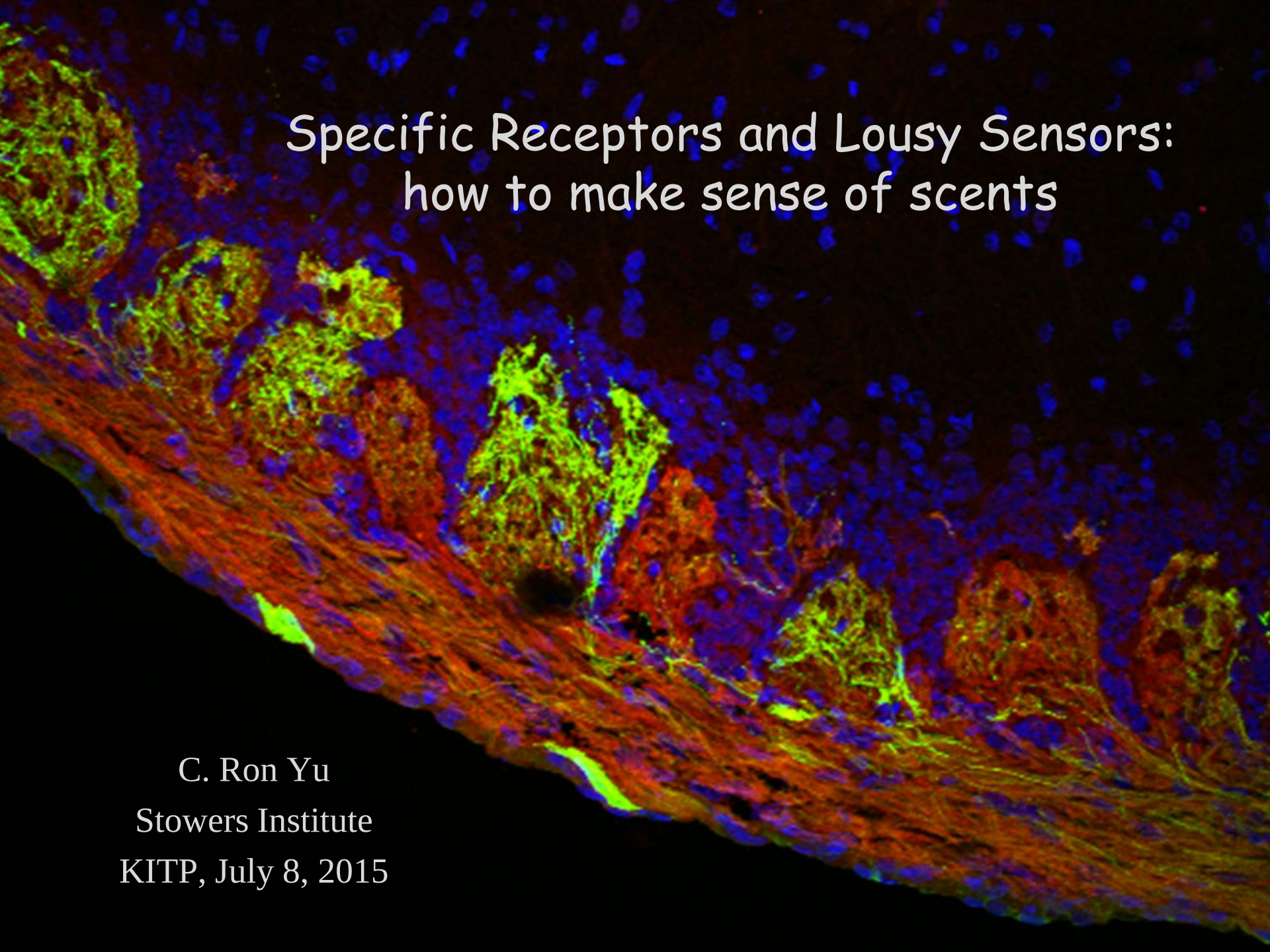
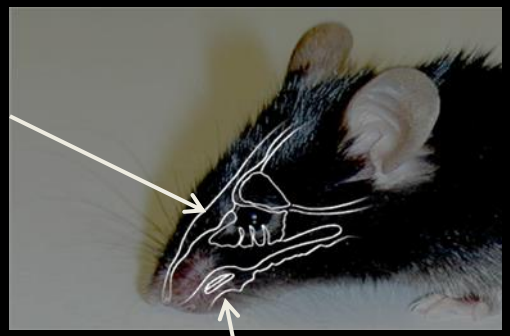
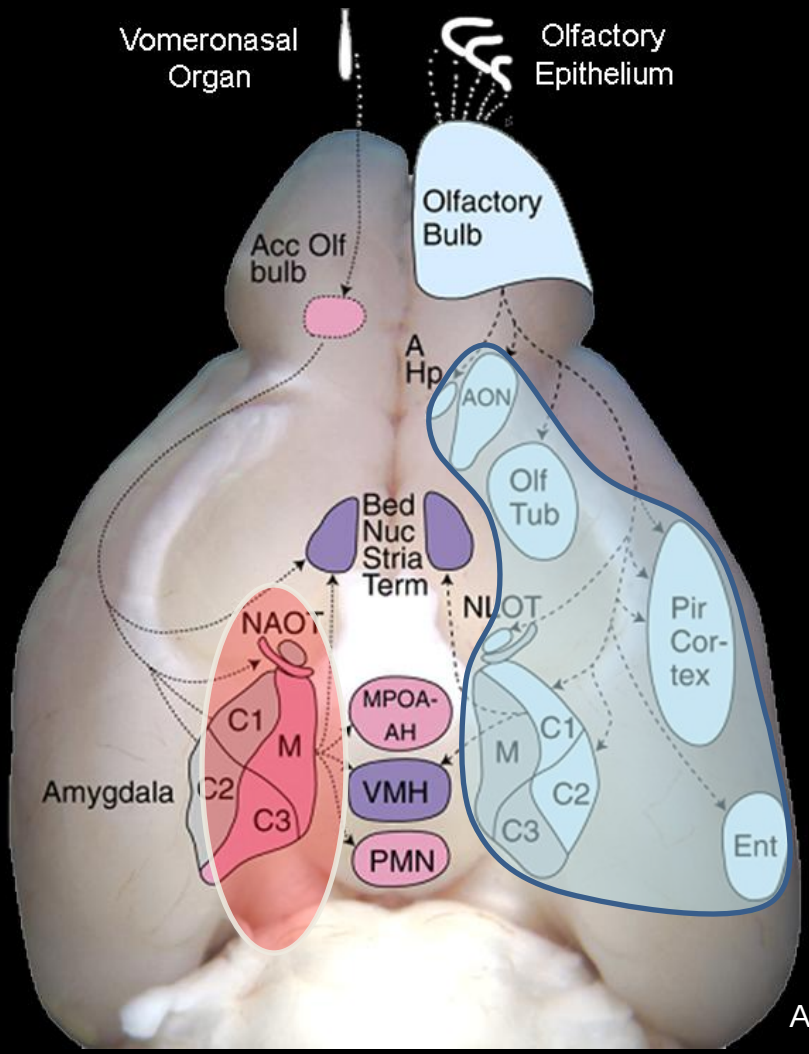
Specific Receptors and Lousy Sensors: how to make sense of scents



