



NEWSLETTER

of the European Society for Animal Cell Technology

December 2007

A Word from the Chairman

Florian Wurm

Dear Friends,

The year ends and we all thought it was just yesterday when we met on the banks of the river Elbe. I surely will remember the HAUSER Meeting as a wonderful event. However, time passed so fast, and it seems there was little time to reflect. But, let's realize it, things have changed, and we need to think: "Our" ESACT community, now clearly an international society with an American member in our Board (welcome again to Dana Andersen) - is, as seen in Dresden, larger than ever before. This presents to the organizers a more and more challenging situation if we wish to meet **all expectations**. Yes, and in addition, the diversity of topics in our meetings is becoming a true challenge. Even for those "oldtimers" who have been around for some time and have thought to have seen it "all". No, in reality, very few can keep abreast of all the exciting developments that occur in the different corners of our science and technology field. Now, how do we cope with this? Are we becoming too big? Are we becoming "mammoths", soon to be eradicated because we can not be flexible enough to see the "climate change" ?

The executive board of ESACT has had one meeting in Zürich a few weeks ago and we did actually reflect on the past and on the future and decided a few important points. One topic was the structure of our meetings. We are suggesting to the chairman of the next meeting to modify it: at least for one or two of the sessions of the upcoming conference (in Dublin as you know) "double booking", i.e. to running parallel sessions should be seriously evaluated as an option. From the start of ESACT this has been thought to be mortal sin. I don't think it is: our intention is still to maintain as much as we can the entire community together, but let's face it, all of us have one or two themes in cell culture technology and research that do excite us less than our "pet topic". One hoped-for benefit for parallel sessions is that the audience would be smaller and thus be more encouraging to truly discuss

the presentations given. I liked in the past this very open and even at times controversial discussing of questions. This has clearly been reduced in our larger meetings, probably because a large room and a large number of attendees in such a hall is in fact threatening, especially for the younger section of our community. In view of the challenge by the commercial meetings which, due to the success of cell culture technology in providing the basis for multibillion products, are being run at an ever increasing pace and frequency, it is important that we set us apart. We wish to deliver a conference where true science is delivered and discussed with view onto the near and far future. This would also give us a little bit more time for considering more oral presentations from the ESACT poster applicants, thus would probably again strengthen the opportunities for young scientists to become more visible during our meeting.

Another point of discussion was the way how we wish to recognize outstanding contributions in our field. We decided to enforce the visibility of the ESACT AWARD. It shall be given in an advertised ceremony, connected to an Award Lecture, with the distribution of both the ESACT medal and a price money of 5000 Euro. We wish to recognize a technological achievement, rather than give an award for a

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fundamental contribution.

We have to thank two parting members of the executive committee: Dr. Otto Merten, our very able chairman from 2003 to 2007, was before organizer of the wonderful meeting in Tours (1997) and has been a pillar of our community since 1981. Thank you Otto and please, continue to be our outpost of virus and gene therapy issues! The other man who left the XC is Rod Smith who will be remembered as the very efficient chairman for Harrogate - a stylish British meeting in a wonderful setting. Rod has generously agreed to provide help for the upcoming Dublin meeting.... I thought that there had been some problems in the past between the big and the small island up there? Thank you so much, and keep up the good work, Rod!

This brings us right to 2009: As you know we have found a very much "local" chairman for the meeting in

Dublin: our old friend Dr. Michael Comer made himself available. He had become, over the years when we did not see him around anymore at ESACT a very much involved top personality within the emerging biotech scene in Ireland. Due to his excellent management skills and his dedication to the cause he has assembled now a top selection of people with the goal to present to us Dublin as the place to be in Animal Cell Culture Technology these days.... and lots of things speak for such a bold statement (but please read his own words in this newsletter). I wish him the best of time in doing this difficult job, but I know already that he will not fail us.

*Best wishes
your chairman
Florian*

New Members

Christophe Losberger

ESACT welcomes the following new members:

Genzel Yvonne	Max Planck Institute for Dynamics of Complex Technical Systems
Kocourek Andreas	Sartorius Technologies & Services GmbH
Lanero Fidalgo Michaël	GSK Biologicals
Lavery Mark	Intervet UK Ltd
Nagel Frank-Jan	Centocor BV
Poulsen Bjarne Rask	Novo Nordisk A/S

Reminder: In order to activate your membership, please do not forget to pay your subscription as described in the the email you have received.



