

GENETIC MODIFIERS OF CYSTIC FIBROSIS: TWIN AND SIBLING STUDY

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Synopsis:

Background

Cystic fibrosis is the most common life-shortening autosomal recessive disorder in Caucasian's. Patients develop progressive lung disease, pancreatic insufficiency, and other complications as a result of inspissated secretions in epithelial tissues. The primary defect is in CFTR, a chloride channel and regulator of other channels. Although over 800 mutations have been described in the CFTR gene, one, $\Delta F508$, is present on 70% of alleles. Almost 50% of CF patients are homozygotes for $\Delta F508$. A few of the clinical manifestations of CF can be attributed to the mutations in CFTR, such as the pancreatic status (e.g. 98% of $\Delta F508$ homozygotes are pancreatic insufficient). However the severity and progression of lung disease, incidence of meconium ileus, and other common complications are highly variable, even within families. Recently, a modifier locus for meconium ileus has been identified on chromosome 19q13⁶.

Methods

We propose to study twins and siblings with CF. Subjects will be recruited through the CF Center at Children's Hospital & Research Center at Oakland. Blood will be obtained from patients and parents for direct DNA extraction. Once CFTR genotyping and identity is determined, we will use chart review to carefully and completely phenotypically characterize the twins and siblings.

Results/Conclusions

This study has just received IRB approval and is in the process of patient recruitment.