C. Ron Yu
Stowers Institute
KITP, July 8, 2015

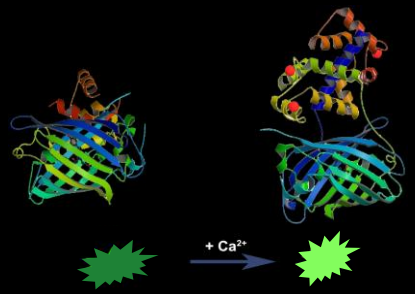
The Mammalian Olfactory Systems

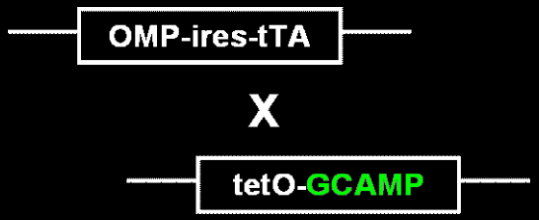


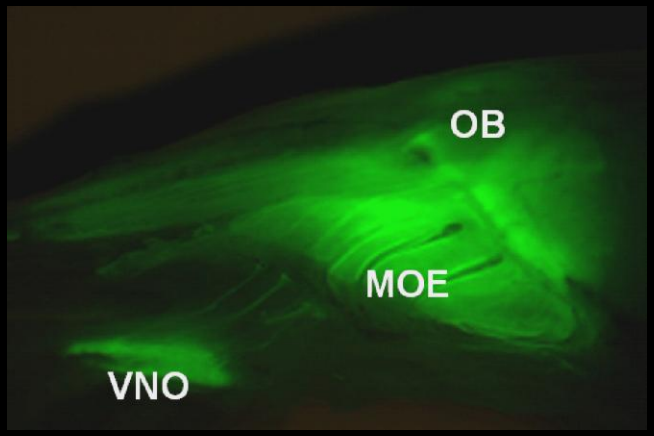


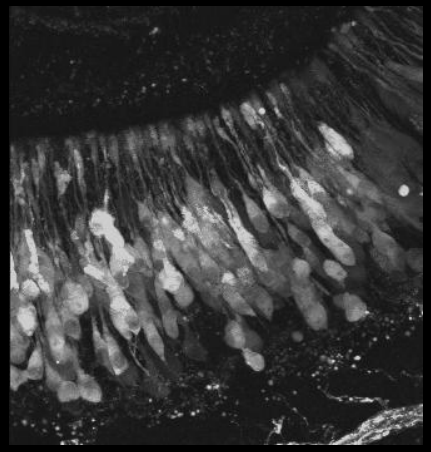
After Meredith 1998

Transgenic Expression of G-CaMP2 in the Olfactory System







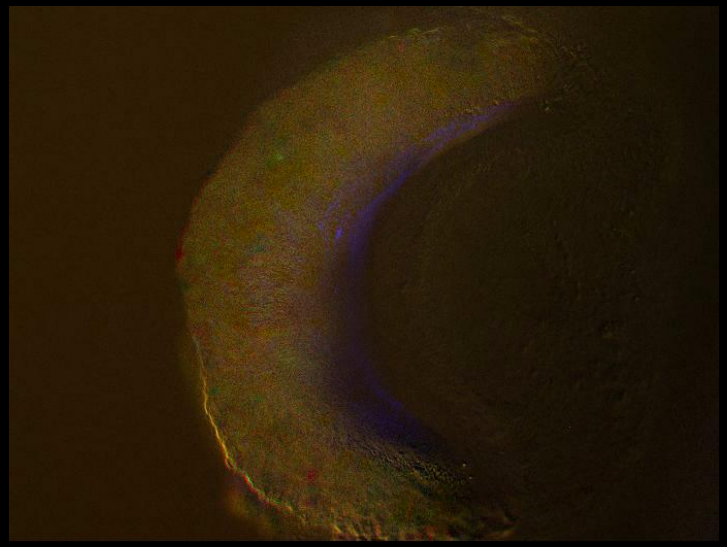


VNO Slice Expressing G-CaMP2

He et al, Science 2008

