# NEWSLETTER: SOCIEDADE PORTUGUESA DE BIOQUÍMICA

December 2023 Edition 1



Fluorescence microscopy of HeLa cells showing the anti-apoptotic protein MCL1 in green and its mRNA detected by RNA-FISH in red.

> Isabel Pereira-Castro and Alexandra Moreira, i3S, University of Porto

## **Editorial**

## WELCOME

#### **Our Newsletter!**

SPB is launching a new series of its Newsletter, which aims to reinforce the communication among SPB members, the dissemination of advances in Biochemistry, and the sense of a collaborative community within SPB.

The first number of this trimestral Newsletter highlights SPB activities during 2023, some of them supported by FEBS and IUBMB, as well as distinctions and awards received by SPB members at the FEBS congress or SPB events, and one fellowship awarded by the PROBio-Africa programme to a student who will perform a research training in Portugal.

In this edition, Graça Soveral (University of Lisbon) tells us about her academic career and the opportunities and challenges as President of SPB (2019–2022) and Vice-President of FEBS (2023).

Additionally, João Laranjinha (University of Coimbra) gives us his perspective on a hot topic in the area of redox biology.

We also highlight several events scheduled for 2024, including the National Congress of Biochemistry, the Clinical Biochemistry Workshop, and several International meetings, as well as the next call for SPB action grants.

Our commitment is to SPB members. Within the scope of SPB's mission, we will continue to strengthen the support of SPB members across all career stages.

We would like to wish all the SPB members joyful holidays and a happy 2024.



Vítor Costa **SPB President** 



# Awars & Distinctions

#### Cecília Arraiano

Coordinating Investigator at ITQB-NOVA and head of the Control of Gene Expression laboratory, received the **FEBS Diplôme d'Honneur**, for her outstanding services to FEBS and to the field of Biochemistry. The award ceremony took place in July 8th, during the 47th FEBS Congress in Tours, France. Cecília Arraiano was chair of the FEBS Working Group on Women in Science from 2013 to 2022. During that time, she integrated the FEBS Executive Committee and Board of Trustees. She was also a member of the Board of the Advanced Courses Committee.



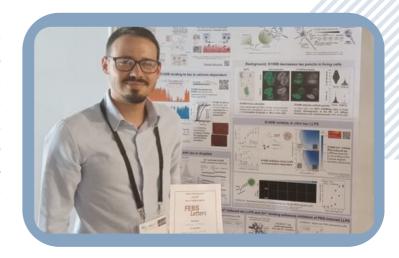
#### Mariana S. Diniz

PhD student at Center for Neuroscience and Cell Biology, University of Coimbra received the SPB Best Oral Presentation Award at the 1st FEBS Redox Medicine Workshop: from cellular signalling to systems physiology and therapeutic targets, in Luso, from May 22nd to 25th, 2023, for her work titled "Offspring's cardiac nitric oxide signaling is influenced by maternal physical exercise during an obesogenic pregnancy".



#### Guilherme Gil Moreira

PhD student at the University of Lisboa received the **BioFactors Best Poster Award** at the 22nd FEBS Young Scientists Forum, in Tours, France (July 6th-8th, 2023), for his work titled "Chaperone regulation of tau liquid-liquid phase separation", and the **FEBS Letter Poster Prize** at the 47th FEBS Congress, 8th-12th July 2023, also in Tours, for his work titled "Tau puncta and liquid-liquid phase separation are precluded by the S100B chaperone".



### **Nigel Francis**

From Cardiff University, UK. received the SPB Best Poster Prize at the "Symposium on Pedagogical Innovation in Biosciences – How to engage students in our practices?", in Aveiro, October 12th–13th, 2023, for his work titled "Simulations as an assessment for learning".



Received a **PROBio-Africa fellowship**. This program aims to foster cooperation between the Federation of African Societies of Biochemistry and Molecular Biology (FASBMB), IUBMB and FEBS, benefiting their members, trainees, and science. Alain Tueche will perform a research training at i3S, Porto, under the supervision of the SPB member Luísa Mesquita Pereira, group leader of the Genetic Diversity group.

He will test compounds isolated from Acacia seyal (Mimosaceae) on triple negative breast cancer cell lines from Sub-Saharan African and European ancestries, exploring the differential behaviour between ancestries in pharmacogenomic terms. Moreover, he will characterize the action of the most promising compounds in genotypic terms through a transcriptomic analysis.







