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EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

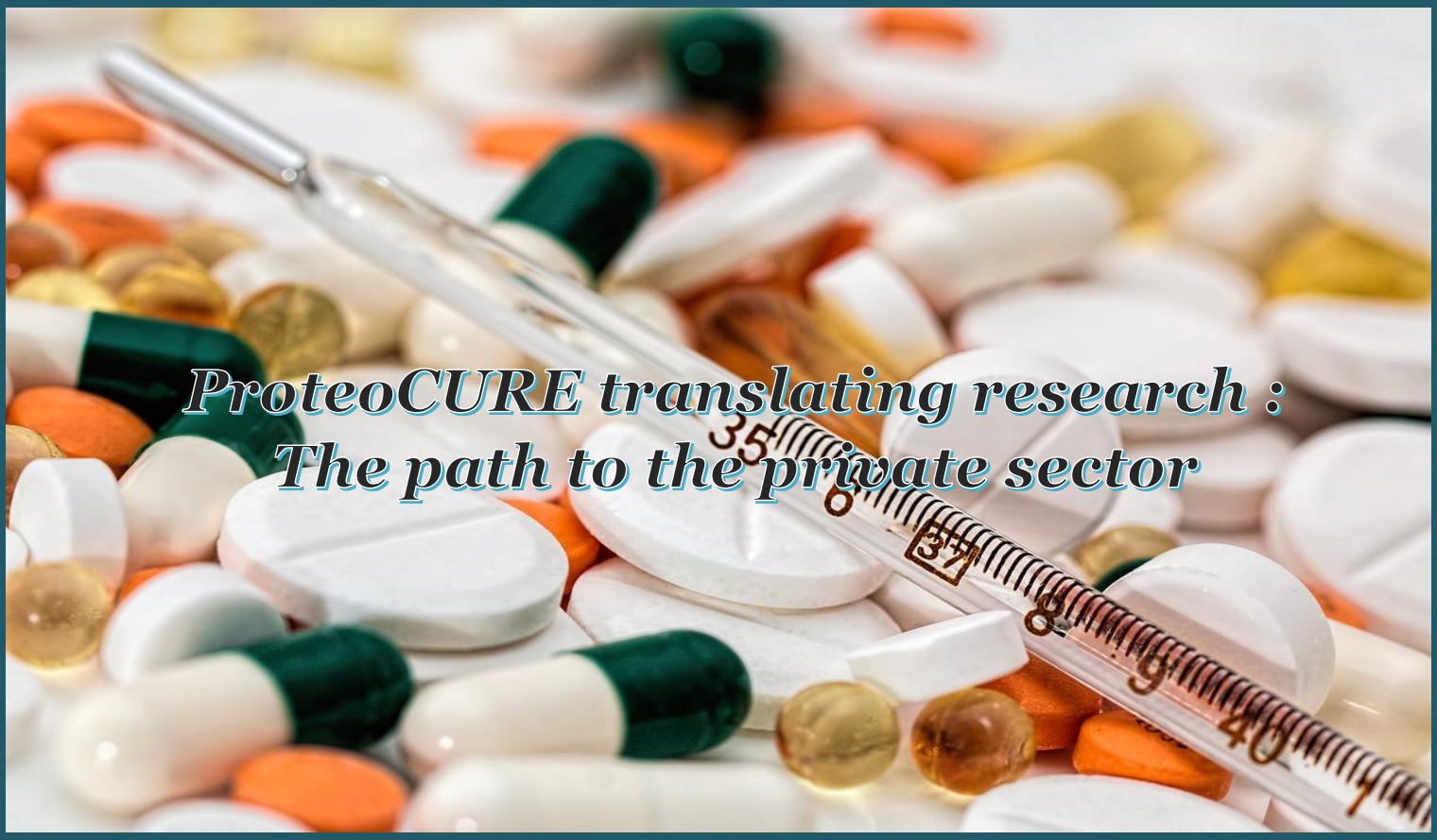
PROTEOCURE Newsletter

06

February 2024 • Winter issue

http://proteocure.eu

A SOUND PROTEOME FOR A SOUND BODY: TARGETING PROTEOLYSIS FOR PROTEOME REMODELING



ProteoCURE translating research : The path to the private sector

ACTIVITIES & HIGHLIGHTS

by the ProteoCURE dissemination committee

ProteoCURE integrates scientist from different generations and thematic orientations. One of the questions scientists have to face is deciding what type of science you want to do. For many of us, fundamental research is “the option”, however it is not always easy to get permanent positions in public institutions. For some others, integrating the private sector is attractive even if we are afraid to lose the intellectual freedom. There is another option that is always open: to collaborate with the private sector. Even of this option is obvious for many of us, it is not always easy to create this type of interactions. In this special number we have contacted 3 scientist that were trained in the 80’s, 90’s and 2000’s that have integrated the private sector and successfully progress in their professional life. They have answered 3 questions to illustrate their point of view of the transition public toward private sectors and how do they thing we can better interact with them.
In this issue you will also find information on the past and future activities and the current open calls that you can apply.

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.

COMING SCIENTIFIC EVENTS

ProteCURE ANNUAL MEETING 2024: SECOND ANNOUNCEMENT

The 3rd PROTEOCURE Annual Meeting. Warsaw, Poland. 7-10, May 2024.

Registration and abstract submission will be available from January 2024 until the end of March 2024.
More information you will find soon on our conference website:https://proteocure2024.sciencesconf.org

Please forward this information to students and postdocs in your lab!

We encourage young scientists to participate:
Slots for short talks are available and will be selected from submitted abstracts; present your research as a poster; Gain experience as session chair; Travel support will be available.
Organising Committee: Oliver Coux (ProteoCure Chair), Rosa Farras (ProteoCure Vice-Chair), Christine Blattner, Efthimios Skoulakis, Justyna McIntyre (Local Organizer), Ulrike Topf (Local Organizer), Laetitia Poidevin (ProteoCure Project Manager).
Venue: Hotel Mercure Warszawa Grand https://all.accor.com/hotel/3384/index.en.shtml
The link to the meeting website is: https://proteocure.eu/annual-meeting-2024/

41st Winter School on Proteinases and Inhibitors. Tiers, Feb 28 – Mar 3 2024

https://www.plus.ac.at/biosciences/the-department/research-groups/brandstetter/winter-school tiers/?lang=en

The Winter School provide a scientifically stimulating and personally outstandingly open atmosphere to researchers on proteolytic enzymes. This Winter School co-organized by ProteoCURE provides a forum primarily to young scientists allowing them to present their exciting and /or intriguing results for discussion with leading experts. The spirit of the Winter School in Tiers attracts scientists from Europe and worldwide, covering diverse and vibrant fields of protease research, such as mechanistic studies on proteases in their molecular, cellular and organismic context. Participate and enjoy this unique event:

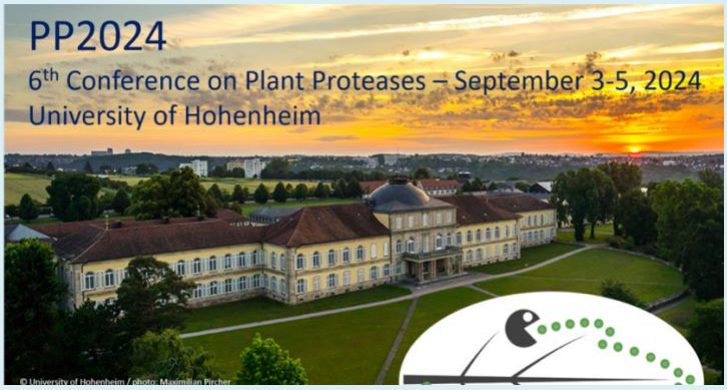
Ligating the Ubiquitin Family: Physiology, Disease, and Future Directions. Bilbao, Jun 24-25, 2024.

https://sebbm.es/actividades-sebbm/2ndsevero-ochoa-conference/

This event is organized by the SEBBM in collaboration with the Fundación Carmen y Severo Ochoa and co-organized by the COST Action ProteoCure. A fantastic lineup of confirmed invited speakers, including Ivan Dikic (GUF), Cristina Mayor-Ruiz (IRB Barcelona), Simona Polo (IFOM), Tim Clausen (IMP), Helen Walden (University of Glasgow), and Jordi Torres-Rosell (IRB Lleida). Selected speakers will complete the programs that includes, poster sessions and short talks.