ESACT 2007: The Organizing Committee.

20th ESACT Meeting 2007 in Dresden - A brief summary

Hansjörg Hauser

This year the biennial conference of ESACT was held in Dresden, Germany, between the 17th and 20th June. It attracted nearly 900 delegates from all over the world. The large attendance and the statistics indicate that ESACT meetings are becoming world meetings in animal cell technology (for statistics see below). It was ESACT's 20th conference, held in the new congress centre of Dresden, located at the Elbe river. The meeting's theme was "Cells and Culture" where the term culture should not only apply to the meeting's content but also recognize the cultural treasures of Dresden.

The German Organizing Committee did an outstanding job to coordinate all events. A novelty was the collaboration with DECHEMA as a meeting organizer. A deal was made between ESACT and DECHEMA that turned out to be advantageous for both sides. Overall, we were very happy with DECHEMA's performance.

Guided by the Scientific Committee the scientific program was organized along with ESACT's tradition to avoid parallel sessions and to give strong emphasis on the posters. A report on the contents of the meeting will not be given. Instead, ESACT has made the abstract book available to everybody as a PDF file:

http://www.esact.org/documents/ESACT07_BoA.pdf

The choice of the conference facilities and the timing of the event turned out to be ideal for the stay in the

Scientific Program		Exhibition	
305	Submissions in total	76	Exhibitors
20	accepted oral	804	Exhibition space (in sqm)
12	accepted short oral		
249	accepted poster		
10	Invited lectures		
5	Keynote lectures		
76	Exhibitors		
Participants (in total 890)			
324	Germany	1	Hungary
38	France	3	Russian Federation
36	Belgium	1	Tunisia
39	Netherlands	1	Egypt
4	Luxembourg	137	USA
2	Italy	7	Canada
96	Great Britain	2	Cuba
18	Ireland	4	Brasil
30	Denmark	1	Uruguay
13	Portugal	3	Argentina
9	Spain	2	Israel
1	Norway	3	India
32	Sweden	3	Singapur
47	Switzerland	10	South Korea
19	Austria	27	Japan
2	Estland	6	Australia
1	Czech Republik	1	New Zealand

ESACT 2007 Poster Prize

1st Prize: Kristina Nehlsen, HZI, Braunschweig P-1.21: Evaluation of a Regulated Antibiotic-free Selection System for Stable Protein Production.

2nd Prize: Jens Kelm, University Hospital, Zürich P-2.08: Microtissue integration into a chronically infarcted Myocardial Wall.

3rd Prize: Roland Schucht, HZI, Braunschweig P-1.22: Stable and predictable expression of proteins, siRNA and therapeutic viruses by Flp mediated cassette exchange.



The Poster Prize Committee chairs Hitto Kaufmann and Heino Büntemeyer during the poster award to Kristina Nehlsen, Roland Schuch and Jens Kelm (standing behind) with Ulrich Behrendt as the representative of Roche the sponsor of these prizes.

pleasant Saxonian city. Given that weather during last summer was comparably nasty, the meeting days were perfect and allowed us to enjoy a boat trip to Pillnitz combined with an excursion to Königstein castle. Thus, the participants could get an impression about the city's architecture and the surrounding landscape.

The exhibition area was fully sold and according to a survey report the overall impression of the exhibitors was very good (as quoted by 90%). The exhibition area was located close to the central lecture room and was mixed with the poster viewing area. This was a main element why exhibitors were very much satisfied with the attendance of their booths.

Following the tradition of recent ESACT meetings the Poster Prize Committee selected in an elaborated and fair procedure three winners who received their awards on the last day's conference party. During this event also the ESACT medal was given to Manuel Carrondo.

