

De-Orphanizing Olfaction

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Cliff and C. diff - Smelling the diagnosis



BMJ



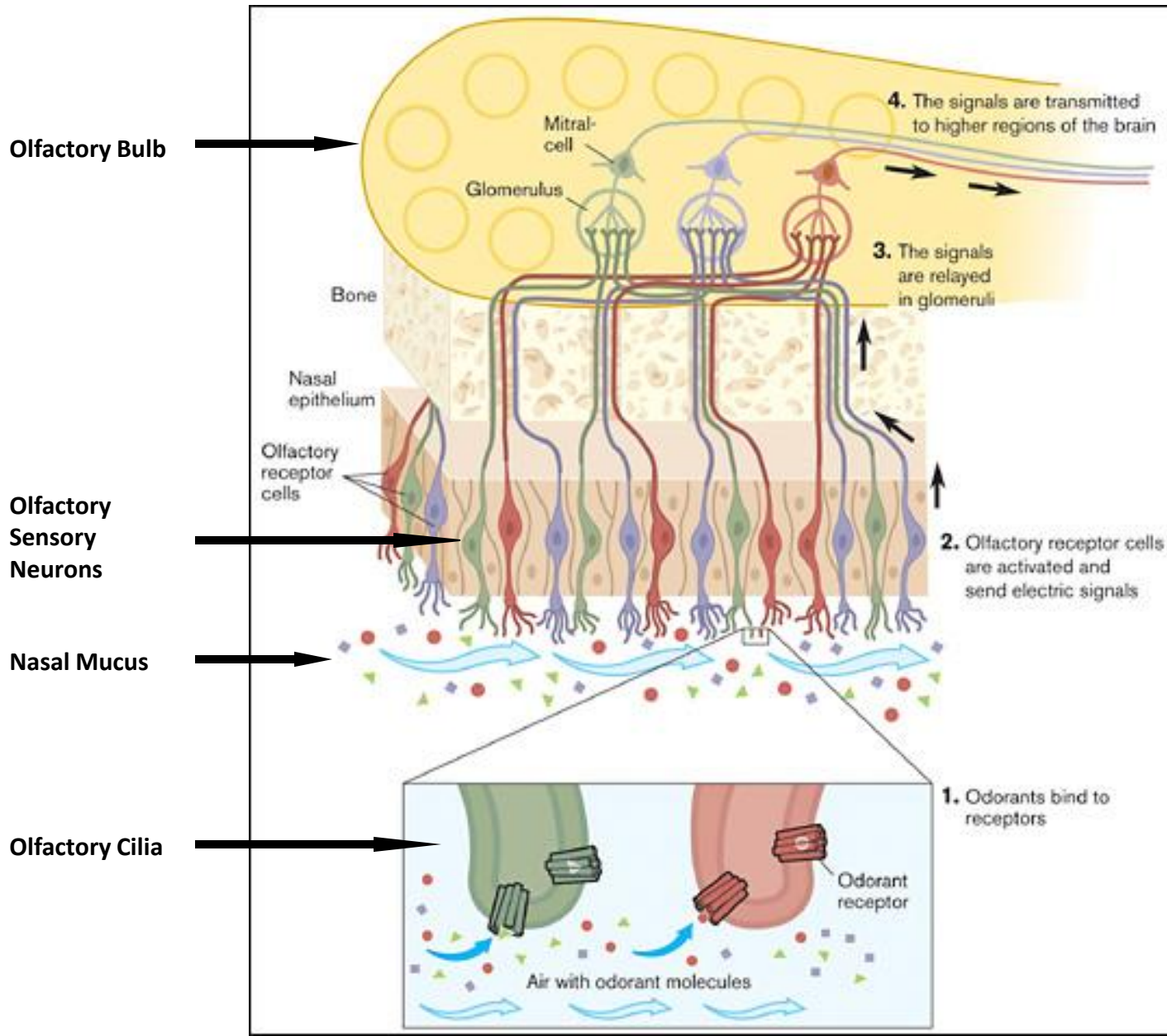
How can he do it?



