

Macrophage Peroxisome proliferator-activated receptor-gamma (PPAR γ) deletion disrupts lipid gene expression in murine alveolar macrophages.

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PPAR γ is a ligand-activated, nuclear transcription factor that regulates genes involved in lipid and glucose metabolism as well as inflammation. We demonstrated that PPAR γ is constitutively expressed in human alveolar macrophages from healthy individuals and markedly decreased in Pulmonary Alveolar Proteinosis patients whose macrophages have a foam cell appearance and have lungs filled with surfactant. These observations suggest a role for PPAR γ in surfactant metabolism. To investigate PPAR γ deficiency in the macrophage, floxed (+/+) PPAR γ conditional mice (FJ Gonzalez) were crossed into a transgenic mouse containing the CRE gene under the control of the murine M lysozyme promoter. Alveolar macrophages were harvested by bronchoalveolar lavage (BAL), from mice at 10-12 weeks of age and pooled from 3-5 mice per set. Histopathological analysis (including periodic acid schiff PAS stain) revealed no abnormalities in the lungs. Analysis of differentials demonstrated increased numbers of foamy oil red O positive (indicating neutral lipid accumulation) macrophages as compared to controls. Interestingly, real time PCR analysis of gene expression (n = 5 sets) revealed that ATP binding cassette ABC transporter A1 was increased 14.9 fold (p = 0.0002); ABCG1, 2.6 fold (p < 0.0001); Apolipoprotein E (APOE), 118 fold (p < 0.0001). Liver X receptor (LXR α) and lipoprotein lipase (LPL) were not different from controls. These results indicate dysregulation in lipid genes in PPAR γ deficient alveolar macrophages.