Poster Session Abstracts

DHQ activates PqSR to initiate transcription of the operon for subsequent virulence factor production. Preliminary data generated from sputum samples by CF outpatients maintaining their lung functions contained a median DHQ concentration of 175 μM (SE 204, n=28). Trends of DHQ during an exacerbation demonstrated a decline in concentration between admission day 1 and final hospitalized day n=3. This study will enroll up to 70 patients and quantify sampling from both outpatient and inpatient groups for two years. Patient data, such as %FEV₁, antibiotic usage, cultured organisms, and CF genotype, will be used to stratify data for trend analysis.

Discussion: This study demonstrated DHQ is an important component of the Pqs system for virulence factor production. Quantification of DHQ in patient samples indicates that DHQ may also be used as a biomarker for exacerbated disease stage since DHQ is linked to both virulence factor production and toxicity towards the host.

376 TAS2R38 GENOTYPE IMPLICATIONS IN BASELINE LUNG FUNCTION IN ΔF508 HOMOZYGOUS CYSTIC FIBROSIS PATIENTS

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Introduction: The bitter taste receptor T2R38 was recently identified to regulate upper airway innate defenses through nitric oxide (NO) production in response to Gram-negative microbial quorum sensing molecules yielding direct bacterial activity as well as stimulating mucociliary clearance (Lee RJ, et al. J Clin Invest. 2012;122:4145-59). Previous investigations demonstrated that the robustness of defensive responses is modulated by common polymorphisms within the TAS2R38 gene which consist of either a proline/alanine/valine (PAV) or alanine/valine/isoleucine (AVI) at positions 29, 262 and 296. Thus the predominant haplotypes are PAV or AVI. Individuals with the PAV/PAV genotype demonstrate the greatest upregulation of NO and mucociliary clearance to quorum sensing molecules. Conversely, those with the PAV/AVI AND AVI/AVI genotype demonstrate minimal antimicrobial or mucociliary clearance activity in response to quorum sensing molecules. It has also been demonstrated that in non-CF patients, those with the PAV/PAV genotype do not require sinus surgery as frequently as other polymorphisms (p value 0.038) (Adappa ND, et al. Int Forum Allergy Rhinol. 2014;4:3-7). While the vast majority of CF patients have radiographic evidence of chronic sinus pathology, it is unclear why some CF patients develop sinusitis symptomatology while others do not and whether this may play a role in pulmonary outcomes.

Methods: Determine whether the protective polymorphism in the TAS2R38 gene (PAV/PAV) is predictive of pulmonary function and sinonasal quality of life (QLo) in an adult CF ΔF508 homozygous population. A prospective study was performed on patients who were genotyped for TAS2R38 and evaluated with a validated sinonasal outcomes test-22 (SNOT-22) as well as baseline predicted FEV₁ % and FVC%. Other factors including age, sex, lung transplant status, body mass index, and diabetes status were also evaluated. A one-way ANOVA was performed for statistical analysis.

Results: We genotyped 43 ΔF508 homozygous patients. The distribution included 8 PAV/PAV, 21 PAV/AVI, and 14 AVI/AVI. The baseline FEV₁ % was 70.3 for the PAV/PAV group and 56.9 for the other polymorphisms (p value 0.089) and the FVC% was 87.5 for the PAV/PAV group and 71.7 for the others (p value 0.065). The mean SNOT-22 score was 21.3 for PAV/PAV and 25.1 for the other genotypes (p value 0.566).

Conclusion: In a homogeneous population of adult CF ΔF508 homozygous patients, the protective T2R38 genotype (PAV/PAV) demonstrates a very strong trend for improved lung function both for baseline FEV₁% and FVC%. Further investigation in a larger population is warranted based on these promising data on a novel bitter taste receptor that may be a disease modifier in the CF population. Supported by the Cystic Fibrosis Foundation Pilot and Feasibility Award as well as the American Rhinology Society Young Investigator Award.