27th ESACT Meeting

European Society for Animal Cell Technology

LISBON 2022

LISBON CONGRESS CENTER 26-29 JUNE

Advanced Cell technologies: Making Protein, Cell and Gene Therapies a Reality

Kuhner shaker

Reliable scale-up
from lab-scale
to production

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Scale-up
while maintaining the quality

The consistent hydrodynamics driven by Kuhner shaking machines allow for an efficient scale-up from microtiter plates to shake flasks and production scales. Our orbitally-shaken bioreactors (OSB) for single-use bags expand the range of shaken cultivations up to 2500 L.

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www.kuhner.com/en/kuhner-technology/scale-up.php

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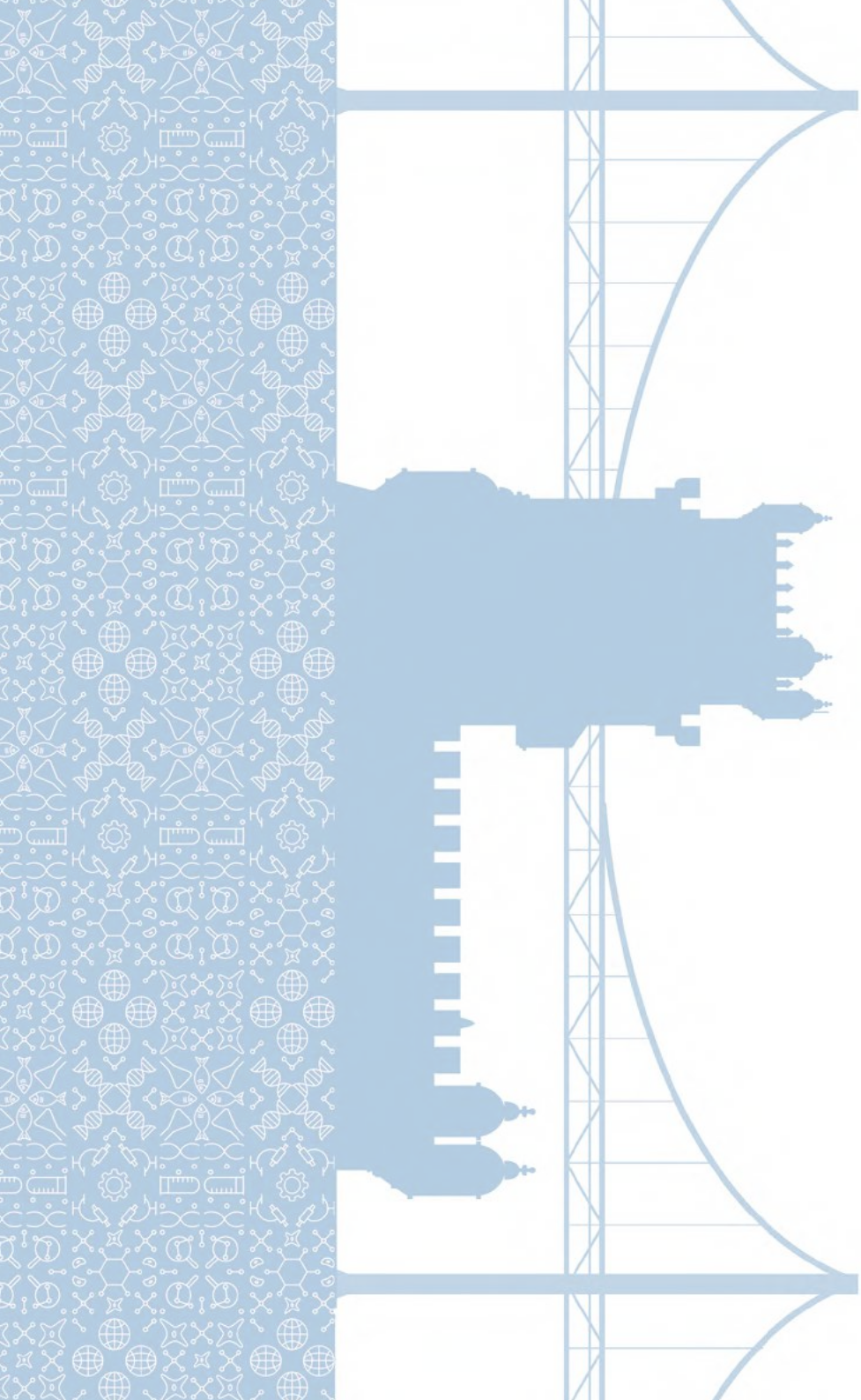

WELCOME FROM THE MEETING CHAIRPERSON

Dear participants,

On behalf of the European Society for Animal Cell Technology (ESACT) and the Organizing Committee, I am delighted to welcome you to the 27th ESACT meeting. What a joy to gather 1000 participants, coming from 33 countries, in beautiful Lisboa. A city embraced by the blue of the Tagus River, cooled by the Atlantic breeze, where the pavement stones shine, reflecting the sun, and the small hills challenge us to discover flowered cozy spots with wonderful views.

Convinced that our community was eager to meet in person, our conference, previously planned for June 2021, was postponed due to the COVID-19 pandemics. From the number of abstracts received, the rapid response of invited speakers, and the remarkable interest of exhibitors and sponsors the decision to proceed with a face-to-face meeting in June 2022 has been fully vindicated. We did all efforts for you to be, and feel, safe at the conference. All the rules from the Health authorities are in place.

The meeting motto - *Advanced Cell Technologies: Making Protein, Cell, and Gene Therapies a Reality* – inspire us to engage and contribute to transform the future of medicines. We will discuss the latest advances in our field, present the most recent tools and technologies and profit from many networking events. All ingredients that make ESACT an unique conference.

The program was designed around six scientific topics, for which the Scientific Committee performed a blinded review of the abstracts and established a ranking based on the quality of the proposals. The ranking was used for the selection of the speakers and to identify the TOP 100 poster abstracts competing for the poster prize. I would like to thank all that have contributed with abstracts, posters and talks, and the Scientific Committee that lent their knowledge and their valuable time to select the excellent contributions. I would also like to thank all the academics and companies that have proposed workshops and symposia for Sunday before the official opening and the ESACT Innovation Award Committee for organizing the nominations received and selecting the ESACT2022 Innovation Award recipients.

My deepest gratitude goes also to the ESACT Executive Committee for their trust, all members of the Organizing Committee for so many hours of dedication to make this conference, the ESACT Frontiers for nurturing ESACT next generations and to the support of Grupo Pacifico Meetings & Events. It has been a 5 years team effort. Also worthy of praise is the fact that a lot of what you see and experience at the conference, would not have been possible without the generosity of our sponsors, for which we are exceedingly grateful.

For those coming for the first time to an ESACT Meeting, I encourage you take advantage of the friendly and inclusive community. We welcome 55 PhD students and early career scientists that received an ESACT2022 grant to attend this meeting. We wish all of you a meeting that meets your expectations, every success for your presentations, new impulses and fruitful interactions with other participants.

We are confident that this will be another great ESACT meeting where our community will celebrate being able to meet, talk and develop new connections and friendships again.

On behalf of the ESACT organizing Committee, I wish you all an outstanding ESACT meeting!

Sejam bem vindos,

Paula Alves
Chairperson of the 27th ESACT meeting
Chairperson of ESACT

WELCOME FROM THE EXECUTIVE COMMITTEE

On behalf of the Executive Committee of the European Society of Animal Cell Technology I would like to warmly welcome you to the 27th ESACT meeting!

We are coming together after the world has been hit by a devastating pandemic. The unprecedented success in developing vaccines and treatments to fight a novel virus has put our field, our academic institutions, our biotech and pharma companies into the limelight. At the same time, the personal exchange amongst all of us has been drastically reduced for two years. However, our inspiration is linked to being together in person! This is when we best learn from each other!

Could there be a better place to reconvene as ESACT community than Lisbon? A city that managed to recover from disastrous events such as the 1755 earthquake. A city that has become a vibrant Biotec and Health Sciences hub and a place where many highly talented scientists and engineers can develop their career.

Making ESACT meetings such a unique event always was a big challenging task. The first post-COVID meeting certainly required extra skill and dedication. This is why I would like to wholeheartedly thank the organizing committee, the scientific committee and the many sponsors of this 27th ESACT meeting.

Enjoy being together!

Best wishes

Hitto Kaufmann
Vice-Chairman of ESACT

ESACT COMMITTEES

ESACT 2022 ORGANIZING COMMITTEE

Paula Alves
iBET and ITQB NOVA Universidade de Lisboa (Portugal) (CHAIR)

Francesc Godia
Universitat Autònoma de Barcelona (Spain)

Alan Dickson
University of Manchester (UK)

Laura Kuhner
Kuhner Ag (Switzerland)

António Roldão
iBET (Portugal)

Gabriel Monteiro
Instituto Superior Técnico ULisboa (Portugal)

ESACT 2022 POSTERS COMMITTEE

Nuša Pristovšek

ESACT Frontiers & Novo Nordisk (Denmark)

Claire Pearce

ESACT Frontiers & XAP Therapeutics (UK)

Francisca Arez

iBET (Portugal)

ESACT 2022 SCIENTIFIC COMMITTEE

Paula Alves
iBET and ITQB NOVA Universidade de Lisboa (Portugal) (CHAIR)

Anne Tolstrup
AbtBioConsult (Denmark)

Chetan Goudar
Amgen (USA)

Damian Marshall
Achilles Therapeutics (UK)

Isabelle Rivière
Memorial Sloan Kettering Cancer Center (USA)

Laura Cervera
Universitat Autònoma Barcelona (Spain)

Laura Palomares
IBT-UNAM (Mexico)

Luis Almeida
CNC Universidade de Coimbra (Portugal)

Martin Fussenegger
ETH (Switzerland)

Mike Betenbaugh
John Hopkins WSE (USA)

Nick Timmins
Artisan Bio (Canada)

Nicole Borth
BOKU (Austria)

Paulo Fernandes
Orchard Therapeutics (UK)

Stefanos Grammatikos
UCB (Belgium)

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28th ESACT MEETING

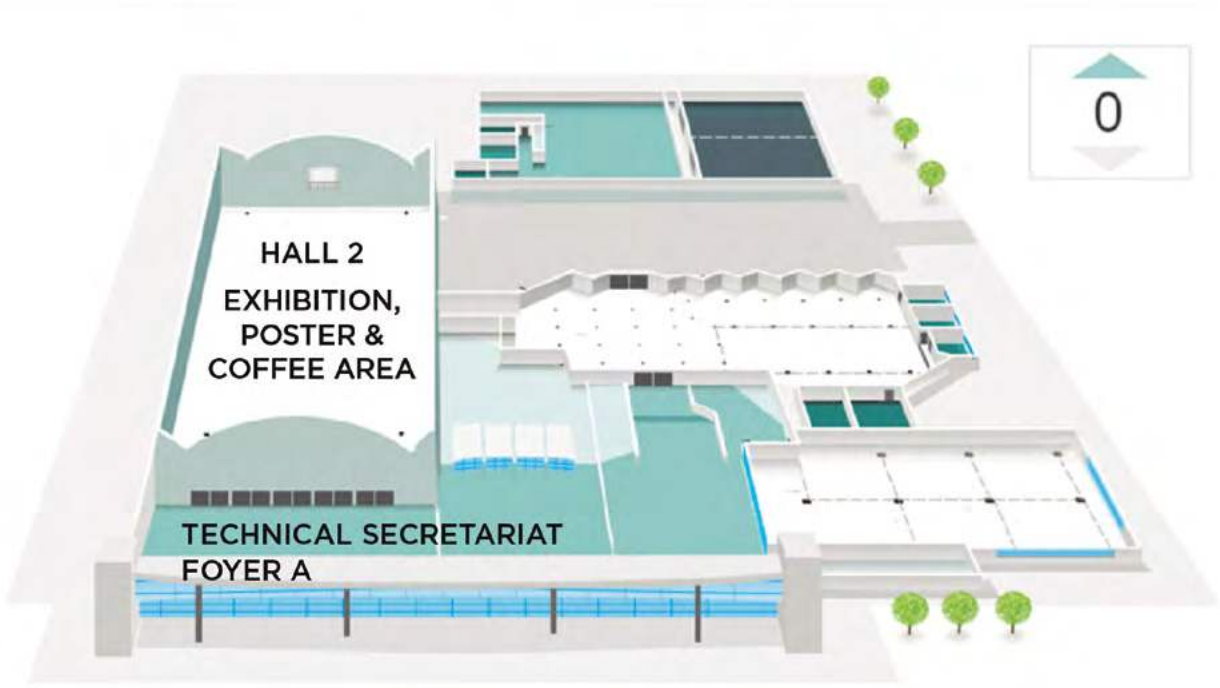
Edinburgh, 23-26 June 2024

www.esact2024.com

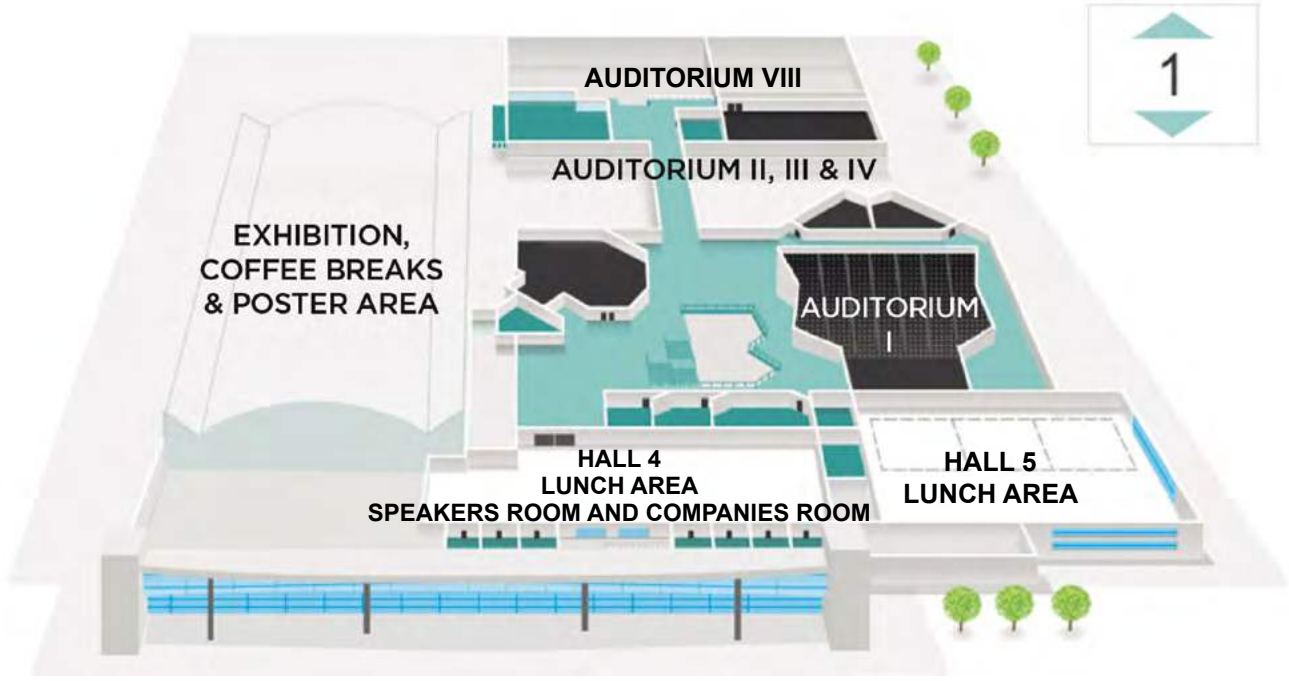
Save the date!!

VENUE MAP

FLOOR 0 - GROUND FLOOR

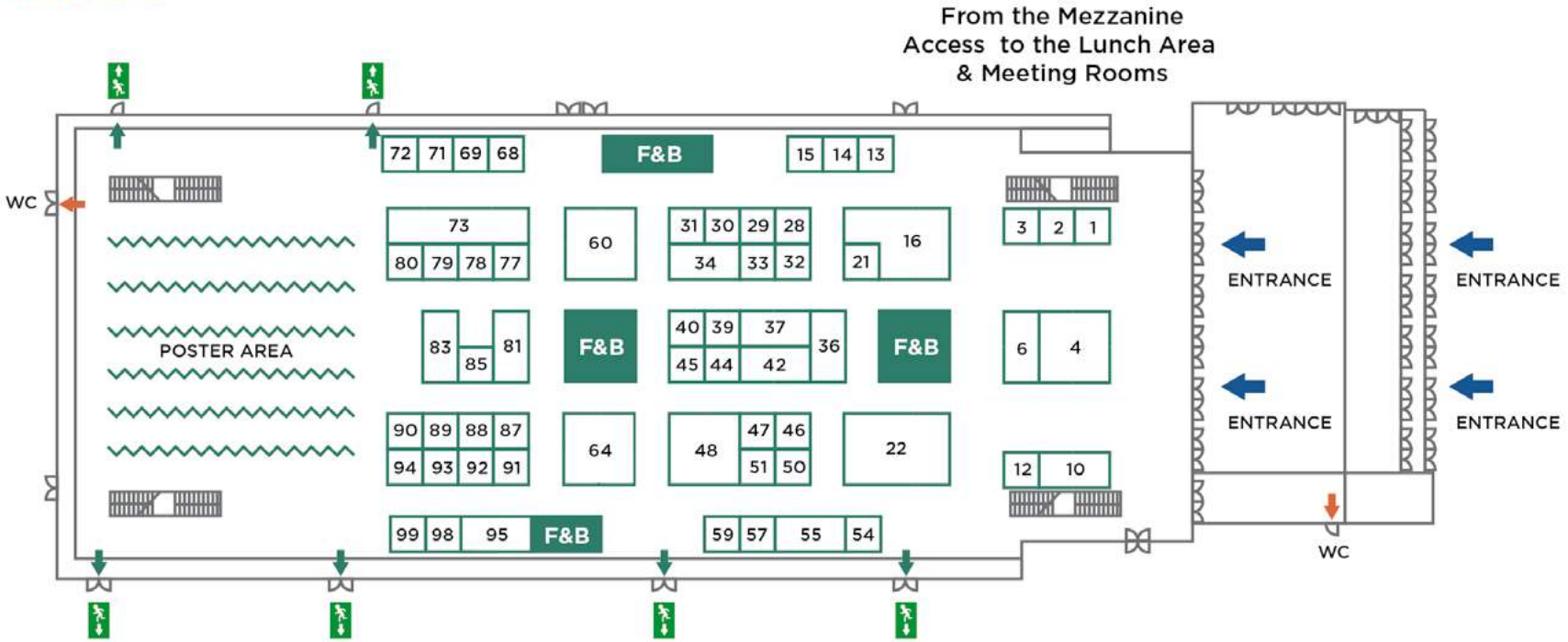


FLOOR 1



EXHIBITION MAP & LIST

LISBON CONFERENCE CENTER
GROUND FLOOR
HALL 2



COMPANY	BOOTH CONFIRMATION
4 BIOCELL	92
4tunnengineering	44
908 Devices	59
Aber Instruments	1
Accellerate	68
Advanced Instruments LLC	95
ALS Automated Lab Solutions GmbH	72
Applikon/Getinge	73
Asimov	14
ATUM	80
BECKMAN COULTER	4
Berkeley Lights, Inc	39
Bioneer	50
Bionet	78
Capricorn-Scientific	29
C-CIT Sensors AG	47
CerCell A/S	42
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c-LEcta GmbH	30
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Cytena/Cellink	12
CYTIVA_GE	60
Demeetra AgBio, Inc	98
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COMPANY	BOOTH CONFIRMATION
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Pall Biotech	48
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REFEYN clx	80
Repligen	37
Roche Diagnostics Deutschland GmbH	81
Sani Membranes	31
SANISURE	55
Sartorius	16
Securecell	33
SEED Biosciences SA	85
SGS Vitrology Limited	32
Sphere fluidics	93
SYNENTEC	40
Tecnic Bioprocess equipment	10
Valitacell	94

JAACT

Japanese Association for Animal Cell Technology

日本動物細胞工学会

JAACT2023

Get Together for the Better Future

Meeting Chairperson: Ken-ichi Nishijima
(Nagoya University)

Program:

Plenary Lectures / ESACT lectures
Symposia: 6 sessions (mAb production, food functions, basic cell biology etc)
Oral and Poster sessions
Technical sessions

http://www.jaact.org/en/

Nov 28 (Tue) –Dec 1 (Fri) 2023

NAGOYA CONGRESS CENTER

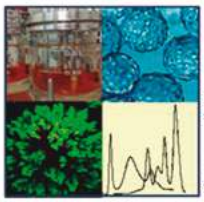
1-1 ATSUTA-NISHIMACHI, ATSUTA-KU, NAGOYA 456-0036 JAPAN

ESACT COURSES - 2022

12TH EDITION

ANIMAL CELL TECHNOLOGY COURSE

18 – 22 Sept 2022, Llafranc (Spain)



Photos: www.ibet.pt

Organizers:
Francesc Gòdia, UAB, ES
Paula Alves, iBET and ITQB NOVA, PT

2TH EDITION

BIOPROCESSING & MANUFACTURING GENE AND CELL THERAPY PRODUCTS COURSE

25 – 29 Sept 2022, Llafranc (Spain)

Photos: www.ibet.pt

Organizers:
Eric J Kremer, CNRS, FR
Joaquim Vives, Servei Terapia Cellular at BST, ES
Paula Alves, iBET and ITQB NOVA, PT

7TH EDITION

CELL CULTURE BASED VACCINES COURSE

2 – 6 Oct 2022, Llafranc (Spain)

Photos: Photos: Dhl & MPI, Magdeburg, www.ibet.pt

Organizers:
Amine Kamen, McGill University, CA
Francesc Gòdia, UAB, ES
Yvonne Genzel, Max-Plank, Magdeburg, DE

6TH EDITION

DISCOVERY & DEVELOPMENT OF NOVEL THERAPEUTICS COURSE

9 – 13 Oct 2022, Llafranc (Spain)

Photos: www.ibet.pt

Organizers:
Catarina Brito, iBET and ITQB NOVA, PT
Hansjörg Hauser, HZI, DE
Heinz Ruffner, Novartis, CH

Application Deadline July 10, 2022

GRANTS

A limited number of grants, covering the course fee will be provided by ESACT and ACTIP.

For more information:

www.esact.org

„I felt that the ESACT ACT Course gave me much needed insight into several aspects of Bioprocess Engineering and for me, as an academic researcher, the opportunity to interact with scientists and engineers working in industry was invaluable." Steve G, Canada

„The ESACT Course in Llafranc was a great opportunity to improve my knowlege in the Biotechnology area. The professors were very attentive and the structure of the course was very organized, providing us comfort and tranquility to enjoy the lectures." Nanditha V., India

Merck

THERE IS A LOT TO SEE & LEARN!

Stop by Merck's booth for short, 5 minute power-presentations addressing hot industry topics.

Power-Presentation Schedule*

Monday, June 27

AM	10:30 AM	GMP-ready Raman PAT platform from R&D to manufacturing
		Process Automation and Data Orchestration for Operational Efficiency
		Data Analytics & Visualization Software for Improved Investigations and Automated CPV
PM	1:45 PM	Is your Virus Safety Strategy Ready for the ICH Q5A Updates?
		Compacted Media: Your Dissolution Solution
		How to intensify your seed train
		How to produce high AAV titers in multiple HEK293 cell lines

Tuesday, June 28

AM	10:30 AM	Is your Virus Safety Strategy Ready for the ICH Q5A Updates?
		Compacted Media: Your Dissolution Solution
		How to intensify your seed train
		How to produce high AAV titers in multiple HEK293 cell lines
PM	1:45 PM	GMP-ready Raman PAT platform from R&D to manufacturing
		Process Automation and Data Orchestration for Operational Efficiency
		Data Analytics & Visualization Software for Improved Investigations and Automated CPV

*Presentation schedule subject to change

Interested in a technology, service or software hands-on demo?

Speak with us about a peer-to-peer consultation or ask for a demo of our data analytics, automation software or Raman PAT Platform. And don't miss all our scientific posters!

Millipore® BioReliance® SAFC®

NETWORKING EVENTS

Exhibitors Reception · **SUNDAY. June 26 at 19:20 auditorium and exhibition hall**

The traders reception and cocktail buffet will take place after the after the first Scientific Session Sunday Evening in the exhibition hall and will be the official opening of the exhibition.

The exhibition provides an opportunity to discover new technologies, materials and services for advancing cell technologies. Catch up with old friends and colleagues in a relaxed atmosphere.

Porto Wine:
From the Douro Valley to the world

Vasco Magalhães · **Wine Consultant**

Postgraduate degree in "Wine Culture and Science" by Universidade Católica do Porto; Lecturer in Master Classes at Universidade Católica do Porto, Universidade de Trás-os-Montes e Alto Douro, Universidade de La Rioja, Spain, Davis University California.

More than 40 years working in the Port Wine trade, (20 years as Port Wine taster, blender, and Master Blender; Founder member of Port Wine Brotherhood.

Teresa Gomes · **Sommelier & Wine Educator**

www.teresagomes.com/eng

Sommelier Course in 2001 amongst other specialized wine courses in both Portugal and the United States. Since 2004, inspired over 17,000 to become Portuguese wine aficionados, have hosted more than 900 wine courses.

Sommelier of the Year Award 2017 by Vinho Grandes Escolhas magazine and shortly afterward was inaugurated into the Confraria do Vinho do Porto, a by invite only Port Wine Brotherhood.

NETWORKING EVENTS

FREE EVENING · **MONDAY EVENING**

Monday evening is free. Catch the metro for a 20 min ride to the very city centre. Discover Lisbon, a city full of authenticity where old customs and ancient history intermix with cultural entertainment. Enjoy the sunset from amazing view points and visit Mirador Sao Pedro de Alcantara, Santa Lucía. Don't forget to visit Mirador de Santa Lucía, Mirador Portas do Sol and the Lisboa Cathedral. Lisbon has the ability to surprise at every turn of its narrow, sloping cobblestone streets!!

NETWORKING ACTIVITY AND DINNER · **TUESDAY 18:00-23:00 Welcome to Belém! An historic city full of culture, tradition, excellent gastronomy and many mysteries!**

Tuesday afternoon (18:00-20:00) you'll have the opportunity to visit Belem, one of the most historic and monumental areas of Lisbon. Located along the Tagus river where ships departed to explore and trade during the Age of the Discoveries, the Belem district houses some of the most important monuments from Lisbon, such as the Jeronimos Monastery, the Belem Tower and the Monument to the Discoveries, and visiting this area is essential.

The ESACT 2022 offers guided walking sightsees and a guided bus sightsee, **Limited places available *per tour*, mandatory to be registered in advance**.

(20:00-23:00). From SUD Lisboa Hall you will have amazing views of the Tagus River, the iconic 25 de Abril suspension bridge and Cristo Rei, adding to the beauty of the already glorious sunset.

On the day of this social event remember to bring the conference badge and the sightsee sticker that were provided to you when checking-in for the conference.

More details available at www.esact2022.com.

CONFERENCE DINNER · **WEDNESDAY 18:00-00:00**

A special event is planned for the closing of the meeting on Wednesday evening, at the Convento do Beato. Come back to the 16th century, when it was a Convent of Monks.

Busses will leave from the Lisbon Conference Centre at 18.00 h. Remember to bring the conference badge and dinner ticket.

Make sure to attend this event which will provide one more opportunity to interact and celebrate!

ACTIP
Connecting Industry Expertise

About ACTIP

Who we are

The Animal Cell Technology Industrial Platform (ACTIP) is an independent non-profit association of European companies and institutions engaged in the industrial use of animal cell technology for research, development and/or production of biopharmaceuticals, vaccines and other preventative or therapeutic approaches. Its main objectives are to bring animal cell technology experts together for networking, keeping up to date on cutting-edge developments and focus on technological and applied-oriented challenges for the industrial use of animal cell technology.

What we do

ACTIP members meet twice a year at a plenary scientific meeting. These informal meetings feature high-level presentations on selected topics of mutual interest, with invited speakers from industry, academia, own member companies, small and medium-sized enterprises and regulatory agencies. In addition to its meetings, ACTIP prepares position papers, monographs, regular newsletters, surveys and supports early career scientists working in animal cell technology through its Fellowship award.

How to join

ACTIP membership is open to companies and institutions located in Europe, engaged in the industrial use of animal cell technology, and performing significant research and development activities for the production of biopharmaceuticals, vaccines, gene & cell therapies or other therapeutic approaches.
For more information about the membership application process please contact the ACTIP secretariat.

ACTIP organizes an ESACT Pre-Conference Academic Workshop "Analytical strategies for improved product characterization and process understanding" on Sunday 26 June 2022.

For contact information, please visit our website: **actip.org**

ACTIP
Connecting Industry Expertise

Fellowship Award

Fellowship Award

ACTIP is connecting industry expertise and promoting talented young scientists active in animal cell technology. Candidates who are awarded the ACTIP Fellowship are invited to present their research to the ACTIP community during a plenary session at one of the upcoming ACTIP meetings. Over the years this has proven to be an excellent way to interact with industry experts and expand professional networks on a European scale.

The award covers all costs to attend a two-day scientific ACTIP meeting and includes a €1000 prize.

How to apply

ACTIP regularly publishes open calls for fellowship applications on its website. For more information about the next call, application process and eligibility criteria please visit actip.org.

We look forward to receiving your application.

IMPORTANT INFORMATION

VENUE

Lisbon Congress Centre
Praça das Indústrias 1, 1300-307 Lisboa, Portugal
+351 21 892 1400
https://lisbonvenues.pt/en/lisbon-congress-center/

TECHNICAL SECRETERIAT

GRUPO PACIFICO MEETINGS & EVENTS
Maria Cubi, 4 - Pral. | 08006 Barcelona (SPAIN)
Tel. +34 932.388.777 | Fax. +34 932.387.488
Email: esact2022@pacifico-meetings.com

OFFICIAL LANGUAGE

The official language of the Meeting is English.
No simultaneous translation will be provided.

BADGES AND SECURITY

It is essential that you wear your personal badge at all times while in the Meeting venue and social events, as it is the official entrance pass to scientific sessions and networking events, and other Meeting activities.
For the Networking Events, it will also be necessary to present the corresponding Voucher that will be provided with the registration package.

DISCLAIMER

The European Society for Animal Cell Technology (ESACT) hereby provides notice to conference attendees and anyone else, that ESACT makes no warranty of any kind whatso- ever, expressed or implied, that any information, materials, techniques or products or anything else presented at this conference is accurate, valid, adequate or fit for any purpose whatsoever. Meeting attendees are solely responsible for determining the validity, adequacy and fitness of any information, materials or products or anything else presented at this conference for any and all uses. Statements and descriptions made by ESACT at this conference and included in conference literature are informational only and are not made or given as a warranty. The views, opinions and statements made at the conference are solely those of the speakers and may not reflect the views of ESACT. Furthermore, speakers may have vested interests in the concepts and products they discuss.

It is further understood and agreed that ESACT shall not be liable whether in contract, in tort, under any warranty, in negligence or otherwise for any kind of claim for loss, damage or expense of any kind arising out of or resulting from the use of any information, materials, products or anything else presented at this conference, and under no circumstances shall ESACT be liable for special, indirect or consequential damages.

ESACT and/or its agents have the right to alter or cancel the conference or any of the arrangements, timetables, plans or other items relating directly or indirectly to the meeting without prior notice for any reason beyond their control. The conference and/or its agents shall not be liable for any loss, damage, expenditure or inconvenience caused as a result of such alteration or cancellation.

INSURANCE AND LIABILITY

It is recommended that participants obtain adequate cover for travel, health and accident insurance before they depart from their countries. ESACT 2022 and GRUPO PACIFICO MEETINGS & EVENTS as organizers cannot accept responsibility for personal injuries, or loss of, or damage to, private property belonging to the meeting participants and accompanying persons.

REGISTRATION AND INFORMATION

DESK OPENING HOURS

Sunday 26th June	08:00-20:00
Monday 27th June	08:00-20:00
Tuesday 28th June	08:00-18:00
Wednesday 29th May	08:00-18:00

SPEAKERS PREVIEW ROOM

Speakers have to provide their presentations in the Speakers Preview Room located on the first floor, Hall 4, in room 1.04 This has to be done no later than two hours before the scheduled time of the session.

SPEAKERS PREVIEW ROOM

OPENING HOURS

Sunday 26th June	08:30-18:30
Monday 27th June	08:00-18:00
Tuesday 28th June	08:00-17:00
Wednesday 29th June	08:00-16:00

WIFI ACCESS

Network: ESACT
Password: ESACT2022

Wifi sponsored by:

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ACCESS TO THE MEETING

The delegate fee gives access to the following:

- Access to all the sessions of the ESACT Meeting.
- Lunches.
- Social & Networking events.

Accompanying person fee gives access to:

- Lunches.
- Social & Networking events.

PERSONAL SAFETY

Lisbon is a safe city. However, we still encourage you to have a care for personal safety and do not deliberately put yourself in unnecessary dangerous situations.

COVID STATEMENT

The ESACT Conference Organising Committee is committed to work hard to offer you a face-to-face meeting while carefully monitoring the worldwide development of COVID-19. We strongly recommend you also keep updated with the current status and specific travel requirements in your country.

RULES IN MAINLAND PORTUGAL

- Mandatory mask:
  - In public transports, taxis and similar passenger transports.
  - Access and visits to care and nursing homes and health facilities.
- General behavior guidelines:
  - Social distancing.
  - Frequent hand washing.
  - Respiratory etiquette.

The ESACT Conference Organising Committee recommends being vaccinated for everyone's sake.

DATA PROTECTION POLICY

The ESACT Conference Organising Committee is committed preserve the data protection policy of all attendees. Your data (full name, affiliation and e-mail) will be shared with the companies, when you visit a stand. If you do not wish to share your contact details, please do not allow your badge to be scanned.

SOCIAL MEDIA/PHOTO/VIDEO POLICY

Please respect authors when publishing in social media, you may not do live tweet (#ESACT22) presentations or take pictures/videos of talks unless the speaker explicitly opts out by stating so at the start of his or her talk and/or has marked slides as Confidential. Taking photos and/or videos of posters without permission is strictly prohibited. (See Poster Policy below).

POSTER POLICY

We expect all participants to treat the posters as the property of the presenter and not attempt to copy them in any way. In the case that a poster presenter wants to give everyone permission to take pictures of his or her work, official "Photography OK" stickers are available from the registration. Taking pictures, videos or otherwise reproducing the posters or any part thereof is not permitted without the permission of the presenter unless a "Photography OK" sticker is found on the poster.

CODE OF CONDUCT

For the ESACT 2022 Meeting, we have established a Code of Conduct to communicate a transparent set of guidelines and rules for acceptable behavior at the Meeting, and to make sure that the ESACT Meeting will continue to be a safe, inclusive, and welcoming environment for all participants and staff. All participants (regardless of their roles) are expected to follow the Code of Conduct at any part of the meeting, both at the official conference venue and at social events off site.

UNACCEPTABLE BEHAVIORS

Unacceptable behaviors include, but are not limited to:

- Intimidating, harassing, abusive, discriminatory, derogatory, or demeaning speech or actions by any participant and at all related events.
- Harmful or prejudicial verbal or written comments or visual images related to gender, gender expression, gender identity, marital status, sexual orientation, race, religion, political orientation, socioeconomic, disability or ability status, or other personal characteristics.
- Violating the rules and regulations of the conference venue.
- Sustained disruption of scientific sessions or other events.
- Unwelcome and uninvited attention or contact.
- Physical assault (including unwelcome touching or groping).
- Harassing or unwanted photography.
- Photographing posters without permission.

TAKING ACTION

- If you feel threatened, witness someone being threatened, or observe behavior that presents an immediate or serious threat to public safety, please contact venue staff/ security or call 112 immediately.
- If you see actions that are in violation with the Code of Conduct, remind the person of the Code of Conduct, or contact venue staff or security.
- If you see someone taking photographs or videos of a presentation or poster (where permission has not been granted), you may choose to remind them of the Code of Conduct policy and ask them to stop photographing the presentation or poster.

Need to file a complaint? Please contact any Conference Organizer (as marked on their badges) or email Meeting Chair. Ms. Paula Alves at esact2022@pacifico-meetings.com. All reports will be handled confidentially.

CONSEQUENCES OF NON-COMPLIANCE

Anyone asked by Conference Organizers, the venue or security staff, or law enforcement officers to stop unacceptable behavior is expected to comply immediately. Retaliation toward official staff or toward someone reporting an incident or after experiencing any of the following consequences will not be tolerated and may result in additional sanctions.

The consequences of non-compliance with the ESACT 2022 Code of Conduct may include:

- Immediate removal from the meeting without warning or refund.
- Restrictions from future meeting attendance.
- Incidents may be reported to the proper authorities.

THE ESACT INNOVATION AWARD

The ESACT Innovation Award is to recognize outstanding **innovators and contributors** to the field of Animal Cell Culture. Technology (ACCT). ESACT has had a profound impact on the development of ACCT-based production of biologicals as human therapeutics as well as diagnostics. Over the years, several landmark contributions have been made by scientists and organizations associated with ESACT, yet, there has not been a mechanism to recognize such contributions and disseminate their impact. This Award aims to fill this need.

For the purpose of this Award and to provide clarity, ESACT defines "Animal Cell Culture Technology" as: Applied science, technologies, systems and processes that enable, facilitate or improve the use of cultured animal cells in research, diagnostic and therapeutic applications.

The Award is presented at the discretion of the ESACT Award Committee during the ESACT bi-annual Scientific Meeting. The award recipient(s) is(are) invited to present the **ESACT Innovation Award Lecture** at the ESACT Scientific Meeting immediately following the award presentation. The invitation to attend the ESACT Meeting includes all travel expenses, accommodations during the Meeting and a waiver of registration fees. The value of the Award will be a sum of 5000 € together with a commemorative plaque.

ESACT Executive Committee members, as well as Award Committee members, are ineligible for the Award during the term of their respective Committee membership and for a two-year period thereafter. All other individuals or organizations that satisfy the Award criteria above are eligible for nomination for the Award.

The 2022 ESACT Innovation Award Recipients

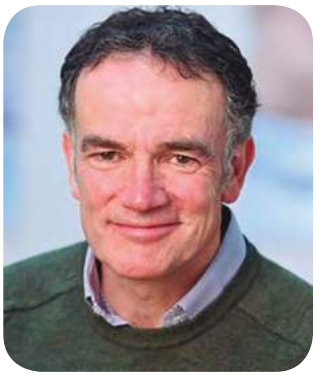
Dr. Richard Wales and Mr. Neil Barg

ESACT has decided to award the ESACT Innovation Award for 2022 to Dr Richard Wales and Neil Bargh for their innovations in automated cell culture technologies to support the development of biotherapeutics.

Dr Richard Wales and Mr. Neil Bargh are recognized as innovators in automated cell culture technologies to support clonal selection and process development for biotechnological products, biopharmaceuticals, vaccines, as well as cell and gene therapies. Notably, they were instrumental in the development, design and technical evolution of the Ambr® bioreactor systems, which closely mimic production bioreactors.

The Ambr® systems have been widely adopted by the biopharmaceutical industry worldwide to accelerate process development and bring life-saving biotherapeutics to the market place.

