

- **Using mouse genetics to study how the brain functions.**

The brain interprets the world through five major modalities of sensation.

Information for sight, sound, taste and touch are relayed to the brain through networks of cellular or neuronal connections.

The sense of smell (olfaction); however, uses specialized bipolar neurons, which can simultaneously identify odors with their dendritically located cilia and make direct connections to the brain with their axonal projections. Thus, olfactory neurons directly convert stimuli from the external world into an internal representation within the brain. In a surprising twist, the same protein (the odorant receptor) that is used for identifying odors is also used for guiding the axonal connection to the brain. The olfactory system detects the universe of odors through ~1000 different odorant receptor coding genes. But, each olfactory neuron makes only one type of odorant receptor. The distribution of neuron types is scattered and equally distributed across the interior lining of the nose, but their axonal projections to the brain are sorted out into discrete units called glomeruli that represent each neuronal type.

To examine how the odorant receptor (OR) functions in odor detection and axonal projections, I have used mouse embryonic stem cell technology coupled with genetic manipulation to alter the expressed OR proteins. Studying these modified OR proteins in vivo, I have found that several additional processes within the neuron are affected. The observed one OR gene expressed per olfactory neuron is maintained even if additional OR genes are added to the genome. I am interested in understanding how olfactory neurons control OR gene expression and how the OR protein provides specificity for axonal projections to form discrete units in the brain.

- **Analysis of embryonic stem cell fates**

During my in depth efforts to modify embryonic stem cells, I have become interested in their development