Nothing great was ever achieved without enthusiasm.

Ralph Waldo Emerson



## Interview

#### **Graça Soveral**

To start the series of interviews of the SPB Newsletters, we talked with **Graça Soveral**, former president of SPB (2019–2022), Full Professor at the Faculty of Pharmacy of the University of Lisbon (FFUL), and group leader at iMed – Research Institute for Medicines.



Can you give us a brief overview of your academic and scientific career?

My career started with the Degree in Pharmacy at FFUL (5 years), that now corresponds to the Integrated Master in Pharmacy. During the course, I attended the Biochemistry classes of Prof. Silveira, a pharmacist Professor of Biochemistry, that taught us Metabolism with such a passion and enthusiasm, that I completely fell in love with Biochemistry and its clinical implications.

Prof. Silveira was also the head of a research center dedicated to investigating inborn errors of metabolism (Centro de Metabolismos e Genética), and had a close collaboration with the Genetics department of Hospital Sta. Maria.

It was there where I was first introduced to research as an undergraduate student, learning and executing biochemical protocols for the diagnostics of genetic diseases caused by enzyme deficiencies, and later as an Assistant Professor in charge of those biochemical analysis for enzyme deficiencies.

This love for Biochemistry really motivated me to, at the end of the degree make my first move into the professional world. From the four possible professional branches of the degree in Pharmacy – Community pharmacy, Hospital pharmacy, Pharmaceutical industry, and Clinical Analysis, I knew that my place was at the clinical biochemistry lab.

So, I started my first job as a clinical analyst at a private clinical lab, where I was responsible for the biochemistry and immunology department. One year after, I applied for a Teaching Assistant position at FFUL, to teach biochemistry to the pharmacy students, and got the position without leaving the clinical lab. Thus, during the next 4 years I managed to keep both positions, at FFUL during the day for teaching and research, and at the clinical lab till late in the evening, performing and supervising the daily analyses and results.

But, as you known, an academic career is demanding in terms of research. At a given moment, I had to decide if I wanted to pursue a scientific career. It was only when a more formal link to academia was at stake, and the work in the clinical lab was becoming too repetitive, that I applied for a fellowship and moved to Montreal, Canada, for one year to do research, investigating new fluorescent enzymatic methods to diagnose a particular metabolic disease.

The results gave rise to my thesis presented at *Provas de Aptidão Científica e Capacidade Pedagógica*, a kind of examination corresponding to a MSc degree that allowed me to continue the academic career at the university. Although I was invited to stay in Canada after that year, I decided to return, to get my position at FFUL now a little more permanent, and engage in a PhD.

For my PhD thesis, I moved my research area to biological membranes and transport, and started working under the supervision of Professor Teresa Moura (at ITQB-UNL, at the time still in the Gulbenkian Science Institute, in Oeiras), who was my PhD mentor.

After completion of the PhD, I continued to work closely and collaborate with Teresa at FCT-UNL in Caparica as an Associate Researcher, and it was only in 2012, when I was promoted to Associate Professor at FFUL, that I moved my lab to FFUL and iMed.Ulisboa. Currently, I am a Full Professor and I lead the Membrane Transporters in Health and Disease research group.

# What has motivated you to Biochemistry and specifically to water transport and aquaporins?

As I mentioned before, my first motivation to work in Biochemistry comes from the very lively teaching of Prof. Silveira – I can still today describe with some detail the Krebs cycle and its different reactions. This was the drive to work in the lab and then to get into the academic world. Looking for something else, led me to Canada, again to work in a biochemical-related subject and then, when looking for the different possibilities for a PhD – not as many in those days as there are today – to choose a biochemical-and pharmacological-related topic.

At the time, aquaporins had not been identified yet, and we were focusing on water transport in general. When these proteins were identified by Peter Agre, later awarded the Nobel Prize (in 2003), motivation was even greater.

And we contributed to the discovery that these proteins are not simple channels selective for water and have other much more complex roles in health and disease.

# What has been your most surprising/exciting discovery?

As I have just mentioned, aquaporins are quite exciting. They were first identified as simple water channels with a selectivity filter of 2.8~Å, but soon after, the selectivity filters in some of them were shown to be slightly bigger, around 3.4~Å – and thus aquaporins were shown to be involved in the transport of some small polar solutes, such as glycerol.