Dr. Richard Wales



Following a first degree in Biological Sciences at the University of East Anglia and subsequently a PhD at the University of Cambridge, Richard completed a 4-year post-doctoral fellowship at the University of Warwick investigating the mode of action of the cytotoxin ricin. Subsequently Richard spent 6 years in the Ag-Biotech sector with Dalgety and DuPont, joining The Automation Partnership (TAP), later to become TAP Biosystems, in 2001. His various positions at TAP always combined both a technical and commercial perspective, working closely with both the engineering and marketing teams, and potential customers to bring new systems to the market. On acquisition of TAP Biosystems by Sartorius in 2013 he transferred to Sartorius central R&D function. Following a 2-year stint in Sartorius business development group, in 2019 he joined the newly established Corporate Research Group led by Sartorius CTO. Currently he has several roles in that group including programme coordination, technology scouting and as head of the Concept-to-Prototype group.

Neil Bargh

Neil graduated from the University of Cambridge in 1992, after completing a 4-year Master of Engineering degree course. Subsequently, Neil joined the Automation Group of The Technology Partnership (TTP). Neil stayed with the same group as it as it transitioned into The Automation Partnership (TAP), later to become TAP Biosystems in 2001 and then acquired by Sartorius in 2013. Early in his career development projects included: automated inhaler testing machines, the original compound storage "Haystack" system and SelecT, a fully automated robotic T-Flask maintenance system. Following a 9-month career break in Australia, Neil has been responsible for the development of ambr® 15, ambr® 250 HT, ambr® 250 Modular and ambr® Crossflow. In 2017 Neil Joined PA Consulting but returned to Sartorius 16 months later to continue his technical leadership role: developing new products that assist biopharmaceutical research and development.

Timelines Change. Flexibility is a Must. Local Supply Chain Access is Critical.

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THE 2022 ESACT MEDALS

Prof. Dr. Roland Wagner

TU Braunschweig, Former Senior Vice-President, Rentschler Biopharma, Germany.

The ESACT medal is being awarded to Roland Wagner for many years of active support to the ESACT and his contributions to education in Cell Culture Biotechnology and to developments in the field of manufacturing of biologics.

Roland Wagner studied biology at the Technical University of Braunschweig, Germany. After his mastser thesis in 1982 about RNA Polymerases in mammals he submitted his doctoral thesis in 1985 revealing synthesis and regulation of nicotine and tropane alkaloids in plant cell cultures. After a one-year PostDoc phase focusing on the large-scale fermentation of *Saccharomyces cerevisiae* for enzyme production, Roland turned his attention on cell culture media development metabolic and engineering aspects of bioprocesses with animal cell cultures and obtained his habilitation qualification and the *Venia legendi* with a professorial thesis at the TU Braunschweig in 1992. The Technical University Braunschweig appointed him adjunct Professor for Biotechnology in 2001.

For more than 20 years Roland headed the Cell Culture Technology Dept. at the German Research Centre for Biotechnology (GBF, now HZI) where he worked on bioprocess development, heterologous protein expression, cell physiology as well as metabolic and tissue engineering. One essential part of his research was the elucidation of ammonium ions in nucleotide synthesis and protein glycosylation. In 2004, Roland moved to Miltenyi Biotec as head of R&D Bioprocess Sciences working on the development of culture media and cultivation strategies for stem cells, hepatocytes, dendritic cells, and cell lines. Since 2008, Roland hold the position as SVP Development at Rentschler Biopharma. The work focused on research and development of new technologies and strategies for high expression and fast track production processes for industrial manufacturing of complex recombinant biopharmaceuticals. In 2010, Roland started establishing Rentschler's gene therapy strategy with a strong orientation on virus-based biologics. After leaving Rentschler in 2021 Roland is currently focusing on his lecturer status at the TU Braunschweig. He has more than 100 publications and holds over 15 patents. He is supervisor of over 30 doctoral and over 50 master and bachelor thesis' and co-editor of two books in Cell Culture Biotechnology. He was also member of the Animal Cell Technology Industrial Platform (ACTIP) where he worked as a member of the steering committee for more than 10 years. Roland is currently chairman of DECHEMA's scientific panel for Cell Culture Technology.

Roland encountered ESACT first time at 1988 during the 9th meeting in Knokke; Belgium. Since than he is member of the society, participated in many ESACT meetings, also contributing to several of these meetings.

Dr. Yvonne Genzel

Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany.

The ESACT medal is being awarded to Dr. Yvonne Genzel for many years of active support to the ESACT and her contributions in the field of cell based vaccines development and production.

Yvonne Genzel is senior scientist in the Bioprocess Engineering group at the Max Planck Institute for Dynamics of Complex Technical Systems (Magdeburg, Germany) since 2001, and is leading the upstream processing team focusing on virus production with mammalian cells. In 2009 she received her habilitation (PD) in "Upstream processing issues in influenza vaccine production using animal cell technology" at the Otto-von-Guericke-University, Magdeburg. With more than 80 peer-reviewed papers on cell culture-based virus production and analytics on this process, experience has been demonstrated.

Before changing to red biotechnology Dr. Genzel had her interests in white biotechnology, as she obtained her Ph.D. in biocatalysis at the University of the Mediterranean, Marseille, France in 2000. Also during her studies of "Technical Biology" at the Technical University Stuttgart, Germany, she focused on biocatalysis. Intensified viral vaccine manufacturing using suspension cell lines in perfusion systems (hollow-fiber based, acoustic or inclined settler), in two-stage bioreactors or hollow fiber bioreactors are currently of main interest. Additionally, microcarrier systems using packed bed reactors for adherent cells are tested. First steps of downstream processing are evaluated to move towards process integration as early as possible. By considering different viruses, such as influenza, Modified vaccinia Ankara (MVA), yellow fever, Zika as well as a fusogenic oncolytic virus (VSV-NDV), experience and data for a knowledge platform is collected to bring process development for applications in vaccines and therapeutic viruses (gene and cancer therapy, defective interfering particles (DIPs) as antivirals) towards next-generation manufacturing.

Yvonne has been participating in many ESACT meetings along her career. In 2013 she was elected to become an Executive Committee member of the European Society of Animal Cell Technology (ESACT), where she was secretary for the term 2015-2017. Since 2016 she co-organizes the 3-day ESACT course on "Cell culture-based viral vaccines" in the ESACT Llafranc Advanced Courses, a course that is running for its seventh edition in 2022.

Prof. Amine Kamen

McGill University, Montreal, Canada.

The ESACT medal is being awarded to Prof. Amine Kamen for many years of active support to the ESACT and her contributions in the field of cell line development and bioprocessing for vaccine and gene therapy vectors production.

Amine Kamen is Professor of Bioengineering at McGill University, and Canada Research Chair in Bioprocessing of Viral Vaccines. He is Researcher Emeritus of the National Research Council of Canada (NRC) where he was employed until early 2014, as head of the Process Development section of the Human Health Therapeutics Portfolio. At NRC, he established one of the North America largest and most advanced governmental center for animal cell culture addressing process development and scale up of biologics. Also, he developed with his team and licensed to industry multiple technology platforms for efficient manufacturing of recombinant proteins and viral vectors and vaccines and led technology transfer to manufacturing sites for clinical evaluation and commercialization.

His current research activities focus on uncovering mechanisms associated with cell production of viral vectors and viral vaccines using functional genomics; cell and metabolic engineering; process analytical technologies; and data sciences for process digitalization to enable streamlining high yield biologics manufacturing processes. He published over one hundred and seventy papers in refereed international journals and acts as consultant for several national and international private and public organizations.

Amine has been participating in many ESACT meetings along his career, starting back in 1993 in Würzburg, Germany, when he became an ESACT member. He has also been contributing in the Committees of some of the Meetings and served in the Executive Committee. In 2016 he initiated and organized a new course on Cell Culture-Based Viral Vaccines in the ESACT Llafranc Advanced Courses, a course that is running for its seventh edition in 2022.

NOTES

We are back! Fostering the next generation of ESACT!!

ESACT
FRONTIERS RETREAT
26TH - 29TH OCT. 2022
VIENNA

After the success of ESACT Frontiers Retreats held in Lyon (2016) and Zagreb (2018), the third edition is planned for October 2022 in Vienna. The retreat is dedicated to early career scientists working in cell culture technology and related fields.

Building on the most valued aspects of the two previous events, this retreat brings:

- **Excellent scientific program, with sessions focused on early career speakers**
- **Dynamic workshops on soft skills and personal development**
- **Even more time for networking and interaction**

More details soon! Until then, save the dates:

From 26th to 29th of October 2022 – IBIS Hotel – Vienna – Austria

Not sure about it? Check our Frontiers Retreat 2016 video on YouTube:

http://bit.ly/2kvkaSI

ESACT Frontiers Retreat is an initiative of ESACT & ESACT Frontiers Program

https://esact.org/esact-frontiers/

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NOTES

Are you a PhD student or a PostDoc within 3 years of graduation? Do you want to present on Animal Cell Technology?

Do you plan to present at a conference other than the ESACT meeting?

ESACT Grant

Why not apply for an **ESACT** Grant?

ESACT Grants provide travel support for PhDs and young academic researchers within 3 years of their graduation from a PhD program. The following may be supported by an ESACT grant:

- Participation in courses and workshops that teach topics of relevance to Animal Cell Technology
- Participation in conferences and meetings to present results in the field of Animal Cell Technology, either as an oral or poster presentation
- Short term research stays at other academic labs

Participation in the ESACT Meeting or courses organized by ESACT is exempt for this program.

Grants provided are a contribution towards coverage of registration fee, accommodation or travel as documented (currently not more than 500 Euros for non-overseas locations and not more than 1000 Euros for overseas locations). In addition, each recipient is awarded a 4-years free ESACT membership.

To apply, please visit www.ESACT.org.

MEETING SCHEDULE

	SUNDAY 26	MONDAY 27	TUESDAY 28	WEDNESDAY 29
08:30 - 09:00	Registration (open all day)			
09:00 - 09:30	ACADEMIC WORKSHOPS A, B and C	KEYNOTE LECTURE Botond Roska	KEYNOTE LECTURE Hildegard Büning	KEYNOTE LECTURE Raymond Deshais
09:30 - 10:00				
10:00 - 10:30		Poster Students Highlights	Selected Flash Presentations	Poster Prize TOP 10 Finalists Flash Presentations
10:30 - 11:00	SPONSORED SYMPOSIA	Coffee break at the Exhibition	Coffee break at the Exhibition	POSTER SESSION III & COFFEE BREAK
11:00 - 11:30		SCIENTIFIC SESSION Data, Data, Data; how to get it and how to use it	SCIENTIFIC SESSION Adaptive Manufacturing: Engineering Quality into your Process (Part I)	
11:30 - 12:00				SCIENTIFIC SESSION Adaptive Manufacturing:Eng Quality into Process (Part II)
12:00 - 12:30	Light Lunch			
12:30 - 13:00		Lunch		
13:00 - 13:30	ACADEMIC WORKSHOPS D, E and F			
13:30 - 14:00				
14:00 - 14:30		Dessert at the Exhibition		
14:30 - 15:00	SPONSORED SYMPOSIA	POSTER SESSION I	POSTER SESSION II	SCIENTIFIC SESSION Challenges and Marvels of Bioprocess Intensification (Part II)
15:00 - 15:30				
15:30 - 16:00				
16:00 - 16:30	Networking Activity	SCIENTIFIC SESSION Beyond Evolution	SCIENTIFIC SESSION Challenges and Marvels of Bioprocess Intensification (Part I)	KEYNOTE LECTURE Robert Deans
16:30 - 17:00	**OPENING SESSION**			
17:00 - 17:30	ESACT INNOVATION AWARD Lecture			**ESACT Medals - Poster Prize CLOSING CEREMONY**
17:30 - 18:00		Coffee break at Exhibition	Announcements	
18:00 - 18:30	SCIENTIFIC SESSION Bio breakthroughs	SCIENTIFIC SESSION Molecular Cell Surgery	NETWORKING ACTIVITY AND DINNER	Transfer to Congress Dinner
18:30 - 19:00				
19:00 - 19:30				CONGRESS DINNER
19:30 - 20:00	EXHIBITORS RECEPTION at the Exibhition	POSTER VIEWING plus DRINKS		
20:00 - 20:30				
20:30 - 21:00				
21:00 - 21:30				
21:30 - 22:00				
22:00 - 22:30				

WORKSHOP SESSIONS

PRE-CONFERENCE WORKSHOPS AND SYMPOSIA

SUNDAY 26TH JUNE · 9:00-10:30
Workshop A – AUDITORIUM VIII

AN ACADEMIA/INDUSTRY XCHANGE PROGRAM FOR EARLY CAREER SCIENTISTS, FOR THE BENEFIT OF ALL – IS THE FRONTIERS VISION FEASIBLE?

Organized by ESACT Frontiers

Speakers: Qasim Rafiq: Unversity College London; Stefanos Grammatikos, UCB

ESACT Frontiers mission is to provide opportunities for Early Career Scientists (ECSs) to personally and professionally develop whilst actively engaging in, influencing, and developing the animal cell technology community. In line with this, ESACT Frontiers are seeking to establish an Xchange program with a view to enabling ECSs to do secondments across academia and industry to experience different environments and increase their skill set, and ultimately benefit the entire ESACT community. To be successful in this, ESACT Frontiers needs your support! Please join us for an Xchange program brainstorming workshop where participants from all sectors and all levels of experience will be in mixed groups discussing topics such as desire for such a program from ECSs, desire from different sectors, funding, solutions to legalities, and benefits for those individuals and sectors involved.

Put yourself in different shoes for 90 minutes: those of an early career scientist, academic leader or industry executive. From this perspective, answer a series of questions as part of a team in order to help ESACT Frontiers determine the value and feasibility of an academia/industry Xchange program for those within 9 years of their most recent qualification. Join ESACT Frontiers, Qasim Rafiq and Stefanos Grammatikos for what is sure to be an interesting event.

SUNDAY 26TH JUNE · 9:00-10:30
Workshop B – AUDITORIUM II

ANALYTICAL STRATEGIES FOR IMPROVED PRODUCT CHARACTERIZATION & PROCESS UNDERSTANDING

Organized by: ACTIP – Animal Cell Technology Industrial Platfor

ACTIP welcomes you to this symposium dedicated to the latest trends in analytical strategies for products expressed in animal cells. Short introductory presentations will set the stage and provide insights into some of the concepts which shape the biologics industry today. The proposed topics will cover aspects such as, but not only, real-time product quality and process monitoring, application of multi-attribute methods during product and process development, platform and high-throughput methods to support accelerated programs and insights into regulatory aspects for product quality/stability. The presentations will be followed by a panel discussion which will allow symposium participants and experts to interact and exchange on this topic. ACTIP is an independent non-profit association of European companies/institutions engaged in the industrial use of animal cell technology for research, development and/or production of biopharmaceuticals, vaccines and other preventative or therapeutic approaches. Its main objectives are to bring animal cell technology experts together for networking, keeping up to date on cutting-edge developments and focus on technological and applied-oriented challenges for the industrial use of animal cell technology. ACTIP also interacts with ESACT for the promotion of animal cell technologies and to support early career scientists in this field.

WORKSHOP STRUCTURE AND SPEAKERS:

Chairs:	Erwin van Vliet (ACTIP, The Netherlands), Jonathan Bones (NIBRT, Ireland), Matthieu Stettler (Lonza, Switzerland)
9.00–9.15 h	**iConsensus IMI project creating a sensing platform for a biopharmaceutical cultivation process and high-throughput system** *Veronique Chotteau, KTH Royal Institute of Technology, Sweden*
9.15–9.30 h	**Development and application of optical sensors to monitor cell culture parameters** *Konstantin Bagnjuk, Rentschler Biopharma, Germany*
9.30–9.45 h	**Application of MS-based characterization workflows in biopharmaceutical development – Recent progress & Case studies** *Dan Bach Kristensen, Symphogen, Denmark*
9.45–10.00 h	**Characterization of key quality attributes of adeno associated virus (AAV) gene therapy products by LC-MS** *Felipe Guapo, National Institute of Bioprocessing Research and Training (NIBRT), Ireland*
10.00–10.15 h	**Bioanalytical tools for characterization of process samples of a rotavirus vaccine** *Sofia Carvalho, iBET, Portugal*
10.15–10.30 h	General discussion & Wrap up

SUNDAY 26TH JUNE · 9:00-10:30
Workshop C – AUDITORIUM III & IV

SINGLE CELL OMICS

Organized by Colin Clarke (NIBRT) and Antonio Roldão (iBET)

The study of cellular biology has been transformed over the last decade through advances in analytical technology such as next generation sequencing (NGS) and the development of new approaches for deep proteomics. While these analyses have greatly improved our understanding of cellular processes, to date the majority of this knowledge gained has been elucidated from the study of millions of pooled cells as a "bulk" sample. A critical drawback of this approach is that heterogeneity, a universal characteristic of all biological systems, is ignored. Bulk sample analysis provides only a "population average" limiting our understanding of complex systems, obscuring heterogeneity and in some cases describing an inferred cellular state in which very few cells (or none at all) may exist.

In recent years rapid technological advances in areas such as cell isolation methods using microfluidics or microwell devices, preparation of NGS libraries from ultra-low quantities of nucleic acids and innovative labelling strategies for MS-based proteomics have enabled the characterisation of DNA, RNA and proteins at single cell resolution. In particular, transcriptome analysis of single cells (scRNA-seq), has matured rapidly and the technique is now cost effective, highly accurate and capable of determining the distribution of expression levels in tens of thousands of single cells.

This workshop will focus on the application of single cell analysis for studies seeking to gain deep understanding of cell factories and cell therapies. The first part of the workshop will introduce participants to scRNA-seq experimental methods and data analyses, including examples of the successful application of single cell transcriptomics to cell factories and cell therapies. In the second part, participants will join working groups to discuss the opportunities and challenges related to the widespread application of the technology to enhance manufacturing of recombinant proteins, gene and cell therapies.

WORKSHOP STRUCTURE:

Section 1. Thematic presentations (15 min each + 5 min Q&A at the end).

- Presentation 1: Overview of experimental methods for single cell omics.
  - *Understanding of single cell libraries preparation (incl. QC, cell isolation methods, sequencing, …), assessing cost-benefit, and examples of applications for production of biopharmaceuticals.*
- Presentation 2: Bioinformatics analysis of single cell omics data.
  - *What are the stages one needs to go through for data analysis? What are the different platforms available?*

Section 2. Working groups (40 min).

- Working groups defined according to thematic lines.
  - Thematic 1: Recombinant protein.
  - Thematic 2: Gene therapy.
  - Thematic 3: Cell therapy.
- Topics/questions to address by each working group:
  - Where´s the high value in using single cell omics?
  - Single cell *vs* bulk omics – which approach is optimal?
  - Do you see value in creating working groups for better annotation of genomes for non-model organisms or creating a cell atlas?
  - What are the major barriers and limitations in using single cell omics? Is it the cost? Is it the lack of bioinformatic platforms? Other?

Section 3. Wrap-up (10 min).

- Summary of major outcomes from working groups activity:
  - Identification of key barriers.
  - Definition of pathways to move the field forward.
  - Tentative timeframe to solidify the field.

SUNDAY 26TH JUNE · 10:30-12:00
AUDITORIUM II
SARTORIUS SPONSORED SYMPOSIUM

SCALE DOWN OPTIMIZATION TO SCALE UP SUCCESS

The commercial success of monoclonal antibodies has paved the way for novel, personalized cell and gene therapies. But the cost and time required to manufacture these life-saving therapies limits their accessibility. To deliver big, pharmaceutical companies may need to start small. Adopting small-scale models that mimic current manufacturing best practices (i.e., inprocess control, quality-by-design, and integrated analytics) can help scale up results – faster.

Following short individual presentations, our distinguished speakers will gather for a panel discussion covering:

- The importance of scale-down models for cost control, process knowledge, and intensifying processes.
- How lessons learned from biopharma have shaped the cell and gene therapy industry, and what we can learn from them going forward.
- Leveraging new technologies (e.g., new PATs, MVDA) to optimize next-generation therapies and scale up.

Speakers:

- Bruno Marques, Head of Process & Product Development, Century Therapeutics.
- Rebeca Real, Upstream Scientist, Process Development, mAbxience.
- Tarik Senussi, Senior Director, Process, Formulation Development & MSAT, Gyroscope Therapeutics.
- Kevin McHugh, Technology Consultant, Sartorius.

SUNDAY 26TH JUNE · 10:30-12:00
AUDITORIUM III & IV
ADVANCED INSTRUMENTS LLC SPONSORED SYMPOSIUM

SECTION 1:

KEY CONSIDERATIONS FOR MANUFACTURING IN CELL AND GENE THERAPY

Speaker: Marta Rucka, PhD, Global Product Manager

Cell and gene therapy (CGT) is one of the most promising and faster growing sectors in biopharmaceutical industry. With the increasing popularity of gene editing and reprogramming of human cells, it is crucial to understand and recognise the differences between steps involved in process development (PD) and commercial manufacturing. The clinical manufacture of a CGT product is governed by stricter requirements vs PD and regulations as per Good Manufacturing Practices (GMP). However, as the cell line development (CLD) technologies continue to rapidly evolve, GMP regulations need to adopt accordingly to meet the demand and reflect the clinical risk profile of these innovate solutions. Importantly, the transfer of practises from PD to GMP-friendly settings can pose several challenges, which with the right planning can be easily avoided. A detailed analysis of the CLD workflow from single cell seeding, through the use of clinical grade reagents to risk and data management, can be extremely helpful in establishing a GMP-compliant manufacturing process early on. During this session we will discuss the following the key considerations for manufacturing of CGT including:

- Best strategies for single cell isolation and homogenous MCB generation.
- Improving CLD efficiency using the right instrumentation and clinical-grade reagents.
- Controlling osmolality to enhance yield, purity and efficiency of AAV Manufacture.

Key words: Cell line development, single cell seeding, clonal outgrowth, data management, GMP, viral vector production, cell and gene therapy, bioproduction, data management.

SECTION 2:

STREAMLINING THE FED-BATCH CLD PROCESS FOR EARLIER SELECTION OF CLONES VIA ICON TITER AND VCD ANALYSER AND INSTISHAKE CELL GROWTH SUPPLEMENTS

Speaker: Paul Butler, Senior Global Product Manager

The trend in Cell Line Development (CLD) isto screen and select clones earlier and with more confidence. At the fed batch stage of the CLD process, particularly in DW 96, 48 and 24 well plates, limited sample availability precludes some measurements from being taken (VCD and titer for example). The low speed of currently available cell counting technologies means that the time taken to analyse, outweighs the benefit of the data. In this talk we introduce the ICON analyser which rapidly measures small volume samples for titer and VCD and combines with confluence and clonality results within the STUDIUS data management platform to make secure, early decisions on best performing clones. Also, we will discuss how our InstiSHAKE supplements for the shaking cell culture and fed-batch stage, improve the outcomes for cell lines to ensure all candidates are considered in the search for best performers.

Key words: Cell line development, data management, shaking fed-batch, Deep Well plate, titer, VCD.

SUNDAY 26TH JUNE · 10:30-12:00
AUDITORIUM VIII
BERKELEY LIGHTS SPONSORED SYMPOSIUM

ADVANCE AND AUTOMATE CELL PROFILING WITH BERKELEY LIGHTS TECHNOLOGY AND TOOLS TO ACCELERATE CELL LINE ENGINEERING AND DEVELOPMENT

Speakers: Rennos Fragkoudis, Edinburgh Genome Foundry Manager at The University of Edinburgh, Renee Tobias, Senior Director, Marketing Antibody Therapeutics at Berkeley Lights

Generation of stable CHO cell lines for biologics manufacturing is a resource-intensive process that can add months to therapeutic or reagent development timelines. Learn how advanced, automated cell profiling technologies like the Beacon. system are removing critical bottlenecks and providing valuable information on function and quality much earlier in the process.

WORKSHOP STRUCTURE

Rennos Fragkoudis from the Edinburgh Genome Foundry core research facility will present how their suite of cutting-edge computational tools and integrated automation technologies have facilitated projects in gene therapy, vaccine development and metabolic engineering. As the first of its kind in a European academic facility, EGF's investment in the Beacon system has provided their customers unparalleled access to state of the art technology to perform previously unworkable high throughput single cell screening experiments.

A panel discussion will follow on the role of advanced screening technologies, automation, and computational tools in accelerating cell line engineering and development projects across academia and industry.

SUNDAY 26TH JUNE · 13:00-14:30
WORKSHOP D – AUDITORIUM II

EFFECTIVE PARTNERSHIPS BETWEEN INDUSTRY, GOVERNMENT, AND ACADEMIA ON BIOPROCESS DEVELOPMENT

Organized by: Barry Buckland (UCL & BiologicB), Manuel Carrondo (iBET) and Carlos Guzman (HZI)

The aim of this workshop is to obtain an overview on diverse institutional ways of driving process development inputs to speed up biological innovations towards first-in-man, as well as improving reliability of manufacturing and reducing costs. Identify concepts and structures used, key success factors and diversity of partnerships and tools to achieve goals, amongst which training highly qualified professionals.

WORKSHOP STRUCTURE AND SPEAKERS:

There are two broad categories of organizations, from essentially public to essentially privately funded, and a spectrum in between.

The following institutions have agreed to participate in presentation and discussion:

- UK
  Catapult, Fernanda Masri
  UCL Vaccine HUB, Martina Micheletti
- EU
  ACTIP, Matthieu Stettler
  ITEM, Fraunhofer – Holger Zieher
  iBET & Genibet, Manuel Carrondo
  Transvac, Stefan Jungbluth
- USA
  CMAT, Krishnendu Roy
  NIIMBL, Kelvin Lee
  Resilience, Rahul Singhvi

Two sets of presentations (more "public" versus more "private") each one followed by discussion "oriented" by the organizers. Presentations of maximum 8 minutes each (goals, key structural/cultural approaches, core competences…).

Outcome – Key success factors, core needs, way forward…

SUNDAY 26TH JUNE · 13:00-14:30
WORKSHOP E – AUDITORIUM III & IV

EXTRACELLULAR VESICLES – FROM BASIC BIOLOGY TO PRODUCTION OF EVS AS NOVEL THERAPEUTICS

Organized by: Johannes Grillari (LBI for Traumatology/BOKU) and João Ferreira (NOVA Medical School)

Extracellular vesicles have raised a strong interest recently as novel biopharmaceuticals. Thereby, 2 different lines of research and development are crystallizing, on the one hand the use of EVs as therapeutics per se, and on the other their use as drug delivery vehicle. In regard to their use as complex biopharmaceutical, there is accumulating evidence for therapeutic activity in various disease models including stroke, myocardial infarction, osteoarthritis, or bone regeneration. They even have been used in a human graft versus host disease patient with extremely positive result. It is hypothesized that beneficial effects that were observed in clinical trials using e.g. mesenchymal stem cells (MSCs)

might well be due to the secretome of these MSCs as opposed to direct incorporation of allogeneically transplanted MSCs. Considering more than 500 ongoing clinical trials using MSC based therapies, we can envision an ever increasing necessity of production systems for EVs. Similarly, the use of EVs as drug delivery/targeting vehicles has by now produced promising results in animal models. In order to give key insights into this fast evolving field, we here apply for a symposium to be held at ESACT2022 in Lisbon, as we see a benefit for all experts in EV based biology and in animal cell culture technology to convene and discuss in order to boost and inspire the respective fields in the quest to produce, purify and finally bring EVs as novel biopharmaceuticals to the patients. Thereby, we will introduce the basic biology of EVs and their isolation and processing; insights into various production processes as well as therapeutic applications.

WORKSHOP STRUCTURE AND SPEAKERS:

- What is an EV?, Kenneth Witwer, John Hopkins.
- Cross-talks in aging and age associated diseases: from EV biology to application, Johannes Grillari.
- Loading of Proteins into Exosomes, João Ferreira.
- EV Production by turbulence stimulation and their application in healing of wounds, Amanda Silva Brun, CNRS.

SUNDAY 26TH JUNE · 13:00-14:30
WORKSHOP F – AUDITORIUM VIII

HOW TO DEVELOP PERFUSION PROCESSES?

Organized by: Veronique Chotteau (AdBIOPRO and KTH) and Yvonne Genzel (Max Planck Institute for Dynamics of Complex Technical Systems)

Perfusion processes have become a reality for biologics biomanufacturing. The leverage and intensification that this mode of operation brings, has attracted many biopharma's towards implementation at different levels, stretching from N-1 bioreactor only to fully integrated continuous USP-DSP.

The basic principle that medium renewal operated under this continuous mode brings nutrients and removes the by-products, is known from everybody but how to develop, optimize, integrate, characterise, scale-up these processes? Which strategy adopt for process development to achieve high intensification with low medium renewal and high product quality?

How much generic can a process be to fit different molecules? Which tools are needed for monitoring (PAT) and control? What is needed for a fair comparison between different modes in terms of yield, productivity, costs and time? How well do we know the effect of these processes on the cells, e.g. by omics, and what should be studied? How does the field tackle these questions today, and what is missing? What are the avenues needed for tomorrow? Compared to glycoproteins, how different are the challenges and approaches for other modalities, such as production of exosomes, viruses or viral vectors?

WORKSHOP STRUCTURE AND SPEAKERS:

In this workshop, these questions will address with talks from academia and industry and with that like to set the stage for a short discussion with the audience on these questions.

- Development of perfusion processes, Veronique Chotteau.
- Integrated continuous USP-DSP from small-scale to pilot-scale, Hubert Schwarz, KTH.
- Industrial perspective on monitoring and control of perfusion processes, Nandita Vishwanathan and Thomas Vuillemin, Merk.
- Transcriptomics as a tool to understand perfusion processes, Meeri Mäkinen, KTH.

- Evaluating end-to-end continuous bioprocesses from economic, environmental and PAT perspectives, Catarina Pereira Galo Neves, UCL.
- An integrated perfusion process for cell culture-based production of MVA virus for vaccination and gene therapy, Sven Göbel, Max Planck Institute for Dynamics of Complex Technical Systems
- Discussion and wrap-up.

SUNDAY 26TH JUNE · 14:30-16:00
AUDITORIUM II
CYTIVA SPONSORED SYMPOSIUM

FROM RESEARCH TO CLINIC: MODERN APPROACHES TO BIOPHARMA COMMERCIALIZATION

Moderator: Andreas Castan, Director Strategic Technologies, Cytiva

The journey from molecule discovery to manufacturing can be challenging and market success is heavily dependent on the swift creation of high-performing processes. Cell culture scientists drive this success by striving for scalable, robust processes that reach target titers and deliver consistent product quality profiles. They must also keep pace with accelerated development timelines, delivering a cost-effective solution to support a viable business case. During this session, seasoned experts will present case studies and hare their insights into overcoming obstacles.

WORKSHOP STRUCTURE AND SPEAKERS:

- Paula Ravnikar PhD, Global Technical Manager, Cytiva, will describe the path to establish a CHO-K1 cell line and cell line development process suitable for the biotherapeutic market.
- Véronique Chotteau, PhD, Assoc. Prof., Director of AdBIOPRO, will speak about the latest advances in the development of continuous biopharma production processes.
- TBC will present key success factors for the successful scaling of bioreactor processes including case studies.
- Artur Padzik, PhD, AAV production manager (or Magnus Gustafsson, PhD, Head of BD), Biovian, will present scaling strategies for gene therapy processes with recombinant adeno-associated virus (rAAV) from lab to production scale.

SUNDAY 26TH JUNE · 14:30-16:00
AUDITORIUM III & IV
MERCK SPONSORED SYMPOSIUM

SHAPING TOMORROW'S BIOPHARMA 4.0 TECHNOLOGIES, TOOLS AND COLLABORATION

The current paradigm shift and digital transformation in biomanufacturing will result in a facility of the future that is truly an ecosystem of intensified, connected & continuous processing seamlessly coupled with uninterrupted data acquisition and analysis. Together, this will make real-time lot release and lights-out manufacturing achievable to the ultimate benefit of patients around the globe, expanding access to affordable life-saving and life-enhancing biotherapeutics.

SECTION I:

WHICH INLINE PAT/QBD TOOL CAN CONTRIBUTE TO ACHIEVING YOUR BIOPROCESSING 4.0 STRATEGY?

Raman combined with chemometric modeling is a standard solution for inline, real-time monitoring of CPPs/CQAs. Improved production capacity and desired product quality can be achieved by controlling the monitored CPPs/CQAs within a specified design space.

Speaker: Fabien Caron Product Manager, Process Monitoring Solutions, Merck

SECTION II:

HOW CAN ADVANCED HIGH THROUGHPUT TECHNIQUES, ANALYTICAL METHODS, AND STATISTICAL TOOLS BE APPLIED TO DEVELOP OPTIMAL PERFUSION CELL CULTURE MEDIA?

Next-gen media optimization requires collecting and interpreting large amounts of data through testing large numbers of formulations, analyzing the samples for critical attributes, and using advanced statistical tools to interpret the results. In this talk we describe how we connect all these tools to improve perfusion media development capabilities.

Speaker: Jeremiah Riesberg, PhD R&D Senior Scientist, Cell Sciences and Development, Bioprocessing, Merck

SECTION III:

WHAT'S THE BEST APPROACH TO OPTIMIZE PROCESS YIELD WITH N-1 PERFUSION TECHNOLOGY AT EARLY AND LATE PHASE?

We will share real-world data from three approaches to N-1 perfusion fitted to the process, development phase, and ultimately to the program's goals.

Speaker: Céline Raymond, PhD Upstream Process Development Manager, Biologics & Viral Vectors CDMO, Merck.

SECTION IV:

A NEW HERO: NOVEL TECHNOLOGIES FOR VIRUS DETECTION IN BIOLOGICS TESTING

While uncommon, contamination events have devastating consequences on biological production in terms of patient supply and clean-up costs. Come and learn about novel methods that are at the forefront of detection of viral contamination and how these are likely to impact biosafety testing as the industry moves to continuous production.

Speaker: Alison Armstrong, PhD Global Head of Technical & Scientific Solutions, Contract Testing Services, Merck

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SUNDAY 26TH JUNE 14:30-16:00
AUDITORIUM VIII
BRISTOL MEYERS SQUIBB SPONSORED SYMPOSIUM

Bristol Myers Squibb™

ADVANCES IN BIOLOGICS, GENE THERAPY AND CELL THERAPY

- **Bioprocessing of Hypo-immune iPSC: Toward Cost-effective, High-quality Allogeneic Cell Therapies,** Bruno Marques, Executive Director, Process & Product Development, Century Therapeutics.
- **Viral Vectors to Maximize the Success of Gene and Cell Therapies,** Carol Knevelman, Vice-President, Head of Process Research & Development, Oxford Biomedica.
- **Product Development Across all Dimensions - Advances in Biologics, Gene Therapy and Cell Therapy in BMS,** Anurag Khetan, Executive Director, Global Upstream and Cell Line Development, Biologics Development, Bristol Myers Squibb.

