K-P-081 **THE CARNITINE SHUTTLE: AN UNTAPPERED TRANSPORTER FOR MITOCHONDRIAL IMAGING**

José Luis Chiara.[1], Blázquez-Moraleja A.[1], Sáenz-de-Santa María I.[2], Chiara M. D.[2], Álvarez-Fernández D.[1], García-Moreno I.[3], Prieto Montero R.[4], Martínez-Martínez V.[4], López Arbeloa I.[4]

[1] Instituto de Química Orgánica General (IQOG-CSIC), Madrid, ***Spain*** *[2] Instituto de Oncología de Asturias (IUOPA), Oviedo, Spain [3] Instituto de Química-Física "Rocasolano" (IQFR-CSIC), Madrid, Spain [4] Universidad del País Vasco-EHU, Bilbao, Spain*

E-mail: jl.chiara@csic.es

Cellular metabolism is enhanced in cancer in order to sustain cell viability and uncontrolled proliferation. In particular, deregulation of lipid metabolism is one of the most important metabolic hallmarks of cancer cells. The carnitine shuttle system (CS), involved in the transport of fatty acids from the cytosol into the mitochondria matrix for oxidation, represents a major bottleneck for lipid metabolism and its reprogramming can play a pivotal role in tumors, suggesting new pathways for prevention and treatment.

We describe herein the first fluorescent probes that are actively channeled into the mitochondrial matrix by the CS in living cells. Our functional probes (**BCTs**) have a minimalist structural design based on the highly efficient and photostable BODIPY chromophore and carnitine as a biotargeting element. **BCTs** selectively label mitochondria regardless of their membrane potential and in an enantiospecific way. The obtained experimental evidence supports carnitine-acylcarnitine translocase (CACT) as the key transporter protein for **BCTs**, which behave therefore as acylcarnitine biomimetics. Slow hydrolysis of the probe in the mitochondrial matrix yields free carnitine and a BODIPY boron acid derivative, which remains within the organelle covalently attached to glycoproteins in the matrix, thus avoiding diffusion of the fluorescence signal.

This simple structural design can be readily extended to other structurally diverse starting BODIPYs to obtain **BCTs** with varied emission wavelengths along the visible and NIR spectral regions and with multifunctional capabilities. **BCTs** are promising research tools to explore the role of the CS in cancer and metabolic diseases.