Hansjörg Hauser

21st ESACT Meeting 2009 “Coming of Age in Ireland”
Dublin, June 7-10, 2009

Michael Comer

Florian Wurm and the Executive Committee are pleased to announce that the venue of the next ESACT Meeting in 2009 will be in Dublin, Ireland. The Chairman of the Organising Committee for this meeting will be Michael Comer assisted by the National Institute of Cellular Biotechnology (NICB; www.nicb.ie) at Dublin City University (www.dcu.ie) with their Director Martin Clynes. The Committee is comprised of key-representatives of Academia, Government Agencies and Industry. By name (alphabetically) in addition to Comer and Clynes:

Beggan, Margaret; *NICB (Secretariat)*, Bonham-Carter, John; *Magellan Instruments*, Byron, Marian; *Irish BioIndustry Association (IBIA)*, Kenny, Gerry; *Industrial Development Agency (IDA)*, Jenkins, Nigel (Chair of Scientific Committee); *National Institute of Bioprocessing Research and Training (NIBRT)*, Magee, Declan; *Enterprise Ireland (EI)*, Marison, Ian; *Dublin City University (DCU)*, Shaw, Reg *Health Research Board (HRB)* and *Wyeth*, Moran, Enda; *Wyeth*, Moran, Matt; *Pharma Chemical Ireland (PCI)*, O’Driscoll, Donnacha; *NICB*, Smith, Rodney; *Alpha Biologics*, Swiderek, Halina; *Roche Switzerland*.

The above will be assisted by an events organising company *Platinum One* headed by Directors; Terri Cullinane & John Burke. The Company has organised many major events in Ireland and abroad.

The Scientific Committee will be Chaired by Nigel Jenkins, NIBRT, Ireland helped and guided by Frank Gannon, Science Foundation Ireland SFI, Terry Papoutsakis, University of Delaware, USA, Martin Fussenegger, ETH, Switzerland, Martin Clynes, NICB, Ireland, Hansjorg Hauser, Helmholtz Zentrum,

Germany, Wei-Shou Hu, University of Minnesota, USA, Rod Smith, Alpha Biologics, UK. We are confident that this group can solicit an excellent scientific programme.

The proposed conference theme is:

*“Coming of Age – Future Horizon
for Cell Technology”*

ESACT will hold its 21st Meeting in Dublin so it seems appropriate to reflect on the past a little and to see how this could impact on our thoughts for the future. The Organising and Scientific Committees agreed that the event in Dublin should focus on looking forward especially to the applications of cell technology and the benefits to the community, the consumers, the environment and those who gain most from the scientific and clinical endeavours i.e. the patients. Therefore as well as the traditional kind of presentation this conference will investigate a slightly different approach to previous ESACT conferences. It will try to focus more on the uses of cellular technology and its many applications and successes indeed along with some of the regulatory obligations that need to be addressed by both large and small companies.

Also, since many of the “oldies” of ESACT are or will be retiring around this time, it was thought appropriate to reflect a little on the past and seek to discover if the “elders” could have predicted the impact of their passions some thirty to forty years ago. So there will be a short panel discussion of as many oldies as we can revive! This will be followed by recognizing and rewarding a presentation that could display results of importance in cell technology that could be plausibly given in 30 years time (judged by the “oldies”). The candidates for this prize would be post docs of <5 years. The prize will be worth having in the form of a medal (gold and/or silver) with perhaps a sponsored long weekend for two! So if you have a predictive and imaginative mind (with perhaps a sense of humour too) and have had a Ph D recently or expect to have one in a year or two put on your thinking caps and watch this space, for Dublin in 2009. By the way Dublin is also quite well known for its “social” prowess.

See you there!

Michael Comer



ESACT 2007: Boat trip to Pillnitz on the Elbe river. In front: Michael Comer, the chairman for the ESACT meeting 2009 in Dublin

Attention with virus contaminated cell lines

O.-W. Merten

Although (or probably because) quality control efforts are continuously increasing in animal cell technology, sometimes surprising news on contaminated cell lines are arriving. Recently a Japanese group (Li et al. in *J. Virol.* doi:10.1128/JVI.00807-07, published on-line ahead of print on 8 August 2007) working on the development of the production of hepatitis E virus-like particles by infecting High Five insect cells (BTI-TN-5B1-4 (Tn5)) with recombinant baculovirus has observed the appearance of unknown viral particles with diameter of 35 nm containing RNA. The study established that these unknown viral particles were nodaviral particles and that they belong to the genus *Alphanodavirus*. The infection of the Tn5 cells with recombinant baculovirus induced the production of infectious nodaviral particles in parallel to the production of the recombinant protein.

The preoccupying fact is that this nodavirus was latently present in the 'High Five' cells and that other freshly purchased ampoules equally contained cells with latent nodavirus infection.