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SCIENTIFIC PROGRAM

SUNDAY 26TH JUNE 2022

16:30-17:00 **ESACT 2022 Opening Session**
Chairperson: Paula Alves

17:00-18:00 **ESACT Innovation Award Lecture**
Presented by Terry Papoutsakis, Chair of the ESACT Innovation Award Committee (ESACT Honorary Member & University of Delaware, USA)

ESACT Innovation Award Committee is pleased to present the 2022 awardees:
Richard Wales and Neil Bargh f*or innovation in automated cell cultures technologies to support the development of biotherapeutics*

ESACT Innovation Award Lecture:
Ambr15; how it happened and what was important

18:00 – 19:20 **Scientific Session: Bio breakthroughs**
Chairpersons: Luís Almeida, CNC Univ de Coimbra, Portugal
Laura Cervera, Univ Autònoma Barcelona, Spain

18:00-18:20 **INV 1** *Manipulating exosome biogenesis to enhance productivity of recombinant cell lines producing engineered exosome therapeutics*
Scott Estes, Codiak BioSciences, United States

18:20-18:40 **INV 2** *Innovating the Manufacturing of Human Mesenchymal Stromal Cells (MSC) and MSC-derived Products through Bioengineering*
Claudia Lobato da Silva, IBB, IST, Univ de Lisboa, Portugal

18:40-18:50 **O 1** *Preservation of critical quality attributes in 3D bioprinted cell-based structures by using natural hydrogels*
Joaquim Vives, Banc de Sang i Teixits, Spain

18:50-19:00 **O 2** *Turning an old medicine into a new therapeutical candidate: from erythropoietin to a novel hyperglycosylated, non-erythropoietic but neuroprotective analogue*
Marcos Oggero, UNL, CONICET, FBCB, Centro Biotecnológico del Litoral/ BioSynaptica SA, Argentina

19:00-19:10 **O 3** *Systems-level discovery of quality attributes and candidate pathways for optimized production of human pluripotent stem cell-derived cardiomyocytes*
Aaron Simons, NSF ERC for Cell Manufacturing Technologies (CMaT), United States

19:10-19:20 **O 4** *Human stem-cell based models to study innate immunity and neuroinflammation in the central nervous system*
Catarina Gomes, iBET, Instituto de Biologia Experimental e Tecnológica, Portugal

19:20-21:00 **Exhibitors Reception at the Exhibition Hall**
Introduction to The Porto wine
by Vasco Magalhães (Wine expert) & Teresa Gomes (Sommelier)
& tasting at Exhibition Hall
Cocktail reception at Exhibition Hall

MONDAY 27TH JUNE 2022

9:00-10:00 **Keynote Lecture**
Restoring vision using optogenetic therapy
Botond Roska, Institute of Molecular and Clinical Ophthalmology Basel (IOB), Switzerland

10:00-10:35 **Poster Student Highlights**
Chairpersons: Nuša Pristovšek, ESACT Frontiers & Novo Nordisk, Denmark
Claire Pearce, ESACT Frontiers & XAP Therapeutics, United Kingdom
Francisca Arez, iBET, Portugal

H1 *3D Bioprinted Cellular Structures for Universal Production of Therapeutics*
Laura Chastagnier, 3d.Fab – ICBMS, France

H2 *Semi-continuous propagation of influenza A virus and its defective interfering particles: Analyzing the dynamic competition to select antiviral candidates*
Lars Pelz, Max Planck Institute for Dynamics of Complex Technical Systems, Germany

H3 *Extracellular Vesicles packaging and delivery of silencing sequences to alleviate a brain disorder*
David Rufino-Ramos, CNC - Center for Neuroscience and Cell Biology of University of Coimbra, Portugal

H4 *Single-cell and Bulk RNA sequencing of insect Sf9 cells during rAAV production*
Nikolaus Virgolini, iBET - Instituto de Biologia Experimental e Tecnológica, Portugal

H5 *Reverse genetics for Influenza A virus to generate genetically engineered defective interfering particles for antiviral treatment and vaccination*
Tanya Dogra, Max Planck Institute for Dynamics of Complex Technical Systems, Germany

H6 *Investigating "Difficult-to-Express" mAb Frameworks in Transient and Site-Specific Integration-Based CHO Expression Systems*
Alana C. Szkodny, University of Delaware, United States

H7 *Artificial miRNAs allow stepwise adjustment of core-fucosylation in CHO cells*
Patrick Schlossbauer, Biberach University of Applied Sciences, Germany

H8 *Raman spectroscopy for monitoring of amino acids and antibody glycosylation in high cell density perfusion culture*
Hubert Schwarz, Competence Centre for Advanced BioProduction Continuous Processing (AdBIOPRO), Royal Institute of Technology (KTH), Sweden

H9 *Lectin-aided flow cytometry reveals a close correlation between cell surface and mAb glycosylation*
Mina Ghahremanzamaneh, School of Chemical and Bioprocess Engineering, University College Dublin, Republic of Ireland

H10 *Development of novel fast-growing Chinese hamster lung (CHL)-YN cells in serum-free fed-batch for monoclonal antibody production*
Puriwat Sukwattananipaat, Graduate School of Engineering, Osaka University, Japan

H 11 *Downstream process design and optimization of GAG HIV-1 based Virus-Like Particles*
Elianet Lorenzo Romero, Universitat Autònoma de Barcelona, Spain

10:35-11:00 **Coffee Break at Exhibition**

11:00-12:30 **Scientific Session: Data, Data, Data: how to get it and how to use it**
Chairpersons: Mike Betenbaugh, John Hopkins Univ, USA
Damian Marshal, Achilles Therapeutics, UK

11:00-11:25 **INV 3** *What can extracellular data tell us about intracellular pathways?*
Cleo Kontoravdi, Imperial College London, United Kingdom

11:25-11:50 **INV 4** *Bioprocessing in the Digital Age: from Process Models, through the Integration of Machine Learning, to Digital Twins*
Alessandro Butté, DataHow AG, Switzerland

11:50-12:03 **O 6** *Biomarker identification for in silico performance prediction of CHO cell lines expressing complex therapeutic Abs*
Stylianiv Papadaki, Roche Diagnostics GmbH, Germany

12:03-12:16 **O 7** *On Digital Bioprocessing and Manufacturing Intelligence: Application of Process Analytical Technology and data analytics for upstream process development and intensification*
Ricardo Suarez Heredia, University College London/University of Cambridge/Merck KGaA, United Kingdom

12:16-12:29 **O 8** *Bioprocess digital twins for biomanufacturing 4.0*
Dong-Yup Lee, SungKyunKwan University, Korea (South, Republic of)

12:30-14:30 **Lunch at Lunch Hall**
Dessert and coffee (will be served at Exhibition Hall)

14:30-16:00 **Poster Session I (at Exhibition Hall)**

16:00– 17:30 Scientific Session: **Beyond Evolution**
Chairpersons: Nick Timmins, Artisan Bio, Canada
Martin Fussenegger, ETH, Swirzerland

16:00-16:30 **INV 5** *CAR T-cell immunotherapy of solid tumours: Parallel learning from the clinic and lab*
John Maher King´s College London, United Kingdom

16:30-16:40 **O 9** *Blueprint from nature: Multi-omics comparison of CHO and plasma cells unveils novel cell engineering targets to improve productivity*
Nikolas Zeh, Boehringer Ingelheim Pharma GmbH, Germany

16:40-16:50 **O 10** *Enabling large therapeutic gene delivery: improving dual AAV vector-intein mediated systems*
Mariana Ferreira, ITQB NOVA & iBET, Portugal

16:50-17:00 **O 11** *Theranostic cells for detection and counteraction of infections by rewiring cellular host defense pathways*
Dagmar Wirth, Helmholtz Centre for Infection Research, Germany

17:00-17:10 **O 12** *Viral protease-based molecular switches for drug discovery and synthetic biology applications*
Nik Franko, ETHZ, Switzerland

17:10-17:15 **Flash 1** *Expanding The Design Space of Synthetic Promoters for CHO Cell Engineering Using Next-Generation Sequencing*
Adrian Bourke, University of Sheffield, United Kingdom

17:15-17:20 **Flash 2** *Multiplexed engineering CHO cells to produce recombinant IgGs with desirable N-glycans via targeted integration*
Nigan Yang Yuan Sheng, Bioprocessing Technology Institute, A*STAR, Singapore

17:30-18:00 Coffee Break at Exhibition

18:00-19:30 Scientific Session: **Molecular Cell Surgery**
Chairpersons: Isabelle Rivière, Memorial Sloan Kettering Cancer Center, USA
Nicole Borth, BOKU, Austria

18:00-18:25 **INV 6** *Turning Genes into Medicines: Prospects and Problems in Development of a Novel Class of Therapeutics*
Kathy High, AskBio, Therapeutics, United States

18:25-18:50 **INV 7** *Guiding mRNA-LNP drug products from early R&D programs to the market – Scale up and production of mRNA LNPs.*
Andreas Wagner, Polymun Scientific, Austria

18:50-19:00 **O 13** *Repairing the repairers: Stabilizing the CHO genome and protein production by editing DNA repair*
Nathan Lewis, University of California, San Diego, United States

19:00-19:10 **O 14** *Influenza A virus-derived defective interfering particles for antiviral treatment*
Sascha Kupke, Max Planck Institute for Dynamics of Complex Technical Systems, Germany

19:10-19:20 **O 15** *An arrayed CRISPR screen reveals Myc depletion to increase productivity of difficult-to-express complex antibodies in CHO cells*
Niels Bauer, Roche Diagnostics GmbH, Germany

19:20-19:25 **Flash 3** *Engineered nucleases targeting the ATXN3 gene for the therapy of Machado-Joseph disease*
Sara Lopes, Center for Neuroscience and Cell Biology (CNC), University of Coimbra, Portugal

19:25-19:30 **Flash 4** *Rational development of recombinant CHO cells based on histone analysis: Identification and experimental validation of stable integration sites*
Oliver Hertel, Bielefeld University, Germany

19:30-21:00 Poster Viewing plus drinks (at Exhibition Hall)

TUESDAY 28TH JUNE 2022

9:00-10:00 Keynote Lecture
Gene Therapy - a new class of medicine
Hildegard Büning, Hannover Medical School, Germany

10:00-10:30 Selected Flash Presentations Session
Chairpersons: Emma Petiot, 3d.FAB/UCBL, France
Niall Barron, NIBRT, Republic of Ireland

Flash 5 *4-1BB and 4-1BBxOX40 bispecific Anticalin®-based payloads to armor cellular immunotherapies for effective localized immune cell stimulation*
Janet Peper-Gabriel, Pieris Pharmaceuticals GmbH, Germany

Flash 6 *Culture of Pluripotent Stem Cells and Derivation of Organoids using Droplet Microfluidics*
Sebastien Sart, Institut Pasteur, France

Flash 7 *Augmented decision making for cell culture process development: from data traceability & accessibility to process modelling*
Wolfgang Paul, Upstream Process Sciences Biotech Sciences, UCB Pharma S.A., Belgium

Flash 8 *Found in translation: Microproteins are a new class of potential host cell impurity in mAb drug products*
Colin Clarke, NIBRT, Republic of Ireland

Flash 9 *Using a cell receptor knock-out strategy to enable stable expression of cytotoxic envelope glycoproteins for lentiviral vector production*
Rodrigo Nogueira, iBET- Instituto de Biologia Experimental e Tecnológica, Portugal

Flash 10 *Endogenous BiP reporter system for simultaneous identification of ER stress and antibody production in Chinese hamster ovary cells*
Jae Seong Lee, Ajou University, Korea (South, Republic Of)

10:30-11:00 **Coffee Break at Exhibition**

11:00-12:30 Scientific Session: **Adaptive manufacturing: engineering quality into your process (part I)**
Chairpersons: Anne Tolstrup, AbtBioConsult, Denmark
Laura Palomares, IBT-UNAM, Mexico

11:00-11:30 **INV 8** *The Application of Mechanistic Models Combined with Statistical Approaches Including Multivariate Visualization and Bayesian Methods to Enable Rapid Process Understanding*
Gene Schaefer, NIIMBL, United States

11:30-11:45 **O 16** *Next-gen glycoengineering: combining cellular and metabolic engineering to fine-tune mAb β1,4 galactosylation*
Apostolos Tsopanoglou, University College Dublin, Republic of Ireland

11:45-12:00 **O 17** *Knowing more from less: a microfluidic toolbox for at-line monitoring of bioprocesses*
Inês Pinto, Science for Life Laboratory & KTH Royal Institute of Technology, Sweden

12:00-12:15 **O 18** *Accurate identification of transgene integration sites and their structure by Cas9 targeted nanopore sequencing in CHO cells*
Klaus Leitner, Austrian Centre of Industrial Biotechnology (acib), BOKU, Austria

12:15-12:20 **Flash 11** *Successful Transfer of Raman Models from Ambr®250 high-throughput systems to larger Scale Stirred Tank Bioreactors*
Jens Traenkle, Bayer, Germany

12:20-12:25 **Flash 12** *Modular mini-factories for the automated and scalable production of ATMPs*
Mario Graeve, Fraunhofer, Germany

11:25-12:30 Flash 13 *Rapid assessment of Aggregation of Biologics in different matrices and from Upstream and Downstream Development Process Stages*
Aris Perrou, PAIA Biotech GmbH, Germany

12:30-14:30 **Lunch at Lunch Hall**
Dessert and coffee (will be served at Exhibition Hall)

14:30-16:00 **Poster Session II (at Exhibition Hall)**

16:00-17:35 Scientific Session: **Challenges and Marvels of Bioprocess Intensification (part I)**
Chairpersons: Chetan Goudar, Amgen, USA
Paulo Fernandes, Orchad, UK
Stefanos Grammatikos, UCB, Belgium

16:00-16:25 **INV 9** *Process Intensification Opportunities, Challenges and Solutions: Product Quality, Harvest and Scale Up Considerations for Intensified Processes*
Bassem Bem Yahia, UCB Pharma, Belgium

16:25-16:40 **O 19** *Process intensification and connected processing for robust, cost effective, and fast manufacturing of monoclonal antibodies*
Sanket Jadhav, Sartorius, Netherlands

16:40-16:55 **O 20** *Overcoming product retention in TFF-based perfusion cell cultures by using low shear magnetically levitating pumps*
Magdalena Pappenreiter, Bilfinger Life Science GmbH, Innovation Management; University of Natural Resources and Life Sciences (BOKU), Austria

16:55-17:10 **O 21** *Migrating a months-long perfusion process to intensified fed-batch*
Lena Thoring, FyoniBio GmbH, Germany

17:10-17:35 **INV 10** *Enabling Intensified Bioprocesses At Scale*
Daniel Karst, Biogen International GmbH, Switzerland

17:35-18:00 Announcement & Networking Activities

18:00-22:00 Networking Activity and Dinner

WEDNESDAY 29TH JUNE 2022

9:00-10:00 Keynote Lecture
Multispecificity – the future of molecular medicines
Raymond J. Deshaies, Amgen Research, United States

10:00-10:30 TOP 10 Finalists - Poster Prize Flash Presentations
The 10 Top Finalists - selected during Posters sessions I and II by the jury will be invited to present their poster

10:30-11:30 POSTER SESSION III & Coffee Break at Exhibition

11:30-12:30 Scientific Session: **Adaptive manufacturing: engineering quality into your process (part II)**
Chairpersons: Anne Tolstrup, AbtBioConsult, Denmark
Laura Palomares, IBT-UNAM, Mexico

11:30-12:00 **INV 11** *Next-generation, feedback responsive cell factories for recombinant protein manufacturing*
Laura Segatori, Rice University, United States

12:00-12:15 **O 22** *Identification and Control of Novel Waste Inhibitory Metabolites In CHO Cell-Cultures*
Sanket Jadhav, University of Massachustts Lowell, United States

12:15-12:30 **O 23** *State-of-the-art strategies for adeno-associated virus product homogeneity assessment*
Marco Radukic, Biofidus AG / Bielefeld University, Germany

12:30-14:30 Lunch at Lunch Hall
Dessert and coffee (will be served at Exhibition Hall)

14:30-16:00 Scientific Session: **Challenges and Marvels of Bioprocess Intensification (part II)**
Chairpersons: Chetan Goudar, Amgen, USA
Paulo Fernandes, Orchad, UK
Stefanos Grammatikos, UCB, Belgium

14:30-14:45 **O 24** *Optimization of continuous HIV-1 Gag virus-like particles (VLPs) harvest using an alternative perfusion approach*
Jesus Lavado, Universitat Autònoma de Barcelona (UAB), Spain

14:45-15:00 **O 25** *The perks of innovating influenza VLP-based vaccine production*
Antonio Roldao, IBET & ITQB-NOVA, Portugal

15:00-15:15 **O 26** *Cell Therapy Process Development with a 2 ml Continuous Perfusion Bioreactor*
Kevin Lee, Erbi Biosystems Inc., United States

15:15-15:30 **O 27** *Ultracentrifugation for AAV manufacturing: non-linear scale-up improves quality & scalability*
Duarte Martins, Takeda, Austria\

15:30-15:35 **Flash 14** *Intensify Viral Vector Manufacturing Using Tangential Flow Depth Filtration (TFDF) platform*
Rachel Legmann, Repligen corp, United States

15:35-15:40 **Flash 15** *A scalable bioprocess strategy for rAAV2 production using a stable cell line system*
Jose Escandell, iBET, Portugal

15:40-15:45 **Flash 16** *Establishment of two suspension adapted stable packaging cell lines for scalable lentivirus production*
Maximilian Klimpel, CSL Behring Innovation GmbH, Germany

15:45-15:50 **Flash 17** *Integrated process for the production and purification of therapeutic mesenchymal stromal cell-derived extracellular vesicles*
Ana Fernandes-Platzgummer, Instituto Superior Técnico, Univ Lisboa, Portugal

16:00-17:00 **Keynote Lecture**
Engineering Biology for future medicines
Robert Deans, Synthego, United States

17:30-18:00 **ESACT Medals Ceremony**
The ESACT Medals are attributed to ESACT members in recognition of their contribution to ESACT activities.
In 2022 Roland Wagner, Yvonne Genzel and Amine Kamen will be awarded with ESACT medals.

ESACT 2022 Poster Prize Announcements
CLOSING CEREMONY

18:00 **TRANSFER TO CONGRESS DINNER**

19:00-24:00 **CONGRESS DINNER**

INVITED SPEAKERS AND ORAL COMMUNICATIONS ABSTRACTS

Sunday 26

18:00-19:30 **Scientific Session: Bio breakthroughs**

Chairs:
Luís Almeida, CNC Univ de Coimbra, Portugal
Laura Cervera, Univ Autònoma Barcelona, Spain

18:00-18:20 **INV 1 Manipulating exosome biogenesis to enhance productivity of recombinant cell lines producing engineered exosome therapeutics**

Scott Estes, *Codiak BioSciences, United States*

Extracellular Vesicles (EV) can transfer functional macromolecules to recipient cells which has spurred an interest in delivering therapeutic payloads with EVs. In addition, ligands displayed on the EV surface can engage cell receptors to activate signal pathways for therapeutic benefit. Given that nature has evolved this communication system, exosomes are believed to have the capacity to deliver therapeutics more effectively with less immunogenicity and less toxicity than synthetic nanoparticles. Significant progress has been made in realizing this potential with the development of effective tools to engineer exosomes with protein, small molecule or nucleic acid therapeutic agents and moving these candidates into clinical trials. As with other new modalities, a challenge has been the development of EV processes to supply demands beyond niche indications or localized routes of administration. There are published reports showing cells respond to unfavourable conditions such as hypoxia or oxidative stress by secreting more exosomes. However, this represents a risky strategy to implement in manufacturing. As an alternative, we hypothesized interrogation of the key pathways associated with EV biogenesis and vesicular transport could identify key regulators amenable to cell line engineering or media strategies to increase productivity.

Both focused CRISPRa and siRNA libraries were transiently transfected in a reporter cell line expressing HiBit luciferase fused to an exosome scaffold protein to monitor the luminescence read out as a surrogate for EV secretion. Leads were subsequently validated by large scale transients and purification and quantitation of exosome to confirm changes in EV output. When available, treatment with pharmacological agents relevant to the lead were also employed as an orthogonal method to validate a hit.

Two significant hits, both key regulators of the cholesterol biosynthesis pathway were identified. Subsequent larger scale transient knockdown of these genes resulted in 5 to 10-fold more exosomes compared to controls. Further studies confirmed inhibition of cholesterol synthesis as the driver of increased EVs rather than other activities such as prenylation which branch off from the Farnesyl-PP intermediate. Extensive biochemical and functional characterization of these EVs revealed no notable changes in their properties other than alterations to the membrane. This finding provides a road map for potential genetic modifications or small molecule media supplements that modulate the cholesterol biosynthetic pathway to create improved host cell lines or media formulations that could significantly increase exosome productivity.

18:20-18:40 INV 2 Innovating the Manufacturing of Human Mesenchymal Stromal Cells (MSC) and MSC-derived Products through Bioengineering

Claudia Lobato da Silva, Department of Bioengineering and iBB-Institute for Bioengineering and Biosciences, Instituto Superior Técnico, Portugal

The robust and scalable cell manufacturing for the cost-effective delivery of safe and potent cell-derived Advanced Therapy Medicinal Products (ATMPs) relies on process engineering tools to understand the impact of cellular features on cell product function and performance, and how do process variables influence the critical quality attributes of the cell product.

Mesenchymal stromal cells (MSC) have been widely exploited as potential therapeutic agents for several conditions due to their intrinsic regenerative and immunomodulatory properties, as well as high proliferative capacity ex-vivo, ease of isolation, multilineage differentiation ability and low immunogenicity. Large cell doses (>1x10^6 cells/kg) have been required for clinical implementation of MSC-based therapies and the success in obtaining those cell numbers starting from different human tissues such as bone marrow (BM), adipose tissue (AT) or umbilical cord matrix (UCM) is dependent on efficient ex-vivo expansion protocols able to comply with GMP. We have established the clinical-grade expansion of human MSC in scalable microcarrier-based stirred bioreactors using serum-/xenogeneic-free (S/XF) culture components and have demonstrated the potential to maximize cell productivity by changing different culture parameters including microcarriers, tissue source and bioreactor configuration.

We are exploring genetic engineering tools to modulate the function of the manufactured MSC in the context of regenerative medicine. Specifically, we are also engineering human MSC to secrete a human codon-optimized version of azurin (hazu), a bacterial protein that in previous studies demonstrated anti-cancer activity towards different cancer models. When using the conditioned medium (CM) retrieved from engineered hazu-MSC, we observed a decrease in cancer cell proliferation in a 2D monolayer configuration for different cancer cell lines, as well as a decrease in cancer cell invasiveness assessed *in vitro* through Matrigel.

Recently, increasing evidence has proposed extracellular vesicles (EVs) as exosomes, as mediators of many of the MSC-associated therapeutic features. In this context, we have adapted the previously established platform for the manufacturing of human MSC using stirred bioreactors to allow the reproducible production of MSC-derived EVs with promising characteristics for biomedical settings.

18:40-18:50 O-01 PRESERVATION OF CRITICAL QUALITY ATTRIBUTES IN 3D BIOPRINTED CELL-BASED STRUCTURES BY USING NATURAL HYDROGELS

Joaquim Vives[1], Lluís Martorell[1], Alba López-Fernández[1], Andrea García-Lizarribar[2], Roger Sabata[3], Patricia Gálvez-Martín[3], Josep Samitier[2].

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Background and novelty: 3D bioprinting is an emerging technology for fabricating complex cell-based tissue-engineering products. However, precise and controlled layer-by-layer assembly of biomaterials and living cells in a desired 3D pattern is compromised by poor resolution and reduced cell viability post-printing. We investigated two formulations of hydrogel-based bioinks loaded with multipotent mesenchymal stromal cells (MSCs) resulting in high recovery of viable cells, while preserving their identity and potency. Moreover, the clinical translation of our approach was achieved by A) using pharmaceutical grade reagents and B) using equivalent species-specific and human MSC.

Experimental approach: Human and ovine bone marrow (BM)-derived MSCs

were isolated, expanded and characterised following established methods (1, 2). Bioinks were formulated using Fibrinogen/Thrombin (F/T; Baxter), loaded with BM-MSC and supplemented with either Hyaluronic acid (HA; Bioibérica) (F/T/HA) or Gelatin methacryloyl (GelMA) (F/T/GelMA) (3). Constructs were bioprinted using a regenHU 3D device (3DDiscovery BioSafety). Post-bioprinting, cell recovery, viability and proliferation were assayed by determining ATP using the CellTiter-Glo® 3D Cell Viability Assay (Promega) and by microscopic inspection upon LIVE/DEAD staining (Invitrogen). In addition, *in vitro* osteogenesis was assessed using StemPro Osteogenic kit (Invitrogen) and alkaline phosphatase (ALP) staining (Sigma-Aldrich).

Results and discussion: 3D constructs were successfully bioprinted by fused deposition modelling using filaments of BM-MSCs-laden composite hydrogels. By visual inspection, 3D architecture was clearly superior using GelMA. In both cases, bioprinted BM-MSCs appeared as viable spherical cells, homogenously distributed within the 3D construct without signs of cell death. Proliferation capacity of 3D printed BM-MSCs in both bioinks was demonstrated by a steady increase of ATP content at days 3 and 7 in expansion medium. Remarkably, fibroblastic morphology of MSCs was acquired by day 3 and cells populated the entire 3D structure. Importantly, MSCs retained ALP^+ osteogenic capacity, reaching a peak of activity 2 weeks after induction. Beyond the biocompatibility of naturally occurring polymers, our results highlight the enhanced protection exerted by designed bioinks on MSCs during the printing process, both reducing shear stress and offering structural support for further proliferation and differentiation. Moreover, we successfully formulated an ovine species-specific 3D construct to be used in sheep, which is a relevant large animal model in translational orthopaedics.

Acknowledgements & Funding: This work has been developed in the context of AdvanceCat with the support of ACCIÓ under the Catalonian ERDF operational program 2014-2020.

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2. Curr Prot Stem Cell Biol (2018) 44:2B.9.1
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18:50-19:00 O-02 TURNING AN OLD MEDICINE INTO A NEW THERAPEUTICAL CANDIDATE: FROM ERYTHROPOIETIN TO A NOVEL HYPERGLYCOSYLATED, NON-ERYTHROPOIETIC BUT NEUROPROTECTIVE ANALOGUE

María De Los Milagros Bürgi[1], Valentina Wandel-Petersen[2], Matías A. Depetris[3], Sofía Giorgetti[2], Marina Etcheverrigaray[2], Gabriela Aparicio[4], Camila Scorticati[4], Sahab Arinrad[5], Anja Ronnenberg[5], Hannelore Ehrenreich[5], Ricardo B. Kratje[1], Marcos R. Oggero-Eberhardt[1].

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Background and novelty: Neuropsychiatric disorders affect millions of people worldwide. They affect the central nervous system and are characterized by their chronicity and progressive evolution. In 2019, 1.5 billion people were diagnosed with some neurological disorder around the globe. Despite their exponential increment, the pharmaceutical market mainly offers medicines to relieve symptoms. Thus, it is necessary to develop new therapeutics which can produce a perceptible improvement in the patients. Human erythropoietin (hEPO) has been used in

clinical trials due to its neurotrophic and cytoprotective properties. However, erythropoietic activity (EA) should be considered as a side effect. Some analogues like asialoEPO, carbamylated-EPO, or EPO-peptides have been developed showing different weaknesses: EA preservation, low stability, potential immunogenicity, or fast clearance.

Experimental approach: Glycoengineering by hyperglycosylation was used as an innovative technology to block the EA of hEPO while preserving the neurological activity and conferring long-lasting actions. A new consensus sequences for N-glycosylation was introduced by site directed mutagenesis within the hEPO sequence responsible for its EA. hEPO-derivatives were then produced by CHO.K1 cell cultures, affinity-purified, and functionally analyzed studying their *in vitro* and *in vivo* EA and neurobiological actions. The *in vitro* neuroactivity was evaluated in neuron's primary cultures by assessing neuritogenesis, filopodia density, synapses formation neuronal rescue from staurosporine-induced apoptosis. The *in vivo* neurobiology was evaluated by the voluntary running performance of young male C57Bl/6N mice during an overnight exposure to Complex Running Wheels (CRW) in their home cages.

Results and discussion: Mut 45_47 (K45 > N45 + N47 > T47), Mut 104 (S104 > N104), and Mut 151_153 (G151 > N151 + K153 > T153) completely lost their EA both *in vitro* and *in vivo*, but preserved their *in vitro* neuroprotective activity. Particularly, Mut 45_47 and Mut 104 were more efficient to stimulate synapses formation *in vitro* than Mut 151_153 that showed a comparable activity respect to hEPO. When analyzing the *in vivo* potency to improve motor-cognitive performance in mice using overnight complex running wheels, only Mut 151-153 was comparable to recombinant hEPO ($p>0.9$ applying Friedman´s test and post hoc Dunn´s corrected multiple comparisons). Finally, the additional N-glycosylation site also improved the pharmacokinetic properties of Mut 45_47 and Mut 151_153 by reducing their clearance in plasma and increasing their half-life in blood.

n conclusion, Mut 151_153 represents an interesting hEPO-derivative with no erythropoietic action that preserves the hEPO neurobiological function to explore its potentiality as biotherapeutic for several neurological disorders.

19:00-19:10 **O-03 SYSTEMS-LEVEL DISCOVERY OF QUALITY ATTRIBUTES AND CANDIDATE PATHWAYS FOR OPTIMIZED PRODUCTION OF HUMAN PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES**

Aaron Simmons, Sean Palecek.

NSF ERC for Cell Manufacturing Technologies (CMaT), Wisconsin, United States.

Background and novelty: Numerous protocols exist for differentiation of human pluripotent stem cells (hPSCs) to cardiomyocytes (CMs). Although these methods have improved in efficiency over the past decade, they remain highly variable in their resultant purities, not only among different source hPSC lines but also between batches in the same cell line. This substantial heterogeneity of hPSC-CM product outcomes points to poorly-understood, highly sensitive, and uncontrolled variables present within the overall process and results in poor overall process robustness.

Experimental approach: Herein, we have undertaken a multi-omic discovery approach to identify key temporal differences in cell attributes between high- and low-purity hPSC-CM differentiations to provide dynamic, systems-level insights into underlying mechanisms which drive these populations to divergent endpoints. Specifically, we are combining metabolomic, proteomic, lipidomic, and transcriptomic analyses collected throughout the differentiation process for high- and low-purity (as assessed by terminal %cTnT+ via flow cytometry) differentiation batches. Key findings are validated by traditional targeted molecular biology techniques (RT-qPCR, Western blots, etc).

Results and discussion: To date we have identified novel putative candidate quality attributes for process monitoring and cellular pathways which may be able to be modulated to augment process robustness in a scaled manufacturing context. Beyond standard single-omic analytical workflows, ongoing work is aimed at integrating these data for deepened insight, including functional integration with systems-scale modeling and high-dimensional machine-learning methodologies to extract dynamic relationships among variables over time. Further confirmatory studies in additional cell lines, and initial investigations into enhancing process robustness (i.e. consistency of high-purity CM differentiations) via target pathway modulation are underway.

In addition to gaining fundamental insights into the underlying biology of the differentiation process, our findings are being applied to 1) identify putative critical quality attributes for use in on- or at-line analytics for continuous process monitoring, 2) enhance process robustness through the development of protocols aimed at depressing off-target pathways and enhancing on-target ones, and 3) establish potential feedforward/feedback control schemes based on real-time analytics to respond to in-process intermediate quality attributes through rational adjustment of process parameters.

19:10-19:20 O-04 HUMAN STEM-CELL BASED MODELS TO STUDY INNATE IMMUNITY AND NEUROINFLAMMATION IN THE CENTRAL NERVOUS SYSTEM

Catarina M. Gomes, Catarina Perdigão, Carolina Gonçalves, Gabriela Silva, Daniel Simão, Catarina Brito.

iBET, Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal.

Background and novelty: The development of gene therapies for central nervous system (CNS) disorders has been hindered by the lack of human-relevant models in which the neuro-immune axis is depicted. Upon infection, astrocytes and the CNS resident immune cells, microglia, undergo activation and express receptors that trigger the production of inflammatory cytokines, through the activation of inflammatory pathways, leading to neuronal death. Still, much of the molecular mechanisms that trigger and sustain human glial activation remain unknown. Here, we present a 3D human CNS in vitro model that recapitulates neuroinflammatory hallmarks and is a suitable platform for preclinical development of gene therapies.

Experimental approach: We explored a neural cell culture methodology pioneered by our team, in which neuron-glia interactions are recapitulated. Neural progenitors derived from human induced pluripotent stem cells (hiPSC) were cultured as 3D spheroids in perfusion stirred-tank bioreactors and differentiated into neurospheroids composed of neurons, astrocytes, and oligodendrocytes. To recapitulate the neuro-immune axis, the incorporation of microglial cells differentiated from hiPSC (iMGL) in neurospheroids was achieved through optimization of culture medium and cell ratio. Neurospheroids with or without microglia were challenged with prototypical neuroinflammatory factors (TNF-α, IL-α, and C1q) and with viral vectors with known tropism towards the CNS, namely human adenovirus 5 (hAdv5) and adeno-associated virus (AAV) serotype 9, an interesting candidate for gene therapy due to its remarkable ability to cross the blood-brain barrier.

Results and discussion: Under inflammatory challenge, neurospheroids displayed upregulation of neuroinflammatory genes (e.g., SERPINA3, and C3), concomitant with the secretion of pro-inflammatory cytokines and chemokines (e.g., IL8 or CXCL8, and CCL2), hallmarks of neuroinflammation. Quantitative transcriptomic (NGS) and proteomic (SWATH-MS) data analyses are ongoing to validate the previous findings. iMGL efficiently infiltrated the neurospheroid 3D structure and adopted a ramified phenotype, while maintaining the expression of typical microglia markers, such as TMEM119, TREM-2 and IBA-1; Functional characterization is ongoing. To access viral

vector immunogenicity, neurospheroids were exposed to hAdv5 and AAV9 with GPF as transgene, at different multiplicities of infection (MOI). Transduction was evaluated in terms of transgene expression and cell toxicity. Ongoing work focuses on characterizing the innate immune reaction to the viral vectors with emphasis on neuron-glial interactions.

Hence, we propose the human neurospheroid model as a useful preclinical model to dissect neuroinflammatory mechanisms and accelerate the development of advanced therapies.

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Monday 27

9:00-10:00 **KEYNOTE LECTURE**

Restoring vision using optogenetic therapy

Botond Roska

Institute of Molecular and Clinical Ophthalmology Basel (IOB), Switzerland

10:00-10:35 **Poster Student Highlights**

Chairpersons: Nuša Pristovšek, ESACT Frontiers & Novo Nordisk, Denmark

Claire Pearce, ESACT Frontiers & XAP Therapeutics, United Kingdom

Francisca Arez, iBET, Portugal

11:00-12:30 **Scientific Session: Data, Data, Data: how to get it and how to use it**

Chairpersons: Mike Betenbaugh, John Hopkins Univ, USA

Damian Marshal, Achilles Therapeutics UK limited, UK

11:00-11:25 **INV 3 What can extracellular data tell us about intracellular pathways?**

Cleo Kontoravdi, *Department of Chemical Engineering, Imperial College London, United Kingdom*

In the era of big data, the challenge shifts from acquisition to analysis. This talk will focus on how models can be used to generate intracellular information using extracellular metabolite data and on how accurate this information is depending on the size and type of model. Specifically, I will present a comparative study between the predictions of generic and cell line-specific genome-scale metabolic models as well as a small-scale metabolic model and experimentally measured growth rates, gene essentialities, amino acid auxotrophies, and ^{13}C intracellular reaction rates. Our results show that while all cell models are able to capture extracellular phenotypes and intracellular fluxes, cell line-specific models better capture gene essentiality and auxotrophy phenotypes, although, in our experience, fail to improve intracellular reaction rate predictions. I will further discuss what an ideal dataset for generating reliable intracellular flux predictions looks like.

11:25-11:50 **INV 4 Bioprocessing in the Digital Age: from Process Models, through the Integration of Machine Learning, to Digital Twins**

Alessandro Butté, *DataHow AG, Zurich, Switzerland*

In this age of technology, the vision of manufacturing industries built of smart factories is not a farfetched future. As a prerequisite for Industry 4.0, industrial sectors are moving towards digitalization and automation. Despite its tremendous growth reaching a sales value of above $230 billion in 2022, the biopharmaceutical sector distinctly lags in this transition. Currently, the challenges are innovative market disruptions such as personalized medicine as well as increasing commercial pressure for faster and cheaper product manufacturing. Improvements in digitalization and data analytics have been identified as key strategic activities for the next years to face these challenges. Alongside, there is an emphasis by the regulatory authorities on the use of advanced technologies, proclaimed through initiatives such as Quality by Design (QbD) and Process Analytical Technology (PAT). In the manufacturing sector, the biopharmaceutical domain features some of the most complex and least understood processes, especially with respect to product quality. Thereby, process models that can transform process data into more valuable information, guide decision-making, and support the creation of digital and automated technologies are key enablers towards more robust processes and more flexible and efficient manufacturing operations. During my talk, with the support of real industrial study cases, I will review the state of process modelling in biopharma; investigate how machine learning can improve process modelling and reduce data requirements, and thus experimental effort, through the use of hybrid models; how such models can also support knowledge transfer across products and scales; and finally how such models can be packaged into digital twins, to enable adaptive and real-time learning and forecasting, process integration and, in general, what can be called Biomanufacturing 4.0.

11:50-12:03 **O-06 BIOMARKER IDENTIFICATION FOR IN SILICO PERFORMANCE PREDICTION OF CHO CELL LINES EXPRESSING COMPLEX THERAPEUTIC ABS**

Stella Papadaki.

Roche Diagnostics GmbH, Munich, Germany.

Background and novelty: During the screening of candidate cell lines in an antibody drug development campaign, there is an emphasis on identifying clones that can deliver high titers of product at the desired quality. For the selection of highly productive, stable and robust monoclonal cell lines able to serve both clinical phases and the market, a large number of clones have to be screened, filtered and further processed, making the clone selection process very demanding in terms of resources and time. As the pace of biotechnology quickens and model-based approaches are now very well establishing, artificial intelligence (AI) and machine learning (ML) models capable of predicting the outcome of bioprocessing, promise to create a pipeline with widely applicable attributes, proven to have correlation with the productivity results. Benefits of these statistical methodologies are lower experimental effort, process transparency, clear rationality behind decisions and increased process robustness.

Experimental approach: In this project we collected high-dimensional multi-omics data derived from 1000 antibody producer clones while in a very early cultivation step of cell line development. For this collection, a high-throughput sample production pipeline was established, to facilitate a robust systematic collection of heterogeneous data. The data library was created following an effective strategy for annotation, storage, quality control and harmonization of large volumes of data, to simplify a rapid data access framework suitable for multimodal computations. The final collection is utilized to develop ML methods for identifying early predictive

markers by screening clones' profiles across various production batches in the early stage, and analyzing their correlation to late stage performance.

Results and discussion: Our approach shows that model-based solutions are the future of bioprocessing and aspires to transform cell line development into an in silico based clone selection methodology which requires less resources to achieve a better success rate than current methods, while being leaner and faster.

Through the development and implementation of this modular, we believe we have set the groundwork towards digitalization of monoclonal antibody development.

12:03-12:16 O-07 ON DIGITAL BIOPROCESSING AND MANUFACTURING INTELLIGENCE: APPLICATION OF PROCESS ANALYTICAL TECHNOLOGY AND DATA ANALYTICS FOR UPSTREAM PROCESS DEVELOPMENT AND INTENSIFICATION

Ricardo Suarez Heredia[1], Nishanti Gangadharan[2], Amy Wood[3], Duygu Dikicioglu[4], Alexandros Kiparissides[5].

[1]University College London (UCL) / University of Cambridge / Merck KGaA, London, United Kingdom; [2]University of Cambridge, Cambridge, United Kingdom; [3]Merck KGaA, Boston, United States; [4]University College London (UCL) / University of Cambridge, London, United Kingdom; [5]University College London (UCL), London, United Kingdom.

Background and novelty: Digital transformation of biopharmaceutical process development has become a rapidly expanding area exploring value creation opportunities across the drug manufacturing lifecycle. This digitalisation has greatly benefited from ongoing developments in advanced sensor technology, robotic high throughput experimental platforms, consolidation of a broad range of analytical techniques, increased computational power and data management systems. Therefore, the steady integration of model-based and data analytics tools to analyse, interpret and use complex real-time and historical data repositories can lead to improve operational efficiency and robustness. Herein, we introduce three case studies to exemplify some of the applications of digital bioprocessing for descriptive, diagnostic, predictive and prescriptive support for upstream process development by combining principles of process analytical technology and process data analytics.

Experimental approach: The first case study introduces a workflow for the development of Raman spectroscopy soft sensors for in-line and real-time monitoring of critical process parameters (CPP) and relevant critical quality attributes (CQA) in mAb secreting CHO cell perfusion cultures. The second case study introduces the implementation of a machine learning (ML) pipeline for the mAb productivity performance prediction and data mining of the impact of nutrient supplementation strategies on growth and productivity of historical CHO cell fed-batch culture data (>120 cultures). The third case study introduces the use of evolutionary computation, particularly genetic algorithms and multigene genetic programming, in combination with automated microbioreactors (ambr®15) for the rapid process design and the intensification of mAb secreting CHO cell perfusion cultures and as a heuristic alternative to the statistical design of experiments (DoE) approach.

Results and discussion: The first case demonstrated the integrated implementation of data pre-processing and processing stages of time-series spectral data for the in-line monitoring of cell culture relevant parameters (growth and productivity), key relevant metabolites, process impurities (HCP, hcDNA) and antibody product quality (N-linked glycosylation, aggregation, charge variants and intactness). The second case highlighted the implementation of data pre-processing and processing methods for a supervised cross modelling framework used to successfully predict the harvest titre based on other process features as early as exponential phase as well as identifying feeding strategies (regime and composition) leading to improved

productivity. The third case study resulted in an accelerated process design screening (perfusion media composition and regime), sensitivity analysis and process improvement based on multi-objective optimization for dynamic perfusion cultures.

Overall, these case studies introduce the future role of digital bioprocessing for manufacturing intelligence in next generation bioprocessing.

12:16-12:29 O-08 BIOPROCESS DIGITAL TWINS FOR BIOMANUFACTURING 4.0

Dong-Yup Lee, Seo-Young Park, Cheol-Hwan Park, Dong-Hyuk Choi.

SungKyunKwan University, Suwon, South Korea.

Background and novelty: Bioprocess for producing a multitude of therapeutic proteins has operational difficulty and complexity since various process parameters and cellular traits significantly affect productivity and product quality during mammalian cell cultures, specifically Chinese hamster ovary (CHO) cells. For example, key performance indicators (KPIs) such as titer and yield as well as critical quality attributes (CQAs) are highly dependent of culture environments with adjustable key and critical process parameters (KPPs and CPPs) including media compositions and bioreactor conditions (e.g., pH, temperature, dissolved oxygen, etc.). In addition, process uncertainty and perturbation often lead to the increase in the product release time and total cost. Therefore, it is highly required to (1) closely monitor their dynamic behaviors, (2) better understand the relationships between KPPs/CPPs and KPIs/CQAs, and (3) finally identify relevant targets which can be timely manipulated to achieve enhanced culture performance, operational efficiency, and reliable product supply.

Experimental approach: Recently, there is a growing interest in industrial applications of the digital twins (DT) which combine physical system and its complementing digital counterpart via real-time data monitoring, thus enabling their interactive communications for the enhanced operational efficiency of manufacturing processes. Thus, we foresee that bioprocess DT can be also developed by incorporating in-line monitoring of bioprocess, data management, advanced data analytics with artificial intelligence (AI), and multivariate statistical and mechanistic models representing the cells and bioreactor for virtually mirroring their behaviors under adjustable process conditions.