6th Conference on plant proteases. Stuttgart, September 3-5 2024.

https://plant-proteases-2024.uni-hohenheim.de/



The conference co-organized by ProteoCURE includes presentations from leading experts and newcomers to the field. It aims to promote scientific exchanges highlighting recent advances and inspire the next generation of plant scientist. Our invited speakers includes Simon Stael, Saskia Hogenhout, Nuria Sanchez-Coll, Renier van der Hoorn, Ralf Reski,, Steven Spoel, Marina klemencic and Zach Adam, among others.

ProteoCURE Training School: Basics and perspectives of mass spectrometry proteomics. Freiburg, September 2024.

This will be a 5 days hands-on training school. More information to be announced.

PAST, ONGOING AND FUTURE STSM

Simon Tack from the Department of Plant Biotechnology and Bioinformatics Ghent University, Belgium to the Department of Molecular Sciences of the Swedish University of Agricultural Sciences (Dec 1-15, 2024)

Tobias Gökler from the Institute of Applied Synthetic Chemistry TU Wien, Vienna, Austria to the department of Chemistry & Pharmaceutical Sciences of Vrije Universiteit Amsterdam, Netherland. (Nov 6 to Dec 23, 2023)

Inci Barut from the Pharmacy Department of the Gazi University, Turkey, to the Institute of Neuroscience and Physiology of the University of Gothenburg, Sweden (Nov 16, 2023 – Feb 02, 2024)

Nerea Ruiz from Centre for Research in Agricultural Genomics, Barcelona, Spain to the Institute of Biologie Paris-Seine (IBPS) at the Sorbonne University, France (Jan 01 – Mar 15, 2024)

Ainoa Sanchez Arfelis from the Faculty of Pharmacy and Food Sciences at the University of Barcelona, Spain, to the Centre for Targeted Protein Degradation at the University of Dundee, UK (Jan 15 – Apr 15, 2024)

Oskar Lipiński from the Insitute of Protein biology and Chemistry of Lyon, France to the Oxford Particle Imaging Centre (OPIC) of the University of Oxford, UK. (Feb 10 -Mar 02, 2024, followed by 3 weeks in May 2024)

Fabian Gerth from the Medical School Berlin, Germany to the University College London, UK (March 10 - 23, 2024)

Javier Anton from the Valencia Biomedical Research Fundation, Spain, to the NOVA Medical School, Lisboa, Proteugal (Jun 15 – Jul 15, 2024)

Announcements-Calls

ProteoCure has re-opened the following calls to facilitate collaboration, knowledge exchange, and the achievement of ProteoCure's objectives:

1) 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.

2) 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.

3) 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.

Application deadline: 15 February 2024

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

PUBLISHING RELEVANT INFORMATION FOR OUR MEMBERS IN OUR WEB PAGE OR NEWSLETTER IS EASY.

Send us an email to: dissemination@proteocure.eu

Successful collaborations, grants awarded, prizes, common publications, scientific events, *etc*.

WEBINARS

Webinars will take place every second Thursdays, 1PM, CET
Starting on February 15

Dr Sala Ambre: Regulation of organismal proteostasis and stress resilience by reproductive and metabolic cues

Abstract: Maintaining a functional proteome is critical to cell survival and is ensured by a complex network of molecular chaperones and degradation pathways that cooperate to promote proteostasis. Failure of these systems during aging is a major driver of cellular dysfunction and many age-related diseases are characterized by pathological protein misfolding and aggregation. Studies using model organisms have revealed that the age-dependent decline of proteostasis capacity is regulated by the reproductive system, with important consequences for organismal health and longevity. Using the Caenorhabditis elegans model system to interrogate the relationship between reproduction and somatic proteostasis, we uncovered a novel transcellular pathway that restores maternal proteostasis and stress resilience when the integrity of the developing embryo is compromised. We found that this pathway utilizes the remodeling of lipid metabolism via a nuclear receptor to enhance cellular resilience to proteotoxic stress. Such regulation of organismal proteostasis by integrated reproductive and metabolic cues may serve to reassess commitment to reproduction and promote somatic endurance when progeny production is not optimal.

