# NEWSLETTER

of the European Society for Animal Cell Technology

January 2013


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## *23rd ESACT Meeting*

### The 23rd ESACT meeting will take place from June 23rd to 26th, 2013 in Lille (France)!

You will find all scientific and practical information on www.esact2013.com.

Registration and abstract submission are now open. **Deadline for abstracts is January 16th, 2013 and will be strictly observed.**

On Sunday afternoon, from 14:00 to 15:30, still ahead of the official opening of the ESACT Meeting, academic workshops will be organized.

Till January 31th we encourage you to suggest topics for the academic workshops. For further information or to propose a specific topic and organize a workshop, please contact Martine Marigliano at marigliano@transgene.fr.

We are looking forward to welcoming you in Lille!

***Yves-Jacques Schneider***

### ESACT 23rd - Better Cells for Better Health

In June 2013, after Vienna, the 23rd Meeting of the series will take place in France, at the Congress Centre of Lille (*Lille Grand Palais*). Lille is a beautiful city, born "out of the water" sometime about 1000 AD. Initially a Flemish city, it changed hands a few times to become Burgundian, then Spanish, and finally French in 1667. In the 19th century Lille was an industrial power and thrived in the metalwork, chemistry and textile industries. Today, Lille is the 4th largest French metropolitan area, an artistic and historic city, but also a centre of economy, higher education and R&D.

Lille is easily accessible by fast intercity train, car or plane, from Brussels, London and Paris international airports. More than 2000 hotel rooms are available within walking distance from the Congress Centre.

For the Lille ESACT meeting, the Scientific Committee decided that the sessions will not be organized on the basis of "traditional topics", but transversally around technology. The general idea would be driven by a **"Systems approach: from prediction to production"** and will aim at "**bringing together the basics to technology**. To reflect the rapid advances in the field of animal cell culture, the Scientific Committee aims at evolving the setup for the plenary sessions to better integrate cell science and all its technological

applications. To achieve this, the final outline of the individual session will only be determined once abstracts have been selected for oral presentations. This will also ensure that the meeting will give the best possible overview of the state of the art in the field in 2013, including the most recent developments.

The Organizing Committee is currently selecting the traditional social events and will particularly focus on the gastronomical and nutritional quality of this event and will also take into account the sustainable development in its organization.

The Scientific and Organising Committees cordially invite you to this event and look forward to meeting old friends, introducing newcomers to the area of animal cell technology and experiencing lively interactions and discussions on the newest hot topics of the field.

See you in Lille!

***Yves-Jacques Schneider***

### Proposals/Nominations for the ESACT XC election

The elections to the ESACT Executive Committee are coming up. The next Committee will be elected during the General Assembly at the 23rd ESACT meeting in Lille, France on June 2013.

An email asking for nominations has been sent to all ESACT members. Please fill-in the form attached to that e-mail and return it by e-mail to roldao@esact.org or marques@ibet.pt together with a short CV and a motivation statement (both from the candidate). You can also propose yourself; in this case, please contact Paula M Alves (marques@ibet.pt) until January 31.

Please respect strictly the deadline for your response: February 4, 2013.

The elections will be prepared and done electronically. A newsletter presenting all nominates CV and motivation letter and the electronic election procedure will be prepared and circulated by March. The dates for the online elections will be defined in the next XC meeting (February 2013).

We thank you for your active participation in this process and look forward to seeing you again in Lille.

***Paula Alves and António Roldão***

## *ESACT Courses*

### 2nd edition of the ACT course organised by ESACT - 2012

***Coordinators:*** *Francesc Gòdia (UAB, Spain) and Paula Alves (IBET, Portugal)*

The second Course on Animal Cell Technology organized by ESACT took place in Hotel Terramar, in Llafranc (Girona, Spain), from September 30th to October 4th 2012. This is an introductory course, providing an overview of the field, from the more basic aspects to the final applications. It is targeted to those starting their research activity in Animal Cell Technology, both from Academia or Companies. It is also of interest to those wishing an up-date of the state-

**2nd edition of the ACT course organised by ESACT - 2012**

of-the-art of Animal Cell Technology in a short intensive Course. The course was well attended, with a total of 27 participants, both from academy and industry, from thirteen different countries.