Results and discussion: In this talk, we summarize and highlight recent advances in the key components within the bioprocess DT platform, present our ongoing efforts to establish key components including "Raman based in-line monitoring system", "deep learning AI model" and "enzyme capacity constrained CHO model", and discuss the current challenges with future research direction towards biomanufacturing 4.0.

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Reference: (1) Park, S.-Y., Park, C.-H., Choi, D.-H., Hong, J.K., Lee, D.-Y., 2021. Bioprocess digital twins of mammalian cell culture for advanced biomanufacturing. *Curr. Opin. Chem. Eng.* 33, 100702. https://doi.org/10.1016/j.coche.2021.100702, (2) Yeo, H.C., Hong, J., Lakshmanan, M., Lee, D.Y., 2020. Enzyme capacity-based genome scale modelling of CHO cells. *Metab. Eng*. 60, 138–147. https://doi.org/10.1016/j.ymben.2020.04.005.

16:00-17:30 **Scientific Session: Beyonf Evolution**

Chairpersons:
Martin Fussenegger (ETH, Switzerland)
Nick Timmins (Artisan Bio, USA)

16:00-16:30 **INV 5 CAR T-cell immunotherapy of solid tumours: Parallel learning from the clinic and lab**

John Maher, King´s College London, United Kingdom

In this two-part presentation, I will first present the results of a dose escalation phase 1 clinical trial of intratumoural panErbB CAR T-cells, administered to patients with head and neck cancer. Thereafter, I will describe two CAR platforms under development by Leucid Bio which are designed to enhance potency and persistence of CAR T-cells. The first of these is dubbed a parallel (p)CAR and consists of a CD28-containing second generation CAR and a 4-1BB containing chimeric co-stimulatory receptor. The second system is referred to as an adapter CAR and simulates the natural configuration adopted by many immune receptors whereby ligand binding and signalling domains are physically separated onto two polypeptides. When compared to traditional linear CAR designs, both pCAR and adapter CAR engineered T-cells demonstrate superior restimulation potential and efficacy in 2D and 3D in vitro tumour/stroma model systems, in addition to a range of cell line- and patient derived-tumour xenograft models.

16:30-16:40 **O-09 BLUEPRINT FROM NATURE: MULTI-OMICS COMPARISON OF CHO AND PLASMA CELLS UNVEILS NOVEL CELL ENGINEERING TARGETS TO IMPROVE PRODUCTIVITY**

Nikolas Zeh[1], Nadja Raab[2], Robin Kretz[3], Linus Weis[2], Larissa Walter[3], Benjamin Lindner[1], Sven Mathias[1], Dienter Stoll[3], Simon Fischer[1], Kerstin Otte[2].

[1]Boehringer Ingelheim Pharma GmbH, Biberach, Germany; [2]Hochschule Biberach, Biberach, Germany; [3]Hochschule Sigmaringen, Sigmaringen, Germany.

Background & Novelty: Chinese hamster ovary (CHO) cells are the predominantly used workhorse for the biotherapeutic industry and efficiently express multiple recombinant proteins including monoclonal antibodies (mAbs) but also difficult to express artificial molecules. However, due to their epithelial-like, ovarian origin they are not naturally specialized for a massive secretion of recombinant proteins. In mammals, terminally differentiated B-cells, so called plasma cells, are responsible for the secretion of high amounts of immunoglobulins (IgGs) after an infection and have been evolutionarily optimized for this task. In this context, plasma cells feature an extended endoplasmic reticulum (ER) and golgi apparatus and are capable for efficient glycosylation. Therefore, plasma cells represent an ideal role model for targeted CHO cell line engineering by taking nature as blueprint.

Experimental approach: The presented study compared IgG producing CHO and immortalized plasma cells using a comprehensive multi-omics analysis comprising transcriptome, proteome, miRNome, surfaceome and secretome. Thereby, differentially expressed genes were identified as promising engineering targets to improve recombinant protein production of CHO cells. We focused on the overexpression of plasma cell specific genes originated from the ER, golgi and the secretory pathway. In addition, CHO cell-specific genes found on the surfaceome or secretome with negative attributes as aggregation were knocked-out by microRNAs. Thereby, we aimed at generating an engineered and improved CHO-plasma hybrid cell line with enhanced productivity.

Results & Discussion: By the comparison of transcriptome, proteome, miRnome, surfaceome and secretome data of CHO and immortalized plasma cells and their

evaluation via DESeq analysis followed by appropriate statistical testing, we identified several gene ontology (GO) terms in the context of ER, golgi apparatus, unfolded protein response and the secretory pathway significantly upregulated in plasma cells. This analysis revealed a subset of nearly 300 promising engineering target genes involved in protein processing for the overexpression in CHO cells and over 200 genes with potential adverse effects as host cell proteins (HCPs). By overexpressing plasma cell specific genes as well as after knock-out of selected CHO specific HCPs, we were able to significantly enhance the productivity IgG expressing CHO cells. In conclusion, we could confirm the suitability of plasma cells as a blueprint for targeted CHO cell line engineering.

16:40-16:50 O-10 ENABLING LARGE THERAPEUTIC GENE DELIVERY: IMPROVING DUAL AAV VECTOR-INTEIN MEDIATED SYSTEMS

Mariana Valentim Ferreira, Ana Sofia Coroadinha.

Instituto de Biologia Experimental e Tecnológica; Instituto de Tecnologia Química e Biológica António Xavier, Lisbon, Portugal.

Background and novelty: Adeno-Associated Viral (AAV) vectors are one of the most well-established vectors used in the clinic for *in vivo* gene therapies. Despite significant improvements since their development, AAV vectors still present several limitations. One major bottleneck is the small packaging size restricting its use to treat diseases requiring the delivery of large genes. To overcome this, dual AAV vector delivery systems relying on homologous recombination have been explored to reconstitute oversize transgenes. Alternatively, protein trans-splicing systems can be used to reconstitute large proteins, being the split-intein DnaE sequence from *Nostoc Punctiforme* (Npu DnaE) currently the most used. However, these approaches present low gene reconstitution efficiencies, demanding higher vector dose administration to attain efficient therapeutic effects. This work seeks to overcome inefficient protein reconstitution rates of current dual AAV vector-intein-mediated systems by applying novel split-inteins with unmatched transplicing rates.

Experimental approach: Comparative studies between Npu DnaE and two optimized split-intein sequences were conducted: engineered consensus intein sequence (Cfa) and cyanophage-like Gp41-1 intein sequence. Initial split-intein protein reconstitution efficiency evaluations were performed by transient transfection of AAV vector transgene expression cassettes in 293T cells, and subsequently by dual AAV vector co-infection. AAV vector transgene cassettes were developed with a split reporter gene, each cassette encoding a frGFP terminal half fused to the respective terminal of each split-intein. The reconstitution of frGFP was evaluated at different time points by Flow Cytometry and Automated Western Blot.

Results and discussion: Transfection studies showed 100% transplicing with all inteins but different frGFP reconstitution rates. Gp41-1 presented up to 2-fold higher reconstitution rates than NPU DnaE, the lowest of all inteins. Moreover, Gp41-1 exhibited fluorescence intensities only 2-fold lower than the frGFP control condition. Dual AAV co-infections were performed to determine the optimal experimental conditions for transduction using AAV2 vectors coding for frGFP and mCherry. Different vector doses ($1x10^4$ to $5x10^4$ Viral Genomes/cell) were tested. Results showed 100% transduction efficiencies with increasing fluorescence intensities at higher doses. A decrease of 40% in fluorescence intensity was observed compared to single infections, suggesting AAV vector competition. Full evaluation on the different dual AAV vector-intein-mediated system is currently undergoing.

This work showed improved protein reconstitution efficiencies, revealing Gp41-1 as a promising new split-intein to be used in dual AAV delivery potentially allowing unprecedent decreased vector doses. Further work optimizing transplicing and transducing is ongoing to improve vector dose in therapeutic administration and enable efficient large therapeutic transgene delivery.

16:50-17:00 O-11 THERANOSTIC CELLS FOR DETECTION AND COUNTERACTION OF INFECTIONS BY REWIRING CELLULAR HOST DEFENSE PATHWAYS

Natascha Gödecke, Jannick Neubert, Juliane Schwarzer, Hansjörg Hauser, Mario Köster, Dagmar Wirth.

Helmholtz Centre for Infection Research, Braunschweig, Germany.

Background and novelty: Mammalian cells have developed potent mechanisms to react to pathogens, however, many pathogens successfully infect their host by suppressing the protective response. To expand the therapeutic strategies against infections theranostic cells that sense and combat infections represent an attractive concept. Using methods of synthetic biology, we rewired the cellular type I IFN signaling cascade activated during viral and bacterial infections with synthetic expression cassettes and evaluated them in vitro as well as in mouse models.

Experimental approach: Upon Crispr/Cas9 assisted genome editing, we generated cells in which the synthetic transcription factor tTA is controlled by the IFN induced cellular Mx2 promoter. This module represents a cellular hub that was connected to various genes of interest that are controlled by the synthetic Ptet promoter. Moreover, feedback loops were implemented for boosted and sustained responses.

Results and discussion: We designed Converter cells in which the IFN-specific hub was connected to reporter genes. Converter cells authentically sense pathogen-induced IFN in a dose- and time-controlled manner reflecting the trigger pulse. To exploit this concept for the detection of viruses that have evolved mechanisms to block IFN responses, we equipped the cells with a positive feedback module to amplify expression of the synthetic cassettes. Such ConvAmplifier cells respond to a transient IFN pulse with sustained expression, resulting in a 'hit-and-run' expression type. Notably, ConvAmplifier cells – but not Converter cells – sensitively detect even infections with viruses that efficiently undermine the cellular IFN response. This demonstrates that the positive feedback module is crucial for boosting weak IFN triggers. Finally, upon connecting the hub to antiviral genes theranostic cells were created which efficiently protect cells from infection.

Together, our results demonstrate that interfacing the cellular IFN signaling cascade with a synthetic positive feedback module provides a strategy to generate pathogen-induced theranostic cells for visualization and counteraction of infections which is functional even when viruses efficiently counteract the IFN response.

17:00-17:10 O-12 VIRAL PROTEASE-BASED MOLECULAR SWITCHES FOR DRUG DISCOVERY AND SYNTHETIC BIOLOGY APPLICATIONS

Nik Franko[1], Ana Palma Teixeira[1], Shuai Xue[1], Ghislaine Charpin-El Hamri[2], Martin Fussenegger[1].

[1]ETHZ, D-BSSE, Switzerland; [2]Université Claude Bernard Lyon, Institut Universitaire de Technologie, France.

Background and novelty: Viral proteases are essential proteins in the virus infectious cycle to process the viral polyproteins into functional sub-units by cleavage at specific amino acid sequences thus representing key targets for anti-viral drug development. Furthermore, the high specificity of viral proteases for their substrates, in combination with small molecules inhibiting their proteolytic activity constitute powerful tools to control human cellular functions, with minimal to none off-target effects as they lack human homologs.

Experimental approach: In this work, we resorted to viral proteases from HIV, HCV, HRV, and from different viruses of the *Coronaviridae* family, to build various molecular switches controlled at transcriptional or post-translational level by clinically approved or safe protease inhibitors. Specifically, we developed modular tunable autoproteolytic gene switches (TAGS) relying on synthetic transcription factors that

self-inactivate unless in the presence of protease inhibitors, which consequently activate transgene expression. Furthermore, we created post-translationally-regulated switches for different applications, in which proteins of interest (POI) are modified to contain a protease cleavage site and the corresponding protease either at POI C'/N'-terminus or within its structure.

Results and discussion: We show that TAGS can report on the activity of different proteases *in cellulo*, providing a robust, fast, and high signal-to-noise response that is selective for corresponding inhibitors, with a sensitivity range that is appropriate for the concentration ranges inhibiting virus replication in cell cultures. We further show that the expression of two transgenes can be controlled simultaneously by multiplexing two orthogonal protease-sensitive gene switches. Mice implanted with TAGS-engineered cells enabled analysis of the activity and bioavailability of protease inhibitors *in vivo* in a virus-free setting. As for the post-translationally-regulated switches, we demonstrated their ability to i) control protein localization, ii) orthogonally control components of signaling pathways, iii) rapidly activate an effector protein bearing a protease cleavage sequence within its structure, by changing from non-functional to functional within a few minutes, confirming the inherent faster activation compared to transcriptional or translational regulation, and iv) achieve inducible control over CRISPR-based genome editing and endogenous gene activation.

Overall, our results suggest that the developed protease-based molecular switches can be valuable to support the establishment of cell-based assays to test new protease inhibitors for future treats and expand the repertoire of small drug inhibited proteases. Their compact design and actuation by clinically tested protease inhibitors show their potential for safe and precise control of next-generation engineered cell-based therapies.

17:10-17:15 Flash 01 EXPANDING THE DESIGN SPACE OF SYNTHETIC PROMOTERS FOR CHO CELL ENGINEERING USING NEXT-GENERATION SEQUENCING

Adrian Bourke[1], Julien Douet[2], Katarzyna Sobkowiak[2], Adam Brown[1], David James[1].

[1]University of Sheffield, Sheffield, United Kingdom; [2]Merck Serono SA, Corsier-sur-Vevey, Switzerland.

Background and novelty: This project expands the design space of synthetic promoters, allowing for greater transcriptional control by inferring design methodology from the cell's genome. Chinese Hamster Ovary cells (CHO) remain the predominant means of producing biopharmaceuticals and the majority of these systems use a Cytomegalovirus (CMV) promoter to drive the genes required for recombinant protein production. However, reliance on a small selection of promoters and the inability to control transcriptional power leads to many products being produced without optimal transcriptional ratios of heavy and light chain, which can affect overall titres. Synthetic promoters can alleviate these issues by providing greater transcriptional power than CMV and enabling fine-tuning of these transcriptional ratios.

Experimental approach: RNA sequencing was performed on days 2, 5 and 10 of Merck's propriety process. The sequencing reads were aligned using Star to the CHO PICR genome and features were assigned using featureCounts. Promoter regions varying from 3600 base pairs (bp) in library 1 to 1200 bp in library 2 of genes with high transcripts per kilobase million (TPM) value were analysed and the most promising transcription factor regulatory elements (TFRE) were taken forward to be tested in repeats of six using secreted alkaline phosphatase as the reporter gene. Concurrently, promoters with mixed populations of TFREs were taken from the literature and tested by the same method. The successive libraries from one to three, built on each other incorporating new TFRE sites and expanding the design space for synthetic promoter design.

Results and discussion: TFREs found in library 1 showed that the abundance of TFRE binding sites in promoter regions of high expressing genes, when normalized against low expressing genes, is a poor indicator of transcriptional activation. Promoters utilizing previous literature and a mix of TFREs, achieved a fold change of 1.8 fold-over CMV. Library 2 took a different approach to the identification of TFREs and found the TPM of the gene encoding the transcription factor is an extremely important element. A new TFRE NFE2l2 was found, which matches the activation potential of the previous top family NFkB. Incorporation of newly found TFRE sequences into library 3 led to an increase in design diversity and when incorporated into previously tested promoters led to increased transcriptional activity of up to 0.4 fold while retaining the same promoter length. Library 3 also led to the creation of fully novel sequences utilising no TFRE sequences previously found in the literature.

17:15-17:20 **Flash 02 MULTIPLEXED ENGINEERING CHO CELLS TO PRODUCE RECOMBINANT IGGS WITH DESIRABLE N-GLYCANS VIA TARGETED INTEGRATION**

Ngan Nguyen Tran Bich, Jianer Lin, Zach Kt Pang, Shi Jie Tay, Mariati Zhang, Jessna Yeo, Terry Nguyen-Khuong, Yuansheng Yang.

*Bioprocessing Technology Institute, A*STAR, Singapore, Singapore.*

Background and novelty: Therapeutic antibodies are decorated with complex-type N-glycans that significantly affect their biodistribution and bioactivity. The N-glycan structures on antibodies are incompletely processed in wild-type CHO cells due to their limited glycosylation capacity. To improve N-glycan processing, glycosyltransferase genes have been traditionally overexpressed in CHO cells to engineer the cellular N-glycosylation pathway by using random integration, which is often associated with large clonal variations in gene expression levels. Combination of heterogenous gene expression and clonal variation have limited the success of achieving desirable glycosylation outcomes for therapeutic antibodies. We developed a CHO targeted integration platform that can overcome such issues by directing transgene integration into specific loci in genome, resulting in stably transfected cells with high levels of phenotypic and transcriptional homogeneity. We aimed to establish this platform for precise multiplexed engineering of both single and multiple genes in the glycosylation pathway to expand the diversity of N-glycan structures that could be produced on antibodies.

Experiment approach: We first utilized our in-house CHO targeted integration platform to overexpress a panel of 42 human glycosyltransferase genes to screen their impact on antibody N-glycosylation. The bottlenecks in the N-glycosylation pathway were identified and then released by overexpressing single or multiple critical genes. We then further optimized the expression of critical genes by using internal ribosome entry site (IRES)-based multi-cistronic vectors with adjustable expression strength.

Results and discussion: Overexpressing B4GalT1 gene alone in the CHO cells produced antibodies with more than 80% galactosylated bi antennary N-glycans. Combinatorial overexpression of B4GalT1 and ST6Gal1 produced antibodies containing more than 70% sialylated bi antennary N-glycans. In addition, antibodies with various tri-antennary N-glycans were obtained for the first time by overexpressing MGAT5 alone or in combination with B4GalT1 and ST6Gal1. Lastly, we produced antibodies carrying various levels of bisecting and a-fucosylated N-glycans by simultaneously fine-tuning the MGAT3 and MAN2 expression in CHO cells. This allowed us to optimize the N-glycans on antibodies for optimal antibody-dependent cellular cytoxicity (ADCC) and complement-dependent cytotoxicity (CDC) activities.

By overcoming position effects and thus minimizing clonal variations, our technology enables the study of gene functions in stable cell pools without the need of isolating clones, facilitating further research toward understanding of the fundamental effects that N-glycans have on antibody pharmacological properties. Moreover, the diverse range of N-glycan structures and the method for producing them in this work also provide opportunities to develop novel recombinant antibodies to address unmet therapeutic application.

18:00-19:30 **Scientific Session: Molecular Cell Surgery**

Chairpersons:
Isabelle Rivière, Memorial Sloan Kettering Cancer Center, USA
Nicole Borth, BOKU, Austria

18:00-18:25 **INV 6 Turning Genes into Medicines: Prospects and Problems in Development of a Novel Class of Therapeutics**

Kathy High, AskBio Therapeutics, United States

This talk will review obstacles that were overcome to reach the current state of the field, with multiple approved products and more in the pipeline. With a focus on AAV-mediated gene therapies, advances in capsid technology, expression cassette design, and analysis and management of human immune responses to AAV will be discussed. Key issues in clinical development, such as choice of controls in Phase 3 studies, and the need to develop and validate clinical endpoints for diseases that have previously lacked any treatment, will be highlighted, and areas of current active investigation, and their potential to expand the addressable patient population, will be noted.

18:25-18:50 **INV 7 Guiding mRNA-LNP drug products from early R&D programs to the market – Scale up and production of mRNA LNPs.**

Andreas Wagner, Polymun Scientific, Austria

Lipid nanoparticles (LNP) are the leading delivery systems for enabling the therapeutic potential of small interfering RNA (siRNA) as well as mRNA for systemic applications. Lipid nanoparticles, currently represent the most advanced platform for RNA delivery, which have now advanced to market products.

During the early days of the Covid-19 pandemic, industry partners reached out to Polymun to set up production processes for mRNA-LNPs together with the respective analytical test methods. Within weeks, a robust and scalable process has been developed, process conditions have been optimized and the process has been adapted to meet requirements for industrial scale. The LNP production process has to meet several requirements, such as simplicity, robustness, potential to scale up and easy handling. Data will be presented, which describe hurdles and solutions throughout these processes.

18:50-19:00 **O-13 REPAIRING THE REPAIRERS: STABILIZING THE CHO GENOME AND PROTEIN PRODUCTION BY EDITING DNA REPAIR**

Nathan Lewis[1], Philipp Spahn[1], Xiaolin Zhang[2], Qing Hu[3], Huiming Lu[3], Nathaniel Hamaker[2], Hooman Hefzi[1], Shangzhong Li[1], Chih-Chung Kuo[1], Yingxiang Huang[1], Jamie Lee[1], Anthony Davis[3], Peter Ly[4], Kelvin Lee[5].

[1]University of California, San Diego, La Jolla, United States; [2]University of Delaware, Newark, United States; [3]University of Texas Southwestern Medical Center, Dallas, United States; [4]University of Texas Southwestern Medical Center, La Jolla, United States; [5]University of Delaware, La Jolla, United States.

Background and novelty: Mammalian cells used for recombinant biotherapeutic protein production are almost exclusively immortalized cells and exhibit extensive genome instability. While this instability has been an asset in successfully developing cell lines capable of suspension growth at high cell densities in chemically defined serum-free media and producing large amounts of product, the cells can frequently lose productivity over time as transgene copies are lost or silenced. This reduced productivity is a major problem associated with this genome instability, as chromosomal aberrations reduce transgene copy number and decrease protein expression. Thus, there is a fundamental need to understand the source of genome instability in mammalian cells used in bioproduction, and to develop approaches to stabilize production cells.

Experimental approach: To identify genetic sources of genome instability, we analyzed whole-genome sequencing data from 11 CHO cell lines. Several deleterious single-nucleotide variants were identified in DNA repair genes. We subsequently compared the DNA damage repair capability of CHO cells with primary Chinese hamster fibroblasts and confirmed DNA repair to be substantially compromised in CHO. Thus, we corrected four DNA-damage repair genes by SNP reversal using a CRISPR-based system or overexpression of damaged factors.

Results and discussion: Correction of key DNA repair genes by single-nucleotide variant reversal or expression of intact cDNAs successfully improved DNA repair and mitigated karyotypic instability. Moreover, overexpression of intact copies of LIG4 and XRCC6 in a CHO cell line, expressing secreted alkaline phosphatase, mitigated transgene copy loss and improved protein titer retention. Thus, by repairing the repairers, we show that DNA repair can be improved, yielding improvements in genome stability in CHO, and provide new opportunities for cell line development for sustainable protein expression.

Acknowledgements & Funding: We would like to express our gratitude to George Yerganian for sharing primary Chinese hamster tissue. We thank Mojtaba Samoudi, Francisco Diaz, Jennifer Santini, Bjørn Voldborg, Alexandra Hoffmeyer and Marcy Erb for technical assistance. This study was supported by the Novo Nordisk Foundation (NNF20SA0066621), NSF (grants 1736123 and 1412365), NIH (CA162804, GM047251, R35 GM119850, and P30 NS047101).

19:00-19:10 O-14 INFLUENZA A VIRUS-DERIVED DEFECTIVE INTERFERING PARTICLES FOR ANTIVIRAL TREATMENT

Marc Hein[1], Najat Bdeir[2], Ulfert Rand[3], Yvonne Genzel[1], Michael Winkler[2], Luka Cicin-Sain[3], Dunja Bruder[3], Klaus Schughart[3], Stefan Pöhlmann[2], Sascha Y. Kupke[1], Udo Reichl[1].

[1]Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany; [2]German Primate Center - Leibniz Institute for Primate Research, Göttingen, Germany; [3]Helmholtz Centre for Infection Research, Braunschweig, Germany.

Background and novelty: Influenza A virus (IAV) defective interfering particles (DIPs) have been suggested as a promising novel antiviral agent. Typically, IAV DIPs harbor an internal deletion in one of their eight viral RNA (vRNA) segments, rendering them propagation-incompetent. Further, DIPs are able to hijack viral resources upon co-infection with fully infectious standard virus (STV), resulting in an antiviral effect. Besides this replication interference, DIP infections also stimulate innate immunity, adding to the antiviral efficacy. So far, DIPs were produced in embryonated chicken eggs. To improve scalability and flexibility of processes and to increase product quality, we established a cell culture-based DIP production system.

Experimental approach: We devised a genetically engineered cell line complementing the defect of DIPs in virus replication. Thus, the need to add infectious STV was abolished, avoiding safety concerns. Specifically, cell lines

expressing the viral PB2 protein (encoded by IAV segment 1 (S1)) were generated. Using these cell lines and reverse genetics for IAV, we reconstituted purely clonal "DI244" - a DIP harboring a deletion in S1. MDCK suspension cells expressing PB2 were used to propagate DI244 in batch and perfusion mode at laboratory scale.

Results and discussion: We yielded very high titers of up to 2.6E+11 DIPs/mL for DI244 production. Next, we established a cell culture-based production process for a novel type of IAV DIP, previously discovered by us using single-cell analyses. Instead of an internal deletion, "OP7" showed numerous point mutations in its S7 vRNA. Intriguingly, OP7 showed a superior interfering efficacy compared to conventional IAV DIPs, i.e. DI244. For OP7 production, we achieved titers of up to 1.1E+11 DIPs/mL in batch mode. Further, infections of mice demonstrated that intranasal administration of produced DI244 or OP7 results in no apparent toxic effects and in a full rescue of mice co-treated with an otherwise lethal dose of IAV. Finally, *in vitro* experiments using human lung cells demonstrated that IAV DIPs even exert an antiviral effect against SARS-CoV-2 replication by stimulating the interferon system. Thus, we propose IAV DIPs as an effective antiviral agent for treatment of infections with IAV, SARS-CoV-2 and potentially additional respiratory interferon-sensitive viruses.

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19:10-19:20 O-15 AN ARRAYED CRISPR SCREEN REVEALS *MYC* DEPLETION TO INCREASE PRODUCTIVITY OF DIFFICULT-TO-EXPRESS COMPLEX ANTIBODIES IN CHO CELLS

Niels Bauer[1], Benedikt Oswald[1], Maximilian Eiche[1], Lisa Schiller[1], Emma Langguth[1], Christian Schantz[1], Andrea Osterlehner[1], Amy Shen[2], Shahram Misaghi[2], Julian Stingele[3], Simon Ausländer[1].

[1]Roche Diagnostics GmbH, Penzberg, Germany; [2]Genentech, Inc., South San Francisco, United States; [3]Ludwig-Maximilians-University Munich, Munich, Germany.

Background and novelty: Complex therapeutic antibody formats, such as bispecifics (bsAbs) or cytokine fusions, may provide new treatment options in diverse disease areas. However, the manufacturing yield of these complex antibody formats in Chinese Hamster Ovary (CHO) cells lack behind monoclonal antibodies (mAbs) due to challenges in expression levels and potential formation of side products. Our aim was to overcome these limitations by a CRISPR/Cas9 based knockout arrayed screening under a production-mimicking setup.

Experimental approach: We performed a CRISPR/Cas9-based knockout (KO) arrayed screening of 187 target genes in two CHO clones expressing two different complex antibody formats in a production-mimicking setup. To prevent clone specific effects, we decided to apply an unbiased screening approach by introducing high-efficiency KOs into CHO expression clones and measure productivity side-by-side to the non-engineered parent clone. We verified the screening result in microbioreactor conditions by testing multiple primary seed bank (PSB) lead clone candidates expressing a range of complex molecule formats.

Results and discussion: We demonstrate that *Myc* depletion strongly increases product expression (>40%). Myc-depleted cells display substantially higher product

titers in industrially-relevant bioprocesses using ambr15 and ambr250 bioreactors. These effects are consistent across multiple additional clones each expressing a distinct complex antibody format. Transcriptomic analysis indicates that *Myc* depletion affects both, transgene transcription and translational machinery of CHO clones and extends their overall production capacities.

Our findings reinforce the mutually exclusive relationship between growth and production phenotypes and provide a targeted cell engineering approach to impact productivity without impairing product quality. We anticipate that CRISPR/Cas9-based CHO host cell engineering will transform our ability to increase manufacturing yield of high-value complex biotherapeutics.

19:20-19:25 **Flash 03 ENGINEERED NUCLEASES TARGETING THE ATXN3 GENE FOR THE THERAPY OF MACHADO-JOSEPH DISEASE**

Sara Lopes[1], Miguel Lopes[1], Rui Nobre[1], Clévio Nóbrega[1], Carlos Matos[1], Ana Ferreira[1], Dina Pereira[1], Neville Sanjana[2], Patrick Hsu[2], F Ann Ran[2], Lukasz Swiech[2], Le Cong[2], Feng Zhang[2], Luís Pereira De Almeida[1].

[1]Center for Neuroscience and Cell Biology (CNC), University of Coimbra, Coimbra, Portugal; [2]Broad Institute of Massachusetts Institute of Technology and Harvard, Cambridge, Massachusetts, United States.

Background and novelty: Machado-Joseph disease (MJD) is an autosomal dominantly inherited neurodegenerative disorder, caused by an over-repetition of the polyglutamine-codifying region in the *ATXN3* gene. Strategies based on the suppression of the deleterious gene products have demonstrated promising results in pre-clinical studies. Nonetheless, these strategies do not target the root cause of the disease, producing an incomplete and/or transient therapeutic effect in target cells or tissues. Recently, genome editing technologies, such as transcription activator-like effector nucleases (TALENs) and clustered regularly-interspaced short palindromic repeat (CRISPR)-Cas9 systems, have been successfully used to permanently inactivate disease-related genes, holding promise for the development of a definitive cure for inherited diseases.

Experimental approach: Here, a panel of customized sequences were designed and constructed aiming at permanently suppressing the human *ATXN3* gene expression. Functional characterization was initially performed in HEK293T cells, through the surveyor mutation detection assay and one sequence of each system was selected for further *in vivo* studies. Adeno-associated viral particles, encoding the referred programmable nucleases, were subsequently delivered in the striatum of a lentiviral-based mouse model of MJD by intracranial injection. Neuropathological markers were assessed 4 weeks after surgery.

Results and discussion: Surveyor mutation detection assay revealed the editing capability of our customized nucleases both in HEK293T cells and in striatal samples of the mouse model. We observed a reduction in the levels of wild-type ATXN3 in human cells and a drastic reduction of the mutant protein in the mouse model, in a dose-dependent manner. Immunohistochemical analysis of mouse brain sections revealed the same tendency for the reduction of aggregates in both TALEN and CRISPR-Cas9 MJD-treated hemispheres. Unexpectedly, despite the efficient reduction of mutant protein expression and aggregation, only the CRISPR-Cas9 system allowed the preservation of neuronal integrity, exhibiting a good tolerability profile.

Overall, this work provides the first *in vivo* evidence of the efficacy of a CRISPR-Cas9-based approach to permanently inactivate the *ATXN3* gene, supporting its potential as a putative therapeutic avenue in the context of MJD.

This work was funded by the ERDF through the Regional Operational Program Center 2020 and National Funds through FCT - CENTRO-01-0145-FEDER-000008, CENTRO-01-0145-FEDER-022095, POCI-01-0145-FEDER-016719, POCI-01-0145-FEDER-029716 and PTDC/BBB-NAN/0932/2014, by SynSpread, ESMI and ModelPolyQ under the EU Joint Program - Neurodegenerative Disease Research; by National Ataxia Foundation, the American Portuguese Biomedical Research Fund and the Richard Chin and Lily Lock Machado-Joseph Disease Research Fund. Sara Lopes was supported by FCT fellowship SFRH/BD/51673/2011.

19:25-19:30 **Flash 04 RATIONAL DEVELOPMENT OF RECOMBINANT CHO CELLS BASED ON HISTONE ANALYSIS: IDENTIFICATION AND EXPERIMENTAL VALIDATION OF STABLE INTEGRATION SITES**

Oliver Hertel[1], Anne Neuß[1], Tobias Busche[2], David Brandt[2], Jörn Kalinowski[2], Thomas Noll[1].

[1]Bielefeld University, Bielefeld, Germany; [2]Center for Biotechnology (CeBiTec)), Bielefeld, Germany.

Background and novelty: Chinese hamster ovary (CHO) cells are the most important platform for production of biotherapeutics. Random integration of a transgene often occurs into epigenetically instable regions of the genome followed by silencing of the gene of interest and loss of productivity during upstream processing. Therefore, cost- and time-intensive clone screening and long-term stability studies are required. Our strategy to overcome these limitations is a rational cell line design by CRISPR/Cas9-mediated site-specific integration into regions harbouring specific histone modifications indicating stable and high expression.

Experimental approach: ChIP-sequencing and RNA-sequencing were performed from a fed-batch cultivation of CHO-K1 cells to identify regions with histone modifications supporting high and stable expression. The reporter gene eGFP was site-specifically integrated into identified sites by CRISPR/Cas9. mPlum was used as a reporter to exclude random integration. Successful targeted integration was confirmed by targeted Cas9 sequencing using nanopores. Stable cell pools were evaluated for productivity, gene copy number, transcription levels and stability during a long-term cultivation over 70 generations with and without selection pressure in comparison to cells generated by random integration.

Results and discussion: In total 709 sites were identified, showing the most promising histone modifications H3K4me3, H3K27ac and not H3K9me3. These were further analyzed and three sites were selected for site-specific integration. Targeted Cas9 sequencing showed correct integration in all three cell pools with a specificity between 23-73%. Already from the beginning of the cultivation, all site-specifically integrated cell pools showed a higher productivity than the random cell pool, whose productivity even rapidly dropped by 75 % by day 21. Two of the three site-specifically integrated cell pools proved to be epigenetically stable. One cell pool (B) showed a slower decline in productivity than the random cell pool, while pool-A could be identified as a real safe harbour, as neither gene copy loss nor transcript level loss occurred. At the end of the long-term cultivation (70 generations), productivity of pool-A was 15-fold higher than in the cell pool with random gene integration, proving that epigenetically active and stable integration sites can be predicted and used by genome-wide histone modification analysis, sequencing and CRISPR/Cas9.

Tuesday 28

9:00-10:00 **KEYNOTE LECTURE**

Gene Therapy – a new class of medicine

Hildegard Büning, Institute of Experimental Hematology and REBIRTH – Center for Translational Regenerative Medicine, Hannover Medical School, and German Center for Infection Research (DZIF), Germany

With the concept of replacing or counteracting the activity of a defective gene, gene therapy human clinical trials were initiated more than three decades ago. However, it took until November 2012 before the first gene therapy, an *in vivo* gene therapy to treat patients with lipoprotein lipase deficiency, received marketing authorization in the Western World. Albeit the number of market approved gene therapies are still low, gene therapy has changed the face of medicine. Indeed, gene therapy represents a new class of therapeutics. It has become an integral part of modern medicine reaching far beyond offering treatment options for monogenic diseases, its initial target. This is maybe best exemplified by the number of approved cancer immunotherapies employing autologous T lymphocytes equipped with a chimeric antigen receptor (CAR). Also, the area of vaccine development greatly benefited from gene therapy since tools and technologies are in use which were initially developed in the context of gene and cell therapy. Through the development of gene editing tools (including the most recent advancements such as prime editing) treatment options have greatly expanded, and the way is paved for the design of treatment strategies that enable a true repair of the underlying disease-causing genetic defects. The talk will provide an overview on basic concepts of gene and cell therapy and will review the status and possible future direction of this new class of medicine.

10:00-10:30 **Selected Flash Presentations Session**

19:25-19:30 **Flash 05 4-1BB AND 4-1BBXOX40 BISPECIFIC ANTICALIN®-BASED PAYLOADS TO ARMOR CELLULAR IMMUNOTHERAPIES FOR EFFECTIVE LOCALIZED IMMUNE CELL STIMULATION**

Janet Peper-Gabriel, Josef Prassler, Stefan Grüner, Eva-Maria Hansbauer, Rachida Siham Bel Aiba, Ahmed Mousa, Hitto Kaufmann, Shane Olwill.

Pieris Pharmaceuticals GmbH, Hallbergmoos, Germany.

Background and novelty: Cellular therapies have achieved remarkable response rates in hematological malignancies but efficacy in solid cancer indications have been limited to date. Multiple lines of evidence show that 4-1BB (CD137) supports T-cell effector functions and persistence and that the combination of 4-1BB with OX40 stimulation further drives synergistic effects in preclinical models. While anti-4-1BB agonistic antibodies have shown immune cell activation in tumor tissues, they are also associated with peripheral immune cell activation, resulting in dose-limiting on-target toxicity. To overcome these limitations, we have generated self-assembling hexavalent 4-1BB and 4-1BBxOX40 bispecific molecules with a limited genetic coding sequence, enabling effective engineering of 4-1BB and 4-1BBxOX40 agonist armored cellular therapies. This results in tumor-localized production and accumulation of the 4-1BB and 4-1BBxOx40 agonist "payloads", potentially providing effective co-stimulation to both engineered cells and bystander immune cells in the tumor microenvironment, driving local anti-tumor immunity with less risk of systemic toxicity.

Experimental approach: Anticalin proteins are ~18 kDa protein therapeutics derived from human lipocalins with high stability and a robust structure. We

utilized phage display technology to generate Anticalin proteins binding to 4-1BB or OX40 with high affinity and specificity. Hexavalent anti-4-1BB or anti-4-1BBxOX40 bispecific engagers were generated by recombinant fusion of either two 4-1BB targeting Anticalin proteins or one 4-1BB and one OX40 targeting Anticalin protein to the human collagen XVIII trimerization (TIE_{XVIII}) domain, separated by a serine-glycine linker to provide structural flexibility. The TIE_{XVIII} domain allows the production of efficiently secreted soluble trimeric proteins resulting in hexavalent binders. Efficient binding and potency of hexavalent anti-4-1BB or anti-4-1BBxOX40 bispecific engagers was investigated in different binding and functional in vitro assays.

Results and discussion: We demonstrated in vitro that the fusion of Anticalin proteins to the TIE_{XVIII} self-assembling domain results in the production of functionally active hexavalent 4-1BB and 4-1BBxOX40 engagers binding with high affinity to their targets. The described agonists drive efficient 4-1BB and OX40 signaling whereby significantly enhancing T-cell effector functions. Furthermore, we demonstrated that the 4-1BBxOX40 bispecific only mediates strong T-cell co-stimulation in presence of 4-1BB and Ox40-positive cells potentially by cross-linking 4-1BB- and OX40-positive T cells, resulting in the generation of a robust and effective anti-tumor immune response with the potential to further enhance efficacy of cellular immunotherapies to expand clinical success to solid tumor indications.

10:05-10:10 **Flash 06 CULTURE OF PLURIPOTENT STEM CELLS AND DERIVATION OF ORGANOIDS USING DROPLET MICROFLUIDICS**

Sebastien Sart.

Institut Pasteur, Paris, France.

Background and novelty: Organoids, the *in vitro* miniaturized form of tissue and organs, are usually derived from differentiating pluripotent stem cells (PSCs). The formation of organoids recapitulates the processes of self-organization, symmetry breaking and tissue patterning that occur during the embryonic development. These morphogenetic events are driven by the creation of specific niches promoting the spatially controlled differentiation into specialized cell types. The biochemical confinement of differentiating PSCs into oil-isolated droplets has the potential to regulate the autocrine signaling that trigger 3D tissue patterning during differentiation, which has not been demonstrated so far. In this work, I demonstrate that droplet microfluidics can generate a unique microenvironment that allows the generation of gastruloids and embryonic-like structures (ELSs), a type of organoids that recapitulate the early steps of the embryonic development. I show that ELSs display a unique head-trunk structure, which demonstrates high degree of similarity with the stage E8.5 of the mouse embryonic development.

