School of Molecular Sciences
Arizona State University

SMS Fall 2021 Seminar Series

Friday Sept 3 | 2:30pm | Biodesign Auditorium*

Sensing, Studying, and Inhibiting Amyloid-β Aggregation using Photoluminescent Metal Complexes

Protein misfolding and aggregation mark the onset of a variety of neurodegenerative diseases including Alzheimer's disease (AD) and Parkinson's disease (PD). For AD in particular, different stages in the misfolding and aggregation of amyloid-β (Aβ) has been related to the development of this disease. Aβ is a relatively unstructured peptide of 39 to 42 amino acids in length, which can form soluble (oligomers) and insoluble (fibrils) aggregates. Amyloid-β fibrils possess a cross-b spine with a regular structure surrounded by large random coil regions. The intrinsic degree of disorder in these Aβ structures makes challenging the study of its structure and interactions with small molecules using traditional laboratory techniques such as X-ray diffraction and nuclear magnetic resonance (NMR). Nonetheless, structural information on the binding of small molecules to Aβ is necessary for developing better diagnostics tools and for drugs targeting to diminish the deleterious effect of Aβ fibrils on neurons. Here we will present our studies on the structure and binding sites of Aβ using Re(I) carbonyl dipyridophenazine complexes. These complexes present unprecedented properties for labeling amyloid aggregates, which involve increase in photoluminescence and selective chemical labeling. We have found that amyloid fibrils get photooxidized by the metal complexes nearby the place of binding. In addition, we discovered that rhenium complexes can photooxidize soluble Aβ monomers on amino acids that are distinct from those in the fibrils, suggesting a different binding place than for the fibrils. We will discuss how finding these photooxidation can help in elucidating molecular binding sites in soluble and insoluble Aβ structures. These photochemical modifications have a profound effect on the folding landscape, as well as the self-assembly and stability of amyloid aggregates.

Angel Martí, PhD

Professor, Rice University

Angel A. Martí obtained his Ph.D in Chemistry from the University of Puerto Rico, Río Piedras under the supervision of Prof. Jorge Colón. Following his postdoctoral training with Prof. Nicholas Turro's at Columbia University in New York, he joined the department of Chemistry at Rice University in Houston in 2008. At Rice, he has been using photochemistry to study a variety of topics including protein aggregation, cellular temperature, and nanomaterials. He is the author of more than 90 publications and has received a variety of awards including the Inter-American Photochemical Society Young Investigator Award in 2013, the New Investigator Award from the American Society for Photobiology in 2014, the Rice University Presidential Mentoring Award in 2019 and was elected Fellow of the Royal Society of Chemistry in 2020

**ZOOM option available: https://asu.zoom.us/j/87081218152*