Limei Ma

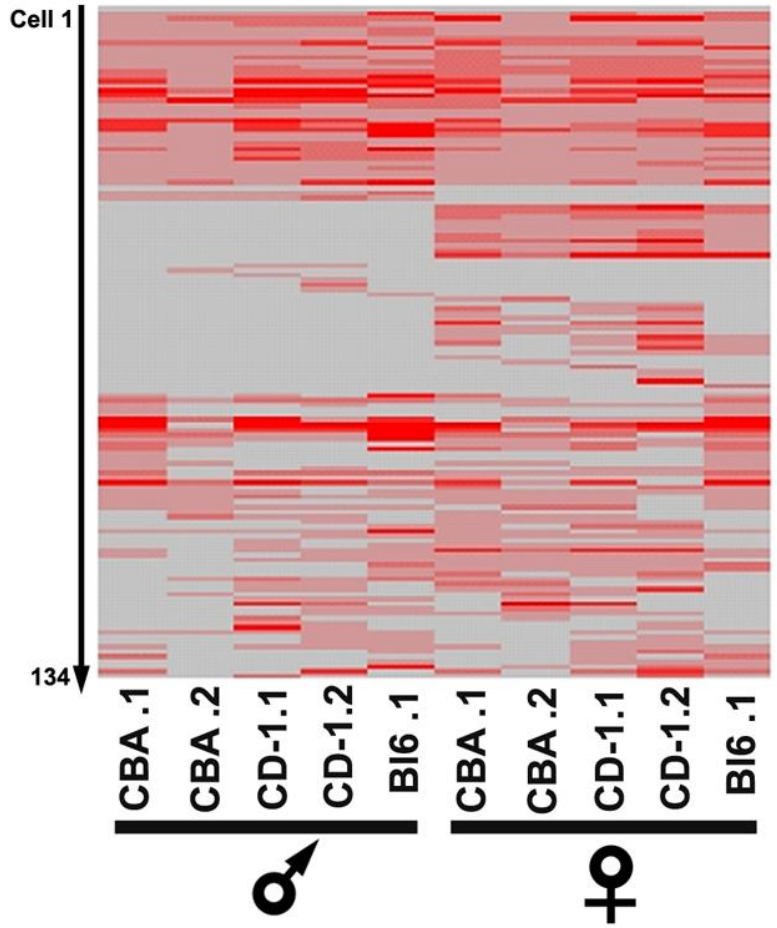
VNO Recognizes Multitude Signals



Male Urine
Female Urine
Predator Urine

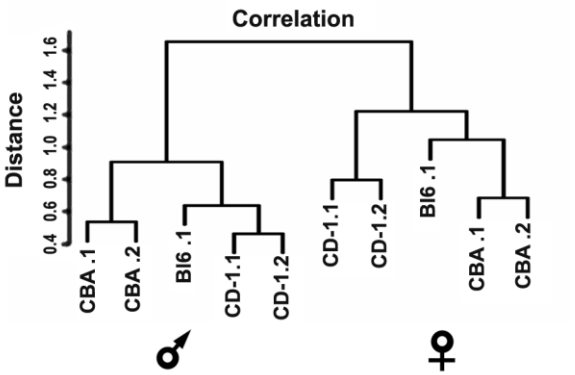
Limei Ma

Recognition of Sexual Cues in the VNO



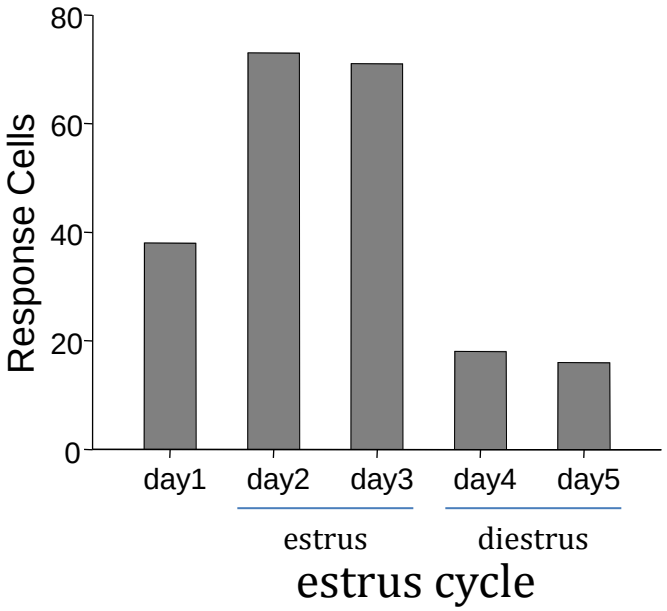
MUSCs Male pheromone detection

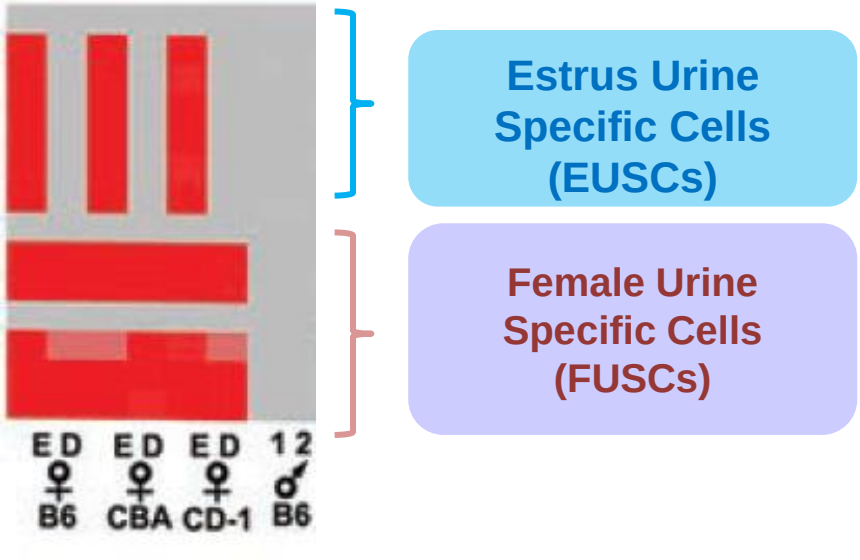
FUSCs Female pheromone detection



He et al, Science 2008

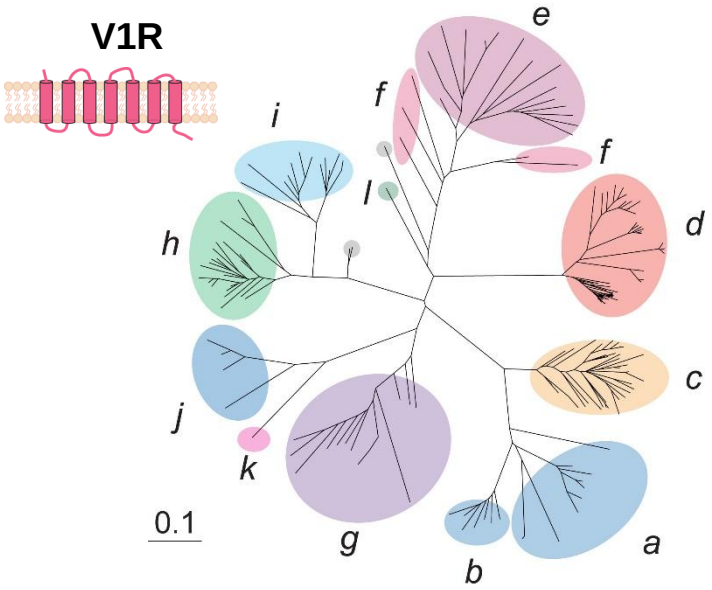
