

GENERATION OF MINILUNGS FROM HUMAN EMBRYONIC STEM CELLS. ANALYSIS OF THE EFFECTS OF VITAMIN D IN THE EXPRESSION OF DNA DAMAGE INDUCED BY BLEOMYCIN.

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The generation of organoids from human pluripotent stem cells allows deeper insight into human development, disease modeling, drug screening and regenerative medicine. Organoids are *in vitro* generated 3D structures containing multiple cell types that are organized similar to an organ, recapitulate some specific organ function and can mimic the responses of real tissues. Different human minilungs (organoids) have been generated from both human embryonic and induced pluripotent stem cells (hESCs and hiPSCs, respectively). We show here the generation of 2D and 3D minilungs from two hESCs lines (AND-1 and AND-2) and have analyzed the effects of vitamin D, and two non-calcemic vitamin D analogs, in the expression of DNA damage induced by the antibiotic bleomycin, an agent widely used to induce lung fibrosis. The results indicate that bleomycin induced DNA double-strand breaks in both types of structures and that vitamin D elevated its number. In addition, the two vitamin D analogs tested were able to reduce the DNA damage observed. The results are discussed in terms of the role of DNA damage in lung fibrosis and the potential use of vitamin D analogs in conditions characterized by DNA damage and senescence such as lung fibrosis.

Biography

Ms. Esmeralda Magro is a third year PhD student in Molecular Biosciences at the University Autonomous of Madrid. She is conducting a research project at the Institute of Health Carlos III, under the supervision of Dr. Alberto Zambrano. She did her M.Sc. thesis at Dr. Zambrano´s lab. This work was related to the role of vitamin D on DNA damage expression and cellular senescence in alveolar epithelial cells type II and human fibroblasts and its potential use as an antifibrogenic agent in Idiopathic Pulmonary Fibrosis (publication under review). She signs this work as co-first author. Currently, she is working on her thesis which is focused on the generation of two and three-dimensional human mini-lungs from human embryonic stem cells to model chronic respiratory diseases, preferably, the Idiopathic Pulmonary Fibrosis (IPF). She is also interested in studying the effect of different drugs and ligands for nuclear hormone receptors in DNA damage expression and cellular senescence in the context of lung fibrosis (*Magro-Lopez E et al., 2017, Viruses)* and (*Magro-Lopez E. et al., 2018, Stem Cell Res Ther).*

Keywords: human embryonic stem cells, minilungs, vitamin D, DNA damage, lung fibrosis.

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