

Presenter: Ludia Pack

Category: Graduate Student

Authors: LUDIA PACK, M. Demagistris, D. Milek, J. Leckenby, M. Noble

Title: 4-AMINOPYRIDINE IS A POTENTIAL THERAPY FOR MULTIPLE ADVERSE EFFECTS OF PACLITAXEL

Abstract: The nasal epithelium acts as a first line defense, continuously exposed to foreign material including microbes (e.g., viruses and bacteria), aeroallergens, chemicals, and pollutants. Part of the nasal epithelium, the main olfactory epithelium (MOE) is the principal site of olfaction (the sense of smell). Disruption of normal functions of this tissue can result in hyposmia, a reduction in the sense of smell or anosmia, total loss of smell, and significant loss of quality of life. The MOE contains multiple cell types, including olfactory sensory neurons (OSNs, which detect odorous molecules), supporting epithelial cells, secretory cells, and immune cells. There is still much to learn regarding communication between these cell types, particularly between neurons and immune cells, and their roles in olfactory dysfunction during inflammatory responses. The capacity for bidirectional neuronal-immune communication in the MOE, is especially relevant in diseases such as allergic rhinitis and respiratory viral infections which are known to often have associated olfactory dysfunction. Many known odorants, such as peptides, proteins, etc., have potentially immunogenic properties, but how these odorants influence the activity and functions of immunogen-sensing OSNs and resident immune cells is not fully understood. We hypothesize that OSN activity influences the immune cell populations and functions in the presence of immunomodulatory odorants. Using single cell RNA sequencing and flow cytometry analysis, we were able to identify OSNs and multiple immune subsets in the MOE. Functionally, using transgenic mice expressing genetically encoded Ca²⁺ indicators, we identified how immunogenic and non-immunogenic odorants impact neuron activity. This was done with mice expressing GCaMP6s, a Ca²⁺-responsive fluorescent protein in OSNs. We isolated the MOE en bloc and exposed the epithelium to a panel of stimuli: 1) amyl acetate, a common olfactory ligand, 2) lipopolysaccharide (LPS), 3) house dust mite extract, and 4) delta-9-THC. Activated OSNs, as shown by increased GCaMP6s fluorescence, were identified in live tissue using objective-coupled planar illumination (OCPI) microscopy. Using the OCPI approach, we observed reliable selective responses in many olfactory neurons to the stimuli. This experimental system establishes a platform to conduct detailed studies investigating how olfactory activity impacts nasal immune responses, filling gaps in our knowledge about the relationships between OSNs and immune cells in the MOE, informing our understanding of olfaction and immunomodulation, and potentially informing our understanding of olfactory dysfunction.