Estrus Dependent and Independent Cues

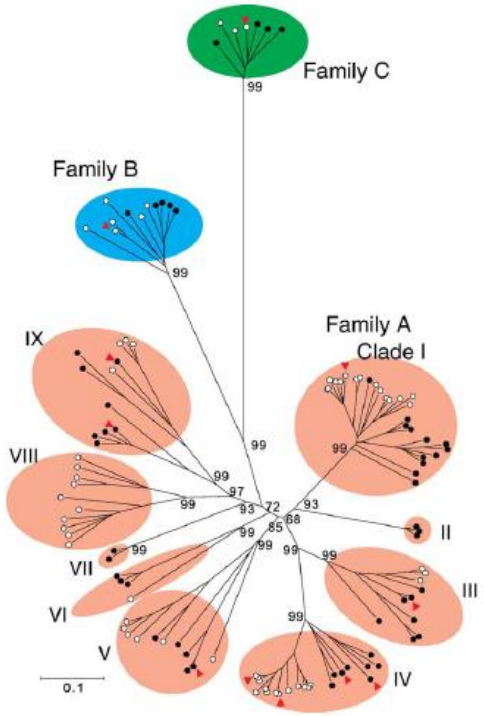


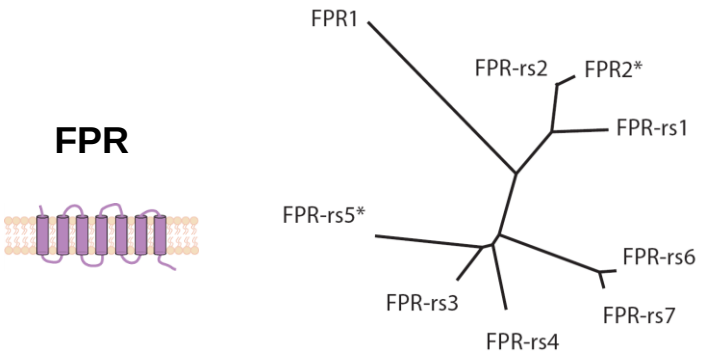


He et al, Science 2008

Vomeronasal Receptor Gene Families

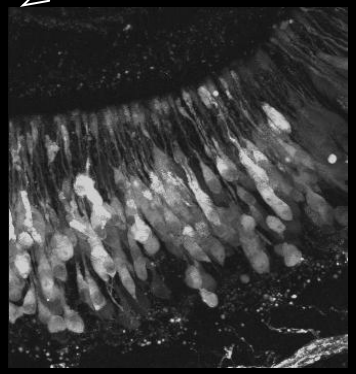






Identification of Vomeronasal Receptor Recognizing Specific Pheromones

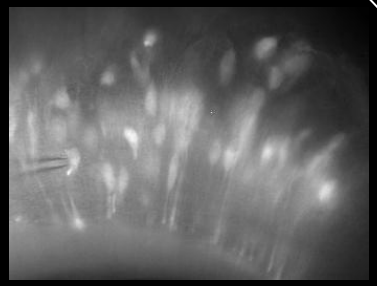
Stimulate with Urine Samples from Multiple Individuals



