

PROGESTERONE RECEPTOR IS CONSTITUTIVELY EXPRESSED IN INDUCED PLURIPOTENT STEM CELLS (iPSCs)

Michele Manganelli¹, Elena Laura Mazzoldi¹, Rosalba Monica Ferraro¹, Marta Parigi¹, Seyed Ali Mir Aghel¹, Mattia Bugatti², Ginetta Collo³, Gabriele Stocco⁴, William Vermi², Luigi Mori⁵, Silvia Giliani¹

¹ "Angelo Nocivelli" Institute for Molecular Medicine, Department of Molecular and Translational Medicine, University of Brescia, Italy, ASST Spedali Civili, Brescia, Italy, 25123, Italy

² Department of Molecular and Translational Medicine, University of Brescia, Italy, ASST Spedali Civili, Brescia, 25123, Italy.

³ Division of Farmacology, Department of Molecular and Translational Medicine, University of Brescia, Brescia, 25123, Italy.

⁴ Clinical Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, I-34127, Italy.

⁵ Department of Clinical and Experimental Sciences (DSCS), University of Brescia, Brescia, 25123, Italy.

Induced Pluripotent Stem Cells (iPSCs) are nowadays a common starting point for wide-ranging applications including 3D disease modeling, drug development and regenerative medicine. Physiological processes like homeostasis, cell differentiation and development are tightly regulated by hormones through binding to their receptors of target cells. Considering their pleiotropic effects, it is important to understand their role also during cell differentiation, in particular for those *in vitro* disease models which include steroid hormone cellular response. We explored the expression pattern of estrogen receptor (ER α) and progesterone receptor (PR) in four different iPSCs, obtained from CD34⁺ progenitor cells and skin fibroblasts with four different methods (episomal vector, Sendai-, Retro- and Lenti-virus). Expression of ER α and PR mRNA were significantly reduced in iPSCs compared to MCF7 breast cancer cells positive control ($p < 0.0001$). Surprisingly, immunofluorescence staining detected only the expression of PR protein in all the different iPSCs cell lines, while ER α was not detectable. These results suggested that active translation occurred, therefore to determine the moment in which PR protein expression arose in iPSCs, we extended the analysis to precursor cells. By flow cytometry analysis we observed that the ~65% of the total population of iPSCs cells expressed only PR, with 100% fold increase compared to hematopoietic stem/progenitor cell (HSPCs) and fibroblasts ($p < 0.0001$), while ER α was not expressed. Our results collectively highlighted for the first time that the reprogramming of somatic cells into iPSCs leads to the expression of PR receptor. These finding would improve future research in iPSCs cell-based disease modelling, being a starting point to better comprehend the molecular mechanisms involved in development and cellular response to treatments.