In principle, the presence of latent virus *per se* might not be a problem, however, in the case of nodaviruses their presence can be an issue because

1st there is a serious risk of contamination by this virus when virus-like particles for vaccine purposes or recombinant proteins for therapeutic purposes are produced using the mentioned cell system, and

2nd nodaviruses (known as viruses infecting insects and fishes) are unique in being able to infect suckling mice and suckling hamsters (Garzon et al. *Arch. Virol.* 113 (1990) 165, Scherer & Hurlbut. *Am. J. Epidemiol.* 86 (1967) 271, Scherer et al. *Am. J. Trop. Med. Hyg.* 17 (1968) 120) with resulting paralysis and death, although no alphanodavirus infections of humans have been reported.

Today nobody knows if the original stock of these cells was contaminated thus we do not know if all established subcultures and all derived subclones of the 'High Five' cells also contain latent nodavirus or not. Therefore, the authors (Li et al.) of the paper further indicated that **all**

cell lines derived from the insect Tn5 cell line should be examined for the presence of such nodaviruses, and that, because of the ability of nodaviruses to establish latent and inapparent infections, all insect cell lines should be screened routinely for the presence of virus.

What does this mean to the producer of biologicals using 'High Five' cells as cell substrate? In the case (the worst case scenario has to be assumed here), that the original stock of the 'High Five' cells was already contaminated and that these cells are used for the production of recombinant proteins for human use or virus like particles for vaccination purposes, either the downstream processing protocol has to be able to eliminate any nodavirus present or potentially present, or, as a total elimination cannot unequivocally be proven, a supplementary virus inactivation step should be added to the purification protocol. Else, 'High Five' should not be further considered for production of biological substances for human use.

How is the situation for other insect cell lines?

- Schneider's cell line 1 (*Drosophila melanogaster* cells): a similar infection by a nodavirus has been reported previously for a sub clone of this cell line (Friesen et al. *J. Virol.* 35 (1980) 741).

- Sf9 cells: With respect to Sf9 cells, Li et al. (*J. Virol.* doi:10.1128/JVI.00807-07) did not find any indication for the presence of a latent nodavirus infection.

- No information is available for other insect cell lines.

And for mammalian cell lines?

With respect to mammalian cells, many virus contaminations have been observed during the past and more details can be found in Merten (*Cytotechnology* 39 (2002) 91).

As a conclusion, I would like to ask any 'cell culturist' to follow the recommendations of Li et al. (*J. Virol.* doi:10.1128/JVI.00807-07) and to be cautious because almost any animal cell is a potential virus producer. Although routine virus testing is a must and a valuable means for reducing the risk of using virus contaminated cell lines, it does not provide absolute safety because of the possibility of new emerging viruses and the permanently existing risk of contaminations by adventitious agents and viruses. Thus the users of animal cells as well as the producers of biotech products by using animal cells have to be attentive to this possible threat and they have to assure the absence of adventitious agents/viruses by any means.

O.-W. Merten, *Evry/F*



Trichoplusia ni

Report on the Biochemical Engineering XV Conference July 15-19, 2007 (Québec City, Canada)

Georg Schmid

After having enjoyed a scientifically very stimulating but “cell culture only” ESACT Meeting in Dresden, Germany in June around 15-20 ESACT participants and/or speakers opted to attend the **Biochemical Engineering XV Conference** held in Québec City, Canada just a few weeks later. From a total of 250 participants 70 colleagues came from outside North America with ca. 35% of all meeting participants working in industry.

This year's conference gave all attendees the opportunity to explore the breadth and scope of biochemical engineering. The conference organizers Mike Betenbaugh (Johns Hopkins University) and Vijay Yabannavar (Trubion Pharmaceuticals) and the organizing /advisory committees had decided to include different sessions dedicated to important research thrusts at the molecular, pathway, organelle, cellular, and multicellular or population level as part of the conference theme of “**Engineering Biology from Biomolecules to Complex Systems**”. In addition, the meeting provided sessions on current “hot” topics such as bioenergy, vaccines, nanotechnology, high throughput/omics technologies, mathematical and systems biology together with sessions dedicated to the biochemical engineering “core areas” (downstream processing, expression platforms, process development, analytics, data analysis, education, and formulations), whereby 6 out of 17 sessions were run as parallel sessions.