Experimental approach: I developed a new droplet microfluidic platform that sustains the long-term culture of mouse embryonic stem cells (mESCs) at the undifferentiated state using reduced culture volumes. The platform is then used to derive several types of organoids from mESCs. In particular, I used this microfluidic chip for the maturation of gastruloids and embryonic-like structures (ELSs). For this purpose, few hundreds of hypoSUMOylated mESCs were first cultivated into water-in-oil emulsions to form polarized gastruloids, which were then encapsulated within Matrigel to allow further maturation into ELSs. The cellular diversity and the structural organization within ELSs were investigated using fluorescent reporter cell lines, *in situ* hybridization, immunostaining, single cell RNA sequencing.

Results and discussion: We show that ELSs generated within droplets display high degree of comparability (*i.e.* gene expression and structural organization) with developing mouse embryos up to stage E8.5. Note that this degree of developmental maturation *in vitro* cannot be achievable using conventional culture vessels. As such,

the differentiation of PSCs into microfluidics droplets provides a novel approach towards the derivation of more functional organoids, in view of tissue engineering and disease modeling applications.

10:10-10:15 Flash 07 AUGMENTED DECISION MAKING FOR CELL CULTURE PROCESS DEVELOPMENT: FROM DATA TRACEABILITY & ACCESSIBILITY TO PROCESS MODELLING

Wolfgang Paul, Steffie Eggermont, Bassem Ben Yahia.

Background and novelty: During the development phase of biopharmaceuticals large volumes of data are generated in many stand-alone hardware devices. Furthermore, with increasing numbers of projects and need to compress development timelines, high throughput and automation systems are being increasingly used. The resulting high pace of data generation augments error rates thereby risking data integrity. In order to ensure a leaner, more efficient and integral data generation we initiated an "e-Transformation" program.

This study provides insights into two main areas: **(a)** strategies and tools for data collection, storage and visualization and **(b)** modeling techniques to transform data into knowledge and decisions for CMC project development application.

Experimental approach: A prior assessment for each cell culture process step and equipment connectivity was performed to map, categorize and highlight gaps where data are generated **(a)**: data traceability, integrity & extractability but also complexity of the systems. Based on this preliminary assessment, a data architecture composed of multiple tools was then designed to close the gaps: middleware, electronic lab notebook, data integration layer and regulatory reporting tools. Moreover, to support CMC project development and decision making **(b)**, multiple modeling tools were developed to focus on specific needs during process development, e.g. clone selection and identification of promising clones for intensified process, process optimization based on mechanistic models both in fed-batch and perfusion mode, bioreactor characterization modeling to support scale-up, and economic models to compare the impact of process changes on facility throughout and cost of goods.

Results and discussion: Through increasing automation and interconnectivity of lab instruments and systems in addition to improving data traceability, extractability and searchability, it is possible to drastically increase development lab efficiency by >20%. Moreover, with the use of mechanistic models of cell culture processes, it was possible to predict cell metabolism and cell culture performance of multiple CMC processes but also to identify new optimized feeding strategies to drastically increase final productivity. Case studies will be presented where the different modeling techniques were applied to troubleshoot process deviations, support scale up but also de-risk the transfer of perfusion processes. In summary, our data architecture combined with process modeling techniques provides a better insight into the impact of process parameters on production yields and product quality, thus improving process understanding and control as well as accelerating process development with a more flexible and agile strategy.

10:15-10:20 Flash 08 FOUND IN TRANSLATION: MICROPROTEINS ARE A NEW CLASS OF POTENTIAL HOST CELL IMPURITY IN MAB DRUG PRODUCTS

Marina Castro-Rivadeneyra[1], Ioanna Tzani[1], Paul Kelly[1], Lisa Strasser[1], Felipe Guapo[1], Ciara Tierney[1], Martin Clynes[2], Barry Karger[3], Lin Zhang[4], Niall Barron[1], Jonathan Bones[1], Colin Clarke[1].

[1]NIBRT, Dublin, Republic of Ireland; [2]DCU, NICB, Republic of Ireland; [3]Barnett Institute, Northeastern University, United States; [4]Pfizer, Bioprocess R&D, United States.

Background and Novelty: Mass spectrometry (MS) has emerged as a powerful

approach for the detection of Chinese hamster ovary (CHO) host cell proteins (HCP) in antibody drug products. The incomplete annotation of the Chinese hamster genome, however, limits the coverage of MS-based HCP analysis. In this study, we performed ribosome footprint profiling (Ribo-seq) to refine the Chinese hamster genome annotation[1].

Experimental approach: Ribo-seq data was captured from a small-scale cell culture model of temperature shift. To arrest translation, we treated cells with harringtonine (initiating ribosomes), as well as cycloheximide and flash-freezing (elongating ribosomes). We performed a transcriptome-wide identification of open reading frames (ORFs) and used this annotation to construct a new protein sequence database. To assess the utility of this database, we carried out HCP analysis of adalimumab. We also analysed changes in translation regulation that occurred upon the reduction of temperature. Finally, a proteomic mass spectrometry was carried out on a CHOK1GS cell line to identify novel proteoforms that were differentially expressed between the exponential and stationary phases.

Results and Discussion: Analysis of translation initiation and elongation using Ribo-seq yielded a refined annotation of the Chinese hamster genome. > 7000 novel Chinese proteoforms including > 5,500 short open reading frames (sORFs) predicted to encode microproteins (i.e., proteins < 100 aa) were identified. 8 microproteins were subsequently detected in adalimumab drug product and sORFs predicted to encode microproteins were found to undergo changes in both expression and translational regulation at reduced cell culture temperature. 79 microproteins were subsequently identified in the CHOK1GS cell line using LC-MS/MS based proteomics with 13 microproteins found to be differentially expressed.

In conclusion, we have shown that microproteins can be found in a mAb drug product and therefore represent a new class of potential HCPs. Ribo-seq is also a powerful approach for monitoring CHO cell translational regulation, providing an additional layer of biological understanding that is not possible with transcriptomics alone. The identification of new proteoforms and extending the annotation of translated regions also enhances the utility of MS-based proteomics to study CHO cells.

Acknowledgements and Funding: The authors gratefully acknowledge funding from Science Foundation Ireland (grant references: 15/CDA/3259 & 13/SIRG/2084).

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10:20-10:25 **Flash 09 USING A CELL RECEPTOR KNOCK-OUT STRATEGY TO ENABLE STABLE EXPRESSION OF CYTOTOXIC ENVELOPE GLYCOPROTEINS FOR LENTIVIRAL VECTOR PRODUCTION**

Rodrigo Nogueira, Ana Filipa Rodrigues, Ana Sofia Coroadinha.

iBET- Instituto de Biologia Experimental e Tecnológica, Apartado 12, 2781-901 Oeiras, Portugal; Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Av. da República, 2780-157 Oeiras, Portugal, Oeiras, Portugal.

Background and novelty: Gene therapy changed the paradigm of modern medicine by providing treatment to previously unmet medical needs, ranging from cancer to monogenic diseases. The use of lentiviral vectors (LV) in gene therapy clinical trials and licensed products has been steadily increasing in recent years. However, their use is challenged by the low yields and poor scalability of current production systems. In this context, establishing efficient and scalable production processes based on high-titer constitutive producer cells, is paramount to sustain the increasing clinical demand of LV-based gene therapies.

This work describes a new approach to establish constitutive LV producer cells stably expressing an engineered, high-titer envelope glycoprotein, GaLV$^{\Delta R}$. This envelope promotes a 5-fold increase in LV titers relative to the original glycoprotein.

Experimental approach: Due its fusogenic properties, GaLV$^{\Delta R}$ expression leads to syncytia formation. Using CRISPR-Cas9, we created a producer cell host deleted for GaLV cell receptor (PiT-1, inorganic phosphate transporter-1), to overcome GaLV$^{\Delta R}$ cytotoxicity.

Results and discussion: PiT-1 knock-out (KO) cells supported stable expression of GaLV$^{\Delta R}$ without syncytia formation while maintaining LV titers. Complementation of these cells with PiT-1 restored the syncytia formation phenotype (upon GaLV$^{\Delta R}$ transfection), supporting a cause-effect relation between PiT-1 KO and the absence of syncytia.

PiT-1 KO cells exhibited a decreased growth rate, however, the later was rescued upon overexpressing of another phosphate transporter (PiT-2). PiT-1 KO cells were further explored in the development of constitutive LV producer cells expressing GaLV$^{\Delta R}$. To that end, PiT-1 KO clones were isolated by limiting dilution and selected by a functional screening based on resistance to GaLV$^{\Delta R}$ transduction. From a total of 37 clones, 6 supported stable transfection with GaLV$^{\Delta R}$. Immunofluorescence-based detection of GaLV$^{\Delta R}$ at cell surface showed different levels of envelope expression across the cell clones. These clones are being characterized and used to establish new constitutive LV producer cells. The different GaLV$^{\Delta R}$ expression levels among established cell clones are being used to study the impact of envelope expression in the final performance of producer cells yield.

This work demonstrates the feasibility of stably expressing fusogenic envelopes by abolishing the expression of its viral receptor in the producer cell host. Additionally, it also provides new cell substrates currently being explored to push the boundaries of constitutive LV production.

10:25-10:30 **Flash 10 ENDOGENOUS BIP REPORTER SYSTEM FOR SIMULTANEOUS IDENTIFICATION OF ER STRESS AND ANTIBODY PRODUCTION IN CHINESE HAMSTER OVARY CELLS**

Minji Kyeong, Jae Seong Lee.

Ajou University, Suwon, South Korea.

Background and novelty: As the biopharmaceutical industry expands, improving the production of therapeutic proteins using Chinese hamster ovary (CHO) cells is important. However, excessive and complicated protein production causes protein misfolding and triggers endoplasmic reticulum (ER) stress. When ER stress occurs, cells mediate the unfolded protein response (UPR) pathway to restore protein homeostasis and folding capacity of the ER. However, when the cells fail to control prolonged ER stress, UPR induces apoptosis. Thus, the UPR pathway is an important pathway involved in protein synthesis and cell death. Previous studies have revealed a correlation between the expression level of BiP and protein productivity. Therefore, monitoring the UPR degree by the amount of BiP could be valuable for achieving high productivity of therapeutic proteins with the desired quality. However, to date, there is no monitoring system for checking ER stress in real time using UPR molecules. In this study, we generated a fluorescence-based UPR monitoring system in CHO cells in which the fluorescence level increased with the expression of BiP in response to ER stress.

Experimental approach: We integrated mGFP into endogenous HSPA5 encoding BiP, a major ER chaperone, and the primary ER stress activation sensor, using clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9)-mediated targeted integration.

Results and discussion: The mGFP expression level changed according to the ER stress induced by chemical treatment and batch culture in the engineered cell line. Using this monitoring system, we demonstrated that host cells and recombinant CHO cell lines with different mean fluorescence intensities (MFI; basal expression levels of BiP) possess a distinct capacity for stress culture conditions induced by recombinant protein production. Antibody-producing recombinant CHO cell lines were generated using site-specific integration based on host cells equipped with the BiP reporter system. Targeted integrants showed a strong correlation between productivity and MFI, reflecting the potential of this monitoring system as a screening readout for high producers. Taken together, these data demonstrate the utility of the endogenous BiP reporter system for the detection of real-time dynamic changes in endogenous UPR and its potential for applications in recombinant protein production during CHO cell line development.

Acknowledgements & Funding: This research was supported by the Samsung Research Funding Center of Samsung Electronics under Project number SRFC-MA1901-09.

11:00-12:30 **Scientific Session: Adaptive manufacturing: enggineering quality into your process (part I)**

Chairpersons:
Anne Tolstrup, AbtBioConsult, Denmark
Laura Palomares, IBT-UNAM, Mexico

11:00-11:30 **INV 8 The Application of Mechanistic Models Combined with Statistical Approaches Including Multivariate Visualization and Bayesian Methods to Enable Rapid Process Understanding**

Gene Schaefer, Senior Fellow at The National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), United States

A current challenge in the development and commercialization of bioprocesses is the need to rapidly develop and validate at scale complex processes to meet both fast to FIH and fast to market goals. The processes are likely to be intensified as well as integrated and possibly continuous to meet capacity and cost of goods constraints. The pressures of an accelerated timeline and more complex processes and/or products require more advanced approaches to be applied to establishing an understanding of the impact on process variability on product quality driven by either raw material variability or changes in scale or equipment. Establishing a relevant scale-down model (SDM) is fundamental to this approach and requires both a combined mechanistic and empirical process model for the design space as well as statistical methods suitable for handling small amounts datasets at the outset but which allow for improved learning or understanding over time. In this presentation, two statistical approaches used in a novel combination will be discussed: multivariate dimension reduction and data visualization techniques, via partial least squares discriminant analysis (PLS-DA), and Bayesian multivariate linear modeling for inferential analysis. The Bayesian multivariate linear modeling allows for individual probability distributions of the differences of the mean of each attribute for each scale while the PLS-DA is used to identify the process performance outputs at the different scales which have the greatest impact on the multivariate Bayesian joint probabilities An example for a fed-batch bioreactor SDM will demonstrate how the method could be used to identify process performance attributes and product quality attributes that capture important aspects of the process. Additional examples extending this analysis to continuous manufacturing will also be discussed. In this latter case, the importance of predicting changes in product quality attributes based on changes in process performance attributes will be significantly greater within

the overall context of an integrated process control strategy due to the limitations on response time to deviations in continuous processing. Opportunities for future improvements in these approaches will also be discussed.

11:30-11:45 O-16 NEXT-GEN GLYCOENGINEERING: COMBINING CELLULAR AND METABOLIC ENGINEERING TO FINE-TUNE MAB B1,4 GALACTOSYLATION

Apostolos Tsopanoglou[1], Mina Ghahremanzamaneh[1], Itzcoatl Gomez Aquino[1], Alfonso Blanco[1], Sara Carillo[2], Jonathan Bones[2], Ioscani Jimenez Del Val[1].

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Background and novelty: N-linked galactosylation is a major source of heterogeneity in commercial monoclonal antibody (mAb) products. In addition, higher levels of galactosylation are reported to enhance mAb effector functions (i.e., Complement Dependent Cytotoxicity (CDC) and Antibody Dependent Cell-mediated Cytotoxicity (ADCC)). Despite the clear need to tightly control mAb galactosylation, strategies to do so remain limited: standard cell engineering strategies are not amenable for real-time control applications, advanced cell engineering strategies require multiple time-consuming genetic engineering events, and metabolic glycoengineering strategies achieve only a narrow range of control at the expense of cell growth and product yield. Here, we present a novel approach that enables real-time galactosylation control across a broad range by feeding a decoy substrate, 2-deoxy-2-fluoro-d-galactose (2FG), to CHO cells that have been engineered to produce hypergalactosylated mAb product.

Experimental approach: CHO-DP12 cells producing a 93% galactosylated mAb were cultured in fed-batch mode, where 2FG was fed (10% on day 3 and 90% on day 5) to achieve concentrations ranging from 0.1mM to 2mM. Daily samples were collected to monitor cell growth and metabolic behaviour, while product titre was quantified with Protein A HPLC. On day 6 of the culture, lectin-aided flow cytometry was used to monitor cell surface galactosylation and samples were taken for mAb LC-MS glycoprofiling.

Results and discussion: Our glycoengineering strategy achieved dose-dependent control of mAb galactosylation ranging from 45% to 93%. No detrimental effect of 2FG feeding on cell growth and mAb titre was observed with up to 2mM of 2FG. With increasing 2FG concentrations, we observed accumulation of undesired aglycosylated mAb product. Upon further analysis, the lowest achieved level of mAb galactosylation (45% galactosylated species) was observed to occur because half of all mAb (at 93% galactosylation) is produced before the first 2FG feed and not due to limited 2FG activity. If 2FG is added earlier to culture or our strategy is deployed in a cell line that yields most of the product after the first 2FG feed, a broader range of galactosylation control can be achieved with lower 2FG concentrations, thus curbing the secretion of non-glycosylated mAb.

With further development, our novel mAb glycoengineering strategy can be deployed for real-time control of mAb glycosylation and contribute to the assurance of a critical quality attribute during biopharmaceutical manufacturing.

11:45-12:00 O-17 KNOWING MORE FROM LESS: A MICROFLUIDIC TOOLBOX FOR AT-LINE MONITORING OF BIOPROCESSES

Inês Pinto[1], Leila Josefsson[2], Saara Mikkonen[3], Debbie Van Der Burg[3], Fabien Abeille[4], David Sergeant[5], Meeri Mäkinen[3], Sebastian Giehring[6], Matthias Stich[7], Christian Krause[7], Cari Sänger[2], Åsa Emmer[3], Aman Russom[1], Veronique Chotteau[3].

[1]Science for Life Laboratory & KTH Royal Institute of Technology, Stockholm, Sweden; [2]Kantisto, Baarn, Netherlands; [3]KTH Royal Institute of Technology, Stockholm, Sweden; [4]Micronit, Enschede, Netherlands; [5]IPRATECH, Mons, Belgium; [6]PAIA Biotech, Köln, Germany; [7]Presens Precision Sensing, Regensburg, Germany.

Background and novelty: Monitoring of the culture components (PAT) is important for process control. Ideally, in-/at-line monitoring of specific proteins, metabolites and CQAs, should be available in a simple, rapid and cost-effective manner. Miniaturized systems with automation of analytical methods are an attractive approach, which can reduce cost and complexity in comparison with sophisticated analytical instruments. In this aim, we have developed a series of novel miniaturised methods, to be integrated and connected to a bioreactor culture.

Experimental approach: We developed a novel microfluidics-based modular system [1] for integration at-line in cell culture and performing (*i*) immunodetection of relevant proteins, i.e. IgG, CHO host cell proteins (HCP), lactate dehydrogenase (LDH), (*ii*) evaluation of antibody glycosylation using specific lectins, (*iii*) analysis of amino acids using microchip capillary electrophoresis [2], (*iv*) analysis of glucose, mannose, galactose, fucose, and lactose [3]. Based on enzymatic activity, optical sensors for the detection of glucose, lactate and ammonia were developed.

Results and discussion: A bead-based multiplexed and versatile microfluidic system for affinity-based protein quantification was developed. This system provided the quantification of proteins directly from the supernatant. It was applied for the quantification of HCP, IgG and LDH, marker of cell viability. The limits of detection were in the ng/mL range with analysis time ≈ 30 min, and provided comparable performance as commercial ELISA kits.

The method was then adapted for the detection of IgG main glycans based on affinity for different lectins. The CE-based method provided the detection of 19 amino acids and was successfully demonstrated for 17 amino acids using microchip electrophoresis. In this proof-of-concept, a good agreement was observed in comparison with measurement by HPLC. A CE method was developed for the analysis of glucose, mannose, galactose, fucose, and lactose, and proved to be transferable to microchip electrophoresis. Finally, these modules of affinity-based protein quantification and microchip electrophoresis were integrated in a proof-of-concept of At-Line Integrated Analytical System, ALIAS, which included as well optical sensors for the detection of glucose, lactate and ammonia.

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12:00-12:15 **O-18 ACCURATE IDENTIFICATION OF TRANSGENE INTEGRATION SITES AND THEIR STRUCTURE BY CAS9 TARGETED NANOPORE SEQUENCING IN CHO CELLS**

Klaus Leitner[1], Nicolas Marx[2], Krishna C. Motheramgari[1], Nancy Stralis-Pavese[2], Nicole Borth[2].

[1]Austrian Centre of Industrial Biotechnology (acib), Vienna, Austria; [2]University of Natural Resources and Life Sciences (BOKU), Vienna, Austria.

Background and novelty: In recent years a trend towards integration of transgenes into pre-selected genomic locations in CHO cells to allow stable and efficient recombinant protein expression could be observed. However, the potential for off-target transgene integration cannot be fully controlled and generated stable cell lines have to be screened for correct integration sites. Targeted Locus Amplification (TLA) sequencing is a common method to determine integration sites. However, due to the short read sequencing used, this technology can not provide information on the precise concatemerization of plasmid integrants. Here, we are demonstrating a fast and reliable method to detect the entirety of transgene integration sites as well as the structure of the integrated sequence in CHO cells using Cas9 targeted nanopore sequencing (nCATS).

Experimental approach: The initial step of nCATS is the dephosphorylation of all DNA ends and CRISPR/Cas9 mediated cleavage at predefined sites. The generation of newly phosphorylated DNA ends at the induced double strand breaks allows site-specific ligation of sequencing adapters and thus enriched sequencing of targeted sites. The prepared DNA is then subjected to long-read nanopore Sequencing, which enables the identification of transgene-genome junctions as well as the precise arrangement of sequences in the integrated plasmid(s). For proof of concept, we performed nCATS by targeting two endogenous genes, B4galt1 and Fut8 in CHO cells. Next, identification of transgene integration sites and their structure was analyzed in a CD4 expressing CHO-K1 cell line where the integrations sites are known.

Results and Discussion: Enriched sequencing of B4galt1 and Fut8 resulted in high on-target coverage and correct identification of the targeted genes, which proved the applicability of nCATS in CHO. For the identification of transgene integration sites, the forward and reverse strand of the CMV promoter of the reporter cell line was targeted by multiple gRNAs. Reads spanning over exogenous and endogenous regions were used to precisely determine and confirm the transgene integration sites. Interestingly, in addition to the integration sites reported by TLA sequencing data, a third integration site was detected by nCATS. Furthermore, the conformation of the integrated sequence was resolved identifying a complex integration of >21 kb consisting of concatemerized plasmid sequences. Importantly, nCATS is a fast (48 hours until final results), versatile and affordable tool to determine integration sites. Additionally, nanopore Sequencing offers the advantage to simultaneously study epigenetic modifications (i.e. DNA methylation) of the targeted genomic sequence, which adds an additional layer of information.

12:15-12:20 **Flash 11 SUCCESSFUL TRANSFER OF RAMAN MODELS FROM AMBR®250 HIGH-THROUGHPUT SYSTEMS TO LARGER SCALE STIRRED TANK BIOREACTORS**

Jens Classen[1], Matthaeus Langer[2], Jens Traenkle[1].

[1]Bayer, Wuppertal, Germany; [2]Bayer, Wupeprtal, Germany.

Background and novelty: The use of spectroscopic sensors for bioprocess monitoring is a powerful tool within the process analytical technology (PAT) initiative of the FDA. Real-time monitoring via spectroscopic sensors enables simultaneous bioprocess monitoring of various critical process parameters including biological,

chemical, and physical variables during the entire biotechnological production process. Raman-based process monitoring, and control is becoming more popular for pilot- and manufacturing-scale bioreactors. However, a challenge is the cost-efficient model building and/ or the application of Raman during process development in high-throughput (HTP) small scale bioreactors, for example Ambr®250. Especially, the Ambr®250 system should allow for quick Raman model building using Design of Experiments (DoE). Current Raman measurements at the Ambr systems require a dedicated set-up (flow cell and Raman probe). In this work we show for the first time that the models generated in such a system can be seamlessly transferred to larger scale bioreactors with true in-line Raman detection.

Experimental approach: We cultured Chinese hamster Ovary (CHO) cells in 10 L stirred tank bioreactor (STR) and in Ambr®250 high-throughput system connected to BioPAT® Spectro spectroscopy platform. During the STR cultivation we collected Raman spectra with an installed in-line Rxn-10 probe with bIO-Optic (Endress+Hauser Optical Analysis). In the Ambr®250 system samples were taken automatically and supplied to a flow cell connected to an Endress+Hauser Rxn-46 probe for BioPAT® Spectro by Sartorius. In both set-ups reference samples were analyzed with the Roche Cedex BioHT metabolite analyzer. Raman models were built and compared across both scales.

Results and discussion: With these experiments, we showed that the Raman model transfer from in-line measurements in STR to measurements in the flow cell connected to the Ambr®250 was successful in both directions (scale-up or scale-down). These findings will help to ensure that Raman can be used efficiently throughout the different development stages.

12:20-12:25 Flash 12 RUNNING TITLE: MODULAR MINI-FACTORIES FOR THE AUTOMATED AND SCALABLE PRODUCTION OF ATMPS

Sarah Kleine-Wechelmann, Andreas Traube, Jessica Horbelt, Martin Thoma, Natalie Gebken, Milena Frahm, Sebastian Puls, Michael Klinger, Markus Schandar, Mario Graeve, Tobias Sauer, Michael Pfeifer.

Fraunhofer Institute for Manufacturing Engineering and Automation IPA, Stuttgart, Germany.

Background and novelty: The class of ATMPs is complex, and the manufacturing processes are heterogeneous. Current processes are often based on autologous cell material and thus allow a batch size of n=1. The manufacturing takes place manually supported by stand-alone devices and non-digitized process control and is therefore time-consuming, rigid and cost-intensive. This leads to limited production capacities. While manufacturing for preclinical and initial clinical testing can be done manually, reaching advanced stages of clinical development and commercialization requires industrialization using automated approaches. A number of automated devices are already in use today, but they quickly reach their limits in terms of scalability.

Experimental approach: We envision an automated and integrated approach for Manufacturing ATMPs, which could be realized in subsequent stages. The short-term path builds on existing infrastructure, supplemented by robotic interlinking and transfer stations, enabling the implementation of automated workflows. In the long term, we imagine the manufacturing of CAR-T cells as a transferable and closed process with full inline control of biological parameters to achieve high quality and standardization in decentralized facilities.

Modularity is a promising concept to enable adaptability and scalability, paving the way for different product classes. We understand modular in this context as a closed system consisting of different modules with standardized interfaces, which allows high flexibility of the individual components and interoperability.

Results and discussion: In order to realize such concept, it is necessary to address key elements within the process chain by new technological solutions. We have developed an approach for future industrial ATMP production based on closed, interlinked subunits (e.g. cell processing and expansion modules) which include in-house developments and commercially available production devices.

The transfer of patient material between modules will be enabled by sterile connections that allow multiple cycles of connection and reconnection. Further technologies focus on automated liquid transfer and analytical sample taking, in order to replace repetitive manual interventions. In addition, application-specific processing units will allow us to address novel processing approaches. The hardware concept will be complemented by standardized and open software architectures that enables digital process execution, monitoring as well as process optimization by digital twin technologies.

With standardization and automation, it will be possible to produce a large number of different cell preparations in shorter time, at lower cost and with higher quality compared to previous market practice. This will enable handling an increasing number of treatment schemes and achieving highly reproducible product quality.

12:25-12:30 **Flash 13 RAPID ASSESSMENT OF AGGREGATION OF BIOLOGICS IN DIFFERENT MATRICES AND FROM UPSTREAM AND DOWNSTREAM DEVELOPMENT PROCESS STAGES**

Aris Perrou, Christian Meissner, Sebastian Giehring.

PAIA Biotech GmbH, Köln, Germany.

Background and novelty: Assessing and controlling aggregation of biologics is vital to ensure safety and efficacy of a biopharmaceutical product. Aggregation can pose an immunogenic risk, which is caused by the formation of anti-drug antibodies against the biologic. Aggregation has been recognized as a major issue for modern therapeutic modalities such as bispecific antibodies and Fc fusion proteins.

Therefore, checking for aggregation propensity is an essential part of developability assessments throughout the whole development cycle, starting from in-silico approaches in the protein design phase to experimental confirmation and analysis in the discovery and upstream and downstream development stages. In these stages, hundreds of samples need to be analyzed and these numbers pose a big challenge for current analytical approaches (mainly size exclusion chromatography, SEC), which are slow and require sample purification.

We have addressed this bottleneck by developing a high throughput aggregation screening assay which allows assessment of aggregation of molecules containing the antibody Fc domain in different sample matrices and cell culture supernatants. This assay is the first assay which is capable of screening hundreds of samples of samples within two hours and without purification of samples. We are presenting different data sets from forced aggregation studies as well as data from Biopharma development partners.

Experimental approach: The new assay is based on the patented PAIA technology and uses specific Fc capture beads in combination with a dye which detects the presence of hydrophobic patches, the root cause of aggregation formation. The assay works in a simple mix- and -measure format and the sample matrix effect is canceled out by a specific, yet simple, background correction technique.

Samples of different Fc containing molecules were generated by temperature stress, characterized by SEC, spiked into different supernatants, and measured with the novel aggregation assay. In addition, samples from different Biopharma partners, both purified and in supernatants and from different cell cultures stages, were assessed with the assay.

Results and discussion: We will demonstrate that the novel aggregation assay can assess aggregation of different biologics at aggregation rates which are relevant for practical applications. The assay is applicable to samples with moderate concentrations of analyte (< 0.5 mg/mL) and in small sample volumes (down to 40 µL). The background correction method allows assessment of aggregation from cell culture supernatants, either directly or after dilution.

16:00-17:30 **Scientific Session: Challenges and Marvels of Bioprocess Intensification (part I)**

Chairpersons:
Chetan Goudar, Amgen, USA
Paulo Fernandes, Orchad, Uk
Stefanos Grammatikos, UCB, Belgium

16:00-16:25 **INV 9 Process Intensification Opportunities, Challenges and Solutions: Product Quality, Harvest and Scale Up Considerations for Intensified Processes**

Bassem Bem Yahia, UCB Pharma, Belgium

Process intensification, both in N-1 (seed bioreactor) and N (production bioreactor) step, is well-developed and has led to very significant titer gains over the last years. Nevertheless, as the high productivity of intensified processes is achieved through very high cell densities, large amounts of impurities are sent through primary recovery to downstream processing (DSP) which could lead to lower product recovery yields, process variability and product quality challenges. In this presentation, we will share a state of the art on intensified processes, focusing mainly on high seeding density (HSD) processes with intensified N-1 step, and highlight some of the increased risks with such processes, i.e. (a) increased challenges during harvest and DSP steps (e.g. depth filter fouling and yield considerations in relation to HCP), (b) impact on product quality attributes (PQAs) and (c) increased risk of performance variability during scale up.

CHO cell processes with intensified N-1 step are used in this study. Harvest step is performed using centrifugation followed by filtration steps. In order to address risk (a) as outlined above, an assessment and optimization of harvest pre-treatment strategy (flocculation) in combination to ranging of physicochemical parameters has been performed. To reduce risk (b), we focused on developing an efficient feeding strategy to control specific amino acid concentrations. Finally, a systematic assessment of key engineering and operating parameters that could impact process robustness and cell culture performance during scale up of HSD processes was performed in small scale in order to mitigate risk (c).

We will show how flocculation with optimized physicochemical parameters impacts harvest (e.g., increases filter capacity and reduces impurity levels) and ensuing DSP steps. We will also demonstrate how key amino acids (e.g. cysteine and tryptophan) significantly impact cell culture performance, PQAs and DSP yield. The data generated were successfully incorporated into *in silico* models to control PQAs both in fed-batch and perfusion mode . Finally, critical engineering and operating parameters impacting cell metabolism and performance during scale up of HSD processes have been identified and will be presented. Using such strategies and with the support of modeling tools to support different aspects of CMC development activities, it is possible to address the challenges and maximize the positive outcomes of HSD processes.

16:25-16:40 O-19 PROCESS INTENSIFICATION AND CONNECTED PROCESSING FOR ROBUST, COST EFFECTIVE, AND FAST MANUFACTURING OF MONOCLONAL ANTIBODIES

Priyanka Gupta[1], Sanket Jadhav[2], Abijar Bhori[3], Himanshu Gadgil[3].

[1]Sartorius, Bohemia, United States; [2]Sartorius, The Netherlands, Netherlands; [3]Enzene Biosciences, Pune, India.

Background and novelty: In a fast-growing biopharmaceutical world, fast paced, flexible, and cost-effective manufacturing has become an inherent requirement for industries to cater to the demand of new therapeutics for complex diseases. Taking the agile approach requires strategic implementation of smarter equipment/ consumables to catch up with the ever-evolving quality requirements and the pace of manufacturing. This is where process intensification comes into play.

In this work, conventional batch downstream processing of monoclonal antibodies (Mabs) was intensified by implementation of flow through membrane and mixed mode resin processes. While optimisation, reduction in the intermediate steps made sure of a seamless conversion of the intensified batch process into connected process. Cost efficiency was further proved by cost modelling in BioSolve for different process scales.

Experimental approach: For a 4g/L titer of Mabs from a fed batch process of CellCa cell line, constant volume elution for a capture step with MabSelect Sure Protein A was optimised to get a desired pH for viral inactivation (VI) conditions. Post VI, implementation of Sartobind Q at 2nd chromatography step in a flow through mode was optimised. Subsequently, ability of CMM Hypercell of being stable and efficient over wider pH range was leveraged to directly feed the elute of Sartobind Q without any load adjustments for pH and dilution for conductivity. After development, all the four operations were run in a connected/ parallel mode.

Results and Discussions: Capture step run in twin column mode gave consistent elute at >91% recovery and >97% purity. Implementation of membrane adsorbers gave higher productivity as compared to conventional resin-based separation due to higher flow rate with full recovery at >98.1% purity. Process optimization for CMM HyperCel achieved by DoE in MODDE produced lowest possible buffer consumption and elution volumes while maintaining the quality (> 98.5% purity with >95% step recovery). Connected process led to significant savings of >50% of the processing time accounting to major increase in productivity of the process. Apart from the time factor, cost modelling in BioSolve, showed immense savings on the consumables (especially methodical storage and reuse of membrane adsorbers for few cycles with consistent output quality attributes), labour, and overall process costs for the connected process.

In a nutshell, this work serves as a blueprint to effectively intensify the Mab processes to reduce the time of operation, improve the cost of manufacturing, while maintaining the quality and consistency of the process.

16:40-16:55 O-20 OVERCOMING PRODUCT RETENTION IN TFF-BASED PERFUSION CELL CULTURES BY USING LOW SHEAR MAGNETICALLY LEVITATING PUMPS

Magdalena Pappenreiter[1], Hubert Schwarz[2], Bernhard Sissolak[3], Alois Jungbauer[4], Véronique Chotteau[2].

[1]Bilfinger Life Science GmbH, Innovation Management; University of Natural Resources and Life Sciences (BOKU), Vienna, Austria; [2]KTH Royal Institute of Technology, Cell Technology Group; AdBIOPRO, Competence Centre for Advance BioProduction by Continuous Processing, Stockholm, Sweden; [3]Bilfinger Life Science GmbH, Innovation Management, Vienna, Austria; [4]University of Natural Resources and Life Sciences (BOKU), Vienna, Austria.

Background and novelty: Tangential flow filtration systems are widely used cell retention devices in perfusion cultures, but significant challenges occur with prolonged operation. A well-known and common issue includes membrane fouling, which leads to low efficiency and increased product retention. Several studies have already investigated the influences on fouling behavior in hollow fibers. In addition to the application of alternating flow profiles, cell lysis, shear stress and membrane pore size have been found to be major contributors to this phenomenon.

Experimental approach: In this work, different process set ups and conditions were tested using magnetic levitation pumps for low shear TFF systems in small-scale perfusion bioreactors (200 ml). Process parameters such as cell growth, cell-specific productivities and product sieving were compared with ATF systems. A novel concept based on the application of reverse flow across the hollow fiber using two magnetically levitating pumps was validated with a CHO cell line producing a recombinant monoclonal antibody (IgG). Applicability to long-term stationary cultures with cell densities of 60 x 1E6 viable cells/mL was confirmed and tested at 2 scales.

Results and discussion: It was found that performance differences in TFF-based perfusion systems are strongly influenced by shear rates, while cellular viability remained unaffected. Product sieving throughout the process could be improved by 20% using 2600 s^{-1} (low shear) in comparison to 5200 s^{-1} (high shear) when using one flow direction. However, minimal product retention has been achieved by reversing the flow of two alternating pumps with a defined short cycle time. This approach makes it a valuable alternative to conventional ATF systems and can be used in various scales.

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16:55-17:10 O-21 MIGRATING A MONTHS-LONG PERFUSION PROCESS TO INTENSIFIED FED-BATCH

Vicky Goralczyk, Lena Thoring.

FyoniBio GmbH, Berlin, Germany.

Background and novelty: We developed a perfusion process for a difficult-to-express human therapeutic expressed in fully human cell host GEX® (Glyco-Express). As the protein proved to be rather unstable when exposed to prolonged cultivation, a perfusion process was the method of choice for protein production, removing protein constantly from the production process. As demands rose due to the protein's potential as an anti Sars-CoV-2 therapeutic, meeting these demands in a cost-efficient was proved to be challenging.

We evaluated the potential of producing the protein in an intensified fed-batch process with n-1 perfusion to narrow the time for production and calculated cost and time impact when shifting the approved process. To our knowledge, so far no approaches are publicly available where an existing perfusion process was migrated to fed-batch and not vice versa.

Experimental Approach: Protein producing cell clones selected for their ability to produce well in a perfusion process were cultivated in different media in a scall scale mock-perfusion approach to select for medium promoting growth in n-1 perfusion. Cells from high cell density cultivation, either from said small scale mock perfusion or out of 1L perfusion runs were inoculated at high cell densities in different media and cultivated in fed-batch mode. Protein was evaluated and compared to protein produced in the master perfusion process. Costs and timelines for both processes were analyzed and set against each other.

Results and Discussion: A 29 day perfusion process was successfully migrated to a 13 day fed-batch after 20 days of n-1 perfusion for expansion with comparable product quality. While titer in intensified fed-batch was increased by 70-fold and total harvest volume to be purified was decreased by almost factor 5, total protein yield for the intensified fed-batch process was only around 60% at the same costs for material and GMP facility production as for the master perfusion process. However, stunning increase in productivity in fed-batch calls attention for further process optimization of the master perfusion process, namely improving medium composition and availability as well as cell state at production.

17:10-17:35 **INV 10 Enabling Intensified Bioprocesses At Scale**

***Daniel Karst**, Ph.D. Senior Manager Process Sciences, Global Manufacturing Sciences, Biogen International GmbH, Switzerland*

Drivers for bioprocess intensification are multiple. Improvements in productivity or simplification of manufacturing operations provide benefits in either dimension of time, quantity, or cost against traditional production platforms.

Although development activities have been widespread, their at-scale implementation in a commercial production environment must meet requirements for process robustness, product quality and regulatory frameworks.

Opportunities range from enhancements of unit operations, the process scheme, application of process analytical technology for control in all process operations, batch release, process automation as well as utilization of advanced data analytics.

Here, we share insights into the variety of process and operational intensifications at Biogen and their implementation at the recently completed next-generation biologics manufacturing facility in Switzerland.

Wednesday 29 Tuesday 28

9:00-10:00 **KEYNOTE LECTURE**

Multispecificity – the future of molecular medicines

Raymond J. Deshaies, Amgen Research, United Sates

Collectively, the biopharmaceutical industry has had an enormous impact on human health through the discovery and development of numerous safe and effective molecular medicines, including both small molecules and biologics. This success has, inevitably, raised the bar on expectations for future medicines. To thrive going forward, our industry will have to make medicines that are even safer and more effective than what came before. This is a tall order, given the relatively small number of high-conviction, accessible targets in most diseases. Nevertheless, opportunities abound, provided that we can surmount the key barriers that restrain many drug development efforts. These include overcoming biological redundancy, managing on-target toxicity/therapeutic index, and conquering so-called undruggable targets. Multispecific medicines that either attack multiple targets simultaneously, localize the action of a drug, or link targets to natural effectors offer a new approach to vanquish these perennial foes. In my presentation I will review the challenges and opportunities and describe approaches that Amgen is taking to develop the next generation of multispecific small molecule and biologic medicines for the benefit of future patients.

