NCCR CHEMICAL BIOLOGY

NEWSLETTER

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EDITORIAL

EPFL's Biomolecular screening facility. © Gerardo Turcatti / EPFL

Chemical Biology is a relatively new discipline which follows in the tradition of Biological Chemistry and Biochemistry. It distinguishes itself from its predecessors as it focuses on the uses of chemistry to probe living systems in situ. The Chemical Biology field is now developing intensively and we can expect many new tools and concepts in the future.

The main goals of the National Centre of Competence in Research (NCCR) Chemical Biology led by UNIGE and EPF Lausanne are to participate fully in these new developments, to become one of the leading scientific centers in this discipline and to train the future leaders in the field.

We believe that novel technologies drive the major scientific discoveries and therefore, we emphasize the development of new techniques and approaches. Interdisciplinarity (chemistry, biology, physics) is at the heart of our endeavor. We also provide an enabling technology in the chemical biology field with our chemical screening platform, ACCESS.

It is with great pleasure that we are launching the NCCR Chemical Biology quarterly newsletter. We wish to keep in touch with members and friends of the NCCR Chemical Biology, but also to reach out to a larger scientific community and inform about the services that we provide.

Each newsletter will have one main theme and a series of interesting and entertaining pieces contributing to a Chemical Biology culture, such as an unusual interview with a distinguished leader in the Chemical Biology field, a choice of important and recent articles in the field selected by one of our investigators and a visually entertaining selection of images produced by NCCR labs or curated from the web.

This first issue has as its major theme **our Chemical Screening Platform ACCESS**: please discover an extensive presentation of its facilities, what role and mission for Switzerland we envision and read about its major achievements, success stories and ongoing call.

CONTENT

Finally, I take this opportunity to inform you about the **International Symposium on Chemical Biology** that will take place at the Campus Biotech in Geneva from January 13 to 15, 2016. We have recruited an outstanding group of speakers in the field and this 2 ½ day meeting will be intense and extremely interesting. Registration is obligatory, but very inexpensive (100 CHF) and travel grants will be available for young researchers. This meeting is a truly unique educational event. Don't miss it.

I hope you will enjoy this first issue. Please read, comment and share!

Howard RIEZMAN
Professor at the Department of Biochemistry, University of Geneva and Director of the NCCR Chemical Biology.

WHAT IS ACCESS ?

Created in 2006, the Academic Screening Platform of Switzerland (ACCESS), a part of the NCCR Chemical Biology, based in the Biomolecular Screening Facility in EPFL, allows scientists throughout Switzerland to perform academic screenings among a library of ~130'000 siRNAs and ~100'000 small molecules. This facility puts its knowledge, know-how and equipment to the service of the Swiss scientific community to harness the power of chemical biology.

ACCESS, which stands for "Academic Chemical Screens in Switzerland", is such a platform. It enables researchers to run from complex phenotypic screens to more classical in vitro biochemical target-based assays and provides a large diverse collection of chemical compounds. Furthermore, ACCESS has competences in chemo-informatics to analyse results and assist with hit expansion.

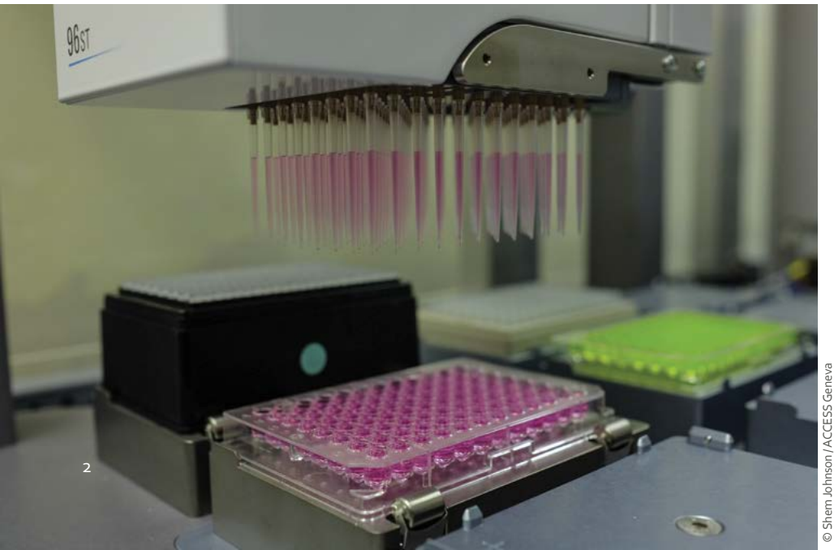
The main core of ACCESS (BSF-ACCESS) is integrated within the Biomolecular Screening Facility (BSF) of EPFL. An antenna of ACCESS (GENEVA-ACCESS) is being developed at the Department of Biochemistry of the University of Geneva.