More recently, some of them were shown to also transport hydrogen peroxide (and we contributed to the identification of one of these).

These discoveries came along with their implication of a plethora of pathological conditions – in which both aquaporin expression and function are altered. We have been working on their role in obesity and cancer, but also contributed to attract new groups to the aquaporin's field and investigate new roles in different organs and implications to several diseases.

# What is (or has been) the major challenge throughout your academic career?

Although the challenges are many – with funding being a major one, I would say that for us that are both researchers and professors, keeping the balance is the major challenge.

We need to be good professors and to invest in our teaching, so that good students keep being attracted to our universities, and later to our research, but at the same time, we need to keep up to very high levels of demand that research asks for - again attracting good (excellent) students to our groups, sustain the publication rate, attracting funding - always without forgetting that you have to be available to your undergrads. Whether we are doing well enough in both fields, is a question that challenges me every day.

### What has meant to you to be SPB President?

Being SPB President was, to me, an opportunity to help consolidating the Portuguese Biochemistry community. We have biochemists at many places – schools of pharmacy, schools of medicine, schools of sciences, research institutes, etc. – and the challenge is to be like a "glue" that brings them together and makes the – limited – resources of SPB available to as many of them as possible, especially in what concerns early career researchers and, on a different note, access to our international partners, particularly FEBS and IUBMB.

# What means to you to be FEBS Vice-Chair (and very soon Chair)?

Becoming FEBS Chair is a consequence of, as president of SPB, having organized the FEBS Congress in 2022, which in fact was a world international congress since it combined the FEBS, IUBMB and PABMB Congresses in one - we called it the World Biochemistry Summit.

Although being part of the Executive Committee, the role of FEBS vice-Chair is more consultive but it gives me the opportunity to represent Portugal and increase the visibility of the Portuguese Biochemistry community among the FEBS and other constituent societies.

This may facilitate new opportunities and help taking advantage of available resources, increasing the number of SPB representatives within the FEBS committees and working groups, and provide SPB with new opportunities to participate in FEBS activities.

### **News & Views**

# A "radical" biochemical view of cognitive enhancement

**João Laranjinha**, Faculty of Pharmacy and Center for Neurosciences and Cell Biology, University of Coimbra.



The brain, representing 2% of body mass in adults, consumes circa 20% of energetic substrates, glucose and oxygen, despite not performing mechanical work, and is dependent on a well-regulated cerebral blood flow (CBF). Curiously, that the brain is energetically expensive given its mass and that it is endowed with fine mechanisms for a precise spatial and temporal control of CBF, delivering energetic substrates to brain areas according to neural activity, has been known since the XIX century (ladecola, 2017).

That is, the mammalian brain has evolved a peculiar mechanism by which CBF (i.e., O2 and glucose deliver) is adjusted in time and space according to changes in neuronal activity and metabolic demand within a small volume of brain tissue (likely within a sphere of a few hundreds of microns of diameter).

This mechanism, the neurovascular coupling, NVC (also known as functional hyperemia as is the basis for brain functional imaging techniques), ensures that the most active areas of the brain get an appropriate amount of energy substrates. This has led to the fundamental concept that the supply of energy may impose a limit on the activity of a neuron and, therefore, on neural communication under normal conditions. The NVC, or more generally, the Neurovascular Unit, operates under a tight network communication among neurons, astrocytes, and vascular cells (smooth muscle cells, endothelial cells and pericytes).

As simple as it may sound, the highly energy-sensitive network involved in delivering energetic substrates to the active areas of the brain (NVC) implies that fluctuations and failure in the communication between neurons and blood vessels results in catastrophic depletion of oxygenation and energy supply to brain cells, and, in the long run, to neuronal dysfunction and cognitive impairment.

Accordingly, mounting evidence from preclinical and human studies demonstrate that NVC dysfunction is a key early factor contributing to the pathogenesis of cognitive decline and vascular cognitive impairment (VCI) in aging and conditions associated with accelerated microvascular aging, including Alzheimer's disease.

Putting it in the simple terms as forwarded by Marcus Raichle, NVC is the root for cognition. This notion is important because raises the premise that by rescuing the functionality of NVC then cognitive enhancement should be observed.