Bio: Ambre Sala is a group leader at the Institute for Integrative Biology of the Cell (I2BC), in Gif-sur-Yvette. She is interested in the mechanisms that orchestrate proteostasis in different cell types and their impact on age-dependent tissue and organismal decline. Her group uses *Caenorhabditis elegans* to model age-dependent protein phase transitions and interrogate the role of proteostasis network components, with a focus on molecular chaperones.
https://www.i2bc.paris-saclay.fr/equipe-protein-homeostasis-in-development-and-aging/

INTERVIEWS WITH SCIENTIST FROM THE PRIVATE SECTOR

Dear colleagues first of all thanks for accepting to answer our questions. The idea of this exercise is to better understand your scientific motivations and priorities that would help us to better interact with you. Please answer our following questions.

1. Many of us started our scientific carrier with fundamental research as it might has been your case. When and why you decided to change to applied/industrial science. How difficult was this transition?
2. Why do you think that intervention at the level of the human proteome by targeting key cellular factors could give better results than genomic therapies?
3. Academics are generally eager to interact with companies but very often find it very difficult, particularly in Europe. Industry/academia interface seems more permeable in the US. In the industry point of view, what are for you the barriers that limit interaction with the academic world?

Roland Hjerpe

Current position:
Senior Principal Scientist in Induced Proximity Therapeutics, at Sygnature discovery, UK
Past positions/ professional carrier:
Postdoctoral researcher in protein homeostasis. University of Glasgow, UK
Postdoctoral researcher in ubiquitin-biology. University of Dundee, UK

Q1. I often get this question from colleagues in academia that are considering work in industry. In a general sense, I think that the difficulty of the transition will depend on the type of company that you join and what you are looking for. Joining a small biotech will have risk profile and role very different from large pharma. In my case, I decided to join a contract research organization (CRO), Sygnature Discovery, where we provide scientific drug discovery services to clients. I took this decision after completing my postdoctoral work, and it was partly based on the challenge of securing a permanent position in academia, and partly on my interest in developing practical drug discovery expertise. The transition was easy, and the company I joined provided training to cover any gaps in my skillset. Six years later, I am still at the same company and enjoy a senior role with varied and stimulating scientific challenges, where I am contributing directly to the development of new drugs.

Q2. I think it will likely be technically more straightforward to develop therapeutics on the protein level, although gene therapy, if successful, would be very powerful. My area of expertise is targeted protein degradation, which is a therapeutic modality that is becoming increasingly popular. In this area, we are seeing the development of small molecules that have the potential to treat diseases that previously were not readily accessible for small molecules on the protein level, for example in neurodegeneration where accumulation of misfolded proteins is a hallmark of disease. Intervention at the protein level, via use of compounds that can clear protein aggregates, is under development by various biotech companies today, and I think that in the next five-ten years we will see many of these entering clinical testing phases. Developing therapeutics that alter the genome for treatment of these disorders will likely be more challenging. Also, targeting proteins may allow better control of pharmacology, as protein activities can be regulated based on the presence, absence and dose of a compound. The pharma industry also has a wealth of knowledge with respect to developing drugs that target proteins, covering development strategies as well as a good understanding of compound liabilities. On the whole, protein- and gene-based therapeutic strategies will probably need to be considered for their merit on a case-by-case basis.

Q3. I think this relates to the different endpoints in industry compared to academia – whereas publishing is essential in the academic setting, this is usually a low priority bonus for pharmaceuticals, CROs, and biotech's, where the endpoint ultimately is to make profit. Large pharma occasionally explores collaborative models with academic research institutes, which can allow industry to access early results that lead into e.g., target identification and validation. From the perspective of working in a CRO, the opportunity for collaboration is limited by funding opportunities that bridge the gap between industry and academia. At my company, our efforts to extend a hand to academia include taking on PhD students that work with us to develop our internal capabilities. This has historically been very successful for us, and students come away with a good understanding of how we work and valuable experience of using technologies and approaches in drug discovery.