While the Biochemical Engineering Conference series is clearly positioned to cover a broad range of topics in biotechnology and is more academia and basic-science driven as other meetings, myself and other participants felt that exactly this was a great additional merit of this conference. Of course, many of us as ESACT members wear (mostly) the cell culture hat, but its always stimulating to see the greater picture and to look over the fence. Here is the link to the conference website for checking out more information if you are interested: www.engconfintl.org/7am.html

In the following I will focus for the main part on sessions/presentations that are of immediate relevance to animal cell culture and that complement it or may even have the potential to compete with it some day in the future.

• **Post-Translational Processing and Molecular Assemblies**

Jim Swartz (Stanford University) presented his group's latest results on cell-free protein synthesis (also presented at ESACT Dresden). Product titers of 400 mg/L were achieved for GM-CSF, likewise 400 mg/L (in 5 hrs) for IGF-1 at the 2 ml, 50 ml and 1 L scales. Quote: “Why cell-free synthesis works so well? 80% of the ribosomes are used in the cell-free system and transcription/translation and folding are performed in the same compartment.”

Laura Palomares (Universidad Nacional Autonoma, Mexico) introduced us to virus-like particles obtained from VP2 and VP6 rotaviral proteins. VP6 on its own can assemble in nanotubes of ca. 50 nm diameter and a length of a few micrometers. It can also form double-layered particles made up of VP6 and VP2. The kinetics of assembly and disassembly of VP6 in nanotubes and virus-like particles was studied.

Martin Gawlitzek (Genentech) gave an overview on the influence of cell culture conditions on glycosylation of recombinant proteins. He covered a broad range of effects on N- and O-glycosylation (including site occupancy, galactosylation and sialylation), e.g. Gal and ManNAc feeding, NANA percentage depends on qp, qp is affected by butyrate addition times, ammonia effects pH and the activity of transferases, temperature and divalent metal ion Mn^{2+} (+ Fe^{2+}) concentrations influence site occupancy.

Matthew DeLisa (Cornell University) presented results and concepts towards a humanization of the N-linked glycosylation machinery in bacteria. Their initial efforts tackle 2 limitations: (1) Prokaryotic oligosaccharyltransferases (OTase) attach glycans to proteins after their folding in the periplasm. Thus glycosylation is decoupled from the translocation machinery and glycosylation sites are constrained within flexible parts of folded proteins. (2) The glycan structure displayed on all prokaryotic N-linked glycoproteins is identical and, as a result, lacks the immense diversity of eukaryotic glycoproteins. This is because the Golgi trimming steps are completely absent from bacteria which lack the necessary compartmentalization. Similar to Markus Aebi at the ETH in Zurich they use synthetic E. coli strains that can perform recombinant N-linked protein glycosylation to introduce a human-like OTase machinery capable of efficient cotranslocational glycan attachment. Second,

they developed methods for intracellular protein assembly resulting in pseudo-compartmentalization within bacterial cells.

- **Downstream Processing**

Alois Jungbauer (University of Applied Sciences, Vienna) described the refolding of *E. coli*-derived proteins in batch and continuous processes. Latest developments using chromatographic refolding can be designed for feed concentrations of unfolded proteins of up to 10 g/L.

Andrew Zydney (Penn State) spoke about the potential application of ultrafiltration for the purification of plasmid DNA for gene therapy and DNA vaccination. Critical process parameters and issues of product quality (i.e. flow-induced elongation of plasmid) were addressed.

Do we really need Protein A (chromatography) for large-scale monoclonal antibody purification was the question put forward in the talk by **Sundar Ramanan** (Amgen). As an example a chromatography-based 2 t per annum process was compared to a non-chromatographic precipitation-based approach. Differences and (dis)advantages were pointed out e.g. differences in HCP removal or the importance of crude antibody titer (0.8 vs 5 g/L) on superiority. In principle, alternative capture operations include precipitation, liquid-liquid extraction systems, crystallization as well as membrane chromatography and filtration. Please refer to a very comprehensive review by Low et al., *Future of Antibody Purification*, *J. Chromatogr. B*, 848(1), 48-63 (2007).

- **Expression Platforms and Accelerating Process Development**

Mark Leonard (Wyeth) reported on benefits of an integrated approach to cell line and platform process development with regard to timelines and process outcome. Several examples were given for cell line stability (“hard to predict”) and candidate selection during manufacturability assessment. Their “generic” DSP process consists of Protein A, AEX, virus filtration and UF/DF steps with the challenge of aggregates remaining. For one antibody a final titer of 10 g/L after 17 days was obtained at the 1 L scale (also presented at ESACT Dresden).