Seven lecturers covered the four days intensive program of lectures: Eleftherios Papoutsakis (U. Delaware, USA), Manuel Carrondo (IBET, Portugal), Hansjörg Hauser (HZI, Germany), Paula Alves (IBET, Portugal), Ashraf Amanullah (Gilead, USA US), Anne B. Tolstrup (Boehringer Ingelheim) and Francesc Gòdia (UAB, Spain). The days in Llafranc where bright and pleasant, the program was very intensive, but still allowing a daily break on the beach. The interaction among lecturers and participants was very dynamic. On Tuesday evening, the group visited some spots in the area and enjoyed a traditional Catalan dinner in Palau-Sator. The opinion from the participants was excellent, and this certainly encourages organizing the Course again in 2013.

***Francesc Gòdia and Paula Alves***

## *Upcoming ESACT Events*

### 3rd edition of the ACT course organised by ESACT - 2013

**Coordinators:** Francesc Gòdia (UAB, Spain) and Paula Alves (IBET, Portugal)

The third Course on Animal Cell Technology organized by ESACT will also be in Llafranc (Girona, Spain), 29th September - 3rd October 2013. The full announcement and web of the Course will be ready early in 2013.

***Francesc Gòdia and Paula Alves***

# *Other events related with ESACT*

### 25th Annual and International JAACT 2012

**International Meeting of the Japanese Association of Animal Cell Technology - "Back to Basics"**

The 25th annual and international meeting of the Japanese Association of Animal Cell Technology (JAACT 2012) took place in Nagoya, Japan from 27 November until 30 November 2012. JAACT is the Japanese counterpart society to ESACT and covers mainly attendance from the Asian area. A long standing partnership with JAACT makes sure that delegates from both sides are invited to the respective meetings between ESACT and JAACT.

This year's meeting was chaired by Takishi Omasa, a well-known molecular biotechnologist who has recently moved from Osaka to Tokushima University. He and his team have organized a refreshing style of JAACT meeting that covered many topics in the area of cellular biology from basic science to applied technology. The program included symposia on

- Biosciences of water and life
- Application of new technologies for assessment of food function and safety
- Cell culture technologies for stem cells
- Cutting-edge technologies in single cell-based analyses and measurements
- Recent advances in CHO-omix technologies
- Advanced engineering in biologics production.

Professor Omasa and his team managed to gather excellent speakers from Japan and the Asian countries (including Yoshinori Fujiyoshi from the University of Osaka, who presented new results on membrane channel structure, Takeharu Nagai who presented exciting optogenetic developments, and Wei-Shou Hu from the University of Minnesota who summarized his experience of cell culture in the post-genomic area). Speakers send by ESACT were Nicole Borth, Florian Wurm and Hansjörg Hauser. The lectures were complemented by a number of excellent short oral poster presentations and a remarkably large exhibition, featuring almost 40 international and Japanese companies.

The scientifically highly interesting meeting was very much appreciated by attendees.

We congratulate the Japanese society on this successful approach.

***Nicole Borth and Hansjörg Hauser***

### 23rd Annual ESACT-UK Scientific Meeting

**9th-10th January 2013, at Loughborough University's Imago Conference Centre at Holywell Park, UK**

The 23rd Annual ESACT-UK scientific meeting was held at Holywell Park Conference Centre at Loughborough University (http://www.esactuk.org.uk/

for details of ESACT-UK and the meeting). This two day meeting had 19 oral presentations covering themes of upstream processes, downstream processes & formulation, high-throughput processes, stem cells & transgenics and "omics and includes a session of oral presentations from early career researchers. In addition, keynote presentations were given by Dr Paul Varley (MedImmune) and Prof David James (University of Sheffield) and research posters were on show throughout the meeting. Residential registration fee included access to all scientific sessions, accommodation for the evening of January 9th and all meals during the conference (details of the venue are given at http://www.welcometoimago.com/conference-venues/holywell-park/)

***Alan Dickson***

## *2012 Events powered by ESACT*

### "Animal Cell Based Technologies" Course

It was held in the city of Santa Fe (Argentina) from 29th October to 9th November 2012, at the School of Biochemistry and Biological Sciences, Universidad Nacional del Litoral (UNL). The organization of the course was held by Dr. Marina Etcheverrigaray and Dr. Ricardo Kratje (Heads of the Cell Culture Laboratory, UNL, Argentina).