Retrospect

BSF was established in 2006 at EPFL as a central "client-oriented" facility within the Life Science Faculty to allow researchers to perform screens with libraries composed of chemicals and siRNA's using both various in vitro and cellular assays, in very diverse fields such as neurobiology, metabolic diseases, infectious diseases and cancer. This represented an ambitious goal, in terms of performing assays in an academic setting and at high throughput rate, as the endeavour required the implementation of a sophisticated infrastructure with industrial rigour.

During the preparation of the NCCR Chemical Biology in 2010, the creation of ACCESS was envisaged. Its implementation within the already well running BSF structure came as a logical solution, but urged to further developing it: the chain-of-custody, quality control, sophisticated storage and hand-out systems, as well as the size of chemical collections and the screening capacity of the infrastructure had to increase in order to perform more chemical screening projects.

Recently, in 2014, an ACCESS antenna was established at UniGE to expand in particular the capacity for high content screening, as well as to give a rapid and in-house access to the several Geneva-based NCCR Chemical Biology groups.



© Shern Johnson / ACCESS Geneva

What does ACCESS offer to NCCR and to Switzerland?

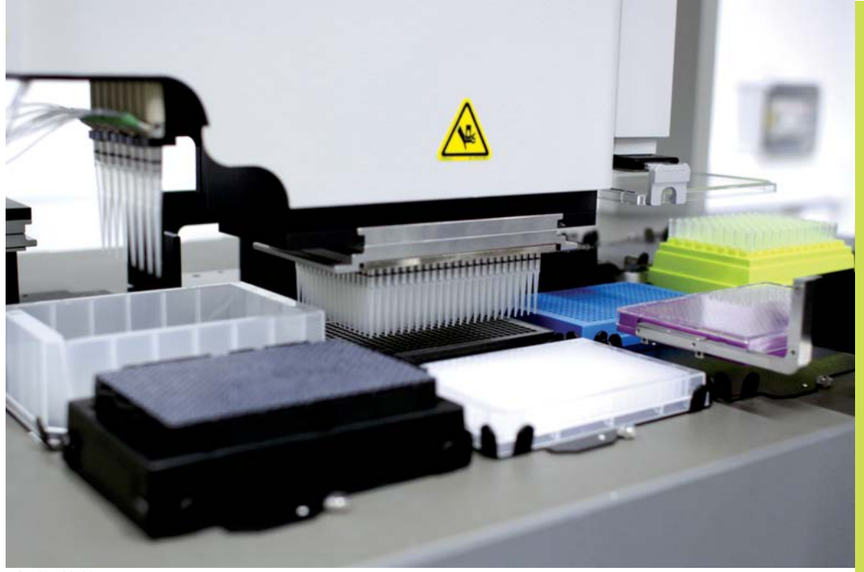
Sound expertise. ACCESS is a bundle of expertise for assay validation – execution and evaluation, which is an essential support for both young and experienced researchers who want to perform screens.

State-of-the-art infrastructure. The robotic infrastructure of ACCESS like the liquid handling systems, including acoustic pipetting and the appropriate expertise is there to provide support in assay development and automation for the screens to be performed.

Plethora of screens possibilities. ACCESS proposes a wide variety of multimode readouts for collecting total microtiter well signal and automated fluorescence microscopy for screening by imaging. Massive screening experiments called "high-throughput screens" (HTS) or image-based "high-content screens" (HCS), and the necessary data management and analysis systems to evaluate these results were established.

Rich chemical library collection. A highly diverse chemical library is available that comprises approximately 100'000 compounds from various commercial sources including a few specific libraries. This assembly of chemical compounds provides large coverage of the chemical 3D-structural space for drug–like molecules, and contains admitted drugs as well as natural compounds.

Swiss Chemical Collection. In complement to it, ACCESS develops a collection of unique chemical diversity obtained from various Swiss chemistry laboratories (the Swiss Chemical Collection-SSC), giving the community access to compounds that cannot be found elsewhere.



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Regular calls for sponsored screening assays. The NCCR Chemical Biology promotes the use of this powerful discovery platform, and has launched recently, and will continue to do so in the future, calls for screening proposals related to chemical biology to the entire Swiss community to be subventioned by the NCCR (see below the corresponding information for the present call). Indeed, for many groups, there is a big barrier to start with screening, both conceptually and financially. The aim of these calls is to promote and facilitate this process, which can lead to exciting results.