11:30-12:30 **Scientific Session: Adaptive manufacturing: enggineering quality into your process (part II)**

Chairpersons:
Anne Tolstrup, AbtBioConsult, Denmark
Laura Palomares, IBT-UNAM, Mexico

11:30-12:00 **INV 11 Next-generation, feedback responsive cell factories for recombinant protein manufacturing**

Laura Segatori, Departments of Bioengineering, Chemical & Biomolecular Engineering, Biosciences. Rice University, United States

The production of soluble and functional recombinant proteins (rProteins) remains one of the main challenges of the field of biotechnology. rProteins are the largest class of therapeutic drugs and are used for the treatment of a large range of diseases, ranging from rare and orphan indications to those affecting millions. The increasing demand in therapeutic proteins has resulted in significant amount of global manufacturing capacity devoted to protein production and substantial effort to improve methods for protein manufacturing.

Manufacturing of rProteins in mammalian cells depends both on cell productivity and cell growth as rProtein overexpression causes accumulation of misfolded proteins and proteotoxic stress, which leads activation of a global response aimed at restoring homeostasis that may ultimately inhibit protein synthesis and reduce cell viability. Because most therapeutic proteins are secretory proteins, protein folding and quality control occurs within the ER. Accumulation of misfolded proteins in the ER triggers activation of the unfolded protein response (UPR), which manifests through activation of three interconnected signaling cascades controlling a *transcriptional* and *translational* regulatory *program* for ER stress attenuation through upregulation of protein quality control. Upon sustained ER stress—typically caused by expression of rProteins—the UPR executes apoptosis.

The outcome of UPR induction, which ranges from stress attenuation to cell death, depends on the relative kinetics of activation of the three signaling responses, which, in turn, is shaped by the intensity and duration of ER stress induced by expression of rProteins. This highly dynamic system requires sophisticated tools for both detection and manipulation. To address the limitation of currently available tools mainly based on exogenous reporters and de-regulated alterations of key UPR genes, we developed a synthetic biology platform technology for (i) monitoring the UPR with high sensitivity and dynamic resolution of the stress stimulus and (ii) manipulating the UPR in response to feedback signals generated by ER stress, with the ultimate goal to enhance the innate cellular capacity to buffer proteotoxic stress.

We have pioneered a platform technology for engineering sense-and-respond cellular devices that detect specific transcriptional signatures, and, in response, activate a biomolecular output, ranging from the expression of diagnostic signals to the actuation of therapeutic program. Our approach is based on the use of the NanoDeg (ACS Synth Biol. 2018 Feb 16;7(2):540-552)—a bifunctional system that mediates proteasomal degradation of a target protein with high specificity and exquisite control over rate of decay. We leveraged this technology to design a platform technology for quantitative, multiplexed profiling of gene expression signatures of the stress response with high sensitivity and dynamic resolution of the stimulus causing proteotoxic stress (Nat Chem Biol. 2020 May;16(5):520-528).

Current work is focused on deploying this technology for manipulating stress signaling pathways in response to feedback signals generated at different stages of rProtein production, with the overall goal to engineer cells for enhanced and sustained expression of rProtein. This talk with describe strategies for engineering cells based on feedback signals that enhance the stress attenuation response

induced in response to proteotoxic stress and delay ER-stress induced apoptosis with respect to activation of the stress attenuation response. Finally, we will describe the design of next-generation cell factories for rProtein manufacturing that tune rProtien expression to the UPR capacity to cope with proteotoxic stress.

12:00-12:15 O-22 IDENTIFICATION AND CONTROL OF NOVEL WASTE INHIBITORY METABOLITES IN CHO CELL-CULTURES

Seongkyu Yoon[1], Michael Betenbaugh[2], Bingyu Kuang[3], Duc Hoang[1], Venkata Gayatri Dhara[2], Jack Jenkins[2], Pranay Ladiwala[2].

[1]University of Massachustts Lowell, Lowell, United States; [2]Johns Hopkins University, Baltimore, United States; [3]AbbVie, Worcester, United States.

Background and novelty: Inefficient intracellular metabolism of CHO cells often prevents cells to fully utilize nutrients to support growth and protein production. Instead, nutrients are diverted into waste by-products which inhibit cell cultures and lower productivity. This study is focus on the identification and control the novel inhibitory metabolites. The identified waste metabolic pathways were further reprogramed through genetic engineering and media optimization under the guidance of genome scale modeling flux analysis.

Experimental Approach: LC-MS/MS based untargeted metabolomics was conducted on CHO-K1 fed-batch process to identify metabolic biomarkers. Targeted metabolomic analysis was performed to validate and assess the impact towards growth and antibody production. Next, the study sought to optimize CHO bioprocess by integrating conventional design-of-experiments (DOE) methodology with genome scale modeling (GEM) flux analysis. Generic CHO-K1 metabolic model was tailored and adapted with CHO fed-batch metabolomic data to obtain a cell line- and process-specific model which allowed screening of specific causation pathways. Finally, a control strategy was developed using an expression vector to modulate the expression of recombinant genes related to metabolic pathways capable of metabolizing toxic inhibitors.

Results and Discussion: The study identified six novel metabolites caused by inefficient cell metabolism which were not previously studied in CHO system: aconitic acid, 2-hydroxyisocaproic acid, methylsuccinic acid, cytidine monophosphate, trigonelline, and n-acetyl putrescine. When supplemented back into CHO fed-batch process, significant suppression effect on cellular growth was observed. The identified metabolites were shown to negatively impact the glycosylation profile of a model secreted antibody, with seven reducing CHO cellular productivity and all eight inhibiting the formation of mono-galactosylated biantennary (G1F) and biantennary galactosylated (G2F) N-glycans. The study established an *in silico* metabolomic platform via genome scale modeling to relate metabolic inhibitors with their nutrient precursors. The critical genes and nutrients were identified using metabolic pathway analysis via GEM, after which metabolites were mapped to cellular metabolic network. By re-allocating internal cellular metabolic fluxes into neighbor pathways, the concentration of metabolites from the transfected subclones significantly decreased as measured through LC-MS. Under these conditions, peak cellular VCD and IVCD of cells were promoted as observed in the reprogrammed clones and optimized media. The study presented a control strategy to improve cellular physiology by mitigating the accumulation of metabolites for cell line evaluation, media optimization and biomanufacturing control.

Acknowledgements and Funding:

NSF I/UCRC grant number 1624684 and AMBIC member companies.

12:25-12:30 **O-23 STATE-OF-THE-ART STRATEGIES FOR ADENO-ASSOCIATED VIRUS PRODUCT HOMOGENEITY ASSESSMENT**

Marco Radukic[1], Tobias Luttermann[2], Benjamin Mueller[2], Kristian Mueller[3].

[1]Biofidus AG / Bielefeld University, Bielefeld, Germany; [2]Biofidus AG, Bielefeld, Germany; [3]Bielefeld University, Bielefeld, Germany.

Background and novelty: Adeno-associated virus (AAV) vectors are prime candidates for gene replacement therapy, which promises lasting treatment for patients with genetic diseases. However, being composed of a protein capsid and a DNA payload, AAV are amongst the most complex biologicals and impose specific challenges to product homogeneity assessment. A combination of novel and conventional approaches can give developers and manufacturers a leading edge in identifying critical process parameters and quality attributes and provide a fast track to an affective therapeutic.

Experimental approach: We combine mass spectrometry (MS) based peptide mapping of the AAV capsid with next-generation Nanopore sequencing of the packaged transgene and further analytical tools, e.g., capillary electrophoreses and surface plasmon resonance (SPR), to provide full and rapid characterization of AAV preparations with respect to their capsid and genomic integrity.

Results and discussion: The AAV capsid and possible modifications to it, as well as heterogeneities in the packaged DNA payload, impose new complexities to homogeneity assessment of these therapeutics. However, we show that new data-intensive methods cover various parameters with few analytical procedures, fast turn-around, and reduced hands-on time. For example, MS peptide mapping provides insights into capsid protein composition, including present host cell protein, amino acid sequence identity, and post-translational modifications. Likewise, rapid Nanopore sequencing provides transgene sequence identity, information on packaged single nucleotide variants, and metrics of transgene recombination events and unintentionally packaged DNA in one experiment. The data is complemented by conventional analyses like SPR to show molecular-level functionality of the therapeutic. Together, we provide a tailored package of analyses that allows developers and manufacturer to engineer quality into AAV therapeutics effectively.

16:00-17:30 **Scientific Session: Challenges and Marvels of Bioprocess Intensification (part II)**

Chairpersons:

Chetan Goudar, Amgen, USA

Paulo Fernandes, Orchad, Uk

Stefanos Grammatikos, UCB, Belgium

14:30-14:45 **O-24 OPTIMIZATION OF CONTINUOUS HIV-1 GAG VIRUS-LIKE PARTICLES (VLPS) HARVEST USING AN ALTERNATIVE PERFUSION APPROACH**

Jesús Lavado-García, Laura Cervera, Francesc Gòdia.

Universitat Autònoma de Barcelona (UAB), Barcelona, Spain.

Background and novelty: The biomanufacturing industry is adapting their processes to a perfusion-based mode of operation to intensify production. Here, HIV-1 Gag VLP production using transient gene expression (TGE), the previously developed extended gene expression (EGE) methodology consisting in sequential retransfections and medium replacement (MR) steps is transferred to bioreactor scale. The optimization of cell culture and operation parameters as well as a thorough selection of the filter unit for the alternating tangential flow (ATF) cell retention

device were performed to achieve continuous VLP harvest operating in perfusion mode.

Experimental approach: Parameters like the time of retransfection, the amount of DNA and the cell specific perfusion rate (CSPR) were optimized using a design of experiment approach (DoE). The optimized bioprocess was then transferred to a 1.5L bioreactor in perfusion. ATF hollow fiber modules of 0.5µm, 0.2µm of pore size from Repligen and the viral harvest unit VHU-1 from Artemis Biosystem were tested. The ratio of unassembled free monomers as well as VLP retention and interaction with the filter membranes were characterize using confocal microscopy, scanning electron microscopy and nanoparticle tracking analysis (NTA).

Results and discussion: After optimization of the values of time of retransfection, the amount of DNA and CSPR and successful bioreactor implementation of the EGE methodology, the time of operation was reduced from 264 to 168 hours post-transfection (hpt) together with a reduction in CSPR, what should translate directly in lower production costs. VLP production improved 8.8-fold, achieving a final concentration of ~$8{\cdot}10^{10}$ VLPs/mL and a total production of VLPs of ~10^{14} particles at 168 hpt. A continuous harvest of VLP was achieved with the VHU-1 filter unit reaching daily harvest rates of ~99%. This work paves the way for further development of scalable cell-based bioprocess for the production of viral particles operating in perfusion mode.

14:45-15:00 O-25 THE PERKS OF INNOVATING INFLUENZA VLP-BASED VACCINE PRODUCTION

António Roldão, Ricardo Correia, Bárbara Fernandes, Sofia B. Carvalho, Ricardo J. S. Silva, Cristina Peixoto.

IBET, Instituto de Biologia Experimental e Tecnológica and ITQB-NOVA, Instituto de Tecnologia Química e Biológica António Xavier, Oeiras, Portugal.

Background and novelty: Increased need for influenza vaccines worldwide justifies the search for novel, flexible, and robust platforms. Insect cells have arisen as a versatile host to produce a variety of complex biopharmaceuticals including vaccines. This study describes advancements in the manufacturing process of influenza hemagglutinin (HA)-displaying virus-like particle (VLP)-based vaccines produced by insect cells, from upstream and downstream processing to analytics and formulation.

Experimental approach: Insect *Sf*-9 and High Five cells were adapted to grow at hypothermic culture conditions (22 ºC) or at neutral pH, and their potential for improved influenza HA-VLPs production compared to non-adapted cell lines. Stable adapted *Sf*-9 cells were later cultured to high cell densities in perfusion, using ATF (*vs* TFF), and continuous operation mode. Influenza HA-VLPs were purified using an in house developed filtration-based approach, which combines a cascade of ultrafiltration and diafiltration steps. Characterization of these viral particles was performed using an array of biophysical and biochemical methods, assessing particle size distribution, purity, surface charge, morphology and thermal stability. Finally, a trehalose-glycerol natural-deep eutectic solvent (NADES) was evaluated as to its potential to improve storage of influenza HA-VLPs.

Results and discussion: Adaptation of stable HA-VLPs producer *Sf*-9 cells to hypothermic growth resulted in up to 12-fold higher expression. Likewise, adaptation of High Five cells to neutral pH induced a 3-fold higher specific HA-VLPs productivity following infection with baculovirus. In both cases, the adaptation process had no impact on VLPs morphology and biological activity. Noteworthy, stable adapted *Sf*-9 cells were cultured in perfusion (up to $100x10^6$ cell/mL) and continuous (~$20x10^6$ cell/mL) operation modes, cell specific productivities staying similar to batch. The filtration-based purification scheme allowed to reduce process time by 30 % when

compared to a standard chromatography-based approach, without compromising scalability and, most importantly, product recovery (~ 80 %). Furthermore, the analytical methods used have shown to be applicable for characterizing VLPs with different complexities, from mono- to penta-valent VLPs, comprising HAs from diverse groups (A and B) and subtypes (H1 and H3). Formulation of HA-VLPs in trehalose-glycerol NADES reduced the HA degradation rate and maintained particles' physical integrity upon storage at 50 °C. At room temperature (20-23 °C), HA-VLPs were stable for one month, demonstrating the potential of TGly for storage under non-refrigerated conditions. Overall, the advancements herein described can be used to assist and/or accelerate influenza HA-VLPs vaccines development.

15:00-15:15 O-26 CELL THERAPY PROCESS DEVELOPMENT WITH A 2 ML CONTINUOUS PERFUSION BIOREACTOR

Kevin Lee[1], Wei Xiang Sin[2], Michael Birnbaum[3].

[1]Erbi Biosystems Inc., Stoneham, United States; [2]Singapore MIT Alliance for Research and Technology (SMART), National University Singapore, Singapore; [3]Massachusetts Institute of Technology, Cambridge, United States.

Background and novelty: With several CAR-T cell immunotherapy products currently marketed for the treatment of hematological cancers, there are increasing efforts to develop better technologies and processes for cell therapies to improve efficacy, reduce variability, and decrease costs. Ways to optimize cell activation, transduction, and expansion for cell-based treatments are improving, but major challenges still exist in experiment reproducibility and robustness during process development. Variability of donor and patient-derived material can confound experiment results. Reagent cost, scarce bench space, and busy scientists can limit the number of experiments possible. Therefore, process development experiments are typically done in milliliter-sized static plates with minimal environmental control and can lead to sub-optimal outcomes.

To address this gap, we investigated a perfusion microbioreactor (Breez™) that can support >400M cells in only a 2mL working volume. This fully closed single-use perfusion bioreactor operates outside of a biosafety cabinet and replicates bench scale perfusion processes at industrially relevant cell densities. The use of integrated microfluidics reduces labor, bench space, and materials, enabling a single donor to be used in many bioreactor experiments.

Experimental approach: T cells were activated, transduced, and expanded in 24-well plates, G-Rex, and Breez and compared. First, activation and transduction were performed in 24-well plates before inoculating each system for expansion. G-Rex and Breez media consumption rates were kept similar during expansion. Next, T cells were activated in 24-well plates, then transferred to each system and transduced and expanded. Lastly, T cells were independently activated, transduced, and expanded in each system. Media exchange rates were optimized in each system to test maximum performance. Cell density, viability, phenotype, transduction efficiency, and cytotoxic activity of anti-CD19 CAR-T cells were compared.

Results and discussion: Breez demonstrated equivalent growth and higher viability compared to G-Rex and 24-well plates for activated CAR-T cells when limiting media exchange to match the G-Rex. However, in follow on experiments with optimized media exchange rates, Breez outperformed, achieving over 200e6 cells/mL and reaching patient dose levels with 800-fold expansion and consistently high cell viability (>95%), in contrast with a maximum of 20e6 cells/mL in the G-Rex. Phenotype, exhaustion, and cytotoxic activity remained equivalent. This data suggests the Erbi Breez can help accelerate cell therapy process development by providing the performance of rocking bags and stirred tanks with the small volumes of well plates and, most surprisingly, while keeping high cell quality despite the expansion and concentrations achieved.

15:15-15:30 O-27 ULTRACENTRIFUGATION FOR AAV MANUFACTURING: NON-LINEAR SCALE-UP IMPROVES QUALITY & SCALABILITY

Duarte Martins, Laura Josefik, Michael Milz, Christoph Repik, Barbara Kraus, Petra Gruber.

Takeda, Vienna, Austria.

Background and novelty: Adeno-associated viruses (AAVs) are currently one of the viral vectors of choice for gene therapy. However, manufacturing of AAV preparations free of empty capsids remains challenging, especially at large scale. This important because regulatory agencies have voiced quality concerns about empty capsids and their adverse effects. Capsid-triggered immune response, liver toxicity and other adverse effects have been associated with high content of empty capsids, therefore their presence in investigational drug products is "undesirable" (FDA CTGTAC Meeting #70, 2021).

Experimental approach: Our approach can be summarized in two steps; first scale factors that impact UC performance were identified. Scale-up of UC rotor volume leads to changes in rotor geometry, which in turn impacts the density media profile (e.g., sucrose gradient). The sucrose gradient is critical because, together with the centrifugal forces, provides the driving force for full/empty AAV separation. Therefore, we characterized the UC cores/rotos from lab-scale through large-scale and identified the scale factors that lead to differences in the density gradient. Secondly, we aimed to compensate scale differences through adjusting the process parameters in order to obtain the same separation performance (i.e., same density media profile).

Results and discussion: We have identified UC core/rotor height as the major factor that impacts the density gradient. Taller cores (higher aspect ratio section) result in steeper gradients while shorter cores (lower aspect ratio section) induce greater mixing during acceleration and thus shallower gradients.

Furthermore, we have scaled the density gradient composition in a non-linear fashion in order to compensate for scale-dependent differences (core geometry). Our non-linear scaling was successful in producing the same gradient across different core/rotor sizes. Finally, we demonstrated the effectiveness of our non-linear scale-up (or -down) approach with an AAV process intermediate. Both online data (UV254nm, UV280 and sucrose gradient) as well as offline data (AAV-ELISA, ddPCR) validated our approach (Figure 1b). In summary, our non-linear approach enables the same UC performance, i.e. full/empty AAV separation, from lab-scale (10 L batch) through large manufacturing scale (500 L batch).

Acknowledgements & Funding: All authors are all employees of Baxalta Innovations GmbH, a part of Takeda companies, which are involved in the development of gene therapy products. The presented work was funded by Baxalta Innovations GmbH, a Takeda company.

15:30-15:35 Flash 14 INTENSIFY VIRAL VECTOR MANUFACTURING USING TANGENTIAL FLOW DEPTH FILTRATION (TFDF) PLATFORM

Rachel Legmann[1], Rene Gantier[1], Mike Bransby[1], João Mendes[2], Ricardo Silva[2], Cristina Peixoto[2], Antonio Roldão[2].

[1]Repligen corp, Waltham, United States; [2]Ibet, Oeiros, Portugal.

Background and novelty: While already approved gene therapies meet important unmet therapeutic needs for a small patient population and with low dosage required at early clinical phase, the new gene therapies currently being developed will address larger patient population and/or using higher dosage needed for global clinical and commercialization. The sub-optimal manufacturing processes for viral vector therapeutic products used for the approved treatments were developed in

research laboratories with technologies not suitable for large-scale industrialization. We used an integrated TFDF platform for process AAV and LV viral vector yield intensification.

Experimental approach: Two experimental studies illustrate the next generation manufacturing process for AAV and LV viral vector intensification using HEK293 cells in suspension. In the first experimental study AAV8 viral vectors were produced in bioreactors from HEK293 cells grown at high cell density in perfusion mode. The performance of the upstream process using TFDF during growth, production and clarification was compared to that of a standard batch bioreactor process. The second case study evaluated the TFDF platform versus regular depth filtration for lentivirus multiple clarification steps. The cell retention filters enabled the continuous harvest clarification of LV particles demonstrating the potential for continuous upstream-downstream processing of secreted LV vectors.

Results and discussion: The TFDF in perfusion mode increased the HEK293 cell density by 2 X fold at time of transfection led to increase of more than 3 X fold of total titer of rAAV8. The cell retention filters enabled the continuous harvest clarification of AAV8 particles present in the media during the virus production, demonstrating the potential for continuous upstream-downstream processing of secreted AAV vectors. The post-lysis recovery of the intracellular AAV8 particles was achieved with the same cell retention filters using an integrated clarification process at flux and throughput up to 900 LMH and >500 L/m2 respectively. The TFDF platform increased lentivirus (LV) yield through multiple harvest approach. The control depth filtration process led to ~70% recovery functional titer yield while the TFDF harvest was at 100%, but more importantly, the TFDF harvest kept the cells intact in the bioreactor and after having replenished the bioreactor with fresh media the cells continued to produce virus and a second harvest was possible leading to a total potent lentivirus yield of ~200% compared to the depth filtration process.

Overall, the TFDF platform enabling meet high vector demand and potentially reduce the cost per dose.

15:35-15:40 Flash 15 A SCALABLE BIOPROCESS STRATEGY FOR RAAV2 PRODUCTION USING A STABLE CELL LINE SYSTEM

Jose Escandell, Filipa Moura, Sofia B Carvalho, Ricardo J S Silva, Patrícia Gomes-Alves, Paula M Alves.

iBET, Oeiras, Portugal.

Background and novelty: Gene therapy based in recombinant adeno-associated virus (rAAV) is being heavily developed in recent years founded on their safety profile and recent breakthrough results in the areas of Haemophilia and Muscular Dystrophy. Although clinical grade rAAV are mainly generated by transient transfection using HEK293 cell line, these platforms are a bottleneck at the commercial stage due to low transfection efficiency when scale up is needed, and high cost of raw materials, such as DNA (GMP grade) required for transfection. A valuable alternative to transient production platforms are stably-transfected producer cell lines systems, since they are more robust and easier to scale-up. Nevertheless, the time needed to establish them, combined with complex production systems, remains the major drawback of stable cell line platforms to become the industry standard. To accelerate the development of stable cell line platforms, we established a rAAV2 vector bioprocess, with the flexibility to be adapted to any serotype, from stable cell line generation to purified sample, using the scalable HeLaS3 system.

Experimental approach: A plasmid containing all genetic material to generate a rAAV2 vector was designed and constructed. Stable-transfected clones were obtained following a strategy previously described[1]. rAAV production conditions were optimized, namely cell concentration at time of infection, multiplicity of

infection (MOI) of Helper virus Adenovirus 5 (Ad5), required for rAAV generation, production media composition and time of harvest. rAAV2 was purified based on membrane-filtration, affinity and size-exclusion chromatography. Scalability studies up to 1L and quality control of purified rAAV using methods such as ddPCR, ELISA, Capillary Electrophoresis and transduction assays were also performed.

Results and discussion: Isolated clone showed specific productivities of $5x10^5$vg/cell and volumetric productivities of $1x10^{11}$ vg/ml with full/empty ratio of 80%, a known Critical Quality Attribute for rAAV vectors. Although it is reported optimal rAAV productions using Ad5 MOI of 10-50 for HeLa stable cell line based systems, we observed that the volumetric productivities increased approximately 70% when Ad5 MOI used was 2-3. Altogether this work describes the generation of stable rAAV producer clones, that could be generated in less than 4 months, coupled to a scalable bioprocess for rAAV2 production supporting high volumetric productivities and the expected vector quality. The transition to these platforms can solve scalability issues and high cost of raw materials of current rAAV production industry standards and boost the development of rAAV-based therapies.

References:

1. Martin,J. et al. Hum. Gene Ther. Methods24,253–269(2013).

15:40-15:45 **Flash 16 ESTABLISHMENT OF TWO SUSPENSION ADAPTED STABLE PACKAGING CELL LINES FOR SCALABLE LENTIVIRUS PRODUCTION**

Maximilian Klimpel[1], Nilakshi Ching[1], Holger Laux[1], Melina Bräuer[1], Vanessa Climenti[1], Nikki Indresh Lal[1], Cedric Vonarburg[2], Martina Biserni[2], Vicky Pirzas[1].

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Background and novelty: Clinical-grade lentiviral vectors are most often produced by transient transfection of adherent HEK293(T) cell lines. These traditional production methods are cost intensive, require large amounts of GMP-grade plasmids and hamper process scalability and reproducibility. To overcome those limitations, we have adapted the two stable packaging cell lines GPRG and GPRTG to growth in suspension. The cell lines serve as a basis for the establishment of suspension based lentiviral production platform enabling serum-free production in stirred-tank bioreactors. As the packaging cell lines are based on a TET-OFF system, the removal of doxycycline is a major challenge. Therefore, we have developed two scalable methods for induction of virus production at bench-scale.

Experimental approach: The already established packaging cell lines were subsequently adapted to growth in suspension using different serum-free media. Stable producer pools were generated by stable concatemeric array transfections using a WASp-T2A-GFP construct and subsequent antibiotic selection. A two-step single cell cloning was performed to select the top producing clones. The generated producer pools were evaluated in small-scale experiments comparing LV production in batch mode with production in semi-perfusion mode by daily medium exchange. The best performing small-scale protocol was scaled up to a 5 L glass bioreactor. For seed expansion at bench scale, the cells are grown to high viable cell density while virus production is suppressed by doxycycline supplementation. The subsequent virus production in the production bioreactor was initiated using a cell washing step or a dilution method.

Results and discussion: The small-scale evaluations of the generated stable producer pools revealed that the production in semi-perfusion mode is superior resulting in several fold higher LV yields and infectious titers compared to production in batch mode. Surprisingly, both cell lines grow to high viable cell densities of >1E7 cells/mL after induction while producing high infectious titer of >1E7 TU/mL for several days, showing the potential for the development of a fully continuous LV production

process. As the production in perfusion mode is superior, we decided to implement the scale-up of the process using the Biosep technology based on acoustic wave separation. We obtained comparable results for virus production at bioreactor scale using two different induction strategies, demonstrating the suitability of the suspension platform for scale up.

15:45-15:50 Flash 17 INTEGRATED PROCESS FOR THE PRODUCTION AND PURIFICATION OF THERAPEUTIC MESENCHYMAL STROMAL CELL-DERIVED EXTRACELLULAR VESICLES

Raquel Cunha[1], Ricardo Silva[1], Sara Rosa[1], Cecília Calado[2], Joaquim Cabral[1], Cláudia Lobato Da Silva[1], Ana Azevedo[1], Ana Fernandes-Platzgummer[1].

[1]Instituto Superior Técnico, Lisboa, Portugal; [2]Instituto Superior de Engenharia de Lisboa, Lisboa, Portugal.

Background and novelty: Human mesenchymal stromal cells (MSC) exert their powerful regenerative and immunomodulatory potential through small secreted extracellular vesicles (EVs). Currently the production of EVs is performed in laborious and time-consuming static culture systems using serum-containing media, and their purification is through ultracentrifugation-based methods. The whole process lacks on resolution, selectivity and capacity. The main goal of this project is the establishment of a fully controlled system for MSC-derived EV production, using defined reagents compliant with GMP standards, and the Integration of a novel scalable purification process for the EV isolation and purification comprising unit operations that are robust, selective and cost-effective.

Experimental approach: MSC from bone marrow (3 donors) were expanded with xeno-free Stempro culture medium on CellStart-pre-coated plastic microcarriers in a 2 L stirred-tank F0 BABY Bionet bioreactor operated under fed-batch and continuous operation modes. Regarding MSC-EVs purification, new chromatographic alternatives - gigaporous resins versus traditional agarose resins and the new-in-market CIMmultusTM EV monolith kit were compared in terms of the resolution and resin capacity by evaluating the recovery yields, and impurities removal. The characterization of the purified EVs was performed according to ISEV guidelines and included methods such as nanoparticle tracking analysis, western blot, TEM and Fourier-Transform InfraRed spectroscopy.

Results and discussion: The impact of different culture conditions (oxygen, shear stress and Temperature) on the expansion of MSC and the production of their EVs, was evaluated. Under the best conditions tested, MSC numbers of $(3.2\pm0.12)x10^8$ and $(5.3\pm0.31)x10^8$ were achieved under fed-batch and continuous operation mode, at days 9 and 12, respectively. Regarding the isolation of the EVs from the conditioned medium, all the resins tested successfully isolated EVs, removing more than 97% of protein content and 95% of host cell DNA.

The robust and in-depth MSC-derived EVs manufacturing process described herein provides a new therapeutic paradigm for cell-free MSC-based therapies.

Funding: This work is financed by national funds from FCT - Fundação para a Ciência e a Tecnologia, I.P., in the scope of the project UIDB/04565/2020 and UIDP/04565/2020 of the Research Unit Institute for Bioengineering and Biosciences – iBB, the project LA/P/0140/2020 of the Associate Laboratory Institute for Health and Bioeconomy - i4HB, and the project EXOPro PTDC/EQU-EQU/3708/2017.

Wednesday June 29

KEYNOTE LECTURE 4

Engineering Biology for a New Era of Therapeutics

Robert Deans, Synthego, United States

The power of gene editing is rippling through our approach to medicine. We can see the impact on many treatment sectors – ex vivo allogeneic cell therapy derived from pluripotent stem cells, correction of inherited disease, and in oncology and designer immunotherapeutics. The ability to study gene associated disease was not enabled 10 years ago, outside of sharing tissues. Now diversity can be brought into a common test bed for modeling using iPSC – from patients and healthy individuals. Curing genetic disease remains limited by high cost viral vectors with associated toxicity risk, where gene editing provides dramatic discounts in COGS and development timelines. And today gene therapies are moving quickly to in vivo delivery of editing complexes using simple lipid nanoparticles. The ability to efficiently knock in large gene blocks has fostered synthetic biology approaches to receptor design and inducible gene circuitry, all of which are in play in the translational stream. How do gene therapies continue to impact this space? As these technology platforms mature likely so must the Regulatory approach, particularly applied to rare and orphan disease, where failures to reduce high manufacturing costs is collapsing the ability to provide patients treatment. CRISPR gene editing provides solutions.

POSTER PRESENTATIONS

- Posters with odd numbers will be presented on Monday 27th June from 14:30 to 16:00
- Posters with even numbers will be presented on Tuesday 28th June from 14:30 to 16:00

Presenting author underlined.

ESACT Posters selected for the ESACT poster prize competition

Bio Breakthroughs

P-001 MANUFACTURING ACELLULAR REGENERATIVE MEDICINES

William Whitford[1], Ankur K. Shah[2].
[1]DPS Group, Dublin, Republic of Ireland; [2]DPS Group, Boston, United States.

P-002 3D BIOPRINTED CELLULAR STRUCTURES FOR UNIVERSAL PRODUCTION OF THERAPEUTICS

Laura Chastagnier[1], Julia Niemann[2], Magali Barbaroux[3], David Pollard[4], Oscar Reif[2], Christophe Marquette[1], Emma Petiot[1].
[1]3d.FAB, Univ Lyon, Université Lyon1, CNRS, INSA, CPE-Lyon, ICBMS, UMR 5246, 43, Bd du 11 Novembre, Villeurbanne cedex, France; [2]Sartorius Stedim Biotech Gmbh, August Spindler Strasse 11 Goettingen, Germany; [3]Sartorius Stedim FMT SAS, avenue de Jouques, 13400 Aubagne, France; [4]Sartorius Stedim North America Inc, 565 Johnson Avenue Bohemia, NY 11716, United States.

P-003 3D BIOPRINTED TISSUE CULTIVATION: THE NEXT GENERATION OF BIOPROCESSES

Emma Petiot[1], Laura Chastagnier[1], Sarah Pragnere[2], Eric Olmos[3], Celine Loubière3[3], Julien Le Boetterf[1], Kleanthis Mazarakis[4], Timo Schmidberger[5], Julia Niemann[6], Magali Barbaroux[7], Christophe Marquette[1].
[1]3D InnovationLab - 3d.FAB - ICBMS Laboratory, Villeurbanne, France; [2]Laboratory of Tribology and System Dynamics, lyon, France; [3]Laboratoire réactions et génie des procédés, nancy, France; [4]Sartorius Stedim UK Ltd, epsom, United Kingdom; [5]Sartorius Stedim Biotech Gmbh, Goettingen, United Kingdom; [6]Sartorius Stedim Biotech Gmbh, Goettingen, Germany; [7]Sartorius Stedim FMT SAS, Aubagne, France.

ESACT

P-004 EXTRACELLULAR VESICLES PACKAGING AND DELIVERY OF SILENCING SEQUENCES TO ALLEVIATE A BRAIN DISORDER

David Rufino-Ramos, Kevin Costa Leandro, Vítor Carmona, Inês M. Martins, Patrícia R. Albuquerque, Rosário Faro, Rita Perfeito, Rui Nobre, Luís Pereira De Almeida.
CNC - Center for Neuroscience and Cell Biology of University of Coimbra, Coimbra, Portugal.

ESACT

P-005 UNRAVELLING THE KNOT: MICROPLASTIC PROPERTIES AND THEIR CORRELATION WITH THE CELLULAR RESPONSE

Matthias Völkl[1], Julia Jasinski[2], Valérie Jérôme[1], Thomas Scheibel[2], Ruth Freitag[1].
[1]University of Bayreuth, Process Biotechnology, Bayreuth, Germany; [2]University of Bayreuth, Biomaterials, Bayreuth, Germany.

P-006 MICROENCAPSULATION OF PRIMARY TONSILLAR B CELLS FOR BIOARTIFICIAL GERMINAL CENTERS VIA SOLUBLE CD40L STIMULATION

Moritz Helm[1], Songyan, Ben Huang[1], Katrin Gollner[2], Ulrich Gollner[2], Valérie Jérôme[1], Ruth Freitag[1].
[1]University of Bayreuth, Process Biotechnology, Bayreuth, Germany; [2]Praxis am Schießgraben, Schießgraben 21, Kulmbach, Germany.

P-007 THE IMPACT OF FN-SILK ON THE MATURATION OF PANCREATIC AGGREGATES TO TREAT DIABETES TYPE 1

Kelly Blust[1], Siqin Wu[2], Carolina Åstrand[2], My Hedhammar[1].
[1]Royal Institute of Technology, Stockholm, Sweden; [2]Spiber Technologies, Stockholm, Sweden.

P-008 BIOMANUFACTURING OF GLIOBLASTOMA MULTIFORME ORGANOIDS USING SMALL SCALE BIOREACTORS

Seungjo (joe) Park, Alexandra Avera, Yonghyun (john) Kim.
The University of Alabama, Tuscaloosa, AL, United States.

P-009 SEMI-CONTINUOUS PROPAGATION OF INFLUENZA A VIRUS AND ITS DEFECTIVE INTERFERING PARTICLES: ANALYZING THE DYNAMIC COMPETITION TO SELECT ANTIVIRAL CANDIDATES

Lars Pelz[1], Daniel Rüdiger[1], Tanya Dogra[1], Fadi Alnaji[2], Yvonne Genzel[1], Christopher Brooke[2], Sascha Kupke[1], Udo Reichl[3].
[1]Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany; [2]University of Illinois, Urbana, Illinois, United States; [3]Max Planck Institute for Dynamics of Complex Technical Systems and Otto-von-Guericke University, Magdeburg, Germany.

P-010 LENTIVIRAL VECTOR PRODUCER CELL LINE GENERATION FOR CHIMERIC ANTIGEN RECEPTOR (CAR) T CELL THERAPIES

Joana S Boura, Radmila Todoric, Jordan Wright, Laura Je Pearson, Emma Burton, Sara Ferluga, Daniel C Farley, Kyriacos A Mitrophanous, Nicholas G Clarkson, Hannah J Stewart.
Oxford Biomedica, Oxford, United Kingdom.

P-011 A NOVEL DISPLAY PLATFORM FOR VACCINE APPLICATIONS BASED ON CHIMERIC VLPS PRODUCED IN CELL SUSPENSION MODE AND SERUM FREE MEDIUM

Ernesto Garay[1], Diego Fontana[1], Lautaro Leschiutta[1], Ricardo Kratje[2], Claudio Prieto[1].
[1]Biotechnological Development Laboratory, School of Biochemistry and Biological Sciences, UNIVERSIDAD NACIONAL DEL LITORAL, Santa Fe, Argentina; [2]Cell Culture Laboratory, School of Biochemistry and Biological Sciences, UNIVERSIDAD NACIONAL DEL LITORAL, Santa Fe, Argentina.

P-012 BOOSTERING THERAPEUTIC EXOSOME SECRETION AND IDENTIFYING HOST CELL LINES FOR PRODUCTION IN A SCALABLE AND INDUSTRY-COMPATIBLE SETTING

Christoph Keysberg, Helga Schneider, Kerstin Otte.
Biberach University of Applied Sciences, Biberach (Institute for Applied Biotechnology), Germany.

P-013 DEVELOPMENT OF HEK293 TRANSFECTION MEDIA PROTOTYPE FOR TRANSIENT RECOMBINANT PROTEIN EXPRESSION AND GENE THERAPY APPLICATIONS

Caroline Tsao[1], Zhou Jiang[2], Peggy Lio[2].
[1]Cytiva, Logan, UT, United States; [2]Cytiva, Marlborough, MA, United States.

P-014 LENTIVIRAL VECTOR REFERENCE MATERIAL - DEVELOPMENT, PRODUCTION, CHARACTERIZATION AND USE

Otto-Wilhelm Merten[1], Aziza Manceur[2], Anja Rodenbrock[2], Sushma Puttaswamaiah[2], Keith Carson[3].
[1]Miltenyi Biotec SAS, Paris, France; [2]CNRC, Montreal, Canada; [3]Bioprocessing Journal, Pensacola, United States.

P-015 HUMAN 3D MODEL OF HEPATIC PLASMODIUM INFECTION: ACCELERATING TRANSLATION OF LIVER-STAGE ACTIVITY OF M5717, AN ANTI-PLASMODIAL DRUG IN CLINICAL DEVELOPMENT

Francisca Arez[1], Diana Fontinha[2], Isabella Ramella Gal[1], Diana Moita[2], Gonçalo Nogueira[2], Christoph Fischli[3], Claude Oeuvray[4], Matthias Rottmann[3], Thomas Spangenberg[4], Catarina Brito[1], Miguel Prudêncio[2], Paula M. Alves[1].
[1]iBET, Instituto de Biologia Experimental e Tecnológica, Apartado 12, 2780-901 Oeiras, Portugal; ITQB-NOVA, Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Av. da República, 2780-157 Oeiras, Portugal, Oeiras, Portugal; [2]Instituto de Medicina Molecular João Lobo Antunes, Faculdade de Medicina, Universidade de Lisboa, Av. Prof. Egas Moniz, 1649-028 Lisboa, Portugal, Lisboa, Portugal; [3]Swiss TPH, Basel 4051, Switzerland; University of Basel, Basel 4003, Switzerland, Basel, Switzerland; [4]Merck Global Health Institute, Ares Trading S.A., Route de La Verrerie 6, CH-1267, Coinsins, Switzerland, a subsidiary of Merck KGaA, Darmstadt Germany, Darmstadt, Germany.