Fernando Ramon-Olayo

Current position:
Head of Screening Sciences, Servier, Paris, FRANCE
Past positions/professional carrier:
Head of Biological Reagents and Assay Development, GSK Madrid, Spain
Screening and Compound Profiling Manager, GSK Spain
Molecular Screening Investigator, SmithKline Beecham

Q1. When I started my PhD I envisaged an academic career, with the powerful tandem of fundamental research and teaching in mind. This changed when I realized that access to academic careers was extremely difficult and founds limited in Spain. I realized that in industry, there were by far more resources to do science and this could be a better option. My PhD being centered around characterization of an enzyme used in the biotransformation of antibiotics in industry, I was presented with an opportunity to join a big pharmaceutical company in the early drug discovery space. The most important challenges in the transition from academia to industry were the high level of automation and the sense of urgency. I had to bring myself up to speed in topics outside the realm of Biology such as mechanical and electronic engineering, physics of light and of fluids, etc. Project management and effective communication became crucial skills to add to my skillset.

Q2. In a nutshell, because the proteome is closer to the phenotype. In fact, tackling disease by acting on the genome is only effective if the causality link is relatively simple, that is, if the mere presence of a single gene is required and sufficient to drive a specific pathophysiological state. This is true only for a reduced number of diseases. For most pathological states, a complex interplay between genes, transcripts, proteins, post-translational modifications and inter-molecular interactions must be taken into account when we establish our therapeutic approach. In recent decades we have witnessed a dramatic drop of the success/investment ratio in pharmaceutical R&D. There is a general consensus that, in order to enable true innovation and provide society with novel therapeutic solutions, we need to encompass more biological complexity than in the recent past. One way to do this is to shift our screening strategy beyond modulation of the biological activity of targets. In fact, targets that have traditionally been deemed of low "druggability" can become more tractable if we aim at modulating their abundance or turnover rather than their activity. In this respect, degraders such as PROTACs and molecular glues are alternatives with great potential as shown by examples already in the clinic.

Q3. In continental Europe I have observed a barrier between academia and industry which is due to misconceptions from both sides. Although the situation has improved since I started my career in the 90s, there is still a lot of progress to make on the establishment of a fluid model of interaction to maximize the combined impact on delivery of new solutions to unmet societal needs. From the academic side there is frequently a simplified view of industrial partners as mere suppliers of financial resources at the best or “vultures” that seek stealing their ideas at worst. From the industrial side, there is also a misconception that their research must remain undisclosed in its entirety and that academic researchers are inefficient and lack strategic direction. However, in recent years, I have seen an increasing number of cases where these behaviours have been replaced by mutual understanding of strengths and constraints. The gap between fundamental and applied research is being filled with an increasing number of individuals that understand the capabilities and expectations from both sides and specialized people (e.g. legal and intellectual property experts) to deal with the mechanisms to ensure a balanced sharing of risks and benefits.

Jean-Christophe RAIN

Current position:
CE0/CSO Hybrigenics services, Paris, FRANCE
Past positions/professional carrier:
Funder member of Hybrigenics pharma
funder three startup companies in the last three years in oncology and cell engineering.

Q1. In the second part of my thesis, I took part in the development of a new yeast double hybrid technology. With Pierre Legrain, my PI, we immediately thought we could turn it into a target identification or service start-up. I helped set up this project while preparing my post-doc. I had obtained a grant from EMBO to go and work with Elisa Izaurralde in Geneva. Finally, we found a venture capitalist for the seeding of the company. So I had two options: leave as a post-doc and try to pursue an academic career, or dive into the Hybrigenics adventure, working alongside Pierre to transfer the technology from the lab to the company. I had a bad night. I decided to let go of the EMBO grant and join an adventure that appealed to me on both human and scientific levels.
Q2. If we consider the actual therapies most of them target protein. I think, it will be the same in the future even if genetic and cellular therapy will take an important place. New therapies developpe around proteome equilibrium manipulation offer new incredible opportunities in particular to extend the druggable space. Open new way to cure is always additional chance for the patient.
Q3. At Hybrigenics Services, academics are valued clients, constituting 50% of revenue and 75% of customers. We take pride in our academic partnerships, ensuring our scientific excellence and affordability. Over 600 papers have been published using data produced by our team. We also engage with academics through French or European grants, enabling us to stay technologically advanced and comprehend evolving needs and markets. However, in France, the complex "Scientific Valorisation System" poses challenges, and despite good intentions, it often falls short of benefiting small companies and research organizations.

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ProteoCURE action receives funding from COST (European Cooperation in Science and Technology) Action CA20113