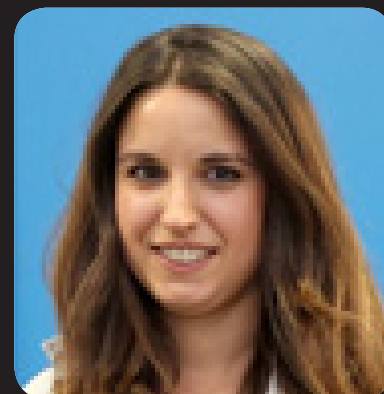


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A ROLE FOR ROS IN THE EPIGENETIC REGULATION OF GENE EXPRESSION

The generation of Reactive Oxygen Species (ROS) as by-products of the highly efficient aerobic metabolism constitutes an inescapable biochemical side effect that can be extremely harmful for cell viability, due to the irreversible oxidation of lipids, proteins and nucleic acids. Nevertheless, eukaryotic cells can also actively generate ROS as essential components of molecular mechanisms regulating key cellular processes, including proliferation and differentiation, through the oxidation of redox-sensitive proteins such as kinases and phosphatases. Here we propose that eukaryotic cells may also use ROS to directly regulate DNA methylation and gene expression patterns through the oxidation of methylated cytosines in CpG Islands (CGI) of target gene promoters. To test this hypothesis, we have used a Protoporphyrin IX-dependent photodynamic treatment as a tool to activate an endogenous production of non-lethal ROS levels in different biological models, including NIH3T3 mouse cultured fibroblasts, E14 mouse embryonic stem cell line, and mouse dorsal and tail skin in vivo. Using this approach, we report that a transient switch-on of ROS production efficiently promotes the dynamic hydroxylation of 5mC in eukaryotic cells and tissues, and changes gene expression patterns. We further report that this ROS-dependent hydroxylation of 5mC occurs also in vitro in a naked DNA molecule in water solution, indicating that the process can take place in a TET-enzyme independent process. As a whole, these results suggest that ROS may be involved in the regulation of gene expression patterns through the dynamic modulation of DNA methylation patterns.

Biography

Since 2014 I am a PhD in cell biology and genetics (UAM). I made different pre-doctoral and post-doctoral research stays at remarkable European institutions. I have participated in 13 R&D projects founded by competitive calls and relevant industrial partners. As a result, I have presented 36 scientific contributions, and I am co-inventor of 3 patents, all currently being commercially exploited, and other two ongoing. Currently I am a post doctoral researcher of the Experimental Dermatology Group, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS, Hospital Ramón y Cajal, Madrid), where I am involved in various research projects mainly focused on regenerative medicine, specifically epigenetics and gene regulation during skin regeneration and hair follicle growth cycle through the endogenous generation of non-lethal Reactive Oxygen Species levels. I also collaborate as associate professor with Universidad Francisco de Vitoria.

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