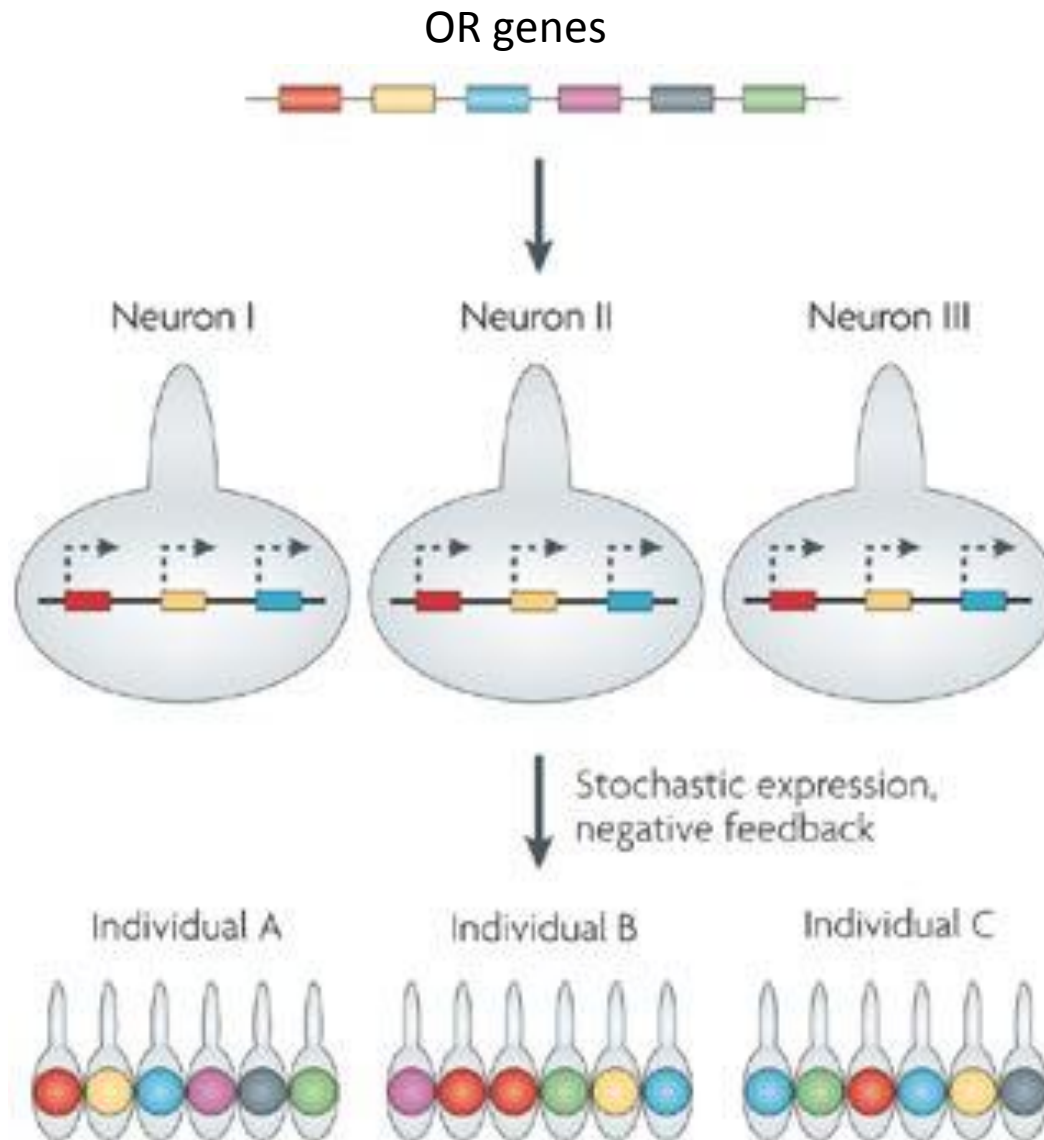
A broad-, sensitive and fine-tuned chemical detector



