



The Newsletter of the European Calcium Society

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Countdown to Strasbourg

With the Strasbourg meeting only a couple of months away, Jacques Haiech would like to remind you that the deadline for reduced registration fees is May 15th, with the Abstract Submission deadline a couple of weeks later. This will be the 9th meeting of the Society, which as many of you know extends a series that began as a “one-off” in Brussels in 1989. Having attended all eight ECS meetings thus far, it is interesting to reflect on the evolution of both the ECS and the biennial meetings over what is now almost two decades. For those of us of a ‘certain age’ it is not at all clear how we ever managed to organise such events before the days of e-mail and the internet. I recently found some of the slides¹ I used in the short talk I gave at that Brussels meeting, and showed them to a couple of PhD students in my lab. They turned them over in their hands and held them up to the light, with expressions of genuine curiosity, as if they were relics from some distant age.

In spite of the technological changes, scientists in general, and especially physiologists, like constants, and one key feature of ECS

¹ Note for younger readers: slides were small transparent plastic sheets upon which data could be printed. For presentation purposes these would be projected onto a screen using back illumination.

conferences that has remained constant over the years is the mix of both calcium-binding proteins and calcium-signaling at the core of the scientific programme. It is this that gives ECS meetings their unique flavour. Every year, many of us travel to and participate in calcium conferences the world over, and the focus of the majority of such meetings tends to be signaling. Calcium-binding proteins thus defines the niche occupied by ECS meetings. Why do I mention this? The ECS board welcomes, and regularly receives, suggestions from members of the Society interested in hosting future meetings. Indeed the location of ECS2008, currently a closely guarded secret, will be revealed in Strasbourg. Therefore, in considering putting forward such a proposal, members need to keep in mind that a balance in the subject matter, between calcium-binding proteins and signaling, is essential. To lose that, would be to lose our identity.

Steve Moss

ECS2006 – a word from the organiser

ECS2006 Meeting: J-60, just after the soccer world championship.

Again, the ECS2006 meeting is attracting young scientists. We will do our best to get them with the experts of the domains and to induce among them “a collaborative attitude”. Science is a network and calcium is the signal although let’s try not to be too extremist.

We are pretty sure that the nice atmosphere of the city of Strasbourg and the Alsatian food will allow friendly and fruitful exchange among the young and the experienced scientists. The weather is going to be between warm and hot, so bring your swimming suit. There is a pool in the hotel and a lake nearby the conference location.

At this meeting, we would like to highlight the emergence of systems biology in the calcium field, and the interface between biology and chemistry. Biology is becoming quantitative and therefore, biological systems may be analyzed in a global manner. A mixture between plant and animal biologists will provide you with fresh views of your own biological questions. New speakers are coming and the program is being finalized. Let's expect some surprises.



New paradigms in biology

The complexity of living organisms has always fascinated the biologists who described it but could not seize it in its globality. Genomics brings knowledge of the complete organization of genomes, and leads the biologist to consider the organization of a living cell as a limited unit which one could quantify overall. Genomics and functional genomics not only established a group of techniques allowing an exhaustive understanding of a cell, but they also changed the paradigms of biology. To the simplistic dogma of the study of living objects being "a gene, a protein, one pathology" is substituted the paradigm of the relationships between objects; "one transcriptional modulus, a network of regulation, a set of symptoms". And thanks to the appearance of the -omic techniques, we are in the train of passing from a qualitative description to a quantitative prediction of the complexity of life, in other words from biology to global biology (Systems biology).

The calcium signal, an entry point to deciphering complexity

Since the fifties, remarkable tools of investigation have been created in order to study the calcium signal, in particular calcium buffers (EDTA, EGTA, BAPTA) then calcium probes (Fluo3, Indo4) and finally systems that allow us to modulate it at will (releasable calcium). The knowledge of the human genome allows a comprehensive census of genes coding for calcium channels (generators of the signal), of

the pumps and the exchangers (suppressors of the signal) and calcium-binding proteins (first cellular stage of deciphering the calcium signal). Cleaned and annotated databases of genes coding for proteins implied in calcium pathways are being constructed. These are cores of nucleation of the knowledge needed to model, then to simulate those networks in a cell at a given time and in a specific physiological state.

