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Conferencia:

***In situ* lipid synthesis: from artificial cells to
cancer therapeutics**

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**University of California – San
Diego – EE.UU**

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Aula de
Seminarios do
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***In situ* lipid synthesis: from artificial cells to cancer therapeutics**

Roberto J. Brea

University of California, San Diego



Roberto J. Brea began his research career as an undergraduate student at Universidad de Santiago de Compostela under the supervision of Prof. Juan R. Granja. After receiving his BSc in Chemistry, he started his PhD studies in the same stimulating environment, working on the construction of functional self-assembling cyclic peptide nanotubes. As part of his doctoral training, he expanded his chemical expertise with stays in the labs of Prof. M. Reza Ghadiri (The Scripps Research Institute, San Diego), Prof. Nazario Martín (Universidad Complutense, Madrid) and Prof. Dirk M. Guldi (Friedrich-Alexander Universität, Erlangen). In 2013, he defended his PhD dissertation (*summa cum laude*).

After his PhD, he joined Prof. Neal K. Devaraj's lab at the University of California, San Diego, working on the fabrication of self-assembled non-natural cellular systems. Only a couple of months later, he was awarded the prestigious and highly competitive Human Frontier Science Program (HFSP) Cross Disciplinary Fellowship to continue his studies on artificial cells.

Since 2018, he has worked as a Project Scientist at University of California, San Diego, focusing his research on the development of chemical strategies to generate self-assembled structures, control *in situ* lipid formation and modulate modification of proteins in living cells and organisms.

During the course of his research career, he has published 35 peer-reviewed articles in high-impact journals (including *J. Am. Chem. Soc.*, *Angew. Chem. Int. Ed.*, *PNAS*, *Nat. Commun*, etc), 3 book chapters and 4 patents. Additionally, he has been recognized with numerous academic and research awards [FPU, V Lilly Prize of Investigation, Medichem Prize, HFSP CDF, USC Extraordinary Doctorate Award, Nanoscale Horizons (RSC) Prize, Hijos de Rivera Award (Best Professional Trajectory), Finalist Career Awards at the Scientific Interface (Burroughs Wellcome Fund), etc].

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Lipids remain one of the most enigmatic classes of biological molecules. While it's well-known that lipids form basic units of structure and energy storage, deciphering the exact roles and interactions of distinct lipid species has proven elusive. How these individual lipids are synthesized, trafficked, and stored are also questions that require closer inspection. Therefore, there has been an increasing interest in developing simple strategies to mimic native lipid formation. Here we address relevant issues about the assembly of lipids and post-translational (de)lipidation of proteins through the development of chemical tools for controlling *in situ* lipid synthesis. Firstly, we describe the use of chemoselective approaches to spontaneously generate and remodel phospholipid membranes from reactive water-soluble precursors. The orthogonality, high reaction rate, and biocompatibility of these methodologies are key features that make them a powerful tool for the efficient encapsulation of relevant biomolecules. Moreover, these biorthogonal strategies successfully drive the *in situ* reconstitution of membrane proteins, with retention of functionality. Secondly, using similar chemical tools, we describe a small-molecule depalmitoylation strategy for the cleavage of native S-palmitoyl groups from proteins in living cells. All these methodologies enable the direct and precise construction of lipids, answering fundamental questions about the origins of membranes and the (de)lipidation of proteins.