European Respiratory Society
Annual Congress 2013

Abstract Number: 1661

Publication Number: P529

Abstract Group: 3.1. Molecular Pathology and Functional Genomics

Keyword 1: Functional genomics **Keyword 2:** Epithelial cell **Keyword 3:** Orphan disease

Title: Evaluation of gene expression during in vitro ciliogenesis to search for novel candidate genes in primary ciliary dyskinesia

Ms. Tamara 10374 Paff t.paff@vumc.nl MD [1,2,3], Dr. Eric 10375 Haarman eg.haarman@vumc.nl MD [2], Dr. Hans 10376 Daniels j.daniels@vumc.nl MD [1], Mr. Youssef 10377 Moutaouakil y.moutaouakil@vumc.nl [3], Dr. Dimitra 10378 Micha d.micha@vumc.nl [3], Mr. Maarten 10383 Massink m.massink@vumc.nl [3], Prof. Piet 14280 Postmus pe.postmus@vumc.nl MD [1] and Dr. Gerard 10387 Pals g.pals@vumc.nl [3]. [1] Pulmonary Diseases, VU University Medical Center, Amsterdam, Netherlands ; [2] Pediatric Pulmonology, VU University Medical Center, Amsterdam, Netherlands and [3] Clinical Genetics, VU University Medical Center, Amsterdam, Netherlands .

Body: Introduction Mutations in genes that are important in ciliary motility often cause primary ciliary dyskinesia (PCD). In half of the patients, causal mutations in any of the eighteen known PCD genes cannot be identified. Aim The aim of this pilot study is to investigate gene expression in respiratory epithelial cells during ciliogenesis. We hypothesized that a) all known PCD genes show similar expression profiles and that b) clustering genes with similar expression may provide novel PCD candidate genes. Methods We collected nasal epithelial curette biopsies from 2 healthy controls. Cells were cultured using a monolayer-suspension cell culture (Willems,T et al. J Cyst Fibros 2004). RNA was isolated at three time points: at the end of the monolayer culture (no cilia), after three days in suspension culture (growing cilia) and at the end of the suspension culture (full grown cilia). Whole genome expression arrays were performed and differential gene expression was analyzed by ANOVA. Results Except for TXNDC3, we observed a time dependent increase in expression levels in all known PCD genes. However, for HEATR2 and CCDC40 this difference did not reach statistical significance. A total of 1511 genes were significantly up-regulated during ciliogenesis. This cluster was highly enriched for genes related to cilia. Conclusion We identified a cluster of 1511 genes that showed an increase in expression levels during in vitro ciliogenesis, including 15 of the 18 known PCD genes. Using this novel application on a larger sample size may provide a more accurate cluster of possible PCD candidate genes.