As in physics, we have to confront simulations of an ideal model with the experimental results obtained by disturbing the biological system, and by looking at the return to homeostasis. Tools were thus developed to disturb one biological system at the genetic level (inactivation or modification of genes), at the RNA level (siRNA for example) and at the protein level by use of pharmacological tools (small molecules able to interact specifically with a given protein). These are essential for setting up and validating models describing living systems, initially to help to simulate and thus to predict the complexity of life before perhaps trying to develop explanatory theories of the biology.



The coming ECS2006 meeting aims to be part of this extraordinary revolution appearing in biology, and we are sure that calcium is the key to open new avenues to explain the living complexity.

Jacques Haiech

Announcements

Postdoctoral Research Position Membrane Protein Research Group Department of Biochemistry, University of Alberta

A Postdoctoral position is available to study the structure and function of endoplasmic reticulum (ER) proteins. The focus of our research program is on the ER associated chaperones involved in quality control of the secretory pathway and modulation of calcium homeostasis. Current research projects include investigation of the role of calreticulin and calnexin in modulation of calcium

homeostasis, intracellular signaling and investigation of function of these proteins in knockout and transgenic mice. We also examine the role of the ER proteins using stem cells as an experimental model to understand the role of ER proteins and ER luminal environment during embryogenesis with special emphasis on cardiac development, cardiac pathologies and neuronal development. As a part of our studies on the dynamics of the ER luminal environment we carry out biochemical and molecular biological investigations on the role of ER luminal proteins in control of many ER functions including ER-nucleus signaling, calcium homeostasis, protein synthesis and folding.

I am looking for an individual who can develop a creative, independent approach to problems within the defined objectives of our research program. Expertise in molecular biology, cell biology and/or biochemistry is desirable. Salary is guaranteed for at least two years.

Selected recent publications from our lab:

Martin, V., et al. 2006. Identification by mutational analysis of amino acid residues essential in the chaperone functions of calreticulin. *J. Biol. Chem.* 281: 2338-2346

Lynch, J., et al. 2005. Calreticulin signals upstream of calcineurin and MEF2C in a critical Ca²⁺-dependent signaling cascade *J. Cell Biol.* 170: 37-47

Méry, A., et al. 2005. Initiation of embryonic cardiac pacemaker activity by inositol 1,4,5-trisphosphate-mediated calcium signaling. *Mol. Biol. Cell* 16: 2414-2423

Knoblach, B., et al. 2003. ERp19 and ERp46, new members of the thioredoxin family of endoplasmic reticulum proteins. *Mol. Cell. Proteomics.* 2: 1104-1119

Papp, S., et al. 2003. Is all endoplasmic reticulum created equal? The effects of the heterogeneous distribution of endoplasmic reticulum Ca²⁺ handling proteins. *J. Cell Biol.* 160, 475-479

Please forward a copy of your curriculum vitae together with the names of two people who will provide a reference to:

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**Academic Posts – Lecturer to Professor
Institute of Ophthalmology
University College London**

Applications are invited from individuals interested in joining the Institute of Ophthalmology up to professorial level. UCL Institute of Ophthalmology is one of the foremost eye institutes in the world with strong core science, translational and clinical programmes. Successful applicants will have a well-established track record of excellence in their discipline. Experience in eye disease is not essential but applicants will be expected to become involved in the broad mission of the Institute to understand basic mechanisms of disease and to develop new therapeutic and diagnostic approaches to blinding conditions. Appropriate areas of expertise include: cell biology, developmental biology, epidemiology, genetics, immunology, pathology, psychophysics, pharmacology, stem cell biology, systems biology and visual science.

Interested individuals should in the first instance visit the Institute web site at <http://www.ucl.ac.uk/iio/> and then follow instructions to contact the search committee.

