higher burden among certain demographic groups. Measures are required to arrest this ominous trend and to eliminate the disparities in outcome among patients hospitalized with NAFLD.

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Reconstruction of Patient-specific Distal Airway Regeneration Patterns in COPD

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OBJECTIVES/SPECIFIC AIMS: The objective of this study was to reconstruct patient-specific distal airway patterns at the tissue- and single-cell resolution and develop personalized distal airway models based on utilization of patient-derived DABCs and autologous region-specific stromal cells. METHODS/STUDY POPULATION: Patient-specific distal airway units, containing parental small bronchiole (<2 mm in diameter, >12th generation) and daughter airway branches, including pre-terminal/terminal bronchioles, leading to alveoli (3-7 units/lung), were dissected. Epithelial and stromal cells were isolated from these units and processed for ddSeq single-cell RNA-sequencing (n=6 samples). Autologous DABCs and stromal cells were isolated, propagated, biobanked, and used for establishment of patient-specific distal airway models (3D-organoids and air-liquid interface-based airway wall model; n=10 samples). Region-specific tissue patterns were evaluated using immunofluorescence and laser-capture microdissection (LCM; n=6 samples). RESULTS/ANTICIPATED RESULTS: Single-cell-based human distal airway transcriptome map (constructed based on the analysis of >6,500 distal airway cells obtained from 6 subjects) identified physiological and COPD-relevant distal airway differentiation patterns, including distal airway-specific secretory phenotype (DASP) characterized with high expression of secretoglobins 3A2 and 3A1, surfactant proteins SFTPB and SFTPA2, and mucin 1, unique signatures of DABCs, and stromal (fibroblasts, smooth muscle, endothelial cell subpopulations) and immune (macrophage, T cells, B cell, mast cells). Immunofluorescence analysis and LCM confirmed distribution of cell type-specific markers with differential expression patterns of DABC and DASP signatures. Patient-derived DABC-stromal co-culture models reproduced 3 regenerative patterns: 1) physiological (high DABC-clonogenic potency, establishment of polarized differentiated organoids and DASP-expressing epithelia); 2) hypo-regenerative (failure of DABCs to form clones, spheres and mechanically stable differentiated epithelial barrier); and 3) hyperplastic (generation of DABC hyperplasia accompanied in some COPD samples by mucous-cell hyperplasia mimicking in vivo remodeling patterns). DISCUSSION/SIGNIFICANCE OF IMPACT: Patient-specific maps and models of distal airway regeneration patterns have been established in this study, which can be used to identify candidate pathways that mediate disease-relevant airway remodeling and potentially utilized as pre-clinical platforms for developing personalized therapeutic approaches to suppress the progression of distal airway remodeling in chronic lung diseases, including COPD.

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Relation between Dopamine Transporter (DAT1) polymorphism and subjective effects of alcohol among non-dependent drinkers

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OBJECTIVES/SPECIFIC AIMS: Dopamine transporter (DAT1) gene variation is associated with reward-related phenotypes including alcohol response. There is also evidence for a potential moderating role for mu-opioid receptor (OPRM1) gene variation on the relationship between DAT1 variation and alcohol response measures. We aimed at studying the interaction between the DAT1 VNTR and OPRM1 A118G polymorphisms on alcohol consumption and subjective responses among non-dependent drinkers. METHODS/STUDY POPULATION: We employed a progressive ratio (PR) paradigm of intravenous alcohol self-administration (IV-ASA) using the Computer-Assisted Infusion System (CAIS) to assess the motivation for alcohol seeking and consumption in a sample of nondependent drinkers. We used the Drug Effects Questionnaire (DEQ) and Biphasic Alcohol Effects Questionnaire (BAES) to assess subjective response. IV-ASA measures included average breath alcohol concentration (BrAC) and total ethanol infused. Peripheral blood samples were collected for genotyping. Ethics approval was obtained from the NIH Addictions Institutional Review Board. RESULTS/ANTICIPATED RESULTS: Fifty participants completed the PR IV-ASA session after informed consent. There were significant interactions between the DAT1 and OPRM1 genotypes in subjective effects of alcohol. Simple main effects analysis showed that DAT1 10a allele carriers that were also OPRM1 G allele carriers had significantly higher scores for several measures: "feel the drug effects" ($F(1,46)=6.573$, $P = 0.014$), "feel intoxicated" ($F(1,46)=8.613$, $P = 0.005$) and "feeling high" ($F(1,46)=10.889$, $P = 0.002$) in DEQ and higher sedation ($F(1,46)=4.575$, $P = 0.038$) in BAES. The genotypes statistically significantly predicted average breath alcohol ($F(1,61) =3.295$, $p=0.044$) and total ethanol infused ($F(1,61)=3.632$, $p=0.032$. DAT1 VNTR and OPRM1 A118G polymorphisms taken together accounted for 6.9 and 7.8% of variations in average breath alcohol and total ethanol infused respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: Polymorphic variations in DAT1 and OPRM1 interact with each other in determining subjective effects of alcohol in intravenous alcohol infusion assessing motivation for alcohol seeking and consumption in nondependent drinkers. These epistatic interactions in subjective effects of alcohol are salient in the context of predicting and understanding neurobiological effects of alcohol and thereby the therapeutic responses in treating alcohol use disorders.

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Super Bingers: Traits and Patterns Associated with High-Intensity Drinking

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OBJECTIVES/SPECIFIC AIMS: This study attempts to evaluate the drinking patterns and traits of individuals who partake in high intensity drinking, defined as binge drinking at 2 or more times

https://doi.org/10.1017/cts.2019.353 Published online by Cambridge University Press