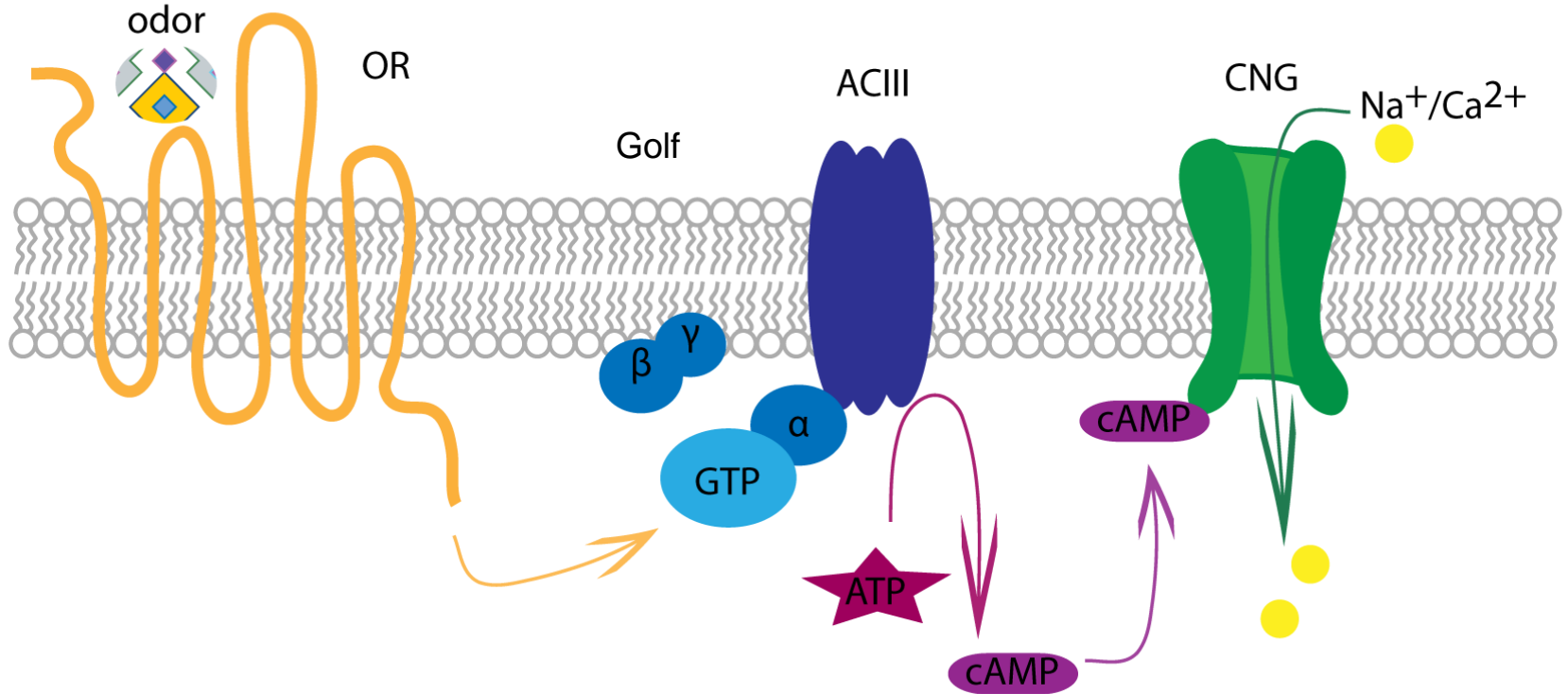
The mammalian olfactory system