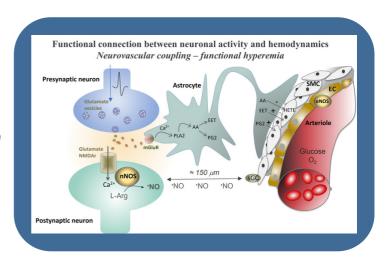
A significant question, then, is what are the messengers, conveying the information among cells within the tridimensional neurovascular unit space in the brain. It sounds clear that a full picture relating neurovascular processes and cognition requires multimodal approaches to bridge molecular mechanisms and cellular function.

A complementary strategy, guided by the theory formulated by Harold Morowitz (1979) that "the flow of energy through a system acts to organize that system", is to identify the most fundamental biochemical messenger operating within the tridimensional network that regulates the flow of energetic substrates from blood vessels to active neural cells, supporting biological organization and function.

Despite the extensive investigations and advances in the field over the last decades, a clear definition of the mechanisms and mediators underlying this process is still elusive.

This is accounted for by the difficulties in measuring the process in vivo in a dynamic fashion, allied with the intrinsic complexity of the process, likely enrolling diverse signalling pathways and numerous molecular messengers that reflect the specificities of the neuronal network of different brain regions and the diversity of the neurovascular unit along the cerebrovascular tree.

A few years ago, Lourenço et al. (2014), on basis of dynamic and real-time recordings of NVC in the brain of rats provided strong evidence that nitric oxide (NO) synthesized by the neuronal isoform of NO synthase (nNOS) is the key modulator of the communication between active neurons and nearby localized blood arteries. Nitric oxide is a relatively stable free radical and ubiquitous cell messenger that participates in many physiological processes, notably vasodilation.



The physicochemical properties of nitric oxide (NO) as an intercellular messenger, in particular the way it conveys information via volume signaling, translate into advantages of communication in the brain.

The nNOS is activated at synapses when neurons fire and the NO produced, because it is small (no specific interactions with targets or "receptors"), hydrophobic (readily permeates biomembranes) and exhibits a high diffusion coefficient, will repeatedly diffuse in and out of a cell over the time span of its half-life, acting as an intercellular messenger and conveying information associated with its profile of change in time and space. By this way, via volume signaling, NO can synchronize the activity of neurons with vascular cells located away (no need for physical contacts between neurons and vascular cells) but within the tridimensional space of the neurovascular unit, to control the communication among cells in a "wireless" fashion.

Overall, in vivo studies in mammals, including humans, support that an operational NVC, allocating energy resources according to neuronal activity, is a most fundamental biochemical process that underline biological organization to support cognition.

This process is critically mediated by a diffusible intercellular radical messenger, nitric oxide. Vascular cognitive impairment and dementia associated with aging has emerged as one of the major public health challenges of our time.

Thus, it is tempting to suggest that maintaining such a "radical biochemistry" operative in the brain (NO-mediated functional NVC), cognitive performance might be enhanced during aging and aging-associated diseases.

This has already been demonstrated in rats. As for the humans, we reasoned that rat's biochemistry might not explain everything about humans but it is a good approach, showing the feasibility of developing strategies to sustain functional NVC responses in individuals at risk for cognitive impairment.

#### References:

- Iadecola, C. (2017). The Neurovascular Unit Coming of Age: A Journey through Neurovascular Coupling in Health and Disease. Neuron 96, 17-42.
- Lourenco C.F. et al. (2014) Neurovascular coupling in hippocampus is mediated via diffusion by neuronal derived nitric oxide. Free Radical Biology & Medicine 73:421-429.

## **SPB** activities



# 1st FEBS Redox Medicine Workshop: from cellular signalling to systems physiology and therapeutic targets

Luso, May 22nd - 25th, 2023

### Report by Bárbara Rocha, University of Coimbra

This workshop aimed to bridge the gap between basic and clinical/applied research in the field of redox biology, spanning several physiological systems and diseases. In addition to the thematic sessions, the program included 3 special lectures: an opening lecture by the IUBMB speaker Prof. Enrique Cadenas (USA), a Women in Science Lecture, by Prof. Cristina Polidori (Germany) and a Closing Lecture by Prof. Jose Vina (Spain). There was also a special session dedicated to bioanalytical tools and a round table to debate strengths and limitations of the methods used in redox biology research. Career development sessions included one focusing on communication skills in science and a second oriented towards writing and published scientific articles and the publication process.

