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517 Inhaled Nicotine Salt Counteranions Induce Airway Inflammation and Promote a Neutrophilic Asthma Phenotype

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RATIONALE: The popularity of electronic cigarettes (e-cigs) that utilize nicotine salts has rapidly increased since the introduction of JUUL pods in 2015. The immunotoxicology of nicotine salts in the respiratory tract is understudied. We hypothesized that nicotine salt counteranions induce airway inflammation and alter immune responses to inhaled allergens independent of nicotine.

METHODS: The nicotine salt counteranions lactate, levulinate, salicylate or benzoate (5% solution) were administered to C57BL/6J mice by oropharyngeal aspiration daily for three days (acute exposure model) or three times weekly for three weeks (persistent exposure model). In some studies, mice were also exposed to house dust mite (HDM) allergen alone or in combination with benzoate three times weekly for three weeks. Airway inflammation was assessed by enumeration of inflammatory cells in bronchoalveolar lavage fluid and lung histology.

RESULTS: Acute exposure to nicotine salt counteranions induced an influx of neutrophils into the airways. Persistent exposure to nicotine salt counteranions resulted in a mixed neutrophilic and lymphocytic airway inflammatory response. Neither acute nor persistent exposure to nicotine salt counteranions caused airway eosinophilia. In a HDM-mediated allergic airway inflammation model, co-exposure to benzoate and HDM increased the percentage of airway neutrophils but decreased the percentage of eosinophils compared to HDM alone.

CONCLUSIONS: Both acute and persistent exposure to nicotine salt counteranions induces airway inflammation in mice independent of nicotine. Benzoate also induced neutrophilic inflammation in a HDM-mediated allergic airway inflammation model, suggesting that exposure to e-cigs containing nicotine salts may promote a neutrophilic asthma phenotype.

518 Loss of sense of smells associated with sour taste is a possible diagnostic marker for COVID-19

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RATIONALE: SARS-CoV2 infection causes loss of sense of smell. We hypothesized that specific smell loss is associated with COVID-19.

METHODS: Patients recruited for the study within 48 hours of COVID-19 test at Montefiore Medical Center, Bronx, NY were evaluated for sense of smell by UPSIT (University of Pennsylvania Smell Identification Test®). A follow-up UPSIT score was recorded after ~6weeks of the first visit. Paired t-test was used for statistical analysis.

RESULTS: Patients with similar distribution of age, gender, race, and disease severity were included into the study. At baseline, there was no significant difference in smell recognition between COVID-19+ (N=14) and COVID-19-negative patients (N=6) (54 (IQR 43-70) and 71 (IQR 39-80), p=0.5). Among COVID-19+, eight patients (57%) recovered their sense of smell with the UPSIT score increasing from 49%-correct (IQR 40-63) to 69%-correct (IQR 61-85), p=0.01. Five patients (36%) had no recovery of the sense of smell, and there was a significant worsening in the score from 60%-correct (IQR 48-78) to 55%-correct (IQR 45-68), p=0.04. Among COVID-19+ patients, 79%, 71.4, 64.3, 64.3%, 79% and 64.3% subjects were unable to detect the smells of lime, pickle, lemon, orange, soap, and banana respectively at baseline.

CONCLUSIONS: SARS-CoV2 infection results in complete or partial anosmia associated with inability to smell "sour" items, banana, and soap. More than a third of COVID-19 patient did not recover their sense of smell at ~6weeks. Objective evaluation of the sense of smells in COVID-19 patients may be used as marker of disease and for monitoring sense of smell recovery.

519 Integrative Proteomics and Phosphoproteomics of Asthmatic Airways following RV Infection

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RATIONALE: Rhinovirus (RV) infection is associated with 60-80% of childhood asthma exacerbations in the emergency department. Global proteomics and phosphoproteomics were performed using human precision cut lung slice (PCLS) airways from deceased asthma and non-asthma donors with and without infection with RV in order to confirm previously identified dysregulated pathways and identify new areas of investigation.

METHODS: PCLS were prepared from 5 asthma and 4 non-asthma donor lungs for phosphoproteomic analyses. PCLS were infected with RV39 or treated with vehicle for 48 hours. Carbachol induced airway bronchoconstriction was measured pre-/post-infection. PCLS were collected and airways were microdissected for LC-MS/MS. Proteins and enriched phosphopeptides from each sample were labeled with TMT10plex isobaric tags and peptides were identified on an Orbitrap Eclipse Tribrid mass spectrometer.

RESULTS: Asthma donors showed airway hyper-responsiveness to carbachol after RV infection (Control uninfected -0.6207, infected -0.4877; p=NS; Asthma uninfected -0.7113, infected 1.099; p<0.001). Global comparison between asthma and non-asthma airways identified 412 proteins and 1049 phosphopeptides differentially expressed using a p-value < 0.05 and an absolute fold change > 2 threshold. Comparison of asthma + RV to non-asthma + RV identified 381 significant proteins and 763 phosphopeptides. Pathologic pathways were identified with integrative bioinformatics and human protein-protein interactome network analyses. Dysregulated pathways in asthma infected compared to non-asthma infected involved inflammatory responses, TNF-a signaling, Interferon-g response, and IL-6/STAT3.

CONCLUSIONS: Asthma donor airways were hyper-responsive after infection with RV, and this finding was associated with dysregulated pathways in the inflammatory response compared to similar non-asthma donors.