

LTRC Concept Sheet # 10-99-0004

FOLLOW-UP OF GENOME-WIDE ASSOCIATION SIGNALS IN COPD

ABSTRACT

Two recent genome-wide association studies in COPD have identified three genomic regions that are likely to contain COPD susceptibility loci; these regions include the *FAM13A* gene on chromosome 4, a locus near the *HHIP* gene on chromosome 4, and a block of genes on chromosome 15 including the *IREB2* gene and several components of the nicotinic acetylcholine receptor. However, the key genes and functional variants within those regions have not yet been proven. Examination of gene expression and protein levels of genes within those GWAS loci is an essential next step. We hypothesize that functional SNPs in or near *HHIP*, *FAM13A*, and *IREB2* affect the expression of these genes in COPD, which in turn promotes the development of COPD. Using previously obtained COPD lung tissues from the LTRC, we have found differences in gene expression for *HHIP* and *FAM13A* between COPD cases from the LTRC and control lung tissues obtained from other investigators.

However, the mild IPF subjects obtained from LTRC and the LTRC COPD subjects also showed reduced levels of gene expression for *HHIP* and *FAM13A* than the available control lung tissues. In order to determine whether there were differences in the preparation or preservation of the control lung tissues that we obtained previously, we are requesting 20 control lung tissue samples to compare to the 20 previously obtained COPD lung tissue samples with FEV1 < 80% predicted from the LTRC. In order to relate genetic variants in *HHIP*, *FAM13A*, and *IREB2* (as well as additional COPD GWAS loci to be identified in the future) to gene expression and protein levels, we are also requesting DNA samples that correspond to the control lung tissues provided.