Education and training. A major mission of ACCESS is to educate the users in both the trade of screening as well as in the methods of performing rigorous data analysis, and lead/hit validation and optimisation. In this respect, novel software is developed and implemented, and courses or workshops are regularly organized at both EPFL and UNIGE antennas to train users on these applications.

Focus on the Swiss Chemical Collection

Chemists in Switzerland produce a plethora of molecules of very diverse and novel structures. By adding these compounds to the **Swiss Chemical Collection**, these molecules will be preserved at BSF-ACCESS and made available to the Swiss community for their bioactivity testing in a large number and variety of assays.Currently, over 500 compounds have been deposited, verified and incorporated into the BSF-ACCESS collections.

SCC is a perfect example of a win-win situation: the chemist valorises his compounds and the screener might find a perfect hit!

ACCESS: a success?

In the context of ACCESS, the term "success" acquires a multifaceted meaning. It could refer to the establishment of a large compound collection and its efficient maintenance, or to the education of users and the elaboration of data evaluation strategies. Furthermore, it could refer to the creation and validation of a novel screening-compatible assays, to the identification of a "hit" yielding interesting biological insight, even to the development of a hit into a potential therapeutic agent and the formation of start-ups formed from compounds discovered within its premises.

All these successes certainly bring satisfaction and are important to argument and motivate the presence of ACCESS. But there is one additional success factor that should not been forgotten: the BSF-ACCESS team, which unites a group of highly experienced and motivated staff to keep the facility operational in terms of compound management, assay development and infrastructure, assist the clients and establish new assays and novel technologies with hard labour and rigour.

EPFL BIOMOLECULAR SCREENING FACILITY BSF ACCESS ACADEMIC SCREENING PLATFORM FOR SWITZERLAND

ACCESS GENEVA ACADEMIC SCREENING PLATFORM FOR SWITZERLAND

ACCESS IN NUMBERS

Thanks to ACCESS developments the capacity of the platform has been increased. From 2013 onwards, more projects have been handled and brought to completion in a shorter time, depending on the complexity and novelty of the individual screens.

According to current human and infrastructure resources available and using statistics based on deliverables for the period 2013-2015, BSF-ACCESS has the operational capacity for handling and finalizing 15-20 primary screening projects per year of different kinds and sizes:

- 4-5 projects targeting > 50'000 compounds
- 5-6 projects targeting 5'000 to 10'000 compounds
- 6-9 projects targeting < 5'000 compounds

It is important to highlight that most of the projects require hit confirmations through dose responses and other validation procedures, which are not accounted for in the above statistics. These steps are time and resources consuming with respect to the relative low number of data points generated but they represent necessary high added-value tasks to any screening campaign.

CALL FOR SCREENS

The NCCR Chemical Biology is launching a call for chemical screening proposals organized by BSF-ACCESS. The selected projects will be sponsored by the NCCR Chemical Biology after project evaluation by the ACCESS steering committee.

Only members from non-profit Swiss Academic Institutions are entitled to apply exclusively for high impact Chemical Biology projects.

The selection procedure will be based on Chemical Biology scientific relevance and feasibility for adapting the proposed assay to a high throughput screening format.

Download application form from
http://bsf.epfl.ch

Deadline for submission:
December 15, 2015

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FROM ACCESS TO SUCCESS

The efficiency of the platform and the significant added value of successful collaborations between academic research groups and ACCESS were demonstrated as shown by the amazing stories behind ACCESS's very first large-scale screens.

New approaches for tackling neuropathic pain

Old drugs have often poorly understood mechanisms of action. An excellent example is sulfasalazine, which has been heavily used since 1942 as an anti-inflammatory and analgesic agent in rheumatoid arthritis and ulcerative colitis. Only recently has the group of Professor Kai Johnsson from the NCCR Chemical Biology, based at EPFL, identified sulfasalazine as an efficient inhibitor of tetrahydrobiopterin (BH_4) biosynthesis and postulated that inhibition of BH_4 biosynthesis contributes to its mechanism of action (ref. 1). Specifically, the group was able to show that sulfasalazine is a potent inhibitor of sepiapterin reductase (SPR), the final enzyme in the biosynthesis of BH_4.

In independent work, the group of Professor Clifford Woolf at Harvard Medical School had shown that elevated levels of BH_4 are related to chronic neuropathic and inflammatory pain, and hypothesized that inhibition of BH_4 production could relieve pain (ref. 2 and 3). If only a more potent SPR inhibitor with better pharmacokinetic properties than sulfasalazine were available!

