



*Enhancing opportunities
for a change:
let's make it happen!*

Past and ongoing STSM

*Sevda Recbertik, 16-29/04/2023, from the INSERM Strasbourg to the Institute for Experimental Internal Medicine of Magdebourg, Germany.

*Jan Dohnalek, 15/03-13/06/2023, from the Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences to the Department of Biotechnology and Biomedicine of the Technical University of Denmark.

*Alice Maiocchi, 03/04-30/06/2023, from University of Milan to Paul Scherrer Institute, Switzerland.

*Bernardo R. Oliveira, 08/05-30/06/2023, from Constructor University (previously, Jacobs University) to Instituto Universitario de Bio-Organica Antonio González, University of La Laguna, Islas Canarias.

*Busra Binarci, 03/07-01/09/2023, from Middle East Technical University, Ankara to the University of Cambridge, UK.

*Dong Xie, 01/07- 30/09/2023, from Institute for Integrative Biology of the Cell, CNRS Gif Sur Yvette to Max Planck Institute of Biochemistry, Martinsried, Germany.

*Clément Daviaud 01/09 to 18/09/2023 From the Université La Rochelle to Institute of Virology and Immunology Mittelhäusern, Switzerland.

ACTIVITIES HIGHLIGHTS

by the ProteoCURE dissemination committee

The second ProteoCURE annual meeting in Zagreb (12-15/06/2023) was attended by nearly 100 participants from academia, clinics, and the industrial sector, all of whom were interested in various fields of protein degradation. They shared their recent advances and proposed collaborative actions. Plenary and poster presentations were given by ProteoCure members, detailing their work to date and projects for which they are seeking collaborations. Presentations included the role of crucial cellular factors and processes in acute and chronic diseases, as well as how proteostasis can be controlled by small molecules or other bioactive compounds. We also had presentations on new therapeutics and discussed possible solutions at the interface between basic research, patient treatment, and the pharmaceutical industry. During the meeting, we were able to discuss unpublished data, propelling us to the forefront of proteostasis research. It successfully facilitated connections between academia and the medical/industrial sectors, enhancing the growth of our european network.

Several topics were discussed including protein modification and turnover, molecular chemistry and its use to tackle multiple diseases. Keynote speakers of the annual meeting were Ivan Dikic (Institute of Biochemistry II Goethe University Medical Faculty, DE), Michael Glickman (Technion Israel Institute of Technology, IL), Michal Sharon (Weizmann Institute of Science, IL), Jörn Dengjel (University of Fribourg, CH), Tommer Ravid (The Hebrew University of Jerusalem, IL), Ulrike Topf (Polish Academy of Sciences, PL), Ron Hay (University of Dundee, UK), Agnès Noël (University of Liège, BE), Marina Klemenčić (University of Ljubljana, SI), Stefan Pöhlmann (Georg August University Göttingen, DE). STSM fellows presented their project and experience at the STSM session in a very dynamic and interesting round of talks.

You can visit our video of this meeting at: <https://www.youtube.com/watch?v=VxTBbqyMtxg>

Future initiatives were discussed, including future meetings, training schools, support for STSMs, participation of ProteoCure members in dissemination activities, or the inclusion of members from ITC countries to attend international meetings. Questions from ProteoCure members about these actions were addressed through open discussions.

These exchanges will enable a much better utilization of resources and expand our possibilities for interactions among members of our network in the future. The associated 5th management committee meeting gathered 32 members, among whom were 26 management committee members representing 20 countries and 7 additional core group members. Minutes of this meeting have been recorded and will be made available to ProteoCure members via the ProteoCure website.

Other grants attributed by Thematic ProteoCURE groups

Dissemination Conference Grantees:

Nuray Erin, to attend the 7th Cancer Immunotherapy and Immunomonitoring Conference in Lithuania (CITIM-2023 <https://www.canceritim.org/program>) on 24-27/04/23.