A group of 15 professors were invited, from Europe and America (Germany, Spain, Portugal, USA, Canada, México, Brazil, Chile, Argentina and Uruguay, and 10 collaborators participated in the lab activities.

30 participants for the complete course (theoretical and practical parts) were selected considering that they do not have many opportunities to access to this kind of practical courses. Selected participants were from Argentina, Brasil, Chile, Perú, México, Cuba and Uruguay, mainly Master and PhD students.

The scientific program was divided in 3 main activities: lectures, workshops and practical sessions. Since the theoretical lectures were open to the public, many students and researchers from Uruguay, Argentina, Brazil, Perú and Chile who did not received fellowships attended nevertheless the lectures.

Local accommodation of invited speakers and participants was done at www.hotellossilos.com.ar/ all together in order to have good chances of interaction among them. The main sponsors of the Course were UNU-BIOLAC, Amsud-Pasteur, UNL and ESACT.

All the participants were really grateful with the scientific level and organization of the course, coming to a very successful event. Much collaboration between the speakers and the participants was established that will contribute to improve the quality of the research and the exchange of students in the region and the world.

***Marina Etcheverrigaray***

### XIV BELACT Meeting

The Belgian Group for Animal Cell Technology was created in 1992 by P. Dewaele, L. Fabry, D. Malarme, A. Miller and J. Werenne, some of whom were and still are active ESACT members. The main aim of BELACT was and continues to be to promote the communication of knowledge and experience among Belgian animal cell

**SPBACC 2011 – Lectures group at COPPE-UFRJ**

technology researchers and industrial practitioners.

BELACT has been closely affiliated with ESACT throughout the decades and ESACT has frequently sponsored financially or with student bursaries the bi-annual BELACT Meeting. In 2012 the 14th meeting of the series took place on December 14 at the Erasmus campus of the Free University of Brussels. The one-day meeting was entitled "Advanced models of (stem) cells in toxicology, pharmacology, safety assessment, and cell therapy". Prominent speakers included Cedric Blanpain who spoke on multipotent cardiovascular progenitors during development and pluripotent stem cell differentiation and Sabine Costagliola who presented her work on deriving functional thyroid tissue from pluripotent stem cells. Particularly noteworthy was also the presentation of Sonja Baeken from the Federal Agency for Medicines and Health Products of Belgium, who shared her views on regulatory acceptance and use of in vitro methods for non-clinical testing of human medicinal products. The well-rounded and informative agenda of the meeting was further enhanced by a non-Belgian presentation of Christoph Giese of ProBioGen AG (Germany) on a human lymphoid organ model for predictive testing of immunogenicity, immunotoxicity and immune functions in vitro.

The meeting was powered by ESACT and as part of the sponsorship a young researcher was chosen by the Scientific Committee of the BELACT Meeting to receive an ESACT bursary to attend the 23rd ESACT Meeting in Lille in June 2013 and to present her work there. The award went to Ira Espuny Camacho of the Free University of Brussels, who presented her work on corticogenesis from human pluripotent stem cells.

**Stefanos Grammatikos**

# *ESACT Office*

## Welcome to New Members

ESACT welcomes the following new members (period Feb 2012 – November 2012):

Steffen Zeng (Boehringer Ingelheim)
Deniz Baycin Hizal (MedImmune)
Harald Bradl (Boehringer Ingelheim)
Markus Michael Müller (Boehringer Ingelheim)
Nienke Vriezen (Synthon)
Christian Kaisermayer (GE Healthcare)
Till Wenger (Boehringer Ingelheim)
Matthieu Stettler (Biotech Process Sciences)
Patrick Schulz (Boehringer Ingelheim)
Pani Apostolidis (Air Liquide)
Anja Puklowski (Boehringer Ingelheim)
Emmanuel Guedon (CNRS)

## Important Reminders

Two important reminders to all ESACT members: 1) in order to activate/renew your membership, please do not forget to pay your subscription as described in the e-mail you have received; 2) all applications for ESACT memberships **MUST** be written in English.