Motivated by these results, a robust screening assay was developed at BSF-ACCESS, aiming to find additional SPR modulators and using for the first time a 54'000-compound chemically diverse library designed by the BSF-ACCESS team. This resulted in the identification and validation of highly potent SPR inhibitors, which were shown to reduce the BH_4-dependent biosynthesis of neurotransmitters in cellular assays.

Encouraged by the possibility to reduce chronic pain through SPR-inhibition and the molecules identified by the compound screen, Woolf, Johnsson and Kevin Pojasek from Atlas Venture, launched in 2013 Quartet Medicine, a start-up dedicated to produce new compounds to treat chronic pain and inflammation with a focus on controlling BH_4 levels.

One year after its creation, this promising start-up was highlighted by Nature Biotechnology as one of the Top Academic Start-ups of 2014. Very recently (07.10.15) Quartet Medicine successfully completed a $23 million dollar A-series financing, among which investors are Atlas Venture, Novartis Venture Fund and Pfizer. The company is based in Cambridge, Massachusetts, and has research efforts underway with collaborators in the US, Europe and Asia. In a nutshell, the ACCESS platform generated new BH_4 biosynthesis inhibitors that are now, thanks to the creation of Quartet Medicine, in further development for the treatment of chronic pain and inflammation.

Jacques SAARBACH & Ruud HOVIUS

Jacques Saarbach is a PhD student in Organic Chemistry (Professor Nicolas Winssinger), UNIGE and Ruud Hovius is a Senior Scientist in the Laboratory of Protein Engineering (LIP; Professor Kai Johnsson), EPFL

Innovative therapeutics for unmet medical needs in oncology

Working in close collaboration with the group of Professor Freddy Radtke at EPFL, BSF ACCESS performed screening campaigns of about 75'000 compounds (including the 54K-compound chemically diverse collection) using an innovative co-culture cellular assay to identify novel small molecules capable of modulating Notch signaling, a key cellular pathway controlling oncogenesis and cancer stem cells.

After hits validation and confirmation experiments, valuable newly identified chemical entities triggered drug discovery programs through the creation of the company Cellestia Biotech co-founded by Professor Freddy Radtke and Dr Rajwinder Lehal. The company has a Worldwide Exclusive License Agreement signed with EPFL since June 2014.

Gerardo TURCATTI

Director of the BSF-ACCESS facility (EPFL) and head of the ACCESS project.

Ref. 1: Chidley et al. A yeast-based screen reveals that sulfasalazine inhibits tetrahydrobiopterin biosynthesis. Nat. Chem. Biol. 7, 375 (2011) doi: 10.1038/NChemBio.557.

Ref. 2: Tegeder et al. GTP cyclohydrolase and tetrahydrobiopterin regulate pain sensitivity and persistence. Nat. Medicine 12, 1269 (2006). doi: 10.1038/nm1490.

Ref. 3: Latremoliere et al. Reduction of neuropathic and inflammatory pain through inhibition of the tetrahydrobiopterin pathway. Neuron 86, 1393–1406 (2015) doi: 10.1016/j.neuron.2015.05.033.

HIGH CONTENT SCREENS AT ACCESS GENEVA

How to run an image-based high-throughput experiment?

To answer this question a three-day hands-on course was organized in Geneva last June by NCCR Chemical Biology members Prof. Jean Gruenberg and Dr. Dimitri Moreau. Eight interested researchers from chemistry, pharmacy and other life science disciplines came to the ACCESS location at the Biochemistry department (UNIGE) to receive an introductory training.

Participants learned in alternating lectures and practical sessions how to plan, conduct, record, view, analyze, and interpret a high-through-put experiment. Lectures supplied the theoretical background starting from the assay design and sample preparation, followed by an introduction to automated imaging and machine-based image analysis and leading to the generation of an analysis pipeline and data analysis using different types of statistics. A large part of the course was dedicated to practical sessions that allowed the participants to get to know the fluidic dispenser for cell seeding or the plate washer for sample preparation and staining. The most exciting part was the image acquisition using the automated microscope coupled to the training in image analysis.

The workshop can be considered a success ifthe learned skills are applied by participants after its completion: in our case, six out of the eight participants are now conducting their own screening experiments using the platform.

J. Thomas HANNICH

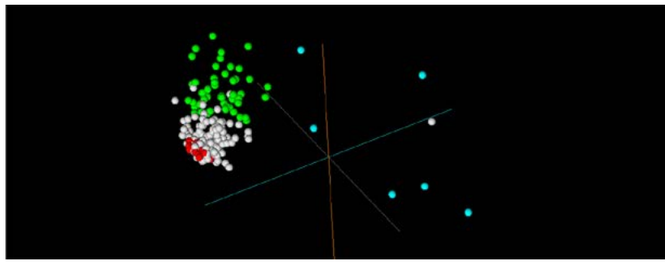
Post-doctoral fellow in Professor Howard Riezman's laboratory at UNIGE.