Niki Chondrogianni, to attend the Diet and Optimum Health Conference 2023 Precision Health: Living Better, Longer, USA (<https://lpiconference.org/>) on 17-21/09/2023

ITC Conference Grantee:

Kathrin Bach to attend the 12th General Meeting of the International Proteolysis Society in Singapore (<https://www.dbs.nus.edu.sg/ips2023/>).

Create your ProteoCURE thematic group following the example of the Nedd8/Rub1 group. During our last annual meeting, Dimitris Xirodimas (Montpellier, France) announced the decision made with other ProteoCure members to create a group devoted to Nedd8/Rub1 issues. The idea is to foster communication and exchange between these groups, to improve collaborations, sharing of knowledge, tools, models etc. This initiative is definitely in line with ProteoCure objectives. Follow the example ! Do not hesitate to contact other ProteoCure members to create a group on your favorite topic! We will do our best to support such groups. There is already a forum on ProteoCure website that can be used for such purpose, and we can build on the website other specific features on request.

ABOUT OUR SCIENTIFIC EVENTS

Joint meeting with the SFBBM. Paris, 22-24/05/2023

A collaborative effort between the 'Cellular Proteolysis group' of the SFBBM (French Society of Biochemistry and Molecular Biology) and Working Group 1 (WG1) of ProteoCure took place in Paris from May 22-24, 2023. With 248 registered participants, WG1's objective is to promote the exchange of knowledge, innovative approaches, and therapeutic solutions in various biological processes and pathologies. The overarching theme of the meeting centered on proteostasis and its diverse impacts on the physiology of animals and plants.

This gathering provided a valuable opportunity for the French Proteolysis community, deeply involved in ProteoCure and WG1, to collaborate and share scientific advancements. The central location of Paris facilitated the attendance of researchers from across Europe. A special issue of Biochimie, an International Journal of Biochemistry and Molecular Biology, is planned to promote the meeting's topic and acknowledge ProteoCure's contributions. Additionally, the panel included individuals from industry (LVMH, MedExpress) and startups (OxiProteomics, Kantify).

Organized by Carmela Giglione, Gilles Lalmanach, Bertrand Friguet, and Chahrazade El Amri, the sessions covered WG1's key scientific areas, including Inflammation, Cancer, Autophagy, Omics, Drug Design, Host-Pathogen Interactions, and Aging & Neurodegenerative Disorders. The event attracted 93 participants from various European countries, Israel, and Korea, including young researchers and industry representatives. The scientific program featured lectures, oral presentations, and industry insights, highlighting crucial developments in each field.

EMBO workshop « SUMOylation: from discovery to translation ».

Pavia de Varzim, Portugal 25-28/09/2023.

The past decade has increased our understanding of the cellular and pathophysiological roles of SUMO modifications, extending its functions to the regulation of immunity, pluripotency, stress response and dynamics of molecular condensates. Such progress in understanding the roles and regulation of SUMOylation opens new avenues for the targeting of SUMO to treat disease.

The aim of this EMBO Workshop is to integrate perspectives on the function of SUMOylation from the fields of biochemistry, molecular cell biology, structural biology, genetics, plant science, pluripotency, immunity, oncology, neurodegeneration and drug discovery. We will stimulate exchanges between established and young scientists, as well as between basic scientists, clinicians and industry, to stimulate the growth of translational SUMOylation research to tackle challenges in health and agriculture.

<https://meetings.embo.org/event/23-sumoylation>



Founded by the European Union

COST (European Cooperation in Science and Technology) is a funding agency for research and innovation networks. Our Actions help connect research initiatives across Europe and enable scientists to grow their ideas by sharing them with their peers. This boosts their research, career and innovation

ANNOUNCEMENTS

CALLS FOR FUNDING FOR ACTIVITIES HAPPENING AFTER OCTOBER 31st, 2023

ProteoCure has launched several new calls to facilitate collaboration, knowledge exchange, and the achievement of ProteoCure's objectives:

1) Meeting Organization or Co-organization: ProteoCure is seeking proposals for meetings that align with its objectives and are of interest to its members. These can include ProteoCure-specific meetings or those co-organized by ProteoCure.