Wim Quax (University of Groningen) and **Timothy Dodge** (Genencor) presented data on using *Bacillus subtilis* and *Trichoderma reesei*, respectively, as expression platforms for biopharmaceuticals. Of course, both hosts have been used extensively to produce homologous proteins, i.e., industrial enzymes, over the past several years. Both genomes are sequenced. With *B. subtilis* a final titer of > 300 mg/L

for fully functionally active huIL-3 (133 AA, 1 correctly formed S-S bond) was achieved when using multiple protease-deficient strains. Among other points, a better understanding of the *Bacillus* “secretion stress” system and the disulfide oxidoreductases has led to these improvements. The filamentous fungus *Trichoderma reesei* is one of the most efficient cellulase producers and has a long history in producing hydrolytic enzymes. Several mutant strains can produce cellulases of 40 g/L and the major cellulase, CBH I, accounts for about 50% of all its secreted proteins. Thus, the strong *cbh1* promoter has been used to construct highly-efficient expression vectors to yield homologous and heterologous proteins. As with other filamentous fungi e.g. *Aspergillus niger*, *T. reesei* can be used to produce full-length antibodies and Fab fragments in a fusion protein approach in a typical 5-day fed-batch fermentation. Glycosylation is of the high-mannose type as expected in fungi and yeasts.

Relevant to all ESACT colleagues that are concerned with the expression of 7 transmembrane receptor (7TM), or G-protein coupled receptor (GPCR), proteins for structural studies **Michelle O’Malley** (University of Delaware) gave a highly interesting presentation on engineering approaches to GPCR expression in yeast. **Anne Robinson’s** group has established an expression system for the human adenosine (A2a) receptor, as well as the eGFP and 6His tagged forms, in *Saccharomyces cerevisiae* using appropriate pre-pro leader sequences to introduce the receptor into the ER membrane. All clones studied exhibited a decrease in the net A2aR-GFP protein production rate over time as determined by various techniques. However, mRNA levels remain high during expression and protein degradation was low. Most importantly, though, the amount of functionally expressed A2aR-GFP per culture (~4 mg/L) is among the highest reported for any GPCR in any expression system. A method to purify the A2aR-His6 protein to homogeneity was established (while maintaining its activity) with yields of greater than 1 mg/L. A poster presented by O’Malley won the **Best Overall Poster Award** of the conference.

- **Analytics and Product Quality Studies in Biochemical Processes**

An example of achieving post-market yield improvements for biologics while maintaining product quality attributes was presented by **Kathy Carswell** (Genentech). Multifactor interactions of % hydrolysate (vs chemically defined), pH, temperature at shift, temperature shift timing, seeding density and basal medium concentration (1.2-1.5x) were evaluated with respect to titer and product quality. Quality as a function of hydrolysate was assessed after the primary recovery step. When settling with an animal

hydrolysate (!) the culture viability could be kept at 60% up to day 14 and the goal of a 50% increase in product titer was met.

Jifeng Zhang (Amgen) elaborated on a cytidine diphosphate and uridine diphosphate modification of Ser54 on the heavy chain's variable region of an undisclosed antibody. It was noticed by the growth of pre-peaks in SEC chromatography in the depth filtrate as a function of time (no aggregation). The molecules were found to be more acidic than the main peak and identified by LC/MS (+385 and +386). Yeastolate used in the preparation of the culture medium contributed to the modification more than any other cell culture component. The conversion could be stopped when medium was protected from light. The exact mechanism of the modification remains unknown.

- **Product Formulation, (In)Stability and Preservation**

Efforts to improve natural proteins while maintaining efficacy and safety were covered in the presentation by **John Beals** (Eli Lilly). In 2 of his examples protein solubility was of main concern (Leptin, FGF). In the Leptin case 2 mutants for hydrophobic surface AAs were created resulting in increased solubility. High injection site reactions were still observed for 1 mutant (similar to the wild-type), whereas the other mutant had improved properties. In a 3rd example the rapid deamidation in 1 CDR of an IL-1beta mAb was noticed.

90% of material was deamidated as function of pH and temperature by day 14. Point mutations were introduced to eliminate the problem, however, all of them failed due to loss of efficacy. Obviously combinatorial changes in CDRs are very critical.