ACCESS GENEVA is a screening platform at the Geneva University Biochemistry department. It provides local support to academic researchers to conduct image-based high content experiments within the ACCESS framework of the NCCR "Chemical Biology" and its activities are in synergy with the ones from the central ACCESS facility at EPFL (BSF-ACCESS).

ACCESS GENEVA provided infrastructure allows conducting screening experiments in Geneva, storing the data on the local server, and analyzing the image data via vpn on a virtual machine from anywhere.

Interested researchers should contact Dr. Dimitri Moreau, in charge of the platform (dimitri.moreau@unige.ch).

Immunostained cell culture showing protein in green and Nuclei in blue (left), quantitative image analysis using MetaXpress® showing protein in green and nuclei in red (right). Image provided by Dr. Dimitri Moreau.



Principal Component Analysis using AquityXpress® to visualize quantitated differences between samples. Image provided by Dr. Dimitri Moreau.

HERBERT WALDMANN

Professor Waldmann's research interests lie in the structural analysis of natural products for Biology Oriented Synthesis (BIOS), which employs biological relevance and prevalidation to identify novel bioactive compounds for the study of biology.

This work includes the design and synthesis of natural product-inspired compound collections and the development of novel enantioselective synthesis methodology, cell-based screening and identification of the cellular targets of bioactive compounds. A major focus of research in the Waldmann group is on the synthesis of lipidated peptides and proteins, in particular of the Ras superfamily and the development of small molecule modulators of their function.

Professor Waldmann is a speaker at the 2016 International Symposium on Chemical Biology, organized by the NCCR next January 2016. His talk is entitled "Hunting the Targets of Natural Product Inspired Compounds". The NCCR Chemical Biology expresses its warmest thanks to him for participating in the event and for accepting to be interviewed. His insightful responses will certainly inspire the reader.

Why do you serve Chemical Biology?

Because it bridges the two scientific disciplines I have found most fascinating since High School. I am a synthetic chemist, a molecule maker by heart, and I am fascinated by the mysteries of biology.

Describe the most intense moment of your career.

At the University of Karlsruhe we had developed the first synthesis methods to prepare the lipid-modified C-terminus of the oncogenic Ras proteins. When these were investigated in the Wittinghofer lab at the Max Planck Institute Dortmund, and the first microscopy pictures came back showing that our peptides mimicked Ras localization I believed I could fly – it was indeed possible for a synthetic chemist who had never attended any biochemistry or biology class at the University to have an impact in biology. The paper got published in Angewandte, the second appeared in Nature, a few years later I became Director at the Max Planck Institute Dortmund, and the Ras proteins have continued to be one of the two major scientific challenges of my life.

Which is the best idea you have ever had?

To develop a logic that puts one of the mightiest forces in the Universe – evolution – into the center of a principle for the design and synthesis of biologically relevant small molecule modulators of protein function: Biology Oriented Synthesis (BIOS).

Do you have a role-model or a driving force?

Not a role model in the classic sense. But my Ph. D. advisor Horst Kunz and my advisor during Post Doc George Whitesides have set examples I try to match. I pay Stuart Schreiber my highest respect for his boldness and risk taking in catapulting organic synthesis into biology.

The philosophy along which lines you lead your lab?

Good science needs the air of freedom and inspiration. I trust in my coworkers. They joined my lab for a reason, and I give them the time to mature and to rise to the challenges we face.

Pick a paper you praise for the elegance of its demonstration.

In chemistry-rooted research it is often that a group of papers matches this criterion. I choose Kevan Shokat's "bump-and-hole" approach. It is Chemical Biology at its best.

Can you shed light on the relevance of inter-disciplinarity for scientific breakthroughs?

Interdisciplinarity often is key to unusual and unprecedented insight. But at least equally often that is not the case. The importance of Interdisciplinarity for breakthrough research is very high but should also not be overrated. One has to be fully professional in one science (at least).

Define research in just three words.

Lots of fun.

How do you match the words beauty and science?

Beauty I often see in artwork, pictures, sculptures which ring a bell in my heart. Science radiates the air of uncharted territory, the adventure to step out into the unknown.

A piece of advice you'd like to give to the young generation of researchers?

Be inspired! One good idea is worth more than weeks of hard work. However, first there is inspiration, then there is transpiration.

