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Respiratory Distress in NPC2 Mutant Mice

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Niemann-Pick Type C is a cholesterol trafficking disorder caused by a mutation in one of two genes, NPC1 or NPC2. Mutation in either gene causes neurodegeneration; loss of NPC2 may cause respiratory failure. Many *Npc2* deficient mice in an F2 intercross with FVB/N suffer from respiratory distress and die within 24 hours postnatally. Histological analysis shows evidence of respiratory distress syndrome (RDS) in these mice. RDS is a major health problem in humans and often stems from incomplete lung development leading to lack of Type I and Type II pneumocytes. To determine whether a developmental problem causes respiratory distress in these mice, we are using Pro SP-C as a marker for Type II pneumocytes and T1#61537; (podoplanin) as a marker for Type I pneumocytes. Immunohistochemistry and Western blots indicate Pro SP-C is present in both wildtype and mutant mice at similar levels, suggesting that the respiratory distress is not due to a defect in Type II pneumocyte development. Electron microscopy has also been done on wildtype and mutant mice to examine lung ultrastructure. Additionally, respiratory distress can be due to lipid abnormalities in pulmonary surfactant. Thin layer chromatography (TLC) will be used to determine any differences in lung lipid content between wildtype and mutant pups. If TLC shows any major differences, high performance liquid chromatography (HPLC) and gas chromatography/mass spectroscopy (GC/MS) will be utilized to further identify and quantify the lipid components of surfactant.