P-016 THE ELEVECTA® HEK293 PLATFORM – AN INNOVATIVE, FULLY STABLE AND HELPER VIRUS-FREE AAV PRODUCTION SYSTEM

Ben Hudjetz, Sabine Schmidt-Hertel, Tamara Grabeck, Annika Bergmann, Julia E. *Hölper, Keerthana Srinivasan, Ahmad Al-Dali, Juliana Coronel, Nikola Strempel, Kerstin Hein, Nicole Faust.*
CEVEC Pharmaceuticals GmbH, Cologne, Germany.

P-017 UPSTREAM PROCESS OPTIMIZATION FOR ADENOVIRUS PRODUCTION IN SUSPENSION HEK293 CELLS

Wen-Yang Tsai[1], Syed Khalil[1], Matt Rosecrans[1], Anna-Barbara Hachmann[2].
[1]Thermo Fisher Scientific, Hunt Valley, Maryland, United States; [2]Thermo Fisher Scientific, Buffalo, New York, United States.

P-018 GENERATION OF TWO STABLE LENTIVIRAL VECTOR PACKAGING CELL LINES AND SUBSEQUENT PRODUCER CELL LINES

Holger Laux[1], Parameswari Govindarajan[1], Nikki Indresh Lal[1], Monica Terrao[1], Adveit Jagirda[1], Martina Biserni[2], Cedric Vonarburg[2], Vicky Pirzas[1].
[1]CSL Behring Innovation GmbH, Marburg, Germany; [2]CSL Behring GmbH, Bern, Switzerland.

P-019 MACROPHAGE-BASED VISUALIZATION OF INFLAMMATION AND LOCAL DRUG DELIVERY

Mario Köster[1], Sandhya Kumar[1], Sami Ullah[1], Hansjörg Hauser[1], Peter Behrens[2], Andreas Kirschning[2], Dagmar Wirth[1].
[1]Helmholtz Centre for Infection Research, Braunschweig, Germany; [2]Leibniz University Hannover, Hannover, Germany.

P-020 AAV PROMOTERS FOR ECTOPIC GENE EXPRESSION IN ABSENCE OF REP OR VIRAL HELPER FACTORS

Sofia Fernandes, Joana Diogo, Ana Sofia Coroadinha.
ibet, Oeiras, Portugal.

P-021 PATIENT-DERIVED MODELS OF THE TUMOR MICROENVIRONMENT FOR DRUG RESPONSE EVALUATION AND BIOMARKER DISCOVERY – ENABLING TOOLS TO ADVANCE PRECISION MEDICINE

Giacomo Domenici[1], Rita Mendes[1], Gonçalo Trindade[1], Maria Teresa Franchi Mendes[1], Ana Félix[2], Saudade André[3], Inês Isidro[1], Catarina Brito[1].
[1]Instituto de Biologia Experimental e Tecnológica, iBET, Apartado 12, 2780-901 Oeiras, Portugal; Instituto de Tecnologia Química e Biológica António Xavier, ITQB, Universidade Nova de Lisboa, Av. da República, 2780-157 Oeiras, Portugal, Oeiras, Portugal; [2]IPOLFG, Instituto Português de Oncologia Francisco Gentil, Rua Prof. Lima Basto, 1099-023 Lisboa, Portugal; CEDOC, Centro de Estudos de Doenças Crónicas da Faculdade de Ciências Médicas, CEDOC-FCM-NOVA, Universidade Nova de Lisboa, R. Câmara Pestana 6, 1150-078, Lisbon, Portugal, Lisbon, Portugal; [3]IPOLFG, Instituto Português de Oncologia Francisco Gentil, Rua Prof. Lima Basto, 1099-023 Lisboa, Portugal;, Lisbon, Portugal.

P-022 SEARCHING FOR BINDING TARGETS INVOLVED THE VIRUS-CELL SURFACE INTERACTION OF SARS-COV-2 TO DEVELOP A NEXT GENERATION OF VACCINES AND ANTIVIRALS

Rodrigo Nogueira[1], Tiago Vaz[1], Maria Fonseca[1], Paul Helbling[2], Ana Sofia Coroadinha[1], Ana Filipa Rodrigues[1].
[1]iBET - Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal; [2]Dualsystems Biotech AG, Zurich, Switzerland.

P-023 SCALE UP CHALLENGES OF AN ONCOLYTIC VIRUS MANUFACTURING PROCESS

Matthias Schad, Orsolya Hamusics.
Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach an der Riss, Germany.

P-024 AAV PRODUCTION IN INSECT CELLS WITHIN A CHEMICALLY DEFINED MEDIA PLATFORM

Alexis Bossie[1], Sharon Harvey[2].
[1]Lonza, Silver Spring, United States; [2]Lonza, Walkersville, United States.

P-025 IN VITRO TRANSCRIPTOME AND PROTEOME REMODELING OF ACTIVATED CARDIAC FIBROBLASTS SUPPORTS TARGET PRIORITIZATION IN CARDIAC FIBROSIS

Maria Raquel Moita[1], Cláudia Diniz[1], René M. Hoet[2], Ana Barbas[3], Marta Marques Silva[1], Daniel Simão[1].
[1]iBET, Instituto de Biologia Experimental e Tecnológica; ITQB NOVA, Instituto de Tecnologia Química e Biológica António Xavier, Universidade Nova de Lisboa, Oeiras, Portugal; [2]University of Maastricht, Department of Pathology, CARIM-School of Cardiovascular Diseases, Maastricht, Netherlands; [3]iBET, Instituto de Biologia Experimental e Tecnológica; Bayer Portugal, Lisbon, Portugal.

P-026 HUMAN INDUCED PLURIPOTENT STEM CELL-DERIVED EXTRACELLULAR VESICLES FOR CELL-FREE CARDIAC REPAIR

Ana Filipa Louro[1], Marta Paiva[1], Ana Meliciano[1], Pedro Vicente[1], Henrique Almeida[1], Gerardo Cedillo[2], Joost Sluijter[2], Jos Malda[2], Miguel Castilho[2], Paula Alves[1], Patrícia Gomes-Alves[1], Margarida Serra[1].
[1]iBET - Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal; [2]UMCU - University Medical Center Utrecht, Utrecht, Netherlands.

P-027 MEDIA DEVELOPMENT STRATEGIES TO INCREASE AAV TITER AT LARGE SCALE

Louise Galuski[1], Sarya Mansour[1], Gino Stolfa[1], Amanda Zunic[1], Ana Coroadinha[2], Sofia Fernandes[2], Ana Isabel Almeida[2], Jennifer Schieber[1], Matthew Smonskey[1].
[1]Thermo Fisher Scientific, Grand Island, United States; [2]Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal.

P-028 PRODUCTION OF HIGH-QUALITY PLASMID IN A NOVEL CHEMICALLY DEFINED MEDIUM

Celine Martin[1], Neelanjan Sengupta[2], Elizabeth O'hanlon[2], Alex J. Jones[2], Stacy Holdread[2], James W. Brooks[2], Sofia Fernandes[3], Ana Coroadinha[3].
[1]Thermo Fisher Scientific, Villebon sur Yvette, France; [2]Thermo Fisher Scientific, Hunt Valley, United States; [3]Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal.

P-029 A 3D CULTURE PLATFORM TO REPRESENT THE IMMUNE MICROENVIRONMENT IN BREAST CANCER AND ITS MODULATION BY ADVANCED THERAPIES

Nuno Lopes, Sofia Batalha, Giacomo Domenici, Catarina Brito.
Instituto de Biologia Experimental e Tecnológica, iBET, Apartado 12, 2780-901 Oeiras, Portugal; Instituto de Tecnologia Química e Biológica António Xavier, ITQB, Universidade Nova de Lisboa, Av. da República, 2780-157 Oeiras, Portugal, Oeiras, Portugal.

P-030 PARTNERING TO SOLVE CELL THERAPY MANUFACTURING AND FUNDING AND GAPS – WHAT DOES THE FUTURE HOLD?

Eytan Abraham.
National Resilience, San Diego, United States.

P-031 ENGINEERING EXTRACELLULAR VESICLES FROM MESENCHYMAL STROMAL CELLS USING MINICIRCLE-DERIVED RNA INTERFERENCE TECHNOLOGY

Cristiana Ulpiano, Ana Fernandes-Platzgummer, Cláudia L. Da Silva, Gabriel A. Monteiro.
iBB - Institute for Bioengineering and Biosciences and Department of Bioengineering, Instituto Superior Técnico - Universidade de Lisboa., Lisboa, Portugal.

P-032 SUPPLY OF CUSTOMIZED SINGLE-USE-MIXER'S UNDER TIGHT CIRCUMSTANCES BECAME AN ISSUE UNDER COVID

Per Stobbe.
CerCell A/S, Herlev, Denmark.

P-033 EXPRESSED PROTEIN YIELDS IN CELL FACTORIES CAN BE PREDICTED BY HIGH THROUGHPUT ASSESSMENT OF TRANSFECTION-POSITIVE CELL POPULATION

Ly Porosk, Kaido Kurrikoff.
University of Tartu, Tartu, Estonia.

P-034 NOVEL SYRIAN HAMSTER ANTI-PD-L1 EXHIBITS ROBUST ANTI-TUMOUR CONTROL IN PANCREATIC DUCTAL ADENOCARCINOMA AND IS POTENTIATED BY ONCOLYTIC ADENOVIROTHERAPY

James Clubb[1], Tatiana Kudling[1], Lyna Haybout[1], Mykhailo Girych[1], Firas Hamdan Hissaoui[2], Víctor Cervera-Carrascon[3], Joao Santos[3], Dafne Quixabeira[1], Santeri Pakola[1], Camilla Heinio[1], Saru Basnet[1], Victor Arias[1], Riikka Havunen[3], Suvi Sorsa[3], Annabrita Schoonenberg[1], Abdullah Erikat[4], Joel Schwartz[5], Ilpo Vattulainen[1], Vincenzo Cerullo[1], Akseli Hemminki[1].

[1]University of Helsinki, Helsinki, Finland; [2]University of Maryland Medical Center, Baltimore, United States; [3]TILT Biotherapeutics, Helsinki, Finland; [4]Kings College London, London, United Kingdom; [5]University of Illinois Cancer Center, Chicago, United States.

P-035 SCALABLE PRODUCTION OF SMALL EXTRACELLULAR VESICLES (SEV) FOR IMMUNE THERAPY: INTEGRATING MANAGEMENT OF CELLULAR STRESS IN UPSTREAM PROCESSING

Laurence De Beaurepaire[1], Thibaud Dauphin[1], Claire Boursier[1], Claire Nouguier[1], Mathilde Laubert[1], Mailys Le Devehat[1], Lucie Grare[1], Quentin Le Yondre[1], Quentin Pruvost[1], Eugénie Lahet[1], Dominique Jegou[1], Philippe Courcoux[2], Aurélien Dupont[3], Julien Pichon[4], Laurence Dubreuil[5], Mayeul Collot[6], Blandine Lieubeau[1], Grégoire Mignot[1], Jean-Marie Bach[1], Steffi Bosch[1], Mathilde Mosser[1].

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NOTES

Data, Data, Data: How to get it and how to use it

P-036 MULTI-OMICS PROFILING OF A CHO FEDBATCH CULTURE UNRAVELS EFFECT OF PH ON ANTIBODY TITER AND PRODUCT QUALITY

Alison Lee[1], Yee Jiun Kok[1], Meiyappan Lakshmanan[1], Dawn Leong[1], Lu Zheng[1], Hsueh Lee Lim[1], Shuwen Chen[1], Shi Ya Mak[1], Kok Siong Ang[1], Neil Templeton[2], Taha Salim[3], Xiaona Wei[4], Eric Gifford[4], Andy Hee-Meng Tan[1], Xuezhi Bi[1], Say Kong Ng[1], Dong Yup Lee[1], Wai Lam W. Ling[3], Ying Swan Ho[1].
[1]Bioprocessing Technology Institute, Singapore, Singapore; [2]Merck & Co. Inc., West Point, United States; [3]Merck & Co. Inc., Kenilworth, United States; [4]MSD International GmbH, Singapore, Singapore.

P-037 COMBINING ADVANCED 3D CELL MODELS WITH OMICS METHODOLOGIES TO UNVEIL THE PROTECTIVE ROLE OF NATURAL BIOACTIVE COMPOUNDS TOWARDS COLORECTAL CANCER

Ana Catarina Macedo[1], Margarida Leite[1], Inês Prazeres[1], Sandra Silva[2], Lucília Pereira[3], Ana Guerreiro[2], Patrícia Gomes Alves[1], Inês Isidro[1], Margarida Serra[1], Maria R Bronze[4], Cristina Albuquerque[3], Teresa Serra[1].
[1]iBET/ITQB NOVA, Oeiras, Portugal; [2]iBET, Oeiras, Portugal; [3]IPOLFG, Lisboa, Portugal; [4]iBET/ITQB NOVA/FFUL, Oeiras, Portugal.

P-038 FLUX BALANCE ANALYSIS (FBA) BASED EVALUATION OF THE CELL STATE FOR ENABLING TARGETED PROCESS OPTIMIZATION

Katrin Paul, Lisa Kemper.
Novartis, Langkampfen, Austria.

P-039 IMPROVING BIOREACTOR PERFORMANCE USING MOBILE SENSORS

Martin Ellegaard Pedersen.
Freesense, Copenhagen, Denmark.

P-040 ARE GENOME-SCALE MODELS (GEMS) FIT FOR PURPOSE? - ASSESSING THE INTRACELLULAR AND PHENOTYPIC PREDICTIVE CAPABILITY OF CHO CELL GEMS

Benjamin Strain, James Morrisey.
Imperial College London, London, United Kingdom.

P-041 MONITORING OF VIABLE CELL CONCENTRATION USING ONLINE BIOMASS SENSORS (DIELECTRIC SPECTROSCOPY)

Christian Kaisermayer, Brendan Bannon.
Novartis, Schaftenau, Austria.

P-042 ANALYSIS OF CHO CELL MITOCHONDRIAL SEQUENCE HETEROPLASMY AT A SINGLE CELL RESOLUTION

Alan Foley, Niall Barron, Colin Clarke, Nga Lao.
NIBRT, Dublin, Republic of Ireland.

P-043 BIOREACTOR SCALING MADE EASY: NAVIGATING THE DESIGN SPACE

Andreas Castan[1], Helena Öhrvik[1], Nagaraj Konduru[2].
[1]Cytiva, Uppsala, Sweden; [2]Cytiva, Bangalore, India.

P-044 UNDERSTANDING THE TRANSCRIPTIONAL RESPONSE TO ER STRESS IN CHINESE HAMSTER OVARY CELLS USING MULTIPLEXED SINGLE CELL RNA-SEQ

Ioanna Tzani[1], Marina Castro Rivadeneyra[1], Stefano Boi[1], Niall Barron[1], Colin Clarke[2].
[1]NIBRT, Dublin, Republic of Ireland; [2]National Institute for Bioprocessing research and Training, Dublin, Republic of Ireland.

P-045 INTEGRATED ANALYSIS OF SINGLE CELL CHROMATIN ACCESSIBILITY AND GENE EXPRESSION IN CHINESE HAMSTER OVARY CELLS

Ryan Hagan, Colin Clarke.
NIBRT, Dublin, Republic of Ireland.

P-046 INTEGRATED CONTINUOUS BIOMASS ESTIMATION IN FIXED-BED BIOREACTORS: ADVANCES IN PAT CORRELATE A PREDICTIVE MODEL WITH EFFECTIVE IN-LINE SENSORS

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P-047 CHARACTERIZING BASAL AND FEED MEDIA EFFECTS ON MAMMALIAN CELL CULTURES BY SYSTEMS ENGINEERING APPROACHES

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P-048 DEEP LEARNING POWERED BIOPROCESS CONTROL

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P-049 RAMAN SPECTROSCOPY FOR AUTOMATED MONITORING AND CONTROL OF BIOPHARMACEUTICAL PROCESSES

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P-050 MINING NGS DATA TO IDENTIFY ENDOGENOUS RETROVIRAL SEQUENCES IN CHO CELLS

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P-051 LIFE AT THE PERIPHERY: UNVEILING THE CHO SURFACEOME ENABLES KNOWLEDGE-BASED ENGINEERING APPROACHES

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P-052 AUTOMATION SCREENING AND EXPANSION OF CHO-K1 GS HOST CLONE CANDIDATES: A NEW CHO PLATFORM FOR BIOLOGICS DEVELOPMENT

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P-053 SINGLE-CELL AND BULK RNA SEQUENCING OF INSECT SF9 CELLS DURING RAAV PRODUCTION

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P-054 LEVERAGING ARTIFICIAL NEURAL NETWORKS FOR CELL ENGINEERING OF CHO CELLS

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P-055 VALIDATION OF COMPUTATIONAL TOOL FOR NGS-BASED ANTIBODY DISCOVERY

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P-056 INCREASED THROUGHPUT IN UPSTREAM DEVELOPMENT BY AUTOMATED BOLUS FEEDING USING QUBICON

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P-057 APPLICATION OF A TARGET PREDICTION WORKFLOW TO IDENTIFY POSSIBLE MIRNA-MRNA INTERACTIONS IN CHO CELLS

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P-058 ESTABLISHING A VERSATILE CELL CULTURE MODELLING TOOLBOX FOR APPLICATION IN UPSTREAM PROCESS DEVELOPMENT

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P-059 INLINE MONITORING OF GLUCOSE AND LACTATE IN AN ADHERENT CELL CULTURE PROCESS WITH SINGLE USE FTIR SPECTROSCOPY AND ONE-POINT CALIBRATION

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P-060 SWATH-MS AS A STRATEGY FOR HOST CELL PROTEIN IDENTIFICATION AND QUANTIFICATION TO SUPPORT BIOPROCESS DEVELOPMENT

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P-061 COMPARING THE SUBCELLULAR PROTEOME OF CHO TO PLASMA CELL DERIVED, ANTIBODY SECRETING CELL LINES

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P-062 ACCELERATED CELL CULTURE PROCESS DEVELOPMENT ENABLED BY HYBRID MODELING AND INTENSIFIED DESIGN OF EXPERIMENTS

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P-063 CENTRAL DATA MANAGEMENT AND MODEL-BASED CROSS-DEVICE PROCESS CONTROL ON A PERFUSION SHOWCASE

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P-064 REAL TIME DIGITAL TOOL ON THE SHOP FLOOR TO SUPPORT DECISION MAKING IN BIOMANUFACTURING

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P-065 REGRESSION OF GLUCOSE- AND VIABLE CELL CONCENTRATION IN CHO CELL FERMENTATIONS WITH ARTIFICIAL NEURAL NETWORKS

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P-066 SINGLE-CELL CHARACTERIZATION USING IMPEDANCE-BASED SPECTROSCOPY

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P-067 INCREASING EFFICIENCY AND QUALITY IN PROTEIN, CELL AND GENE THERAPEUTICS RESEARCH AND DEVELOPMENT USING AN ALL-IN-ONE WORKFLOW PLATFORM

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P-068 REAL-TIME PRODUCT QUALITY PREDICTIONS USING DATA DRIVEN AND HYBRID MODELS

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P-069 DATA CLEANING FOR MACHINE LEARNING MODELS IN THE CELL CULTURE INDUSTRY

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P-070 TOTAL/INFECTIVE TITERS: THE UNCERTAINTY ON ADENOVIRUS STABILITY

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P-071 MODELING CHINESE HAMSTER OVARY METABOLISM - BENCHMARKING & APPLICATIONS

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P-072 ANALYZING PERFUSION PROCESSES IN AN INTEGRATED PROCESS DEVELOPMENT PLATFORM

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P-073 CETSA-MS FOR PROTEOME-WIDE CHARACTERIZATION OF SORAFENIB TARGET ENGAGEMENT PROFILE IN HEPATOCELLULAR CARCINOMA

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P-074 MEDIA POWDERS SHELF-LIFE EXTENSION: INCREASING MANUFACTURING FLEXIBILITY

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P-075 ISERA: CLUSTER-BASED AUTOMATED SELECTION OF ANTIBODY PHAGE DISPLAY CANDIDATES

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P-076 MODEL-BASED STRATEGIES FOR ENHANCED UPSTREAM DESIGN & CHARACTERIZATION

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P-077 METABOLIC FOOTPRINTING AND MACHINE LEARNING REVEAL METABOLIC SIGNATURES ASSOCIATED WITH TREATMENT RESPONSE IN OVARIAN CANCER

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P-078 LESSONS LEARNED FROM A MULTIYEAR CHO OMIC INITIATIVE

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P-079 USE OF GENOME-BASED METABOLIC MODELING TO IDENTIFY PROCESS SOLUTIONS TO SOLVE RAPID LACTATE ACCUMULATION

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P-080 NGS AND PHAGE-DISPLAY: RETRIEVING V_L:V_H PAIRED INFORMATION AND ASSESSING SIX CDR DIVERSITY SIMULTANEOUSLY

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P-081 A SYSTEMATIC, MODEL-BASED APPROACH FOR DECISION MAKING IN UPSTREAM DEVELOPMENT – CONSIDERATIONS REGARDING CLONE SELECTION AND CELL EXPANSION

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P-082 A 3-FOLD TITER INCREASE IN FED-BATCH CHO CELL CULTIVATION USING MULTI-OMICS DRIVEN MEDIUM DESIGN

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P-083 MASS SPECTROMETRY ANALYTICAL TOOLBOX FOR THE COMPREHENSIVE CHARACTERIZATION OF BIOTHERAPEUTICS

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P-084 FEEDING STRATEGY DESIGN FOR CONTROL OF IGG GLYCOSYLATION IN CHO CELL PERFUSION CULTURES

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P-085 COMBINING MULTIVARIATE DATA ANALYSIS AND METABOLIC FLUX ANALYSIS TO EXPEDITE MEDIA SELECTION AND OPTIMIZATION FOR CHO CLONES

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P-086 DEVELOPMENT OF AN ANALYTICAL PLATFORM FOR PAT MONITORING OF AN ETANERCEPT BIOPROCESS THROUGH AN INTEGRATED CHEMOMETRIC MODELLING APPROACH

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P-088 ENHANCEMENTS FOR A MORE RELIABLE SINGLE-USE PH SENSOR

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Beyond Evolution

P-089 HUMAN ANTI-FGF-2 MABS DERIVED FROM A MURINE ANTIBODY BY A PHAGE DISPLAY LIBRARY

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P-090 HUMAN NEUTRALIZING MONOCLONAL ANTIBODIES AGAINST SARS-COV-2 VARIANTS: FROM BLOOD COLLECTION TO *IN VIVO* ANIMAL TESTING

Tania Manieri[1], Adriele Oliveira[1], João Batalha-De-Carvalho[1], Daniela Takata[1], Viviane Botosso[1], Sonia Andrade[1], Ana Guimaraes[2], Ana Moro[1].
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P-091 CHARACTERIZATION OF CHO CELLS OVEREXPRESSOR OF C-MYC AND ITS RELATIONSHIP WITH MTOR PATHWAY IN THE PRODUCTION OF RECOMBINANT PROTEIN

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P-092 GENETICALLY ENCODED BIOSENSORS FOR VIRUS DETECTION: ENABLING THE DEVELOPMENT OF ANTIVIRAL THERAPIES

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P-093 AN IMPROVED VECTOR DESIGN UTILISING SYNTHETIC ELEMENTS FOR EFFICIENT TRANSIENT MONOCLONAL ANTIBODY EXPRESSION IN CHO CELLS

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P-094 REVERSE GENETICS FOR INFLUENZA A VIRUS TO GENERATE GENETICALLY ENGINEERED DEFECTIVE INTERFERING PARTICLES FOR ANTIVIRAL TREATMENT AND VACCINATION

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P-095 GAIN CONTROL OVER YOUR PROTEIN PRODUCTION; GLYCOSYLATION, TITER AND DEVELOPMENT

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P-096 NEW CELL ENGINEERING METHOD FOR INCREASING PRODUCTIVITY OF RECOMBINANT THERAPEUTIC ANTIBODIES UP TO 10-FOLD IN BATCH CULTURES

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Molecular Cell Surgery

P-097 RECONSTRUCTION OF AMMONIA METABOLISM VIA GLUTAMATE DEHYDROGENASE ENHANCES RECOMBINANT PROTEIN PRODUCTION IN CHINESE HAMSTER OVARY CELL CULTURE

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P-098 DEFINING UBIQUITOUS CHROMATIN OPENING ELEMENT (UCOE®) MOLECULAR MECHANISMS OF ACTION FOR EXPEDITING THEIR BIOTECHNOLOGICAL APPLICATIONS

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P-099 INCREASED CLONE PRODUCTIVITY BY LOWERING STRENGTH OF SELECTION MARKER: AN IMPROVEMENT OF THE CHOZN® CHO K1 CELL LINE DEVELOPMENT PLATFORM

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P-100 RECOMBINASE-MEDIATED CASSETTE EXCHANGE (RMCE) USE FOR CELL LINES DEVELOPMENT MONOCLONAL ANTIBODY PRODUCER, IN CHO CELL

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P-101 NON-VIRAL TRANSFECTION OF PRIMARY HUMAN B-CELLS

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P-102 A NOVEL, TARGETED INTEGRATION PLATFORM FOR EVALUATION OF VECTOR ELEMENTS IN CHO CELLS

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P-103 ORCHESTRATING A SWEET SYMPHONY: MIRNAS SETTING THE TONE FOR GLYCOSYLATION

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P-104 DEVELOPMENT OF RECOMBINASE-BASED TARGETED INTEGRATION SYSTEMS FOR PRODUCTION OF EXOGENOUS PROTEINS USING TRANSPOSON-MEDIATED LANDING PADS

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P-105 A BLUEPRINT FROM NATURE: MIRNOME COMPARISON OF PLASMA CELLS AND CHO CELLS TO OPTIMIZE THERAPEUTIC ANTIBODY PRODUCTION

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P-106 COMPARISON OF ADVANCED SINGLE CELL ISOLATION TECHNOLOGIES FOR THE GENERATION AND SELECTION OF MONOCLONAL PRODUCTION CELL LINES

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P-107 LEVERAGING A TRANSPOSASE-MEDIATED SEMI-TARGETED TRANSGENE INTEGRATION SYSTEM TO ENABLE WARP SPEED DEVELOPMENT OF A MONOCLONAL ANTIBODY

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P-108 EPIGENETIC TARGETING OF TRANSPOSONS DELIVERS HIGH QUALITY PRODUCER CELL LINES FOR COMPLEX PROTEINS

Thomas Rose, Sven Krügener, Anneliese Krüger, Sophia Sörensen, Anne Furthmann, Fränzi Creutzburg, Karsten Winkler, Susanne Seitz, Annett Hillemann, Volker Sandig.
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P-109 RAPID GENERATION OF GENETICALLY ENGINEERED CHO-K1 CLONES USING THE NOVEL GENE EDITING TECHNIQUE, CAS-CLOVER

Tiffany Mclamarrah, Iona Stephen, Michael Hoffman, Kathryn Selvitelli, Thomas King, Jennifer Tedstone, Victor Cairns, Christine Demaria.
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P-110 THE EFFECT OF N^6-METHYLADENOSINE MODIFICATIONS ON MRNA STABILITY AND EXPRESSION IN CHO CELLS

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P-111 INVESTIGATING "DIFFICULT-TO-EXPRESS" MAB FRAMEWORKS IN TRANSIENT AND SITE-SPECIFIC INTEGRATION-BASED CHO EXPRESSION SYSTEMS

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P-112 IMPROVEMENT OF ERYTHROPOIETIN PRODUCTION, BY EXPRESSING OF C-MYC IN CHO CELLS BATCH CULTURE, AND USE OF GALACTOSE/LACTATE HIGH CONCENTRATION MIXTURE

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P-113 GET-CHO: A STANDARDIZED AND UNIFIED GENOMIC, EPIGENOMIC AND TRANSCRIPTOMIC COMPENDIUM OF CHO CELLS FOR RATIONAL CELL LINE DEVELOPMENT AND ENGINEERING

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P-114 GENE EXPRESSION PROFILING OF HIGH-PRODUCER VLPS INSECT CELLS VIA RNA-SEQUENCING

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P-115 ENHANCING CHO CELL PRODUCTIVITY THROUGH A NOVEL DUAL SELECTION SYSTEM USING ASPG AND GS IN GLUTAMINE FREE MEDIUM

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P-116 ARTIFICIAL MIRNAS ALLOW STEPWISE ADJUSTMENT OF CORE-FUCOSYLATION IN CHO CELLS

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P-117 OVEREXPRESSION OF THE MITOCHONDRIAL PYRUVATE CARRIER: AN EFFECTIVE CELL ENGINEERING APPROACH AGAINST WARBURG EFFECT IN CHO CELLS

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P-118 SYNTHETIC BIOLOGY-BASED GENOME EDITING APPROACHES FOR CHO CELL ENGINEERING TO DEVELOP NEW CHASSIS FOR ENHANCED DIFFICULT TO EXPRESS PROTEIN PRODUCTION

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P-119 TARGETED INTEGRATION OF ANTI-APOPTOTIC GENES TO ENHANCE THE PERFORMANCE OF CHO CELL CULTURES

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P-120 GENERATING SYNTHETIC POLYCLONAL ANTIVENOMS USING CHO CELL COCKTAILS ENGINEERED BY RECOMBINASE MEDIATED CASSETTE EXCHANGE TO REDUCE CLONAL VARIATION

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P-121 ARTIFICIAL C1Q GLOBULAR REGIONS FOR C1Q-IGM INTERACTION STUDIES

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P-122 MISSING IN ACTION: IDENTIFYING EFFECTOR GENES TO RESCUE PROTEIN PRODUCTION IN CHO CELLS

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P-123 SCREENING OF PROMOTERS FOR SELECTIVE PRESSURE RESISTANCE EXPRESSION: IMPACT ON GROWTH AND PRODUCTIVITY OF CHOZN® CHO K1 CELLS

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P-124 TARGETED GENE INTEGRATION FOR RAPID & MORE PREDICTABLE PRODUCTION OF THERAPEUTIC PROTEINS IN CHO CELLS

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P-125 GALMAX: MODEL-INSPIRED GLYCOENGINEERING FOR BIOPHARMACEUTICAL QUALITY ASSURANCE

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P-126 COUPLING CRISPR INTERFERENCE WITH FACS ENRICHMENT: NEW APPROACH IN GLYCOENGINEERING OF CHO CELL LINES FOR THERAPEUTIC GLYCOPROTEIN PRODUCTION

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P-127 REPROGRAMMING OF CHINESE HAMSTER OVARY CELLS TOWARDS ENHANCED PROTEIN SECRETION

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P-128 TARGETED DNA METHYLATION OF ENDOGENOUS PROMOTERS AND THE CMV PROMOTER ENTAILS DISTINCT AND SUBSEQUENT HISTONE MODIFICATION CHANGES IN CHO CELLS

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P-129 PROFILING LNCRNA -PROTEIN INTERACTIONS IN CHO CELLS

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P-130 CHOSOURCE CHO-K1 ADCC+ CELL LINE FOR ENHANCED THERAPEUTIC POTENCY

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Horizon Discovery, Cambridge, United Kingdom.

P-131 TARGETING OF EXTRACELLULAR VESICLES VIA DE NOVO ANTIGEN BINDING CD81

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P-132 OPTIMISATION OF A LENTIVIRAL DELIVERY STRATEGY TO SUCCESSFULLY CONDUCT GENOME-WIDE CRISPR-CAS9 SCREENS IN SUSPENSION-ADAPTED CHO CELL LINES

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Adaptive Manufacturing: Engineering quality into your process

P-133 5-THIO-L-FUCOSE A NOVEL SUGAR ANALOGUE FOR BOOSTING CLINICALLY RELEVANT ANTIBODY RESPONSES
Martina Zimmermann, Melanie Nguyen, Christine Weiss, Aline Zimmer.
Merck KGaA, Darmstadt, Germany.

P-134 ESTABLISHING A ROBUST WORKFLOW TO IDENTIFY HIGH-PERFORMING GOCHO™ CLONES
Sheffali Dash, Michelle Sabourin, Paula Ravnikar.
Cytiva, Marlborough, MA, United States.

P-135 GENERATING A ROBUST HOST CELL LINE, GOCHO™, FOR A CELL LINE DEVELOPMENT PLATFORM
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ESACT **P-136 QUANTITATIVE ASSESSMENT OF DESIRABILITY OF PLATFORM CELL CULTURE MEDIA**
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ESACT **P-137 METABOLOMICS BASED MEDIUM OPTIMIZATION FOR BIOMANUFACTURING CONTROL IN CHO CELLS**
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ESACT **P-138 KINETICS OF NK-92 METABOLISM AND FUNCTIONALITY IN PSEUDO-STATIC CULTURES**
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ESACT **P-139 CHEMSTRESS® CHO PROFILING TECHNOLOGY TO MONITOR DEEP CELL FUNCTION IN A CLONE STABILITY TRIAL**
Alessandra Prinelli, Eligio Iannetti, Paul Dobson, Jerry Clifford.
ValitaCell, DUBLIN, Republic of Ireland.

P-140 NEW ANTIBODY FORMAT ASSOCIATED CHALLENGES FOR IN-PROCESS ANALYTICS
Jonathan Stern, Quentin Demeyere, Frédéric Delouvroy, Wolfgang Paul.
UCB Pharma, Braine l'Alleud, Belgium.

P-141 NON-INVASIVE, NOVEL OPTICAL AND DIELECTRIC METHODS TO DETECT CHANGES IN CELL METABOLISM DURING A BIOPROCESS
Michael Butler, Adam Bergin, Evangelia Flampouri, Laura Breen.
NIBRT, Dublin, Republic of Ireland.

P-142 SPIKING-BASED RAMAN MODEL CALIBRATION OF PERFUSION CELL CULTURE USING A HARVEST LIBRARY
Patrick Romann.
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P-143 AUTOMATED BIOPROCESS MONITORING ENABLED BY A CHO SENSOR CELL LINE
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P-144 CELL CULTURE APPLICATIONS OF HYCLONE™ CLASSICAL MEDIA AND SERUM
Johanna Rodhe, Ann Lövgren.
Cytiva, Uppsala, Sweden.

P-145 UNLEASHING THE FULL POTENTIAL OF THERAPEUTIC PROTEIN MANUFACTURING - *RENTSCHLER BIOPHARMA'S STATE-OF-THE-ART EXPRESSION PLATFORM*
Britta Reichenbächer, Sebastian Schwamb.
Rentschler Biopharma SE, Laupheim, Germany.

P-146 RAMAN SPECTROSCOPY IN BIOPROCESS MONITORING: PRACTICAL CONSIDERATIONS
Luís Bernardo Silva, Quentin Demeyere, Jan-Sebastiaan Uyttersprot, Jonathan Stern, Wolfgang Paul.
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P-147 SATELLITE-BASED SCALE-DOWN MODELS FOR EARLY UPSTREAM PROCESS DEVELOPMENT: A SMART LAB APPROACH
Vanessa Henriques, Malo Lafont, Jimmy Stofferis, Alexandre Super, Marie-Françoise Clincke, David Bulnes, Wolfgang Paul.
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P-148 IDENTIFICATION OF MISPAIRING OMIC SIGNATURES IN CHINESE HAMSTER OVARY (CHO) CELLS PRODUCING A TRI-SPECIFIC ANTIBODY
Maria João Sebastião[1], Jose Miguel Escandell[1], Jin Zhang[2], Michael Hoffman[2], Christine T Demaria[2], Bruno Figueroa[2], Patrícia Gomes-Alves[1].
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P-149 FLUORESCENT-LABELLED EVS TO EASE THEIR QUANTIFICATION AND TRACKING AS A TOOL FOR MANUFACTURING BIOPROCESS DEVELOPMENT
Maria José Sanchez, Pau Leivar, Salvador Borrós, Cristina Fornaguera, Martí Lecina.
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P-150 APPLYING INTENSIFIED DESIGN OF EXPERIMENTS TO MAMMALIAN CELL CULTURE PROCESSES

Lisa Junghans, Verena Nold, Beate Presser, Erich Bluhmki, Thomas Schwab, Bettina Knapp, Stefan Wieschalka.
Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany.

P-151 DIRECTEDLUCK™ FOR BISPECIFICS – A TRANSPOSASE SYSTEM STREAMLINES CELL LINE DEVELOPMENT WITH PRODUCT QUALITY FOCUS

Volker Sandig, Annett Hillemann, Thomas Rose, Susanne Seitz, Daniel Rehm, Karsten Winkler, Sven Krügener.
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P-152 BIOANALYTICAL TOOLS FOR THE QUANTIFICATION OF IN-PROCESS AND FINAL PRODUCT SAMPLES OF A ROTAVIRUS VACCINE

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P-153 D-OPTIMAL MIXTURE DESIGN OF EXPERIMENTS TO OPTIMIZE A MONOCLONAL ANTIBODY PRODUCTION PROCESS

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P-154 INNOVATIVE FAST ELISA FOR AT-LINE MONITORING OF BIOLOGICAL ACTIVE PRINCIPLE. APPLICATION TO MONOCLONAL ANTIBODIES TITRATION

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P-155 A HIGH PERFORMING EASY-TO-USE MEDIA AND FEED SYSTEM FOR CHOK1SV GS-KO® CELL LINES-BASED PRODUCT MANUFACTURING

Josi Buerger[1], John Mattison[1], Harrison Garner[1], Lucy Tate[1], Aymaan Rahman[1], Kelly Molder[1], Ivan Carubelli[1], Mohsina Baig[1], Preeti Phanse[2], Olivier Bertini[2], Alexis Bossie[3], Deirdre Raduns[3], Scott D'andrea[3], Colin Jaques[1], Kenneth Low[3], Harsh Amin[1].
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P-156 CHARACTERIZATION OF SARS-COV-2 SPIKE PROTEINS SAMPLES PRODUCED IN GLYCO-ENGINEERED CHO CELL LINES WITH ORTHOGONAL ASSAY TECHNOLOGIES

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P-157 MONITORING OF FC FUSION PROTEIN SIALYLATION DURING CELL LINE AND UPSTREAM PROCESS DEVELOPMENT USING LECTIN-BASED GLYCAN SCREENING ASSAYS

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P-158 PAT TOOLBOX FOR REAL TIME PRODUCT CQA MONITORING IN PERFUSION BIOPROCESSES

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P-159 DIFFERENCES IN N-GLYCOSYLATION OF CHO-S AND CHO-K1 CELLS AND THE IMPACT OF ANTIBODY PRODUCTION ON GLYCOSYLATION CAPACITIES

Roberto Donini, Stuart Haslam, Cleo Kontoravdi.
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P-160 ESTABLISHMENT OF AN EFFICIENT PLATFORM PROCESS FOR DEVELOPMENT AND MANUFACTURING OF ANTIBODY-ANTICALIN FUSION BISPECIFICS

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P-161 HOLLOW-FIBERS AND FLAT-SHEET CASSETTES HIGH THROUGHPUT OPTIMIZATION AND COMPARISON IN A TFF PROCESS FOR AAV PURIFICATION ON THE AMBR CROSSFLOW

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P-162 USE CASES OF RAMAN PAT PLATFORM TO ENABLE QUALITY CONTROL, REAL-TIME MONITORING, AND CONTINUOUS AUTOMATION ACROSS UPSTREAM PROCESSES

Célia Sanchez, Johan Sarrazin, Céline Duchemin, Baptiste Mourcet, Johan Cailletaud, Fabrice Thomas.
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P-163 ANTIBODY CAPTURE BASED ON MAGNETIC BEADS FROM CULTURE AT DENSITY > 100 X 1E6 CELLS/ML

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P-164 EFFECTS OF MICROCARRIER CONCENTRATION ON MESENCHYMAL STEM CELL CULTURE

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P-165 INNOVATIVE FUNCTIONAL CHARACTERIZATION OF MSC BY VALITACELL CHEMSTRESS® TECHNOLOGY FOR MEDIA DESIGN & QUALITY CONTROL

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P-166 PROOF-OF-CONCEPT OF A NOVEL CELL SEPARATION TECHNOLOGY USING MAGNETIC AGAROSE-BASED BEADS

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P-167 CHALLENGES IN MASS SPECTROMETRY MULTI ATTRIBUTE METHOD (MAM) IMPLEMENTATION: FROM SAMPLE PREPARATION TO BATCH ANALYSIS

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P-168 COMPARISON OF DIFFERENT REGRESSION METHODS FOR REAL-TIME MONITORING OF CHO CELL CULTURE PROCESSES USING IN SITU RAMAN SPECTROSCOPY

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P-169 SCALABILITY EVALUATION OF A 50L STIRRED TANK BIOREACTOR PLATFORM TO PRODUCE ADENO-ASSOCIATED VIRAL VECTORS (AAV) USING HEK293F CELLS

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P-170 STABLE OVEREXPRESSION OF MIRNAS FOR THE PRODUCTION OF DIFFERENTIALLY GLYCOSYLATED ANTIBODIES IN CHO CELLS

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P-171 PREDICTIVE REAL-TIME ONLINE BIOMASS ESTIMATION (PROBE): IMPLEMENTING AN ONLINE VCD PREDICTION TOOL INTO A LEGACY COMMERCIAL BIOPROCESS

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Bristol Myers Squibb, Devens, MA, United States.