A book, song, poem, music or painting that you spot out and get inspiration from?

"The Physicists" by Dürrenmatt. "A thought that can be thought will be thought".

Herbert Waldmann graduated in 1985 from the University of Mainz under the guidance of Professor H. Kunz in organic chemistry after which he carried out postdoctoral research with Professor G. Whitesides at Harvard University. He was appointed as Professor of Organic Chemistry at the University of Bonn (1991), full Professor of Organic Chemistry at the University of Karlsruhe (1993), and Director at the MPI of Molecular Physiology Dortmund and Professor of Organic Chemistry at the University of Dortmund (1999).

The interview questions were designed by Maria TSEMPEROULI, PhD student in Professor Sugihara's lab at UNIGE, and Phaedra SIMITSEK, COO of the NCCR Chemical Biology.

A SELECTION OF GOOD READING BY ROBBIE LOEWITH

Full Professor at the Department of Molecular Biology UNIGE and Head of the Educational committee for the Master's in Chemical Biology.

DIRECTED EVOLUTION OF APEX2 FOR ELECTRON MICROSCOPY AND PROXIMITY LABELING

The majority of proteins within a cell function as part of multiprotein complexes. Some of these complexes are stable and can easily survive biochemical isolation whereas others, such as kinase-substrate interactions, exist only fleetingly. There are now several ways by which protein-protein interactions can be identified including two-hybrid screening, protein-fragment complementation screens, affinity pull down coupled to mass spectrometry and database mining. Each of these techniques has its own particular advantages and disadvantages. In the present publication, work from the Ting group describes an enhanced version of a novel strategy capable of identifying protein-interaction partners. Specifically, a monomeric peroxidase reporter, APEX2, optimized through directed evolution using a yeast display platform, is expressed as an in-frame fusion with a specific protein of interest. At the desired moment, cells are treated for 1 minute with H_2O_2 in the presence of biotin-phenol and then processed for mass-spectroscopic analyses of biotinylated proteins; tag-dependent biotinylation serves to identify proteins that were in very close proximity to the APEX2 tagged bait protein, i.e. bait-protein-interaction partners. Alternatively, biotinylated proteins can be visualized by fluorescence microscopy using labeled streptavidin or labeling can be performed such that an electron opaque osmium salt is precipitated in the immediate vicinity of the tagged bait protein suitable for electron microscopy studies.

Lam et al Nat. Methods 2015 12:51-54

TUNABLE AND REVERSIBLE DRUG CONTROL OF PROTEIN PRODUCTION VIA A SELF-EXCISING DEGRON

I am preaching to the choir when I state that having access to acute and specific exogenous chemical control over a protein's function is highly desirable for biological studies. However, the identification of protein-specific small-molecule inhibitors is not a trivial task. As an alternative, many groups have exploited chemical-genetic tricks where proteins of interest are modified such that they become sensitized to a generic small molecule. The development of analog-sensitive kinases by the Shokat group is one such example. Another set of examples are the design of degron tags that target a protein of interest for degradation upon administration of exogenous cues ranging from particular wavelengths of light to small-molecules such as the plant hormone auxin. The Lin lab has now published a complementary strategy to inducibly target a protein for degradation called 'small molecule-assisted shutoff' or SMASh. Specifically, this chemical-genetic approach involves genetically appending a sequence encoding for i) a HCV NS_3 protease-recognition site, ii) the NS_3 protease, and, iii) an inherently unstable 'degron' sequence, into the 3' end of the coding region of the gene of interest. N-terminal tagging strategies of proteins are also presented. In the case of this C-terminal tagging construct, the fusion protein is expressed but the degron tag is cleaved off by the NS_3 protease before the degron motive can target the full length fusion protein for destruction. After protease cleavage, the degron portion of the peptide sequence is degraded and an intact protein of interest remains stable. To induce degradation of the protein of interest, asunaprevir, a specific inhibitor of the NS_3 protease, is added to cells. Asunaprevir prevents the cleavage of the degron tag off of the protein of interest and thus the entire fusion protein is rapidly turned over. This inducible turnover is very fast but affects only newly translated protein. Perhaps protein turnover kinetics can be further improved if this degron system is combined with other existing systems that are capable of targeting already synthesized proteins, albeit with slower kinetics (the auxin degron or even PROTAC - Proteolysis Targeting Chimeras - for example).