OMP-tTA:tetO-GCaMP2

Identify Neurons According to Response Patterns

Pick Single Cells



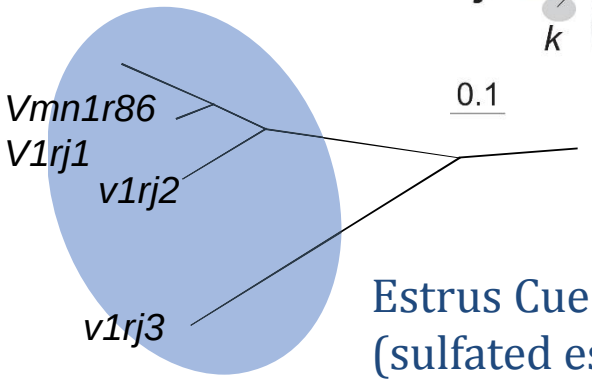
Degenerate RT-PCR

Receptor ID

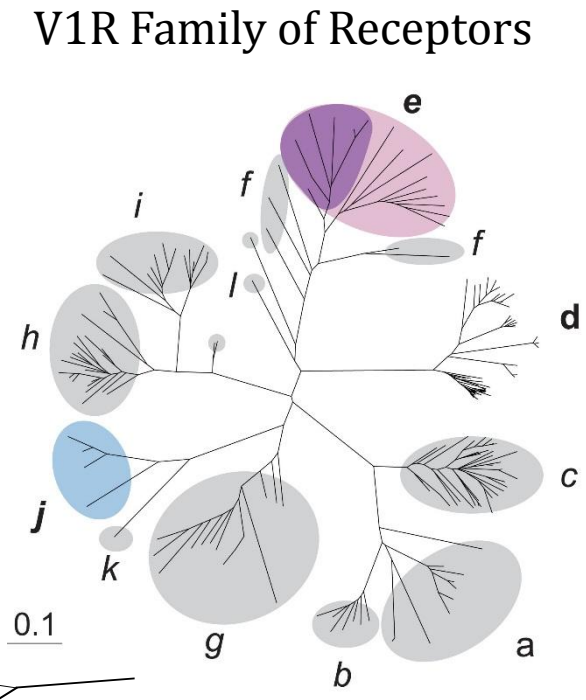
Single Cell RNA Seq

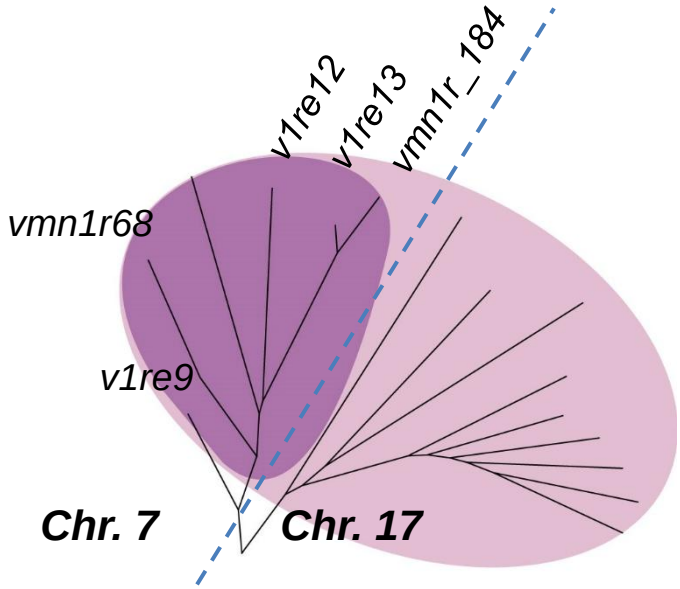
Co-regulated genes

Identification of Female Pheromone Receptors



Estrus Cue
(sulfated estrogen)

