

Conference Report

Medicinal Chemistry and Chemical Biology (DMCCB) Session of the SCS Fall Meeting 2016, University of Zurich, Irchel Campus, September 15th, 2016

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Who said industry and academia have a hard time meeting each other? Certainly not the attendees of the Session of Medicinal Chemistry and Chemical Biology of the SCS Fall Meeting 2016. During this event that took place on September 15th on the Irchel Campus of the University of Zurich, the Division of Medicinal Chemistry and Chemical Biology (DMCCB) held a session endowed by Actelion Ltd, presenting 80 scientific contributions, including 68 posters and 11 talks. After an overview of the activity of the DMCCB in 2016 and the election of the DMCCB Board, the rest of the morning and afternoon sessions, chaired by Yves Auberson (Novartis, President of the DMCCB) and Jean-Louis Reymond (University of Bern, Vice-President of the DMCCB) respectively, showcased top level Swiss medicinal chemistry and chemical biology research. Interestingly, the program presented a very fair mix of academic and industrial oral contributions, with six and five speakers from each domain respectively.

News from the DMCCB

The morning session was opened by *Yves Auberson*, who gave an overview of what has been a very successful year for the DMCCB. Among the highlights of the DMCCB activities, he brought back from the last European Federation for Medicinal Chemistry (EFMC) Council that took place on August 27–28th 2016 in Manchester the news of his election as the next EFMC



Fig. 1. Basel will host the XXVI EFMC International Symposium on Medicinal Chemistry in 2020. This event is a major rendez-vous for European medicinal chemistry.

President for 2018–2020. This appointment will with no doubt strengthen the contribution of Switzerland to Medicinal Chemistry in Europe, and the visibility of the Swiss scientific community. Secondly, the DMCCB managed the successful bid for the XXVI EFMC International Symposium on Medicinal Chemistry (EFMC-ISM 2020) in Switzerland. Taking place on a biannual basis, the EFMC-ISM is the major assembly of industrial and academic medicinal chemists in Europe, usually attracting over 1000 participants. Thanks to this successful application, the 26th edition will be organized by the DMCCB in Basel on September 6–10th, 2020 (Fig. 1). Prof. Karl-Heinz Altmann (ETH Zürich) will be the Chair of the Symposium. Congratulations to the Local Organizing Committee!

Among the announcements regarding major upcoming events for the Division, the ‘Frontiers in Medicinal Chemistry’ meeting will take place in Switzerland for the first time (Bern, February 12–15th, 2017). Co-organized by the DMCCB, the Medicinal Chemistry section of the GDCh (Gesellschaft Deutscher Chemiker) and the DPhG (Deutsche Pharmazeutische Gesellschaft), this international symposium will focus on current developments, novel approaches and cutting-edge technologies in the field of medicinal chemistry and drug research.

To conclude this session, DMCCB Board members were elected by the participants as follows: Yves Auberson (Novartis – President), Jean-Louis Reymond (University of Bern – Vice-president), Leonardo Scapozza (University of Geneva – Treasurer) and Georg Jaeschke (F. Hoffmann – La Roche – EFMC Council Member) were re-elected unanimously. Karl-Heinz Altmann (ETH Zurich – Past president) was re-elected as board member. Two new members integrated the board: Finton Sirokin will take over the role of webmaster to replace Nikolas Stiefl who held this responsibility for six years, and Anaëlle Dumas will be in charge of the DMCCB communication, including its activity on social media. This brings the board to a panel of twelve active members, which is available with all contact details on our website *SCG.ch*.

Top-level Talks



Fig. 2. Martin Hans Bolli (Actelion Pharmaceuticals Ltd), laureate of the KGF-SCS Industrial Science Award 2016 (Photo taken by Simeon Lüthi).

The scientific program of the session was composed of eleven talks from young and confirmed researchers issued from the industry and academia. All of them showcased brilliant presentations about medicinal chemistry hot topics.

The first lecture was given by *Martin Hans Bolli* (Actelion Pharmaceuticals Ltd), who was the laureate of the KGF-SCS Industrial Science Award 2016 (Fig. 2). In this very interesting talk, Dr. Bolli discussed

the unconventional medicinal chemistry success story leading to the discovery of Macitentan, an approved drug for the treatment of pulmonary arterial hypertension. This journey was characterized by the use of *in vivo* experiments assessing compound efficacy and safety to lead the discovery process. Inspiringly, Martin Hans Bolli illustrated how this successful approach can be applied to other drug discovery programs.