Press release

Jellyfish Protein Shows Powerful Neuroprotectant Activity

Chicago, Illinois (April 8, 2006). Quincy Bioscience (Madison, WI) announces that their proprietary technology consisting of the jellyfish protein aequorin has displayed potent neuroprotectant activity in their laboratory studies. Quincy Bioscience has been researching the jellyfish protein for the past ten years and has recently demonstrated a significant ability to keep brain cells alive longer in controlled tests when an ischemic event is administered. Laboratory tests show a 28-45% improvement in cellular protection from death in their rodent models studied. The specific area of the brain studied was the hippocampus, a region that is responsible for short term memory formation. "Without a properly functioning hippocampus, if you looked away from me right now and turned back, you would have to reintroduce yourself to me, having forgotten that we just met," commented James Moyer, Jr. Ph.D. of the University of Wisconsin at Milwaukee (UWM). Dr. Moyer is Quincy Bioscience's primary investigator within the Neurosciences Laboratory at UWM. "Investigating the hippocampus is crucial to understanding the molecules impact on the largest neurodegenerative disease, Alzheimer's."

Quincy Bioscience sponsors research conducted at the University of Wisconsin at Milwaukee to develop aequorin-based technologies for the treatment of neurological conditions such as Alzheimer's, Parkinson's, stroke, Amyotrophic Lateral Sclerosis (ALS) and Huntington's Disease (HD). In each of these disorders there is a known depletion in neuroprotective calcium-binding proteins that is highly correlated with disease progression and severity. Quincy Bioscience's molecule is intended to essentially replace those lost proteins.

"We are very excited to be moving this technology forward. There are many people suffering from these diseases," commented Mark Underwood, President of Quincy Bioscience. "Both academic labs and drug companies are searching for a molecule that can attenuate neuronal loss from calcium-mediated toxicity. We have one. Now it is time to focus on selecting the right partners that can take this to the next level."

A certain species of jellyfish contains the protein aequorin which has the unique property of binding calcium ions within the nervous system of the jellyfish. Humans also need this type of protein to properly protect cells. One of the detriments of the aging process is that humans lose a significant amount of their own cell-protecting proteins. Aequorin is a very similar type of protein with no toxicity issues. Clinical trials are planned to investigate aequorin's impact in patients.

This technology would not be possible without some significant advances in biotechnology manufacturing. Jellyfish protein used to be very difficult to obtain and expensive. Two tons of jellyfish would only yield 125mg of aequorin. Now with safe production techniques the protein is more economically feasible to be utilized as a therapeutic.

"The response to the technology has been very positive from pharmaceutical companies. Since aequorin targets a very important mechanism of action it has the potential for the treatment of several neurodegenerative conditions." Underwood also added. Interest in Quincy Bioscience's technology has been growing as potential licensing partners are looking at applications of this technology towards everything from acute treatments for post-stroke trauma to longer term anti-aging research.

"Having strong science is the key to providing a quality product to our consumer base," added Mike Beaman, Mr. Underwood's partner in Quincy Bioscience. "It is exciting that we can have the opportunity to touch the health of so many others. This protein is rather amazing."

Quincy Bioscience is a biotechnology company based in Madison, Wisconsin. Quincy Bioscience is focused on the discovery, development and commercialization of novel compounds to fight the disease of aging. The company's therapeutic products focus on restoring calcium balance related to neurodegenerative disorders and the destructive age-related mechanisms triggered by calcium. Quincy Bioscience is set apart by its cutting-edge health applications of the jellyfish protein aequorin. Aequorin has proven neuroprotective activity and is being developed for pharmaceutical product applications.

For more information, contact Mark Underwood, President at munderwood@quincybioscience.com or 414-303-0814.

Books

Karl-Wilhelm Koch and Pavel Philippov are editors of a new book entitled "**Neuronal Calcium Sensor Proteins**", which includes 20 chapters written by experts in the field. The book is expected to go into press in a few weeks. Please see the following weblink for details.

https://www.novapublishers.com/catalog/product_info.php?products_id=4214
