EuroSciCon

European Conference on

Agriculture, Horticulture & Epigenetics

February 25- 26, 2019
Paris, France

S Fernandez-Martos et al., Int J Appl Sci Res Rev 2019, Volume: 6
DOI: 10.21767/2394-9988-C1-009

DIRECT HYDROXYLATION OF METHYLATED CYTOSINES BY A TRANSIENT ROS PRODUCTION

S Fernández-Martos[1], MI Calvo-Sánchez[1], V Lombardo[1], H Mjoseng[2], RR Meehan[2], J Espada[1]

[1]Experimental Dermatology and Skin Biology Group, Ramón y Cajal Institute for Health Research (IRYCIS), Ramón y Cajal University Hospital, Madrid, Spain

[2] Genome Regulation MRC Human Genetics Unit MRC IGMM University of Edinburgh Western General Hospital, Edinburgh, UK

Methylation of the 5´position of cytosine (5mC) in CpG dinucleotides is a major epigenetic mark of mammalian genomes, commonly associated with chromatin compaction and repression of gene transcription. DNA methylation, catalysed by the DNA methyltransferase (DNMT) protein family, is not an irreversible chemical modification of the DNA molecule. Methylated cytosines can be further oxidized by the enzymatic action of members of the Ten-Eleven-Translocation (TET) protein family to form hydroxymethyl cytosine (5hmC), which ultimately may activate DNA demethylation by passive and active pathways. These mechanisms provide the DNA methylation process with a strong dynamic potential.

Here we propose that 5mC can be also oxidized directly by reactive oxygen species (ROS). In mammalian cells, ROS are mainly produced as a side effect of the aerobic metabolism and, as such, can be extremely harmful for cell viability. However, ROS are also produced in small amounts by dedicated mechanisms (e. g., lipoxygenases, cyclooxygenases and NOX enzymes), acting as true second messengers in essential cellular processes, including cell proliferation, differentiation or motility.

Supporting our hypothesis, here we show that a transient production of ROS through a Protoporphyrin IX-dependent photodynamic procedure in an aqueous medium containing a methylated DNA fragment, and in the absence of proteins, lipids or carbohydrates, results in the oxidation of 5mC to 5hmC. Using this photodynamic experimental tool, we also provide evidence for the existence of such mechanism in human and mouse origin cultured cells, and also in mouse adult tissues. As a whole, our results suggest that a local production of ROS in the nuclear compartment can be a mechanism contributing to the dynamic regulation of the DNA methylation state.

Biography

I hold a bachelor in Biology (2015) and Master degree in Biomedical Research (2016). During three years I've been a pregraduate student in the Auditory Neurobiology Group, (Facultad de Medicina, Universidad Complutense de Madrid, 2014-2016). Currently I am a PhD Student at 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. As a result, I have participated in 3 R&D projects founded by competitive calls and relevant industrial partners, I have presented 5 scientific contributions, and I am co-inventor of 2 patens currently being commercially exploited (other two ongoing).

fernandezmartossandra@gmail.com