Chung et al. Nat. Chem. Biol. 2015 11:713-720

STRUCTURE-BASED DRUG DESIGN IDENTIFIES POLYTHIOPHENES AS ANTIPRION COMPOUNDS

Alzheimer's disease, Parkinson's disease, Huntington's disease, Lou Gehrig's disease and prion diseases are all neurodegenerative maladies in which protein aggregates accumulate in the brains of patients. These diseases are deadly and incurable. Using a mouse transmissible spongiform encephalopathy model, Herrmann et al set out to evaluate the usefulness of luminescent conjugated polythiophenes (LCPs) as antiprion agents. LCPs bind and stabilize ordered protein aggregates and screens with a chemically diverse library of LCPs identified compounds that increased survival of prion-infected mice. In a very clever twist, SAR analyses were then performed using a fungal prion, the only prion aggregate for which high-resolution structural information is available. NMR studies with such model amyloids revealed structural features seemingly important for aggregate binding.

Based on subsequent in silico analyses including molecular dynamics, rationally designed compounds were generated, some of which showed impressive prophylactic and therapeutic efficacy which, importantly, was translatable to other prion strains. The authors suggest that the most effective LCPs act by hyperstabilizing prion protein oligomers such that higher order infectious aggregates cannot be generated. It is tempting to speculate that LCPs will be effective in treating related neurodegenerative diseases and/or that the experimental pipeline outlined in this manuscript may also identify novel leads to treat these diseases.

Hermann et al. Science Translational Medicine 2015 7:229ra123

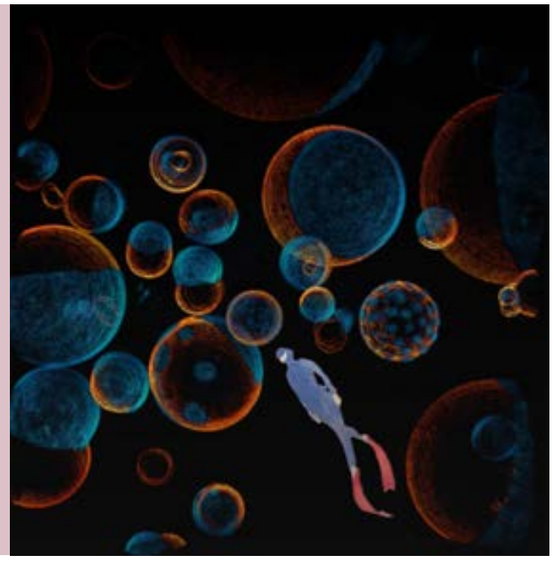
AND NOW FOR SOMETHING COMPLETELY DIFFERENT...

A selection of images that highlight topics in the field of Chemical Biology or are just meant for visual entertainment.

Beautiful chemical reactions
Eight types of beautiful chemical reactions are presented in this short video. Video & editing: Yan Liang (L2Molecule.com).
https://vimeo.com/107976057

Biomembranes
Chemical Biology offers the means to visualize biologically important properties of biomembranes that are otherwise difficult to detect. This image illustrates the concept behind the experimental approach used to visualize membrane organization and tension. Biphasic giant unilamellar vesicles made of Sphingomyelin, Cholesterol and DOPC were labelled with a novel planarizable push–pull probe whose spectral properties are sensitive to the lateral organization of membranes, then imaged by multicolor 3D confocal spinning disk microscopy. This novel class of membrane probe is referred to as "fluorescent flippers", because their chemical structure resembles the flippers of divers.

Dal Molin, M.; Verolet, Q.; Colom, A.; Letrun, R.; Derivery, E.; Gonzalez-Gaitan, M.; Vauthey, E.; Roux, A.; Sakai, N.; Matile, S. "Fluorescent Flippers for Mechanosensitive Membrane Probes," J. Am. Chem. Soc. 2015, 137, 568-571.



RECENTLY COMPLETED - OR ALMOST COMPLETED - PHD THESES

"Mechanism of Dpp Transport and Dpp Gradient Scaling in the Wing Imaginal Disc of Drosophila Melanogaster" by **Maria Romanova Michailidi** (Supervisor: Marcos Gonzalez-Gaitan, UNIGE)

"Addressing Fundamental Questions in Chemical Biology through Biochemical Investigations of Natural Products" by **Simon Sieber** (Supervisor: Karl Gademann, UniBas)

"From privileged natural product scaffolds to PNA-encoded chemical libraries" by **Claudio Zambaldo** (Supervisor: Nicolas Winssinger, UNIGE)

In December: "Lead Optimisation of an Unconventional Small Molecule Notch Inhibitor" by **Viktoria Reinmüller** (Supervisor: Freddy Radtke, EPFL)

NOMINATIONS AND AWARDS RECEIVED BY NCCR CHEMICAL BIOLOGY MEMBERS OR ALUMNI

ERC starting grant received by Javier Montenegro – former postdoctoral fellow in Professor Stefan Matile's lab in 2009, currently running his own lab at the University of Santiago de Compostela, Spain. His research stands at the interphase between organic synthetic and supramolecular chemistry applied to biological systems and the discovery of new materials with focus in the topological control of supramolecular assemblies for broad applications such as differential sensing, nanotechnology, controlled delivery and tubular-templated composites.