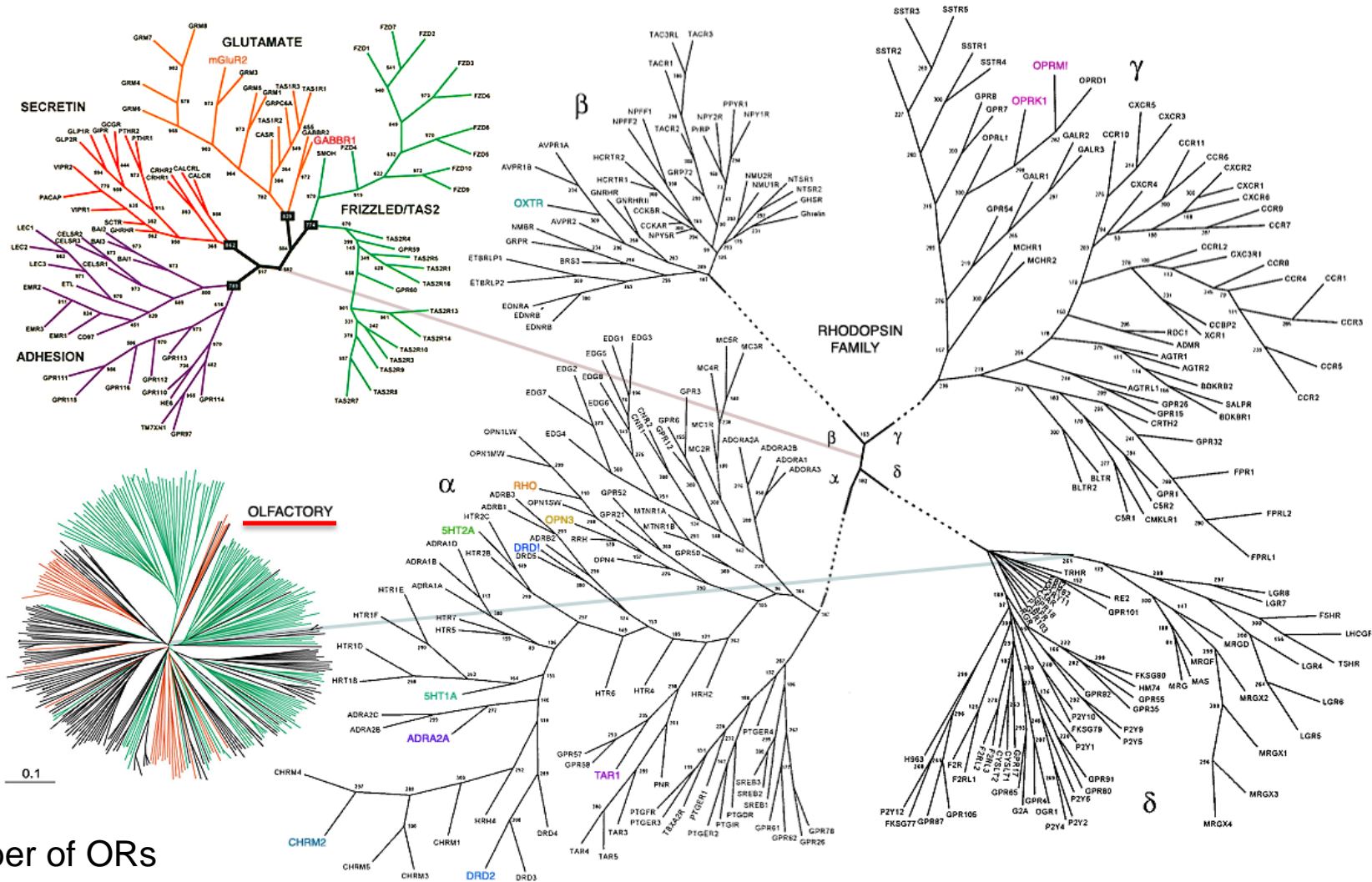
One olfactory neuron – one receptor rule