2) Training School Organization: ProteoCure is providing financial support for organizing Training Schools focused on specialized topics within the scope of the action. These schools aim to train researchers and innovators and may contribute to the goals of the ProteoCure COST Action.

3) ITC Conference Grants: ProteoCure is offering grants to young researchers from Inclusiveness Target Countries (ITC) or Near Neighbour Countries to participate in high-level conferences. These grants cover travel, accommodation, subsistence expenses, registration fees, and poster printing.

4) Dissemination Conference Grants: ProteoCure is offering grants to its members who are invited as speakers at meetings. The grants cover travel or subsistence expenses not covered by the meeting, with a requirement to include information about ProteoCure in their presentations.

5) STSM Call: ProteoCure is launching a call for Short-Term Scientific Missions (STSMs), which are exchange visits between labs aimed at fostering collaboration, sharing techniques, and strengthening the network.

Please visit the ProteoCure Website <https://proteocure.eu/category/calls/> for all the details on these fundings opportunities!

ProteoCURE Interviews

In this new section we will have the opportunity to meet some of our members and to learn about their work or in a special occasion, such as a prize.



We have started with Niki Chondrogianni who recently got The Leopold Flohé Redox Pioneer Young Investigator Award. Niki is a research director from the National Hellenic Research Foundation working at the Institute of Chemical Biology in Athens. She kindly answer to our questions during our annual meeting at Zagreb.

Tell us about this prize and tell us about the work that contributed to receive this recognition.

The Leopold Flohé Redox Pioneer Young Investigator Award is awarded to a scientist < 45 years with outstanding novel findings in the field of biological redox processes, working already independently, and leading an own group of young scientists having published high quality papers.

This prize is sponsored by the Society for Free Radical Research-Europe (SFRR-E) and Oxygen Club of California (OCC). An International Scientific Advisory Board reviews all the nominations for this honorary award.

My work in the field of proteasome regulation and modulation in response to oxidative stress, aging, cellular senescence and neurodegenerative diseases such as Alzheimer's disease (AD) enabled this recognition.

More specifically, we have initially shown that the proteasome expression and function is downregulated during replicative senescence (the best -so far- *in vitro* model to study human aging) and that the β -catalytic subunits are the rate-limiting ones (Chondrogianni *et al.*, *J. Biol. Chem.*, 2003, Chondrogianni and Gonos, *Biogerontology*, 2004). Upon partial proteasome inhibition a p53-dependent irreversible premature senescence is elicited (Chondrogianni *et al.*, *Aging Cell*, 2008). We have also revealed that the proteasome expression and function are maintained in centenarians in levels comparable to the ones found in young rather than in old donors (Chondrogianni *et al.*, *Exp. Gerontol.*, 2000). We thus decided to investigate whether proteasome activation is feasible. We initially attempted proteasome modulation in human primary cells through genetic means and we were among the first ones to reveal that the 20S core proteasome can be activated through overexpression of just one catalytic subunit, namely the β 5 subunit. Our work has revealed that proteasome activation promotes cellular lifespan extension and healthspan amelioration (Chondrogianni *et al.*, *J. Biol. Chem.*, 2005). We then identified natural compounds (mainly constituents of our normal diet) that may act as proteasome activators (Katsiki *et al.*, *Rejuvenation Res.*, 2007, Kapeta *et al.*, *J. Biol. Chem.*, 2010, Chondrogianni *et al.*, *Exp. Gerontol.*, 2010). These results led to an international patent as well as to two anti-aging series of cosmetics in the market based on our results (in collaboration initially with a Greek and afterwards an internationally renowned company).

