

CICLO JORNADAS CIENTÍFICAS  
PROMETEO 2022

# AMINO-NANOZIMES

## Biomedical Applications



**Dra. Olga Iranzo**

Institut des Sciences  
Moléculaires de  
Marseille



**Dr. Peter Faller**

Université de  
Strasbourg



**Dr. Patrick Gámez**

Institut de Nanociència i  
Nanotecnologia de la  
Universitat de Barcelona



24 de Novembre de 2023



11:00 - 14:00 h



Salón de Grados Facultat de Química. Universitat de València.  
(Campus Burjassot)

Organizado por:

**SUPRAMOL**  
*a supramolecular chemistry group*

**ICMOL**  
INSTITUTO DE CIENCIA MOLECULAR

 **GENERALITAT  
VALENCIANA** | **TOTS  
A UNA  
veu**  
Conselleria de Innovación,  
Universidades, Ciencia  
y Sociedad Digital

  
**VNIVERSITAT  
DE VALÈNCIA**



11:00h



**Dra. Olga Iranzo** (*Institut des Sciences Moléculaires de Marseille*)

### **Bioinspired Peptidic Ligands: from Concepts to Applications in Health and Catalysis**

Peptides are an interesting family of molecules that have high potential to develop metal-containing systems with different structures and functionalities. Inspired by Nature, we have been developing different peptidic scaffolds capable of binding different transition metals, among them copper. In this presentation, I will mainly focus on these copper systems covering from their design to their characterization and functional analysis.

12:00h

**Dr. Peter Faller** (*Université de Strasbourg*)

### **Design of peptide shuttles importing Cu into cells and able to prevent ROS induced cell toxicity of Cu-amyloid- $\beta$**

Copper ions are essential for mammals and its homeostasis is tightly controlled. In Alzheimer's disease (AD), Cu-accumulation occurs in amyloid plaques, where it is bound to the amyloid- $\beta$  peptide (A $\beta$ ). In vitro, Cu-A $\beta$  is competent to catalyze the production of reactive oxygen species (ROS), and hence contribute to the oxidative stress in AD. Other groups have shown that molecules that can recover extracellular Cu from A $\beta$  and transport it back into cells has beneficial effects in cell culture and transgenic AD models. However, these Cu-shuttles currently available have limited selectivity. We designed a novel peptide-based Cu shuttle with a selective Cu(II)-binding motif and which is tagged with a fluorophore sensitive to Cu(II)-binding and release. Our shuttles were able to transport Cu ions selectively into PC12 cells and made it bioavailable. Moreover, they were able to withdraw Cu from the A $\beta$  peptide and consequently inhibited the Cu-A $\beta$  based ROS production and related cell toxicity. Hence, these Cu-shuttles could be a valuable new tool for Cu-transport into cells and for mechanistic insights, with potential applications in restoring Cu-homeostasis in Cu-related diseases such as AD.



13:00h



**Dr. Patrick Gámez** (*Institut de Nanociència i Nanotecnologia de la Universitat de Barcelona*)

### **Small histidine-containing peptides to reduce copper-mediated oxidative stress in Alzheimer's disease**

Metal ions are crucial in the human body; however, they can cause serious damage to biomolecules and cells when their metallostasis fails. Misbalanced levels of copper have been found in AD brains where it generates oxidative stress, eventually leading to neuron dysfunction and death. Moreover, copper is found in the synaptic cleft together with the Ab peptide, and it is believed that it stabilizes Ab oligomers, enhancing their toxicity. Hence, copper-capturing drugs represent a promising tool against AD as they may restore natural Ab aggregation into (less toxic) amyloid plaques and prevent copper-mediated generation of oxidative stress. In that context, we are using small peptides containing at least one histidine residue (as effective copper binder) to displace A $\beta$ -bound copper ions and prevent the production of harmful oxidizing species.