

## **Lenti-mediated expression of PPAR $\gamma$ in human and murine alveolar macrophages,**

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Peroxisome Proliferator-Activated Receptor  $\gamma$  (PPAR $\gamma$ ) is a transcription factor involved in lipid and glucose metabolism. Alveolar macrophages constitutively express high levels of PPAR $\gamma$ . Pulmonary Alveolar Proteinosis (PAP) is an autoimmune disease characterized by the high titers of neutralizing anti-GM-CSF (Granulocyte Macrophage Colony-Stimulating Factor) antibody leading to an overaccumulation of surfactant lipid in the lung. Previous studies from our laboratory have shown PPAR $\gamma$  deficiencies in the alveolar macrophages from PAP patients. GM-CSF Knockout mice also have PPAR $\gamma$  deficiencies in the alveolar macrophages and accumulation of surfactant lipid, making GM-CSF KO a good model for studying PAP. We hypothesize that the deficiency of PPAR $\gamma$  in alveolar macrophages leads to accumulation of surfactant. We have developed a lentiviral expression system to study the role of PPAR $\gamma$  in the lung.

Herein, we have utilized this system to successfully generate a lentivirus expressing PPAR $\gamma$  (L-PPAR $\gamma$ ). Successful L-PPAR $\gamma$  transduction of human and murine alveolar macrophages obtained from bronchoalveolar lavage has been confirmed by immunofluorescence microscopy. Preliminary data using real time PCR shows a 16 fold increase in the expression of PPAR $\gamma$  mRNA in the murine alveolar macrophages upon transduction with L-PPAR $\gamma$  vector. Our results suggest that this system provides a reliable approach to study gene expression in primary macrophages. Further experiments are currently underway to characterize the role of PPAR $\gamma$  in lipid metabolism and lung biology.