Professor Robbie Loewith from the Department of Molecular Biology (UNIGE) has been promoted to Full Professorship.

Professor Stefan Matile, from the Department of Organic Chemistry (UNIGE), delivered this summer the Molecular Science Frontier Lecture at the prestigious Institute of Chemistry, Chinese Academy of Sciences (ICCAS), Beijing, China. Professor Matile also received from ICCAS director the certificate of Molecular Science Frontier Lecture Professorship.

The EPFL spin-off Lucentix, fruit of the collaboration between EPFL's Laboratory of Protein Engineering (LIP) and the NCCR Chemical Biology, has received CHF 130'000, the maximum funding granted by Venture Kick, the Swiss leading startup financing platform.

PUBLICATIONS FROM AUGUST TO NOVEMBER 2015

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- Blanc M., David F., Abrami L., Migliozzi D., Armand F., Bürgi J., van der Goot FG. "SwissPalm: Protein Palmitoylation database", F1000Res. 2015 Jul 16;4:261. doi: 10.12688/f1000research.6464.1. eCollection 2015.
- Ronald F. S. Lee, Stephane Escrig, Marie Croisier, Stephanie Clerc-Rosset, Graham W. Knott, Anders Meibom, Curt A. Davey, Kai Johnsson and Paul J. Dyson. "NanoSIMS analysis of an isotopically labelled organometallic ruthenium(II) drug to probe its distribution and state in vitro", Chem. Commun., 2015, 51, 16486—16489, doi: 10.1039/c5cc06983a.
- Gasparini G., Matile S. "Protein Delivery with Cell-Penetrating Poly(disulfide)s", Chem. Commun., 2015,51, 17160-17162.
- Fujisawa K., Humbert-Droz M., Letrun R., Vauthey E., Wesolowski T. A., Sakai N., Matile S. "Ion Pair-π Interactions", J. Am. Chem. Soc. 2015, 137, 11047-11056.
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- Carlini L., Holden S. J., Douglass K. M. and Manley S. "Correction of a depth-dependent lateral distortion in 3D super-resolution imaging", PLoS One.
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UPCOMING EVENTS

Conference: professor Dario Neri
ETH Zurich, December 1, 2015 , SV1717A, 16:15 (EPFL)
"Armed antibodies and targeted cytotoxics for the treatment of cancer and of rheumatoid arthritis: from the bench to the clinic"
Link to the event.

Conference: Professor Frédéric Bard
Institute of Molecular and Cell Biology, Singapore
December 14, 2015, Room 352, 11 a.m.(UNIGE)
"Journey to the Center of the Cell"

International Symposium on Chemical Biology
January, 13 -15, 2016 - Campus Biotech, Geneva
Outstanding speakers, latest advances in the field, world-renowned speakers, academic speed-dating.
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8th Conference of the International PhD program in Life Sciences
January 18 - 20, 2016 - Leysin
An event where the NCCR is a Silver Sponsor! Link to the event.

Workshop on soft skills # 1: Rodriguez Chapin
January, 21 2016, room 352 - UNIGE
Fundamentals on paper writing. The objective of this workshop is to improve participants' ability to draft research manuscripts attractive to high-quality journals.

LS2 Annual Meeting
February 15 & 16, 2016 - Amphimax/Amphipôle, Lausanne.
Topic: "Interdisciplinary Sciences". The program includes a wide array of cutting-edge research from interdisciplinary fields in the Life Science disciplines and plenary talks from internationally renowned speakers as well as numerous educational and career development events. Highlight: A chemical biology symposium will take place on the 2nd day of the meeting from 2:00 pm to 4:00 organised by the DMCCB (Division of Medicinal Chemistry and Chemical Biology) of the Swiss Chemical Society. The NCCR Chemical Biology is a sponsor of the event. Link to the event.

Pre-seed workshop 2016
April 12, 13, 20, 2016 - Fribourg
Organized by the NCCR Chemical Biology and the Swiss Integrative Center for Human Health (SICHH). Two and a half days workshop which tests the marketability of up to 10 high-tech ideas. Includes the participation of experts, investor panels, carefully designed team setting and fast-paced modules. Submission of champion ideas from December 15th 2015 to January 30th 2016.

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