P-172 PRODUCT DEGRADATION DURING DOWNSTREAM PROCESSING

Antonia Pries[1], Simon Fuchs[2], Simon A. B. Riedl[1], Thomas Schubert[2], Tobias Luttermann[1], Christian Schmitz[3], Benjamin Mueller[1].
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P-173 ASSESSMENT OF THE IMPACT OF A MILLING TYPE AND PRODUCTION SITE FOR CELL CULTURE FEED PRODUCTION

Margaux Le Moal, Romain Mette, Martin Bertschinger, Patrick Vetsch.
Ichnos Sciencies SA, La Chaux de fonds, Switzerland.

P-174 OFF-GAS ANALYSIS TO ENHANCE PROCESS MONITORING, TRANSFER AND CONTROL

Amy Nehring, Matthew Demers, Ian Tougas.
Amgen Inc, West Greenwich, United States.

P-175 ADAPTIVE FEED CONTROL IMPLEMENTATION BASED ON A PREDICTIVE GLUCOSE MODEL

Marcus Kirschner, Markus Kneißl, Wolfgang Sommeregger.
Qubcion AG, Wien, Austria.

P-176 PREDICTIVE MONITORING AND CONTROL ACROSS PROJECTS USING DIGITAL TWINS

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P-177 ADVANCING THE MANUFACTURE OF MESENCHYMAL STROMAL CELLS-BASED PRODUCTS WITH AUGMENTED CARDIAC REGENERATIVE POTENTIAL THROUGH GENETIC ENGINEERING AND ENHANCED PROCESS CONTROL

Beatriz Painho[1], Marta Costa[2], Inês Carrondo[1], Margarida Costa[1], Carolina Sousa[1], Rafael Fernandes[3], Maxime Fayel[4], Anne-Catherine Prats[5], Jérome Roncalli[4], Beatriz Pelacho[6], Felipe Prosper[6], Paula Alves[1], Inês Isidro[1], Margarida Serra[1].
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P-178 HIGH-THROUGHPUT TESTING OF NON-LABELLED ANTIBODY-ANTIBODY INTERACTIONS ON OCTET (BLI ASSAY)

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P-179 PREDICTING AND OPTIMIZING PRODUCT QUALITY USING DIGITAL TWINS OF BIOREACTORS

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P-180 STEM CELL EXPANSION ON DISSOLVABLE MICROCARRIERS IN A SINGLE-USE BIOREACTOR

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Getinge Applikon, Delft, Netherlands.

P-181 HIGH-QUALITY SARS-COV-2 S AND RBD PROTEINS TO ASSIST VACCINE DEVELOPMENT AND SEROLOGICAL ASSAYS IMPLEMENTATION

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P-182 SCALABLE PRODUCTION OF METABOLIC AND MIRNA PRE-CONDITIONED MESENCHYMAL STROMAL CELLS IN A MICROCARRIER-SUPPORTED BIOREACTOR TOWARDS THE TREATMENT OF MYOCARDIAL INFARCTION

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P-183 ON-LINE AUTOMATED PROCESS CONTROL MONITORING SYSTEM FOR MULTIPLE CRITICAL QUALITY ATTRIBUTES PRODUCT CHARACTERISATION

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P-184 ANALYZING AAV – A STORY OF PROBLEMS AND SOLUTIONS

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P-185 ADVANCING AAV QUALITY THROUGH USE OF IN-LINE PAT IN DOWNSTREAM PURIFICATION (DSP) WITH POTENTIAL TO SIGNIFICANTLY REDUCE PROCESS DEVELOPMENT TIMELINES

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P-186 ADVANCED CELL CULTURE PERFORMANCE BY RATIONAL MEDIA DESIGN BASED ON IN-DEPTH PROCESS UNDERSTANDING

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P-187 HOW MODELING, MONITORING AND STATISTICS CAN BE USED TO DESIGN CELL CULTURE PROCESSES LESS IMPACTED BY RAW MATERIAL VARIABILITY

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P-188 GS PIGGYBAC®: LIFTING UP YOUR CLC EXPECTATIONS TO A NEW LEVEL

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P-189 RECOMBINANT CD19 AS SCREENING TOOL FOR CAR T CELL IMMUNOTHERAPY: TRICKS AND TIPS FOR THE PRODUCTION

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P-190 FUNCTIONAL TRIMERIC SARS-COV-2 ENVELOPE PROTEIN EXPRESSED IN STABLE CHO CELLS

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P-191 UNDERSTANDING BOTTLENECKS IN RECOMBINANT PROTEIN EXPRESSION: SIGNALS IN THE PHOSPHORYLATION CASCADE AS REGULATORS?

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P-192 TECHNOLOGY INNOVATION THROUGH ADAPTIVE AND CUSTOMIZED CELL CULTURE AUTOMATION

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P-193 BIOMARKER DISCOVERY FOR EARLY AND EFFICIENT CLONE SELECTION

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P-194 A HIGHLY SENSITIVE CAPILLARY ELECTROPHORESIS METHODOLOGY FOR VIRAL VECTORS PURIFICATION MONITORING

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P-195 HIGH-THROUGHPUT PRODUCTION OF *IN VITRO* 3D CELL SYSTEMS

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P-196 AUTOMATED QUALITY CONTROL AND SORTING OF HIPSC-DERIVED NEURAL ORGANOIDS

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P-197 A NOVEL, ONE-STEP GLYCO-ENGINEERING APPROACH TO PRODUCING HIGH TITERS OF HUMAN-TYPE SIALYLATED IGG'S IN CHO CELLS

Annemarie De Jel, Chantal Van Den Berg-Tilburgs, Elena Gugiatti, Tomás Aguirre González, Bart Engels, Raymond Verhaert, Maurice Van Der Heijden.
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P-198 RAMAN SPECTROSCOPY FOR MONITORING OF AMINO ACIDS AND ANTIBODY GLYCOSYLATION IN HIGH CELL DENSITY PERFUSION CULTURE

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P-199 TRANSCRIPTOMICS AND MODELLING TO UNDERSTAND THE BENEFITS OF LOW PERFUSION RATE

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P-200 IMPROVING PROTEIN TITER AND QUALITY IN CHO CELLS WITH EFFICIENT-PRO MEDIUM AND FEED SYSTEM

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P-201 MODULATING OF N-GLYCAN FUCOSYLATION OF IGG1 USING GLYMAXX® TECHNOLOGY AND FUCOSYLATION MONITORING WITH A HIGH THROUGHPUT LECTIN-BASED GLYCAN SCREENING ASSAY

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P-202 LECTIN-AIDED FLOW CYTOMETRY REVEALS A CLOSE CORRELATION BETWEEN CELL SURFACE AND MAB GLYCOSYLATION

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P-203 CHARACTERIZATION OF LIPID CONCENTRATE AND INFLUENCE OF ITS OXIDIZED LIPID CONTENT ON MONOCLONAL ANTIBODY PRODUCTION BY MURINE HYBRIDOMA CELL LINE

Rémy Moisant.
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P-204 USE OF HIGH-THROUGHPUT LECTIN-BASED GLYCAN ASSAYS FOR ACCELERATING UPSTREAM PROCESS DEVELOPMENT AND MEDIA OPTIMIZATION FOR BIOSIMILAR MONOCLONAL ANTIBODIES

Aris Perrou, Laura Limbach, Sebastian Giehring.
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P-205 CHEMSTRESS® CHO MEDIAQC TOOL TO ASSESS MEDIA VARIATION BY CELL PROFILING

Alessandra Prinelli, Eligio Iannetti, Patrick Hoey, Jerry Clifford.
ValitaCell, DUBLIN, Republic of Ireland.

P-206 APPLICATIONS OF IN-LINE RAMAN SPECTROSCOPY TO MONITOR AND CONTROL BIOREACTOR IN BIOPHARMACEUTICAL MANUFACTURING

Francois Carruzzo, Florence Monard, Tuan-Tu Tran, Jean-Louis Boyé, Rémy Moisant, Anthony Baud, Véronique Deparis.
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P-207 RAPID & HIGH THROUGHPUT IGG QUANTIFICATION IN CELL CULTURE SUPERNATANT

Brian Murphy, Eligio Iannetti, Hannah Byrne, Jerry Clifford.
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P-208 SUSPENSION MDCK CELL LINE DEVELOPMENT BY AUTOMATED SINGLE-CELL CLONING & SCALE-DOWN INTO AMBR®15 MICROBIOREACTORS IN CHEMICALLY DEFINED MEDIUM

Tilia Zinnecker[1], Ilona Behrendt[1], Maverick Lau[2], Angelika Hinkelmann[2], Najd Badri[2], Kristin Thiele[2], Diogo Araujo[2], Yvonne Genzel[1], Udo Reichl[3].
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P-209 GMP MANUFACTURING OF COMPLEX BIOTHERAPEUTICS FOR CLINICAL TRIALS

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P-210 USING CE-HPMS FOR ACCELERATED PROCESS DEVELOPMENT OF A MAB-EXPRESSING CELL LINE

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P-211 A RHABDOVIRUS-NEGATIVE SF9 CELL LINE (SF-RVN®) AND CHEMICALLY DEFINED INSECT MEDIUM FOR PRODUCTION OF RECOMBINANT PROTEIN AND AAV

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P-212 DESIGN SPACE DETERMINATION AND PROCESS OPTIMIZATION OF CRITICAL QUALITY ATTRIBUTES IN AAV GENE THERAPY MANUFACTURING

Seongkyu Yoon[1], David Mcnally[2], Michael Betenbaugh[3], Kelvin Lee[4], Ashli Polanco[1], Yongsuk Lee[1], Qiang Fu[1].
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P-213 THE STABILITY OF MONOCLONAL ANTIBODIES AND THEIR HIGH GALACTOSE GLYCOFORMS

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P-214 HIGH THROUGHPUT SCREENING FOR PRODUCT QUALITY ATTRIBUTES EARLY DURING MAMMALIAN CELL LINE GENERATION

Katharina Koether, Michaela Strotbek, Claudia Knoll, Corinna Ruedi, Rebecca Krieg, Jürgen Fieder, Simon Fischer, Sebastian Puengel, Dennis Blank, Joachim Baer.
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P-215 ENGINEERING PCV2'S VLP AS A NEW AND ADAPTABLE BIOTECHNOLOGICAL PLATFORM FOR VACCINE DEVELOPMENT

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P-216 COMPARRISON OF DIFFERENT CHO CELL CULTIVATION PLATFORMS USED IN CELL LINE DEVELOPMENT

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P-217 FLEXIBILITY: WE ALL WANT IT IN OUR FEED

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P-218 IMPACT OF IRON RAW MATERIAL IMPURITIES ON CHO CELL PERFORMANCE AND RECOMBINANT PROTEIN PRODUCT QUALITY

Christine Hilde Weiss, Janine Stephanie Caspari, Corinna Merkel, Aline Zimmer.
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P-219 BIOMANUFACTURING USING SINGLE-USE SYSTEMS: CASE STUDY OF FLUOROPOLYMER MATERIAL

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Challenges and Marvels of Bioprocess Intensification

P-220 A NEW, CHEMICALLY DEFINED CELL-CULTURE MEDIUM PROTOTYPE FOR DIRECT ADAPTATION OF BHK-21 SUSPENSION CELLS TO SERUM-FREE GROWTH

Ann Lövgren[1], Rena Baktur[2], Angel Varela-Rohena[2].
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P-221 PROCESS DEVELOPMENT FOR LENTIVIRAL VECTOR PRODUCTION USING ADHERENT CELL CULTURE SYSTEMS

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ESACT **P-222 THE EKKO™ AND EKKO™ SELECT: ACOUSTIC-BASED CLOSED AND AUTOMATED SYSTEMS FOR CELL AND GENE THERAPY CGMP MANUFACTURING**

Maria Mora, John Cushman, Regan Sakurada, Krishna Kumar, Robert Scott, Bart Lipkens, Rui Tostoes.
MilliporeSigma, Springfield, United States.

P-223 L-CYSTINE-DIPEPTIDES – CHOOSING THE RIGHT SEQUENCE TO MAXIMIZE CHO CELL PRODUCTIVITY

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ESACT **P-224 INDUSTRIAL PRODUCTION OF CULTURED RED BLOOD CELLS: A MODEL OF FUTURE LARGE-SCALE CELL THERAPIES FINALLY WITHIN REACH**

Guillaume Rousseau.
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P-225 ADDRESSING CELL CULTURE AS A ROOT CAUSE FOR POLYSORBATE DEGRADATION AND PARTICLES IN DRUG PRODUCTS

Inn Yuk.
Genentech, Inc., South San Francisco, United States.

P-226 IMPROVING PROTEIN TITERS IN CHO CELLS WITH A NEXT GENERATION MEDIUM AND FEED SYSTEM

Massimo Ferretti[1], Yoana Hammer[2], Megan Pajak-Lee[2], Mary Reynolds[2], Fatima Zara[2], Anna-Barbara Hackmann[2], Paul Gulde[2], Chengjian Tu[2], Rich Hassett[2], Christopher Brau[2], Ryan Boniface[2], James W. Brooks[2].
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ESACT **P-227 VALITA®AGGREGATION: A HIGH-THROUGHPUT AGGREGATION SCREENING TOOL FOR BIOLOGICS DISCOVERY AND MANUFACTURING**

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P-228 PRODUCTION OF INFLUENZA A VIRUS- DERIVED DEFECTIVE INTERFERING PARTICLES FOR ANTIVIRAL THERAPY IN A HIGH CELL DENSITY PERFUSION CULTIVATION

Marc Hein[1], Anshika Chawla[2], Prerna Arora[3], Maurizio Cataneo[4], Michael Winkler[3], Stefan Pöhlmann[3], Yvonne Genzel[5], Sascha Kupke[5], Udo Reichl[5].
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P-229 TOWARDS THE PRODUCTION OF A FUSOGENIC ONCOLYTIC RVSV-NDV VIRUS IN PERFUSION MODE

Sven Göbel[1], Ingo Jordan[2], Volker Sandig[2], Jennifer Altomonte[3], Yvonne Genzel[1], Udo Reichl[1].
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P-230 CHEMICALLY DEFINED SERUM-FREE PLATFORM FOR THE PRODUCTION OF GLYCOSYLATED RHSCF WITH IMPROVED PROLIFERATIVE ACTIVITY USING HEK293 CELLS AS BIOFACTORIES

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P-231 COMPUTATIONAL SIMULATION AS A PREDICTIVE TOOL FOR BIOREACTOR DESIGN AND PERFORMANCE

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P-232 LARGER AND SMALLER SCALE NK T-CELL COLLECTION AND CELL WASH WITH UNIFUGE AND UFMINI SINGLE USE CENTRIFUGE

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P-233 CELL LINE AND UPSTREAM PROCESS DEVELOPMENT FOR HIGH DENSITY PERFUSION PROCESSES: STRATEGIES FOR LARGE SCALE HIGH QUALITY CONTINUOUS UPSTREAM PROCESSES

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P-234 UNDERSTANDING THE CELL DENSITY EFFECT IN TRANSIENT TRANSFECTION: THE ROLE OF EXTRACELLULAR VESICLES

Pol Pérez Rubio, Jesús Lavado García, Laura Cervera Gracia, Francesc Godia Casablancas.
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P-235 GENERATION OF INDUCIBLE LENTIVIRAL VECTOR PACKAGING CELL LINES USING MODULAR PLASMIDS

Danielle Fairbrass, Radmila Todoric, Louis Frost, Joana Boura, Helen Maunder, Kyriacos A. Mitrophanous, Nicholas Clarkson, Hannah J. Stewart.
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P-236 MULTI-LAYERED ROTATIONAL MATRIX BIORREACTOR: A NEW DESIGN FOR SPECIAL ADHERENT CELL CULTURE APPLICATIONS

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P-237 EVOLUTION OF A CLARIFICATION PLATFORM STRATEGY USING A NOVEL CHROMATOGRAPHIC CLARIFICATION TECHNOLOGY

Arnaud Brisson, Agathe Drape, Laetitia Macon, Valerie Besset, Stephanie Seguin Huet.
Sanofi, Vitry sur Seine, France.

P-238 COMPARATIVE ANALYSIS OF LENTIVIRAL VECTOR PRODUCTION UNDER DIFFERENT CULTURE CONDITIONS FOR CAR-T CELL GENERATION

Mariane Cariati Tirapelle[1], Ana Luiza Lomba[1], Renata Silvestre Nacasaki[1], Amanda Mizukami[2], Virgínia Picanço E Castro[2], Dimas Tadeu Covas[2], Kamilla Swiech[1].
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P-239 OPTIMIZING SCALABLE PRODUCTION OF ADENO-ASSOCIATED VIRAL VECTORS FOR GENE THERAPEUTICS

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P-240 OPTIMIZATION OF A CELL CULTURE CLARIFICATION PLATFORM PROCESS WITH THE AIM OF BOOSTING THE RECOVERY OF BISPECIFIC ANTIBODIES

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P-241 IMPLEMENTATION OF A NOVEL AUTOMATED SAMPLING SYSTEM FOR HIGH DENSITY CELL CULTURE PROCESSES

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P-242 QUALIFICATION OF A SINGLE-USE DISK STACK SEPARATOR FOR MODERN MAB UPSTREAM PROCESSING AT PILOT SCALE

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P-243 INTEGRATING PERFUSION AND CLARIFICATION FOR IMPROVED AAV PRODUCTION

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P-244 ADVANTAGES OF CHO CELL PROCESS INTENSIFICATION IN STATE-OF-THE-ART SINGLE-USE BIOREACTORS

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P-245 STRATEGIES FOR EFFICIENT DEVELOPMENT OF THE CELL CULTURE MEDIA AND FEEDS OF THE FUTURE

Valentine Chevallier, Antoine Piednoir, Clarisse Huygues, Fabienne Coddens, Bassem Ben Yahia, Wolfgang Paul.
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P-246 EVALUATION OF THE PALL'S ALLEGRO™ STR BIOREACTOR FOR USE IN CULTIVATION OF MAMMALIAN SUSPENSION CELLS AND LENTIVIRAL VECTOR PRODUCTION

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P-247 DEVELOPMENT OF NOVEL FAST-GROWING CHINESE HAMSTER LUNG (CHL)-YN CELLS IN SERUM-FREE FED-BATCH FOR MONOCLONAL ANTIBODY PRODUCTION

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P-248 OVEREXPRESSION OF SAR1A IN CHO CELLS AND ITS EFFECTS ON ANTIBODY PRODUCTIVITY

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P-249 RAPID CONSTRUCTION OF PERFUSION CHO CELL CULTURE PROCESS BY USING SIMULATOR CONSIDERING THE CHARACTERISTICS OF IN-LINE SENSORS

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P-250 BIOSORPTION OF LEACHABLES IN CELL-BASED THERAPIES

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P-251 DRESSED FOR SUCCESS: IMPROVED PROCESS SCALING BY INTEGRATING CELL PHYSIOLOGY AND PHYSICAL PARAMETERS USING MVDA, DOE AND AMBR® SYSTEMS

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P-252 BOOSTING MONOCLONAL ANTIBODY PRODUCTIVITY OF FED-BATCH PROCESSES BY RECOVERING VIABLE CELLS

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P-253 ENABLING BIOMASS AND CSPR CONTROL IN THE 'EPIC' 250ML PERFUSION BIOREACTOR SYSTEM

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P-254 TARGETING COST-EFFECTIVE LARGE-SCALE MANUFACTURING FOR R-AAV VECTORS BY TRANSIENT TRANSFECTION USING PALL ALLEGRO STR BIOREACTOR

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P-255 PROCESS INNOVATION TO REDUCE TRACE METAL CONTENTS IN SOY PROTEIN HYDROLYSATES FOR CELL CULTURES

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P-256 PROTEOMICS INVESTIGATION OF THE ROLE PLAYED BY TEMPERATURE INDUCED ER STRESS MECHANISMS IN BIOPRODUCTIVITY OF CHINESE HAMSTER OVARY (CHO) CELLS

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P-257 A NEW VIABLE CELL COUNT AND VIABLITY LABEL-FREE METHOD FOR HIGH-THROUGHPUT CELL CULTURE MONITORING

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P-258 SCALE-X™ TECHNOLOGY PROVIDES DIVERSE APPROACH FOR VIRUS MANUFACTURING IN SCALABLE MANNER

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Exothera SA, Jumet, Belgium.

P-259 NOVEL GAS DELIVERY, DISTRIBUTION, AND SCALABILITY STRATEGIES FOR MEETING INCREASED OXYGEN DEMAND IN INTENSIFIED BIOREACTOR PROCESSES

Marisa Maher, Amy Wood, Sualyneth Galarza, Jonathan Cain, Amy Mei, Vivian Gasca, Samantha Whitney, Diana Perez.
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P-260 CAPTURE OF MABS VIA PRECIPITATION, A SOLUTION FOR CONTINUOUS DOWN-STREAM PROCESSING

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P-261 DEVELOPMENT AND CHARACTERIZATION OF THE ASIMOV LENTIVIRAL VECTOR PRODUCER CELL LINE SYSTEM

Kevin Smith.
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P-262 CELL CULTURE PRODUCTION OF A BIOACTIVE RECOMBINANT EQUINE CHORIONIC GONADOTROPIN (RECG, FOLI-REC®): REPLACEMENT OF ANIMALS AS A SOURCE OF PMSG

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P-263 PROCESS INTENSIFICATION OF HBMP2 PRODUCTION USING REPEATED TRANSIENT GENE EXPRESSION

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P-264 DOWNSTREAM PROCESS DESIGN AND OPTIMIZATION OF GAG HIV-1 BASED VIRUS-LIKE PARTICLES

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P-265 NEED FOR BLEED: RATIONAL IMPROVEMENT OF CHINESE HAMSTER OVARY (CHO) CELLS FOR PERFUSION CULTURE

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P-266 *EFFECT OF TEMPERATURE AND GLUTAMINE ON PRODUCTION AND POLYMERIZATION STATE OF IGA PRODUCED BY MOUSE MYELOMA CELLS OVEREXPRESSOR OF XBP1(S)*

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P-267 USING N-1 PERFUSION AND COMPACTED MEDIA INTENSIFIES THE SEED TRAIN

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P-268 DEVELOPMENT, MANUFACTURING AND CONTROL OF A CONTINUOUS MANUFACTURING PROCESS

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P-269 DESIGN & CONSTRUCTION OF A TRULY CONTINUOUS AND AUTOMATED PROCESS SKID FOR THE PRODUCTION AND PURIFICATION OF A MONOCLONAL ANTIBODY

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P-270 FULLY AUTOMATED ON DEMAND CELL CULTURE MEDIA PREPARATION FOR PERFUSION BIOREACTORS

Lisa Wolowczyk, Christian Schultheiss, Luis Ayala Solares, Niklas Welzenbach, Mona Bausch, Jochen Sieck.
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P-271 SCALE UP OF A LENTIVIRAL PRODUCTION PROCESS FROM THE ICELLIS® NANO BIOREACTOR TO THE ICELLIS 500 + BIOREACTOR

Miriam Tuschy-Mori[1], Kaitlynn Bayne[2], Odette Becheau[2], Nathan Hazi[2], Isabelle Pelletier[3], Pragati Agnihotri[3], Volga Pasupuleti[3], Ziv Sandalon[3], Young Do[3].
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P-272 PROCESS DEVELOPMENT FOR RECOMBINANT ADENO-ASSOCIATED VIRUS PRODUCTION USING A DESIGN OF EXPERIMENTS MODEL

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P-273 SCALABLE PRODUCTION OF RECOMBINANT ADENO-ASSOCIATED VIRUS IN DIFFERENT SINGLE-USE BIOREACTOR PLATFORMS

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[1]Protein & Viral Production, Uppsala, Sweden; [2]Viral Vector application, Uppsala, Sweden.

P-274 DEVELOPMENT OF AN ALTERNATIVE TO AFFINITY-BASED CAPTURE CHROMATOGRAPHY OF AAV USING MONOLITHS

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P-275 MOVING TILT-123 ONCOLYTIC ADENOVIRUS FROM BIOPROCESS DEVELOPMENT TO CLINICS

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P-276 CHO-BASED VACCINE PRODUCTION PROCESS INTENSIFICATION AND PLATFORMIZATION

Sébastien Colette, Quentin Zune, Patrick Dumas, Monica Tello Soto, Michèle Lecocq, Ludovic Peeters, Hao Chen.
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P-277 METABOLIC DECOUPLING OF CHO CELLS TO REGULATE CELL GROWTH AND RECOMBINANT PROTEIN PRODUCTION

Rita Singh, Shrikant Kumar, Ashok Kumar, Niraj Kumar.
Translational Health Science and Technology Institute, Faridabad, India.

P-278 DESIGN, PRODUCTION AND TESTING OF A TOOLBOX OF SARS-COV-2 ANTIGENS FOR PRECISION VACCINATION

Khaled Trabelsi, Ali Nairouz, Dana Ashour, Nariman Al Mustapha, Ahmad Ramadan Ramadan, Noureddine Ben Khalaf, Mohamed-Dahmani Fath Allah.
Arabian Gulf University, Manama, Bahrain.

P-279 ENHANCE YOUR CELL LINE DEVELOPMENT PROCESS WITH SOLENTIM'S STUDIUS™ POWERED ECOSYSTEM TO PROVIDE CONSISTENT, DATA DRIVEN, ACCELERATED WORKFLOWS

Camilla Domeneghetti.
Solentim, Advanced Instruments, Solent House, Wimborne, United Kingdom.

P-280 CONCERTED PROPERTIES OF TWO NOVEL HYPERGLYCOSYLATED PEPTIDE TAGS: FROM IMPROVING BIOLOGICAL ACTIONS TO FACILITATING THE DETECTION AND PURIFICATION OF BIOTHERAPEUTICS

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P-281 ULTRA-HIGH CELL DENSITY CELL BANK-BASED IGG PRODUCTION WITH CHO CELLS

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P-282 PROCESS INTENSIFICATION WITH AN ADAPTABLE AND SCALABLE UPSTREAM CHO PLATFORM

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P-283 HIGH THROUGHPUT PROCESS INTENSIFICATION WITH A 2 ML CONTINUOUS PERFUSION BIOREACTOR

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P-284 MODEL-BASED INTENSIFICATION OF AAV PRODUCTION IN INSECT CELLS

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P-285 CLEAR IT UP! – ALLUVIAL FILTRATION FOR EFFICIENT CLARIFICATION OF (SUSPENSION) HEK293 PROCESS HARVEST IN AAV PRODUCTION

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P-286 OPTIMIZATION OF *EX VIVO* UMBILICAL CORD BLOOD-DERIVED NATURAL KILLER CELL EXPANSION AND PRODUCTION OF DERIVED EXTRACELLULAR VESICLES UNDER STATIC CONDITIONS

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P-287 IMPROVED EXPANSION OF ISOLATED T CELLS TO SUPPORT CAR-T THERAPY INNOVATION

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P-288 REDUCTION OF TRISULFIDE BOND FORMATION IN MONOCLONAL ANTIBODIES BY CELL CULTURE MEDIA AND FEED OPTIMIZATION

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P-289 EVALUATION OF WAVE BIOREACTORS FOR DIFFERENT PERFUSION CULTURES APPLICATIONS

Agathe Drapé, Stéphanie Seguin-Huet.
Sanofi, Vitry sur Seine, France.

P-290 TOWARDS AN INTEGRATED BIOPROCESS FOR SCALABLE PRODUCTION AND ISOLATION OF MESENCHYMAL STROMAL CELL-DERIVED EXTRACELLULAR VESICLES FOR CARDIAC REPAIR

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P-291 HIGH CELL DENSITY PERFUSION PROCESS FOR RAAV PRODUCTION BASED ON TRANSIENT TRANSFECTION

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P-292 INTENSIFICATION OF THE FED-BATCH PROCESS USING N-1 PERFUSION

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P-293 DEFEATING HYPOXIA INDUCED PRODUCTION LOSSES DURING CONTINUOUS PRODUCTION

Nikolas Zeh, Patrick Schlossbauer, Nadja Raab, Florian Klingler, René Handrick, Kerstin Otte.
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P-294 DEVELOPING SCALE DOWN HIGH THROUGHPUT CULTIVATION SYSTEM AND SPENT MEDIA ANALYSIS PLATFORM FOR CHO CELL CULTURE MEDIA DEVELOPMENT AND OPTIMIZATION

Eva Diem, Ali Safari, Swapnil Chaudhari, Dirk Müller.
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P-295 OPTIMIZING SARTORIUS CELL LINE DEVELOPMENT PLATFORM FOR BIOPHARMACEUTICAL PRODUCTION, USING THE ALS CELLCELECTOR™ SINGLE CELL CLONING TECHNOLOGY

Katrin Brosch, Juliana Bischof, Rathangadhara Nammalwar, Kristin Thiele.
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P-296 USING A GLUTAMINE DIPEPTIDE AS GLN SOURCE IN CHEMICALLY DEFINED MEDIA INCREASES TITER AND PRODUCT QUALITY IN HEK 293-BASED AAV-PRODUCTION

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P-297 MULTI-OMICS STRATEGY FOR CELL CULTURE MEDIUM OPTIMIZATION TO PRODUCE BIOTHERAPEUTICS

Paul Gulde, Chengjian Tu, Alex Abreu, Vyncent Nguyen, Km Shams Ud Doha, Andrew Campbell.
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P-298 SEAMLESS CMC ACCELERATION OF NBE PROJECTS FROM CLD TO FIH TO ADVANCE UCB'S PIPELINE

Richard Davies[1], Matthew Allen[1], Matthew Hinchliffe[1], Donal Mactiernan[1], Wolfgang Paul[2].
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P-299 PROCESS ANALYTICAL TECHNOLOGY (PAT) AT MANUFACTURING SCALE: BENEFITS AND CHALLENGES

Valérie Duret, Daniel Karst, Oliver Steinhof, Thomas Villiger, Dave Kolwyck.
Biogen, Luterbach, Switzerland.

P-300 DEVELOPMENT OF A FEED MEDIUM TO IMPROVE AAV PRODUCTION IN HEK293 FED-BATCH CULTURE

Catherine Nguyen, Omid Taghavian, Hamid Soleymani, Tannaz Goodarzi, Shahram Shahabi, Chandana Sharma.
FujiFilm, Santa Ana, United States.

P-301 A NOVEL PROCESS INTENSIFICATION APPROACH TO IMPROVE THE EFFICEINCY OF THERAPEUTIC PROTEIN MANUFACTURING

Prasad Babu Kakarla[1], Dirk Mueller[2], Lukas Klein[2], Johannes Lemke[1], Markus Schulze[1], Thomas Kruse[1], Martin Saballus[1], Jens Matuszczyk[1], Markus Kampmann[1], Gerben Zijlstra[1].
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P-302 DEVELOPING AND INTEGRATING A CONTINUOUS BIOMANUFACTURING PLATFORM FOR PROCESS INTENSIFICATION AND PRODUCT CONSISTENCY

Bethany Kerr.
CPI, Darlington, United Kingdom.

P-303 THE TITER GAP – A HOLISTIC APPROACH TO UNDERSTANDING HIGH AND LOW HEK293 PRODUCER CELL LINES IN AAV PRODUCTION PROCESSES

Niklas Kraemer, Vera Ortseifen, Luisa Vetter, Kathrin Teschner, Alyssa Vetter, Tim Steffens, Stefan Northoff, Sandra Klausing.
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P-304 AFFINITY CHROMATOGRAPHY-BASED PROTOCOLS FOR PURIFICATION OF NEUROTROPIC AAV VECTORS

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P-305 NOVEL IDEAS FOR PRODUCT RECOVERY FROM FED-BATCH PROCESS USING ATF

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P-306 SCALABLE MANUFACTURING OF HUMAN MESENCHYMAL STROMAL CELL-DERIVED EXTRACELLULAR VESICLES WITH ANGIOGENIC POTENTIAL

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P-307 ENHANCING PRODUCTION OF THE MALARIA ASEXUAL BLOOD-STAGE VACCINE CANDIDATE PFRIPR5 IN INSECT CELLS BY MODULATING EXPRESSION VECTOR AND CULTURE TEMPERATURE

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P-308 DISCOVER AND IMPLEMENTATION OF AN AFFINITY LIGAND FOR LENTIVIRAL VECTOR PURIFICATION

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P-309 THE EFFECT OF CELL DENSITY ON THE PLASMID UTILIZATION FOR THE PRODUCTION OF ADENO-ASSOCIATED VIRUS VIA THE TRIPLE-TRANSFECTION METHOD

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P-310 AUTOMATION OF A FEEDING STRATEGY THROUGH THE REAL-TIME MEASUREMENT OF GLUCOSE IN FED-BATCH CULTIVATION

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P-311 OVERCOMING BARRIERS IN VIRAL VECTOR MANUFACTURING: SMALL MOLECULE TARGETING OF ANTIVIRAL DEFENCES

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P-312 MASSIVE PRODUCTION OF HIPSC-DERIVED HEPATOCYTES FOR PRIMARY HYPEROXALURIA TYPE 1 DISEASE MODELLING AND THERAPY

Pedro Vicente[1], Joana I. Almeida[1], Inês E. Crespo[1], Inês A Isidro[1], Maren Calleja[2], Juan Rodriguez-Madoz[2], Felipe Prosper[2], Anders Aspegren[3], Paula Alves[1], Margarida Serra[1].
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P-313 STRATEGY FOR PERFUSION MEDIUM OPTIMIZATION IN MICRO-SCALE ERBI BIOREACTORS COMBINED WITH DESIGN OF EXPERIMENTS METHODOLOGY

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P-314 SINGLE IN-LINE BIOMASS PROBE DETECTS CHO CELL GROWTH BY CAPACITANCE AND BACTERIAL CONTAMINATION BY CONDUCTIVITY IN BIOREACTOR

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P-315 DEVELOPMENT OF SCALABLE LENTIVIRAL VECTOR PRODUCTION PLATFORMS: METABOLIC INSIGHTS AND KEY BIOREACTION PARAMETERS

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P-316 RECELLULARIZATION OF ACELLULAR LIVER SCAFFOLDS WITH FUNCTIONAL HIPSC-HEPATOCYTES GENERATED USING NATURE-INSPIRED BIOPROCESSES

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P-317 INVESTIGATION OF ER STRESS MECHANISMS IN RECOMBINANT CHO CELLS: ROLE OF UBIQUITINATION

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P-318 PREDICTING THE PERFORMANCE OF PERFUSION MEDIA IN A CONTINUOUS BIOREACTOR FROM SMALL-SCALE PERFUSION MIMICS

Luis Rodriguez, Martin Santillan, Ociel Ferreyra, Catherine Nguyen, Aylar Sharafkhanian, Niki Fujimoto, Chandana Sharma.
Fujifilm Irvine Scientific, Inc, Santa Ana / R&D Bioproduction, United States.

P-319 INTEGRATED CONTINUOUS BIOMANUFACTURING AT PILOT-SCALE SUITABLE FOR PH-SENSITIVE MONOCLONAL ANTIBODIES

Veronique Chotteau[1], Hubert Schwarz[1], Joaquín Gomis Fons[2], Madelène Isaksson[2], Julia Scheffel[1], Andreas Castan[3], Sophia Hober[1], Bernt Nilsson[2].
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P-320 PROCESS INNOVATION TO INCREASE ZINC LEVELS IN PROTEIN HYDROLYSATE FOR BIOPHARMACEUTICAL PRODUCTION

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P-321 DEVELOPMENT OF SCALE-DOWN SYSTEM FOR PERFUSION PROCESSES

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P-322 USE OF HIGH-RESOLUTION UNTARGETED LC-MS TO OPTIMIZE THE STABILITY OF CELL CULTURE MEDIA AT ROOM TEMPERATURE

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Merck KGaA, Darmstadt, Germany.

P-323 HIGH YIELDING LARGE-SCALE TRANSIENT EXPRESSION OF BIOTHERAPEUTICS IN CHO: BEYOND PRECLINICAL DEVELOPMENT

Kitty Agarwal, Juan Camilo Gonzalez Rivera, Todd Ryder, Lorena Pena, Peter Onyskiw, Lakshmi Kandari, Anurag Khetan.
Bristol-Myers Squibb, New Jersey, United States.

P-324 INTENSIFICATION OF CELL CLARIFICATION BY A NOVEL SINGLE-USE APPROACH: FLUIDIZED BED CENTRIFUGATION WITH INTEGRATED FILTRATION

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P-325 CONSIDERATIONS FOR BIOSAFETY TESTING OF CELL AND GENE THERAPIES

Richard Adair.
SGS, Glasgow, United Kingdom.

P-326 TIGHT CONTROLLED SCALABLE PERFUSION-SUBS FROM 250 ML AND UP

Per Stobbe.
PerfuseCell A/S, Herlev, Denmark.

P-327 BEMSCA: A NOVEL DECISION SUPPORT TOOL FOR THE OPTIMAL DESIGN OF A LARGE-SCALE HUMAN INDUCED PLURIPOTENT STEM CELL EXPANSION BIOPROCESS

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P-328 EXPANSION AND CARDIAC DIFFERENTIATION OF HUMAN INDUCED PLURIPOTENT STEM CELLS AS AGGREGATES IN SINGLE-USE VERTICAL-WHEEL™ BIOREACTORS

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P-329 MODEL-BASED INTENSIFICATION OF CHO CELL CULTURES: ONE-STEP STRATEGY FROM FED-BATCH TO PERFUSION

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P-330 CONTINUOUS HIGH-CELL-DENSITY INSECT CELL CULTURES FOR GAG-HA VLP-BASED VACCINE PRODUCTION

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