We would like to stress once again that the official ESACT e.V. bank account to which you should transfer the membership fees, if you which to use this method, is the following:

Deutsche Bank
Account Nr: 0189191
BLZ: 27070024
IBAN (EUROS): DE55 2707 0024 0018 9191 00
IBAN (GBP): DE28 2707 0024 0018 9191 01
BIC: DEUTDEDB270

Please note that for transfers in Euros within Germany the Account Nr and BLZ are needed while for transfers outside Germany IBAN and BIC are needed. All bank transfers should be in Euro or GBP. Membership fees are 20€/year or 17GBP/year and all costs associated with the transfers should be assumed by the members.

**IMPORTANT NOTES:**

We encourage all ESACT members to use the bank transfer method rather than the PayPal system for the payment of membership fees due to economic reasons related with the transaction cost of PayPal for ESACT. In the era of online banking, transferring into the ESACT account should be as easy as PayPal.

All ESACT accounts in Belgium, Switzerland and the UK to which ESACT members were used to transfer their membership fees have been closed. Effective immediately, for future payments of membership fees please use the ESACT e.V. bank account provided above.

***Stefanos Grammatikos and António Roldão***

## ESACT´s "New Look"

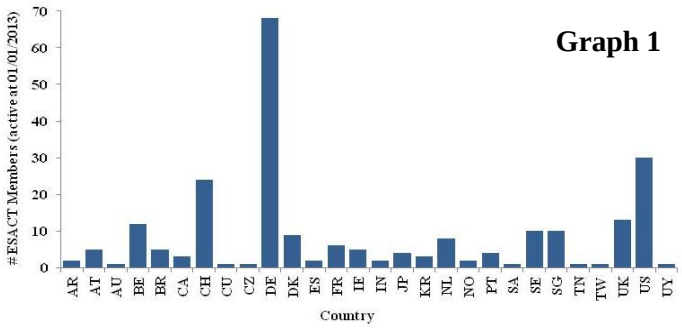
As announced early this year, ESACT webpage has a "new, modern look". All features of the old website are maintained. The website is fully operational and can be accessible through www.esact.org. Explore it and let us know your opinion. In addition, help us maintaining the website updated by sending us comments, suggestions, information... via our contact module (go to contacts in www.esact.org).

In the members area you can edit your profile, renew your membership and download documents such as the minutes from the ESACT General Assemblies. This last feature is only available for members with valid memberships. Other documents such as the **proceedings of the 22nd ESACT meeting on Cell Based Technologies, Vienna, Austria, 2011** can be accessible via our website, under the Library/Proceedings menu in www.esact.org. We would like to take this opportunity to let you know that the proceedings from the 21st ESACT meeting in Dublin, 2009 will be soon available online.

***António Roldão***

## Membership Statistics

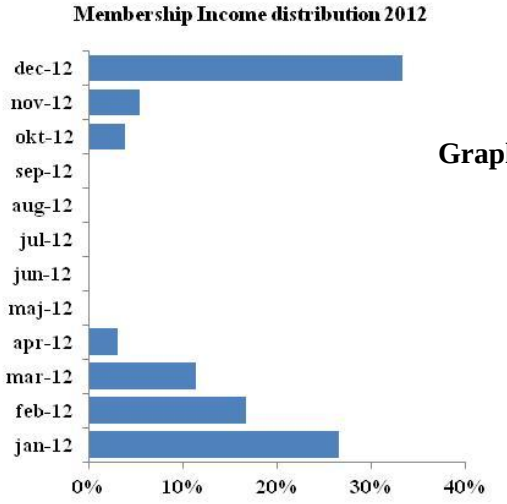
At 07/01/2013, ESACT had 241 active members (members with membership paid) and 432 members with expired memberships. The most represented country is DE (Deutschland), followed by US (United States of America), CH (Switzerland), UK (United Kingdom) and BE (Belgium) – see Graph 1 below.