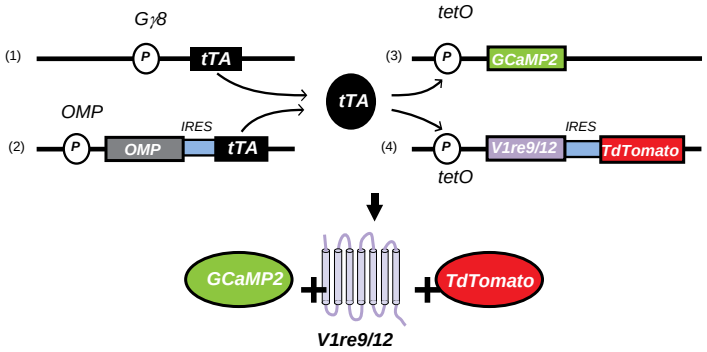


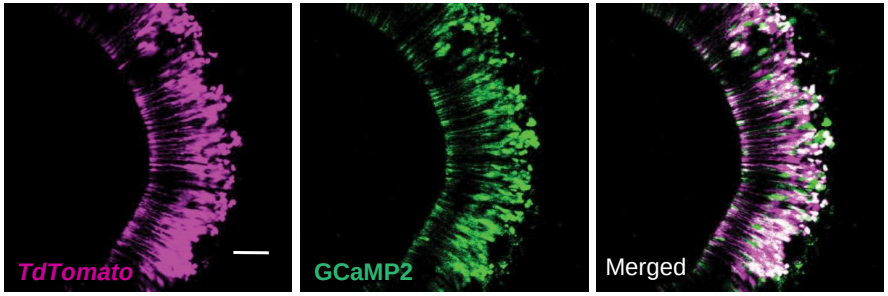


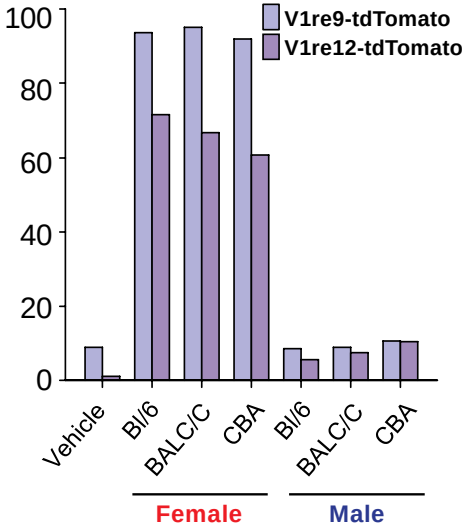
Female Sex Cue

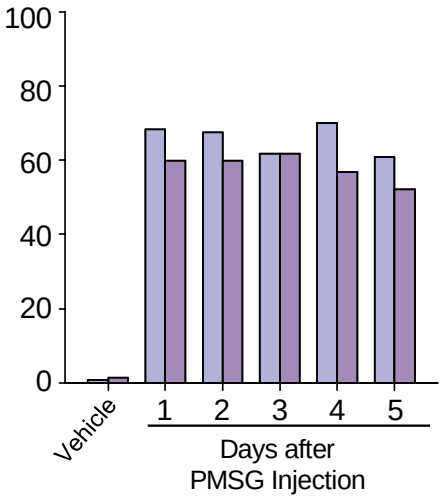
Haga-Yamanaka et al, eLife 2014

In Vivo Assay of Receptor Activity and Pheromone Identification



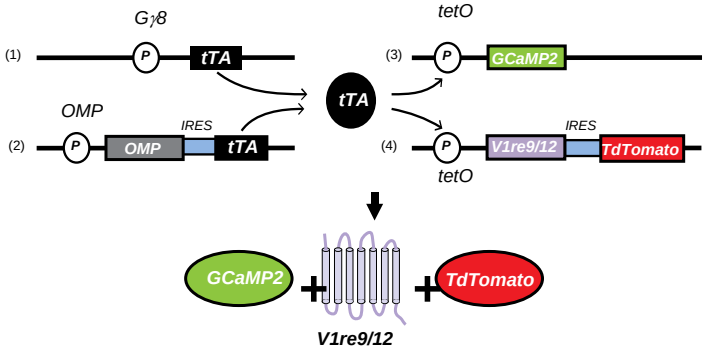


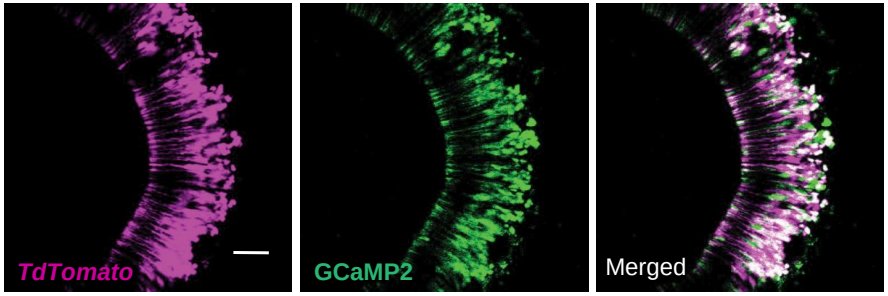


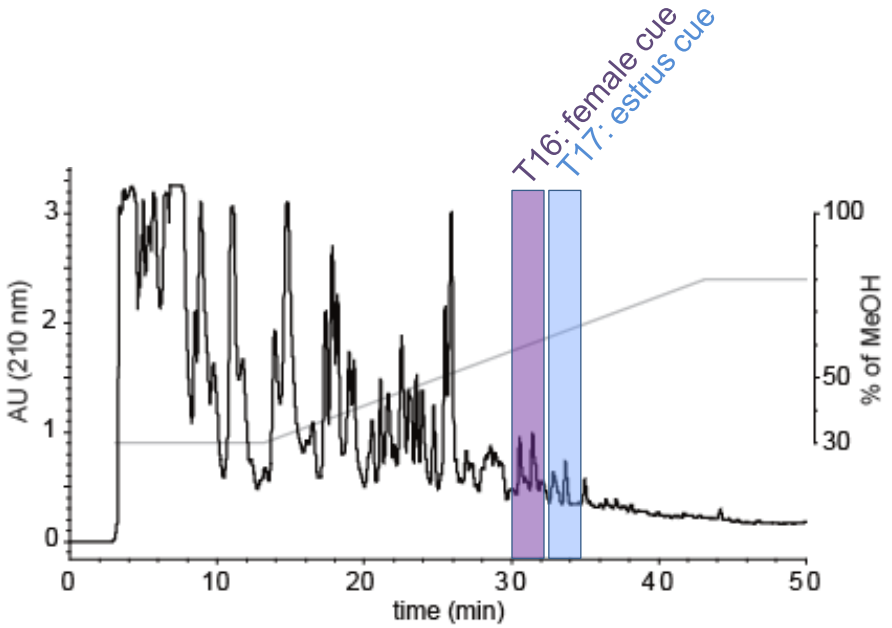


Haga-Yamanaka et al, eLife 2014