Ranjini Ramachander (Amgen) presented on the topic of biophysical characterization of antibodies and fusion proteins for manufacturability assessments for early stage candidate screenings. They use a whole array of biophysical tools for determining the impact of aggregation and misfolds on secondary (Far-UV CD, FTIR, Raman) and tertiary structure (Near-UV CD, ANS binding, Raman, DLS, analytical ultracentrifugation) to characterize candidates and pick

candidates if bioactivity and PK are identical. So far, they looked in depth at 15-20 mAbs, all different. A database is being built up.

Posters/Plenary lectures: The broad range of topics covered in the oral presentations was equally matched by the ca. 150 posters that were on display. In a series of plenary presentations **Guido Grandi** (Novartis Vaccines) described approaches to develop e.g. universal Group B streptococcus and serogroup B meningococcus vaccines using genome-derived vaccine discovery and **David Robinson** (Merck) put the challenges and opportunities for the pharmaceutical industry in perspective, stressing the importance in the development of novel medicines to expand the druggable space from small molecules to biologics (hormones, mAbs, fusion proteins, etc.) and beyond to oligonucleotides (RNAi).

Another real highlight of the conference was the **Amgen Lecture** presented by **George Georgiou** (University of Texas) with a challenging and "provoking" title for each and every cell culture colleague: **NO-CHO**. In his presentation he described the isolation of full-length IgG antibodies expressed in *E. coli*. Full-length HCs and LCs are secreted into the periplasm, where they assemble into aglycosylated IgGs that are captured by an Fc-binding protein that is tethered to the inner membrane. After permeabilizing the outer membrane, spheroplast clones expressing "E-clonal

antibodies" and recognizing fluorescently labeled antigen, are selected by flow cytometry. Screening of a library constructed from an immunized animal yielded several antibodies with nanomolar affinities toward the protective antigen of *Bacillus anthracis* (Mazor et al., *Nature Biotechnology*, 5, 563-565 (2007)).

In a nutshell: A great conference well worth attending.

Look out for Biochemical Engineering XVI in 2009!

Georg Schmid



ESACT 2007: Manuel Carrondo receives an ESACT medal from the hands of the meeting chairman Hansjörg Hauser.

Notes from the 20th ESACT General Assembly

Stefanos Grammatikos

The 20th General Assembly (GA) of ESACT took place during lunchtime on June 19, 2007, as part of the 20th ESACT Meeting (Dresden, International Congress Center, June 17-20, 2007) and was attended by approximately 60 ESACT members. Florian Wurm (Chairman) welcomed all attendees and presented the agenda of the Assembly which traditionally covers a number of organisational and administrative matters, reports on areas of activity of the Executive Committee (XC), updates on the current and future ESACT Meetings, the results of the XC elections as well as a discussion session featuring feedback/input from ESACT members. A summary of major topics presented and discussed is given below:

ESACT Finances: Treasurer's Report

Martin Fussenegger (Vice-Chairman) reporting for Alain Bernard (Treasurer, excused) presented the current financial balance of ESACT. The financial situation of ESACT is healthy and features a substantial financial reserve. This reserve is considered to be a minimum financial cushion necessary to ensure the continuity of ESACT Meetings, to sustain the activities of the Society between Meetings and to absorb potential financial losses incurred by an ESACT Meeting. While Meetings have been successful in the recent past and the XC is always planning for success, the fact that ESACT Meetings have become huge and represent a large financial liability must not be overlooked.

Membership Issues: Secretary's Report

Stefanos Grammatikos (Secretary) opened this part by updating the audience on the definition of an Active ESACT Member, a term recently coined to mean the Member who shows sufficient interest in ESACT by paying membership fees up to the current year. Following the introduction of an easy-to-use electronic payment system and a number of reminders sent to members, the members' database was cleaned up to reflect this definition. According to this system ESACT has 266 active members (on June 19, 2007). A very large majority of members (77%) still comes from Europe. All continents are represented (15% Americas, 6% Asia, 2% Middle-East/Africa/Australia). 65% of ESACT's members are based either in Germany (21%), the United Kingdom (14%), Switzerland (9%), Sweden (6%), Belgium (5%), Denmark (5%), or Ireland (5%), which is representative of the level of activity in animal cell technology (ACT) in those countries (though not always proportional to their size).