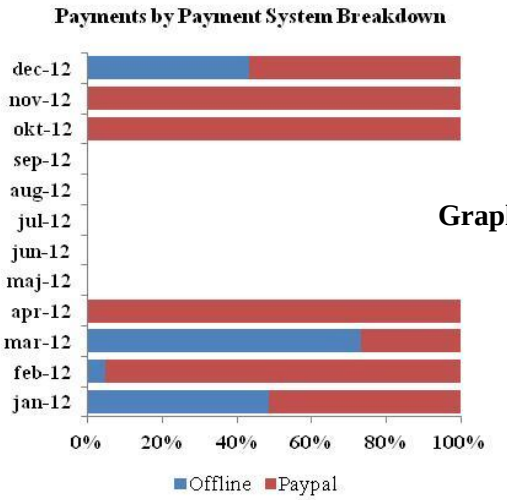

**Graph 1**

Graph 2 shows how the ESACT membership income was distributed along the year of 2012. The Top-4 months (months with highest membership payments) were January, February, March and December 2012.

ESACT members continue to have at their disposal two payment systems for the payment of membership fees, off-line payment or PayPal. Graph 3 on next page reports the payments made in 2012 by payment system breakdown. It is possible to state that both systems are used almost evenly.

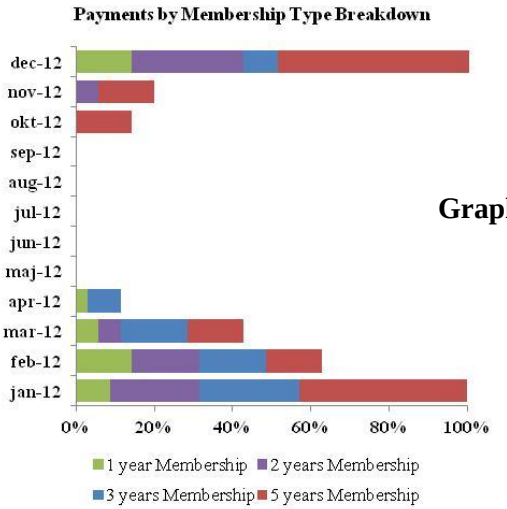



**Graph 2**




**Graph 3**

Mandatory to newly accepted members, 5-years memberships continue to be the preferred membership type for most ESACT members (Graph 4).




