Hunter College of the City University of New York
Department of Biological Sciences
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A Gene Choice Enhancer Generates a Monoclonal Nose Expressing Predominantly One Odor Receptor in Mice

Olfaction, the sense of smell, is a sophisticated chemical detection system that allows terrestrial animals to recognize and distinguish thousands of odor molecules in the air, playing crucial roles in their lives. Central to this system are odorant receptors (ORs) that constitute the largest multigene family and are expressed in olfactory sensory neurons (OSNs). ORs are expressed in an unusual monogenic and monoallelic manner such that any given OR allele is represented in the OSNs by just a few thousand OSNs. The mechanism behind OR gene regulation remains unclear. The identity of the high affinity ligands for most human ORs remains unknown since ORs are poorly expressed through in vitro expression systems making them difficult to characterize.

To understand the mechanism of OR gene choice and decode human olfaction, we have been generating mice with human OR transgenes by using an OR gene choice enhancer transgene system that we have developed capable of expressing an OR in millions of OSNs. This increased number of cells led us to establish an ex vivo odor activation bioassay with extracted olfactory cilia found on the dendritic tips of OSNs.

Recently, we identified a novel single-copy human OR transgene, OR10G4, with our OR gene choice enhancer. Remarkably, OR10G4 is expressed in approximately 80% of olfactory neurons uniformly across the olfactory epithelium. The high number of OSNs and cilia expressing OR10G4 facilitates the identification of its most potent ligand to date, achieved through both liquid and vapor phase delivery methods. A screening platform such as this one may lead to correlations between odor perception and the highest affinity OR. We believe that the insertion locus of OR10G4 will facilitate a CRISPR based pipeline for a sensitive and highly scalable ex vivo odor screening platform for all human ORs allowing us to take a giant step towards decoding human olfaction.

Here is the link to our recent work
https://www.science.org/doi/full/10.1126/scisignal.abm6112

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Host: Paul Feinstein