The audience then had the opportunity to hear:

- **Kristina Goncharenko** (University of Basel, F. P. Seebeck) with her talk ‘Deciphering the catalytic mechanism of the sulfoxide synthase EgtB’, who described a model of the catalytic mechanism of an unusual non-heme iron enzyme that catalyzes the formation of sulfur-carbon bonds.
- **Brigitte Fiege** (University of Basel, T. Maier) described the rational development of antagonists of FimH, a bacterial lectin attaching glycoproteins on urothelial cells, preventing clearance from the bladder and enabling infection in a talk entitled ‘A sticky interaction: Optimizing the hydrophobic stacking between the tyrosine gate of the bacterial lectin FimH with antagonists’.
- **Frédéric Stauffer** (Novartis Pharma AG) showcased ‘The discovery of a potent and orally available Dot1L inhibitor’. Here, a structurally novel series of Dot1L inhibitors was described. These bioavailable compounds might present a solution to certain acute leukemia caused by the misdirected catalytic activity of Dot1L, an enzyme responsible for histone methylation.
- **Romain Siegrist** (Actelion Pharmaceuticals Ltd), in ‘Optimization of 1,4-disubstituted benzodiazepines as selective and brain penetrant triple calcium T-Channel Blockers’, related the optimization of highly potent compounds that were largely impeded by their poor physicochemical properties and low stability, leading to a compound with interesting *in vivo* efficacy in a model of absence epilepsy.
- **Pascal Röthlisberger** (Institut Pasteur, M. Hollenstein) presented a method to elucidate the three-dimensional structure of oligonucleotides involving derivatization with an L-fucose residue to trigger interaction with a protein that serves as co-crystallization agent in his talk ‘A FUC/LecB system to crystallize versatile nucleic acid structures’.
- **Martin Pouliot** (Syngenta Crop Protection) described the ‘Synthesis and oomycete fungicidal activity of a new family of inhibitors targeting an oxysterol binding protein’.
- **Tobias Brüttsch** (ETH Zürich, K.-H. Altmann) presented his work on the synthesis and SAR around polyketide with highly unsaturated macrolactone core structure in a talk entitled ‘Stereoselective synthesis and biological evaluation of highly potent new (–)-zampanolide derivatives’.
- **Robert Pulz** (Novartis Institute for Biomedical Research) presented the ‘Discovery of a potent and selective reversible BTK inhibitor for the treatment of autoimmune diseases’, describing SAR efforts to improve physicochemical properties, metabolic stability and solubility of a lead to present a compound that showed efficacy in two animal models.

- **Erika Crane** (University of Basel, K. Gademann) described the ‘Investigations for new therapeutic targets for neurodegenerative disease’ using activity-based protein profiling studies driving the discovery of novel hits in the context of neurodegeneration and identification of new targets of relevance to the mechanism of action of withanolide A.

Focus on the Winner



Fig. 3. Olivia Paula Schmidt, winner of the Medicinal Chemistry & Chemical Biology best presentation award.

The best oral presentation award went to **Olivia Paula Schmidt** (University of Zurich, N. W. Luedtke), who convinced the jury composed of Yves Auberson (Novartis), Jean-Louis Reymond (University of Bern), Georg Jaeschke (F. Hoffmann – La Roche) and Michele Leuenberger (University of Bern) with the presentation of her work on the ‘High kinetic stability of T-Hg^{II}-T and DNA polymerase inhibition’ (Fig. 3). In her thrilling talk, Olivia Paula

Schmidt described the use of ^{DMAT}, a new fluorescent thymidine mimic composed of 2'-deoxyuridine fused to dimethylaniline, to characterize Hg^{II} binding to duplex DNA. The fluorescence quenching of ^{DMAT} upon Hg^{II} binding was used to assess the exceptionally high kinetic stabilities of T-Hg^{II}-T base pairs. Their results showed that the kinetically stable T-Hg^{II}-T base pairs have the potential to disrupt DNA metabolism including DNA–DNA strand-displacement reactions and enzymatic DNA synthesis. The work of this young scientist may contribute to explain the poorly understood cytotoxic activities associated with Hg^{II} exposure.

Four prizes were also distributed for the best poster presentation awards in Medicinal Chemistry & Chemical Biology. These awards were attributed to **Fabian Brockmeyer** (Northeastern University) and **Marc Heitz** (University of Bern). Runners-up for this prize were **Fahimeh Moradi-Afrapoli** (University of Basel) and **Isabel P. Kerschgens** (University of Zurich).

The DMCCB warmly congratulates the winners, thanks all participants for their overall excellent scientific contributions that highlight the outstanding level of Swiss research in the field, and hopes to see you in Bern on February 12–15th, 2017 at the ‘Frontiers in Medicinal Chemistry’ event.

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