In Vivo Assay of Receptor Activity and Pheromone Identification



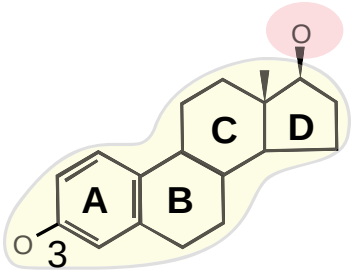


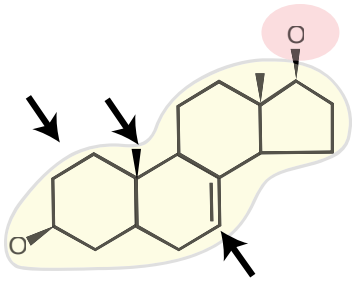


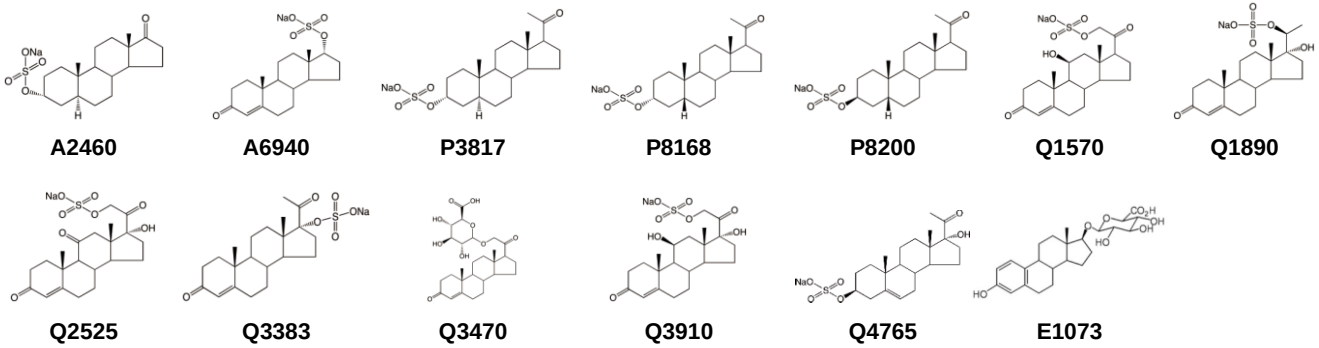
Haga-Yamanaka et al, eLife 2014

Highly Specific Activation of V1rj Receptors

	~10^{-10} M	~10^{-9} M	~10^{-8} M	~10^{-7} M	~10^{-5} M
V1rj2	E1072	E1050	E1103	A7864 E0588 E1100	A2398 P2135 E0893 A2534 P3865 A8530 Q5545
V1rj3	E1103		E1050		A2398 P2135 A7864 E1100



