

### **6.03 Induced Pluripotent Stem Cell-derived Alveolar Epithelial Type 2 Cells – A Novel Model to investigate Sex Hormones and their Role in Pulmonary Fibrosis**

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**Background:** Idiopathic Pulmonary Fibrosis (IPF) occurs predominantly in men over the age of 60 years and women after the onset of menopause, implying a role for sex hormones in disease development. Mouse models suggest that estrogen affects IPF pathogenesis. Research in human models is lacking. We hypothesize that type 2 alveolar epithelial (AT2) cells respond to sex hormones and that human iPSC-derived AT2 cells (iAT2s) can be used to model this.

**Methods:** Non-diseased iAT2 cells were treated with control, estradiol or testosterone. Expression of AT2 marker genes and sex hormone receptors was measured by RT-qPCR. Bulk RNA sequencing was executed to investigate iAT2 response to these sex hormones. ESR $\beta$  and GPER1 expression on protein level was investigated using Western Blot Analysis.

**Results:** Significant expression of ESR $\beta$  and GPER1 was shown on the protein and RNA level in iAT2 cells and were downregulated following estradiol treatment. Expression of SFTPA1 and SFTPC was downregulated following estradiol treatment but upregulated following testosterone treatment.

**Conclusion:** This is the first report of sex hormone treatment of human iAT2 cells and explores their effect on typical cell expression markers and human disease pathways. Our preliminary data shows opposing effects of estrogen and testosterone on surfactant genes.

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