Given that our work that far was conducted in cellular models, we then moved to a multicellular model, namely *C. elegans*. We created transgenic animals overexpressing *pbs-5* proteasome subunit (the orthologue of $\beta 5$ subunit) and we showed that this overexpression was sufficient to induce all three proteasomal activities. The transgenic animals were more resistant to oxidative stress, they exhibited lifespan extension and they were healthier (healthspan amelioration). More importantly, when the overexpression took place in nematodes that are models for AD, the paralytic phenotype of these animals was delayed while the animals exhibited reduced levels of various A β forms (Chondrogianni et al., *FASEB J.*, 2015). We have also shown that natural compounds with proteasome activating properties can elicit similar phenotypes when fed to the animals throughout their lifespan (Papaevgeniou et al., *Antiox. Redox Signal.*, 2016). More recently, we identified the first proteasome activator derived from the marine ecosystem leading the nematode but also human primary cells to healthspan improvement and resistance to proteotoxic stress (Vasilopoulou et al., *Redox Biol.*, 2022). Our ongoing work aims to reveal the potential cell non-autonomous regulation of the proteasome function (Panagiotidou et al., *under revision*). In total, our work has contributed to the understanding of the proteasome regulation and role in the progression of aging (*in vitro* and *in vivo*) and has added further value on the identification of natural or synthetic compounds that can be used in anti-aging and anti-aggregation strategies.

Why investigations on the redox field are so important?

Redox reactions are tightly linked and vital to basic functions of life, such as photosynthesis or respiration, among many others. Our lives are literally dependent on redox reactions and redox regulation. The redox signaling is central in the molecular pathways that are implicated in development, life, death and diseases. Therefore, the redox field has enormously evolved and represents one of the fields that cannot be ignored as the necessity to study redox involvement and regulation can appear anytime in any lab regardless of the main focus of the lab. Free radicals are everywhere, changing the game. They can be “good” or “bad” for us and this is why the redox field is so important.

What are the challenges you still have to face to progress in this area?

One of the main disappointments in the field of redox biology and aging is the failure of various antioxidants in clinical trials. Findings in cellular and organismal models are not fully verified in humans. Nevertheless, although the outcome is negative, this should not annul the previous findings. There are several possible reasons for the negative outcomes. For example, many antioxidants have been chosen for clinical trials due to their availability and not to their outstanding performance. Vitamin E is such an example. Especially if we refer to the effects of antioxidants supplementation on human aging, it is possible that the trial did not last long enough or did not start early enough. Experimental details such as the chosen cohorts, the duration and the initiation point (age) or the tested concentration, represent the potential factors that can negatively affect the final outcome. But those failures should only point out the challenges and indicate where we are still behind knowledge-wise. The negative outcome indicates that we probably need: 1) a better understanding of oxidation mechanisms at the basis of the aging process, 2) more reliable and specific markers of oxidative damage as well as of antioxidant status, 3) to specify the therapeutic window in which an antioxidant supplementation may be beneficial, 4) a deeper knowledge of the physiology of the elderly, as one size does not fit all. Failure is more frequent in life sciences than success, but these failures should act as a driving force for an improved future trial.

Why do you think it is important to encourage young investigators to continue doing research in your field and in general in life sciences. What would you do to help them?

I am active in the field of redox regulation of proteolysis and proteostasis. All these notions are vital and govern cellular physiology and well-being. Although a lot of work has been done and many regulatory pathways have been revealed, there are still many processes in both health and disease states that are not elucidated. This is why young investigators are absolutely required to continue working in this field and to further develop it. Elucidation of the involved pathways and regulatory mechanisms will enable the possibility to identify bioactive compounds or to design new ones that can maintain the “normal” function or can “repair” the abnormal one. Research in life sciences can be difficult and depending on the country or the place each one is working, it can become even more difficult, but at the end of the day, even for a tiny moment, you are the only person in the world that has achieved/revealed/found a tiny piece of the huge puzzle of life. And this is what keeps you going.

What a senior scientist can do for the younger ones is to remember that he/she was once in their shoes, to stand by them, to listen to their fears and doubts and to show them that this is something really normal (it has happened to everyone) and frequent (still happens even in senior researchers) but not enough to keep them away from their dreams. As a member of the SFRR-E, I urge young scientists to join this society. It is a friendly society that really cares about young researchers and does everything in its power to help them as much as possible and to give them the necessary boost to carry on and to evolve. The award I got is only one of these boosters that are generously offered by SFRR-E. I am really grateful to this society.

Follow us