Each thematic session included 2 invited lectures, one focusing on basic research and the other on clinical or applied research in redox. Each session was followed by 3 oral presentations selected from submitted abstracts. In addition, 6 posters were selected by the evaluation panel for flash presentations in the final day of the workshop. This designed allowed for a span of talks from highly accomplished senior scientists and PhD students and post-doctoral researchers, considered very positively by participants.



# SPIB2023 - Symposium on Pedagogical Innovation in Biosciences - How to Engage Students in Our Practices?

University of Aveiro, October 12th-13th, 2023

# Report by Margarida Fardilha, University of Aveiro

The symposium was organized by the University of Aveiro and University of Minho, in association with SPB, FEBS and IUBMB, and focused on promoting active learning methods that enable students to engage more deeply with the course material, student engagement strategies that foster a sense of community and collaboration in the classroom, and leveraging research in science education to enhance the learning experience.

Through interactive presentations and workshops, the SPIB2023 provided a valuable opportunity for educators, researchers and professionals to collaborate and exchange ideas on how to improve biosciences education and prepare the next generation of bioscience professionals. Three SPB grants and 3 FEBS grants were awarded to students. Poster sessions were also organized, and selected talks presented.

Furthermore, distinguished Professors were chosen by the students as the recipients of "Best Professor" award from their respective departments. The event ended with a closing message highlighting its success and Nigel Francis (Cardiff University, UK) being awarded a prize for the best poster (sponsored by SPB) for his work in the use of PeerWise for biochemical teaching.



# Workshop on Biochemistry of Aging, 2nd edition

November 7th, 2023 (online)

# Report by Paula Ludovico, University of Minho

The second edition of the "Workshop on Biochemistry of Ageing" aimed to join researchers and students interested in the complexity and multifactorial mechanisms of ageing, by facilitating and disseminating science, joining interests around senescence, new models, biochemical processes, discoveries and therapies. It was also an opportunity of reflection in a field that greatly accelerated in the last decade, emerging as one of the most important and determining areas of scientific research requiring different perspectives and approaches.

In this edition, two topic sessions on Ageing and Cancer and Ageing and Neurodegenerative Disorders were featured and opened by plenary talks by Eric Solary (Institut Gustav Roussy, France) and Tarja Malm (University of Eastern Finland, Finland), respectively. These sessions besides other internationally renamed speakers (e.g., José Pedro Castro, Máté Maus, João Duarte Pereira, Marzia Perluigi and Jens Pahnke), included firetalks selected from PhD students participating. The "Workshop on Biochemistry of Ageing" had more than 200 registrations resulting in an attendance of 180 national and international participants.

### RNA solutions to infectious and noncommunicable diseases

ICBAS, University of Porto, Open symposium (Nov 27th 2023) + Exhibition (Nov 27th-Dec 13th), 2023

### Report by Maria Strecht Almeida, University of Porto

RNA Solutions brought together around sixteen people for a multidisciplinary discussion around therapeutic RNA solutions, in the context of science-society interaction. This event was supported by the Science and Society program of FEBS. The symposium featured contributions from molecular biology (Maria Carmo-Fonseca, University of Lisbon), immunology (Luís Graça, University of Lisbon), sociology (Ana Delicado, University of Lisbon) and communication design (Heitor Alvelos, University of Porto) and was moderated by Jorge Pedrosa (University of Porto).

The importance of collaborations between different scientific disciplines was emphasized, reinforcing the conviction that something new and more accessible to different audiences can emerge from this type of crosstalk.

On the same day, an exhibition was opened that seeks to show the visual culture of RNA research, bringing images produced in the areas of life and health sciences for an appreciation outside that scope. Their reading in a new context can be done in its aesthetic dimension, constituting another way of bringing science to different audiences.







26/01

#### **SPB Clinical Biochemistry Workshop**

University of Algarve, Faro

**LINK** 

15/03 to 14/04 **SPB action grants:** organization of students Meetings, Workshops, Congresses or SPB Conferences.

LINK

20 -23 /03

**FEBS Education and Training Conference** 

Antalya, Türkiye

**LINK** 

26 - 29/06

23rd FEBS Young Scientists' Forum

Pavia, Italy

**LINK** 

29/06 to 03/07 **48th FEBS Congress** 

Milano, Italy

LINK

22 - 26/09

**Biomolecular Horizons 2024** 

Melbourne, Australia

**LINK**