ESACT Members commented that when considering the interest in ACT matters and in ESACT Meetings the current number of members is regarded to be low. The suggestion was made to set the objective to increase membership by 100% in 5 years.

JIN and Website Information

Christophe Losberger (Head of ESACT Office) gave an update on website issues, in particular JIN (Job Information Network). JIN is successfully established, features a large number of job openings and experiences a large number of visits per day. The audience was urged to spread the word and continue to use/support JIN. The issue of financial support was also mentioned. Generous contribution of Astra Zeneca was acknowledged and a call for further financial support was made.

Dresden 2007 Report

S. Grammatikos reporting for Hansjoerg Hauser (Dresden Meeting Chairman, excused) informed the audience that the 20th Meeting is on its way to becoming a great success as reflected in the record attendance, number of exhibiting companies, overall quality of presentations, the food, the (fortunately) good weather and the social events. This sentiment was shared by the audience, although individual members expressed disappointment from the level of certain oral presentations. For impressions and a summary of the Dresden Meeting statistics please see Hansjoerg Hauser's article in this issue of the Newsletter.

Update 2009 Meeting (Dublin)

Michael Comer (Dublin Meeting Chairman) gave an overview of the current status of the preparations, which are all at a rather early stage. The Organizing Committee is defined, the venue is likely to be City West Resort and the social events will be designed to offer the best in Irish music, song, dance and fermentation.

Information on the 2011 ESACT Meeting and beyond

F. Wurm announced that Prof. Hermann Katinger has accepted to host the 2011 Meeting in Vienna, Austria. Proposals on meeting venue and interested persons to organize the 2013 Meeting are always welcome.

Feedback/Discussion on the Newsletter

F. Wurm and C. Losberger led a discussion on members' perception of the ESACT Newsletter. The

Newsletter was found by the members attending the GA to be a useful communication tool. Members would like to keep receiving the Newsletter and expressed overall interest and enthusiasm in contributing to it with news and articles. The present form of the Newsletter was deemed adequate.

XC Elections 2007

Electronic Voting Concept

S. Grammatikos presented relevant information on the electronic voting concept used for the first time ever in an ESACT XC Election. Main objectives were to simplify voting, eliminate paperwork and maintain anonymity. These objectives have been achieved.

Announcement of Election Results

A total of 109 members voted by the new electronic method (an increase over previous XC elections where 50-80 members typically would vote).

The Executive Committee for the period 2007-2009 has the following composition:

Ordinary Members (elected by the members):

Paula Alves

Dana Andersen

(first XC Member ever to be active outside of Europe)

Francesc Godia

Hansjoerg Hauser

Officers (nominated by the previous Executive Committee):

F. Wurm (Chairman)

M. Fussenegger (Vice-Chairman)

S. Grammatikos (Secretary)

A. Bernard (Treasurer)

M. Comer (Meeting Chairman 2009)

S. Grammatikos thanked all the candidates for coming forward and showing interest in contributing to ESACT matters. F Wurm/S Grammatikos thanked also the previous Executive Committee and in particular Otto Merten and Rodney Smith, who decided to step down, for their contributions to ESACT matters and interests via Meeting organisations and Executive Committee memberships.

Discussion Session: Members' Comments/Suggestions

All comments and wishes of participating ESACT members as expressed during a lively discussion are summarized according to category below:



ESACT MEETINGS

- More bursaries and financial support for academics
- Avoid putting all participants in one big and expensive hotel, by also offering cheaper hotels
- Consider including in the Meeting program a session on regulatory issues (QbD; PAT), possibly as a workshop if not as a regular session.

ESACT MEMBERSHIP

- From available information (website etc) it is not clear that ESACT Membership is open to the world. Still regarded as a "European Club". Please make this fact clearer.
- The application for membership is not easily accessible
- Strive for more members

EXECUTIVE COMMITTEE

- Include as part of the ESACT Meeting (for example in opening speech or in closing speech) a Review/Report of the Chairman on what happened within the Society in the last two years. What initiatives were taken, what has been achieved etc.
- Consider establishing an ESACT Secretariat (Executive Secretary, part-time or full-time)

The ESACT Executive Committee thanks all members for their feedback, is open for comments, suggestions and criticism at all times (not only during the General Assembly) and will consider all current and future suggestions.

Stefanos Grammatikos

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