BMPS5

Undifferentiated iPS Cells Do Not Regenerate Functional Lung Tissue When Seeded on Native Lung Extracellular Matrix under Biomimetic Culture Conditions

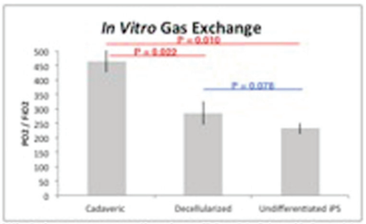
Authors **Heba Al-Siddiqi, Bernhard Jank, Roger Ng, Jeremy Song, Joseph Vacanti, Harald Ott**

Institutions Qatar Foundation, Doha, Qatar
Massachusetts General Hospital, Boston, Massachusetts, USA
Harvard Medical School, Boston, Massachusetts, USA

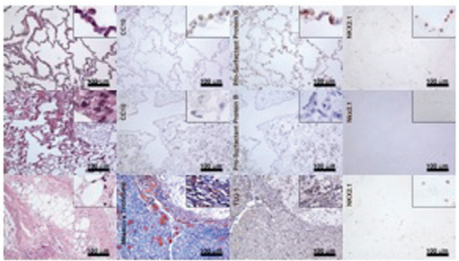
e mail heba.alsiddiqi@gmail.com

Perfusion-decellularized native lungs seeded with human BJ

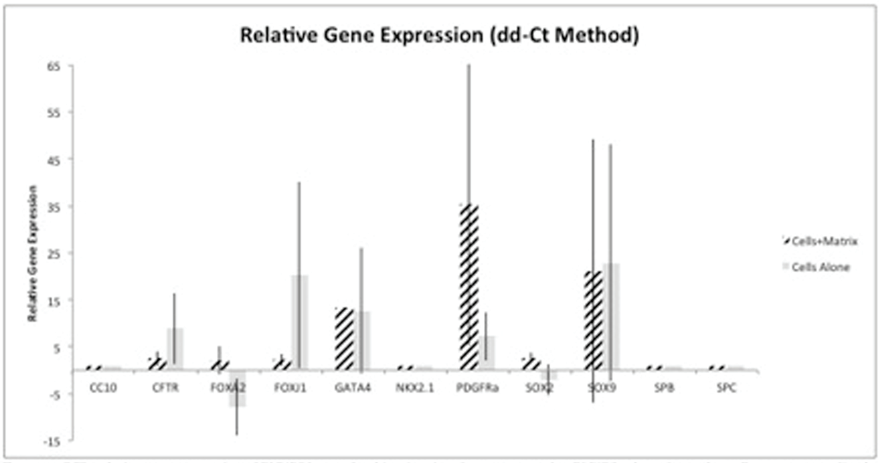
RNA-induced pluripotent stem (BJ-RiPS) and umbilical vein endothelial cells failed to regenerate functional lung tissue as quantified by immunohistochemistry (no detection of TTF1,CC10,and Pro-SPB), gene expression (non-significant differences in lung-specific gene expression as compared to cells cultured under standard conditions), and in vitro lung gas exchange properties. Histological analysis of orthotopically transplanted BJ-RiPS lungs revealed a teratoma (detection of ectoderm: TuJ1, mesoderm: SMA, and endoderm: TTF1).



Whole lungs were ventilated at a FiO_2 of 1, 24cm H_2O positive inspiratory pressure, 7cm H_2O positive end expiratory pressure, and a frequency of 55 breaths/min. Pulmonary venous effluent was measured. Red denotes significant difference (Student's T-test).



Top Row: Cadaveric Human Lung. Middle Row: Undifferentiated RiPS Cells & HUVECs seeded lungs after biomimetic culturing. Bottom row: Bioartificial lungs after orthotopic transplantation. All three germ layers are represented.



Taqman qPCR: relative gene expression of BJ RiPS lungs after biomimetic culture compared to BJ RiPS cultured on geltrex. Data was normalized to 18S and undifferentiated BJ RiPS served as the calibrator for $\Delta\Delta$Ct calculations. Outliers were excluded using Grubb's Outlier Test (α=0.05). Samples with thresholds above 38 cycles were not factor into calculations. There are no significant differences in relative gene expression in comparing cells in matrix versus cells on geltrex (Student's T-Test, P>0.05) for all genes. Biological triplicates and technical replicates were performed.