Rare event of histone demethylation can initiate singular gene expression of olfactory receptors

Awardee: Xiaolang (Sunney) Xie
Award: Transformative Research Award
Awardee Institution: Harvard University

Co-authors: Longzhi Tan* and Chenghang Zong
Co-author institution: Harvard University

In mammals, the sense of smell relies on the peculiar expression pattern of olfactory receptors—the largest subfamily of G-protein-coupled receptors (GPCRs): Each single neuron chooses one, and only one, from all ~1400 receptors genes that are present in a mouse genome. In neurobiology, a longstanding mystery is how such “singularity” can be achieved. We show theoretically that a simple kinetic scheme of receptor gene activation followed by feedback can be solely responsible for the observed singularity, as long as the two time-scales—slow activation by epigenetic modification and fast feedback by transcriptional regulation—are well separated. This example demonstrates how the nervous system utilizes the kinetics of epigenetic changes to direct a dramatic outcome of neurogenesis. In addition, our more recent work sheds light on the spatial patterning—also known as the "zonal" expression—of receptors inside the nose.