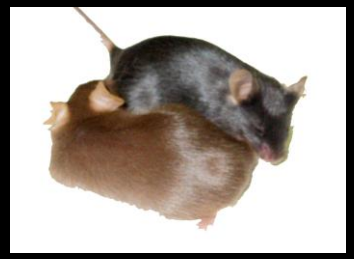




Haga-Yamanaka et al, Frontiers Neurosci, 2015

Pheromone Elicited Behaviors

Encounter



Investigation

Intruder

Territorial Aggression

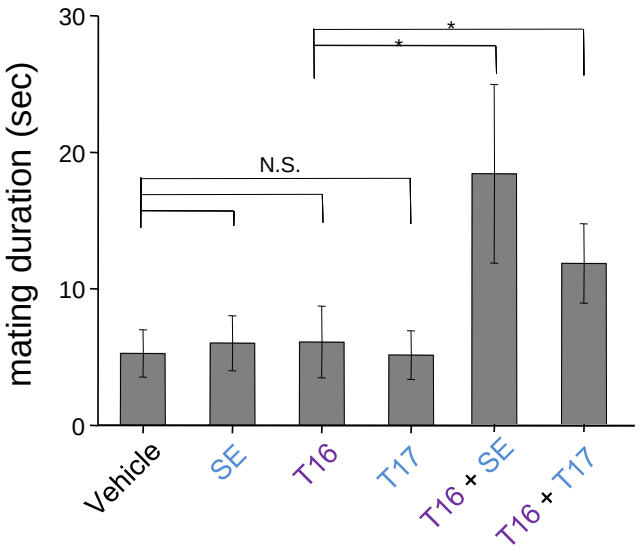
Hierarchical Dominance

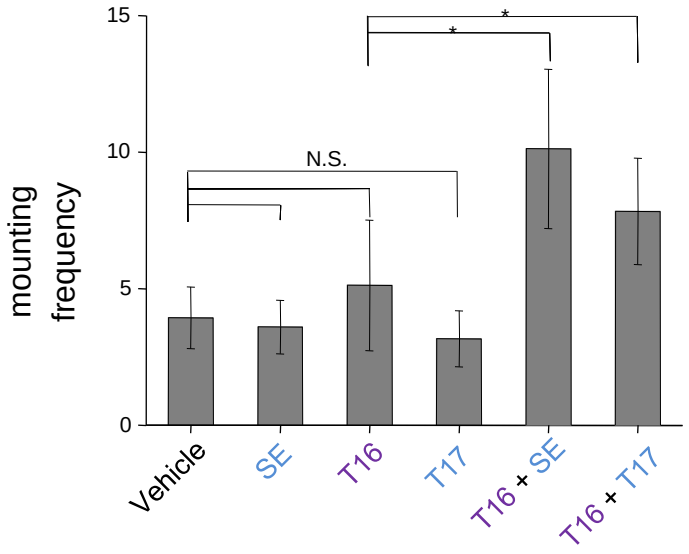
Mate

Mating Rituals

Satiety

Combination of Female and Estrous Fractions Enhances Mounting Behavior





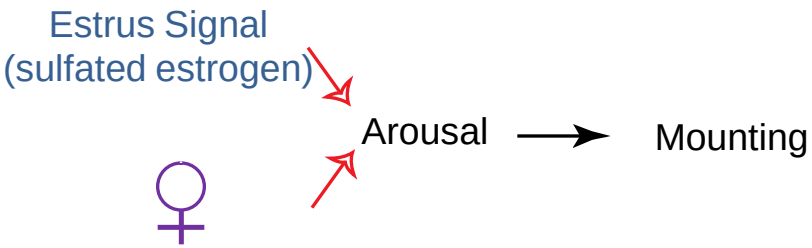
T16: Female Specific Fraction **T17:** Estrus Specific Fractions

SE: Sulfated Estrogens

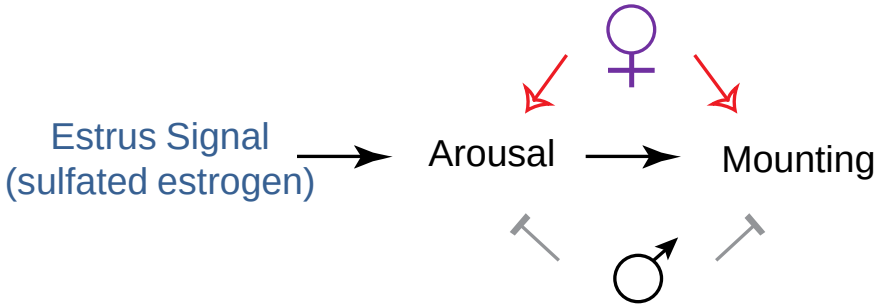
Haga-Yamanaka et al, eLife 2014

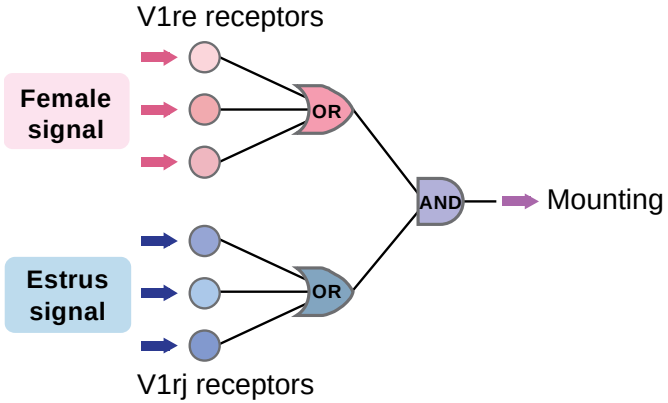
Circuit Models of Mounting Behavior Control

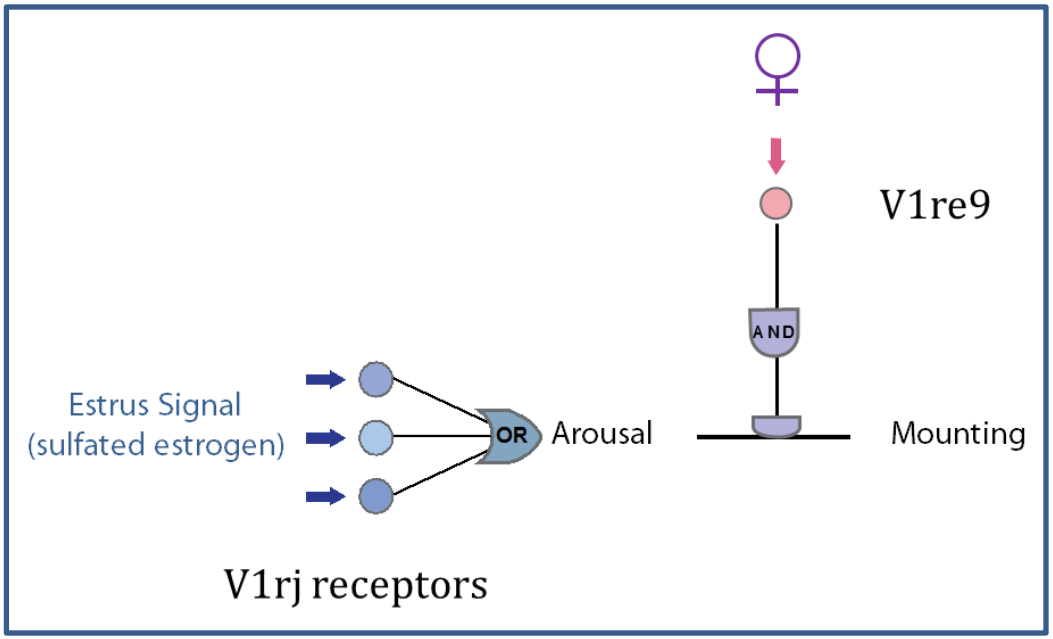
Parallel Integration



Hierarchical Integration







Summary I

- Highly specific vomeronasal receptors are directly linked to specific behaviors
- Pheromone information likely processed by inborn circuits forming logic gates and orchestrating innate behaviors

Acknowledgement

VNO

Jie He
Sachiko Haga-Yamanaka
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