**Graph 4**

# *Contribution Articles*

## Metabolic modelling in animal cell cultures

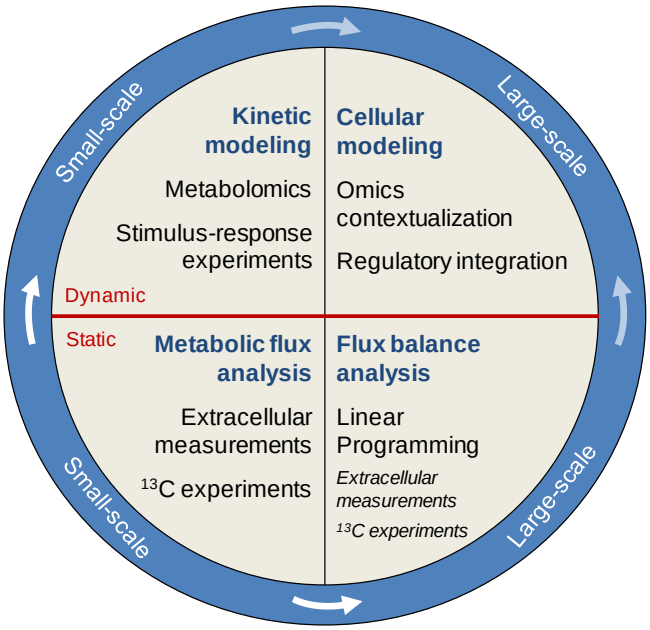
***Nuno Carinhas, IBET, Portugal***

The more recent systems approach to biology has put the study of metabolism in an eminent position to uncover the complexity of cell behaviour. In particular for animal cell culture, the growth and productive phenotypes are an output of metabolic flows within the cell, and a complete mechanistic account of these pathways would provide the biological constraints for industrial biotechnology. However, a significant experimental challenge is the measurement of enzyme kinetic parameters at a large scale, which depends on our ability to quantitatively profile the cellular metabolome, still requiring a cumbersome combination of multiple extraction and analytical methods. While metabolomics is evolving into a mature technology, the knowledge of regulation at the levels of enzyme expression and enzyme activity is highly incomplete, and the application of rigorous kinetic models to animal cells metabolism is in its infancy.

Meanwhile, most metabolic models have been based on steady-state assumptions, such as in classical metabolic flux analysis (MFA). It is assumed that the rate of change of metabolites is much larger than their uptake or secretion by the cell, therefore resulting in negligible intracellular accumulation. Material balancing equations can then be written around each metabolite resulting in a simple linear algebra problem. The expense of metabolic precursors and energy for cellular growth is accounted for by setting stoichiometric reactions for biomass formation based on its composition. Cell culture facilitates the measurement of extracellular concentrations of a number of metabolites in the supernatant, and thus experimentally determine rates of consumption (e.g. sugars, amino acids) and secretion (e.g. lactate, ammonia), as well as cellular growth. Using this approach, several small-scale models were developed for animal cell lines under bioprocess-relevant conditions, including hybridoma and CHO (see [1] for a review). At IBET, we have been studying amongst others the metabolism of *Sf*9 cells during growth and recombinant baculovirus infection in order to address the loss in per cell productivity when cells are infected at later stages of growth [2, 3].

To increase the resolution of metabolic flux estimations, including the determination of reversible and parallel fluxes, experimental and computational methods have been devised to follow the intracellular path of a $^{13}C$ label from medium nutrients. Most of the metabolic studies with labelled substrates in animal cell culture have analyzed the label patterns produced into secreted metabolites [4]. The incorporation of a $^{13}C$ label from glucose into intracellular metabolites started only recently to be studied in CHO cells, integrating the resulting isotopomer dynamics with MFA to provide a more detailed representation of the metabolic flux distributions [5]. Apart from producer cell lines, there has been considerable progress in the study of metabolism of primary animal cell cultures using these techniques. For instance, we have followed and modeled the metabolic distribution of $^{13}C$-glucose in astrocytes, both extracellularly [6] and intracellularly [7].

With the emergence of extensive metabolic reconstructions of several organisms, accompanying the surge in genome sequences available, flux balance analysis (FBA) algorithms for genome-wide fluxome estimation have become popular. The practical effects of large-scale *in silico* metabolic analyses are documented in numerous applications for metabolic engineering of microbial strains (reviewed in [8]). Examples for animal cells include the large-scale reconstruction of mouse/hybridoma [9] and human [10] metabolic networks, but still no significant applications to bioprocess optimization have been reported. With the recent publishing of the genome sequence of the CHO-K1 cell line [11], the way is open to reconstruct a large-scale metabolic network for fluxome investigation. The incorporation of flux constraints from $^{13}C$ experiments and basic extracellular measurements will increase the resolution and accuracy of such models.




Overview of metabolic modeling strategies. Refer to the text for a brief explanation.

Finally, it should be pointed out that the complexity associated with engineering complex, multi-genic phenotypes, such as improving the production yields of recombinant proteins, is much larger than for microorganisms producing small molecules. This is

emphasized by the fact that available metabolic models do not embrace all layers of information that confer the cell phenotype. Nevertheless, these models provide convenient scaffolds to contextualize different types of data, such as transcriptomic and proteomic. Alongside the progress towards dynamic descriptions of metabolism, as well as from smaller to larger scale, the integration with other layers of information, including modeling of regulatory processes, will be essential to accurately predict the phenotypic attributes of efficient animal cell factories.

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***Newsletter Editor***

António Roldão - roldao@esact.org