The olfactory signaling pathway



The human G-protein coupled receptors and the ORs



Number of ORs

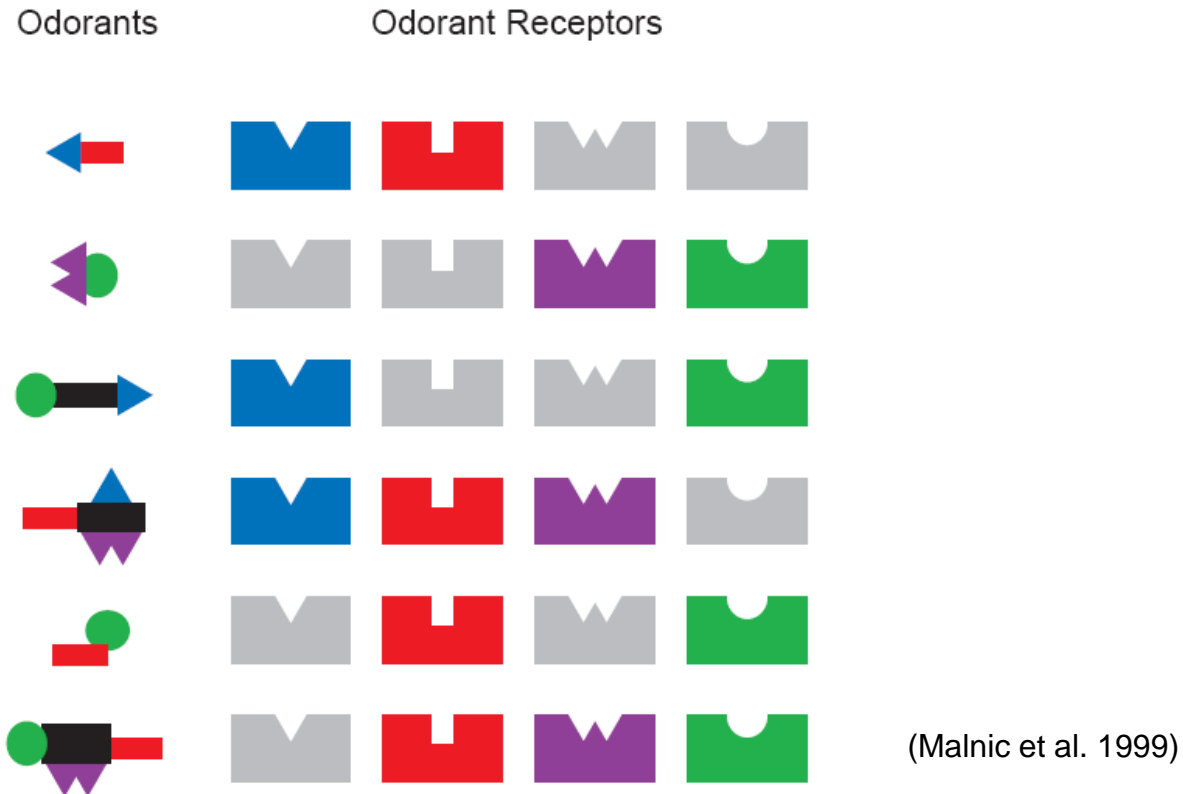
Human 396

Mouse 1130

Rat 1207

Dog 811

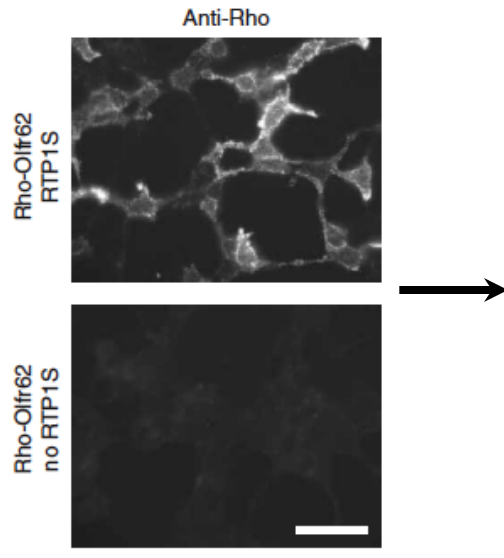
A combinatorial odor coding



1. How many and which ORs are activated by a given odor?
2. How does each OR contribute odor perception?

Functional expression of ORs in heterologous cells: Importance of Receptor-Transporting Proteins (RTPs)

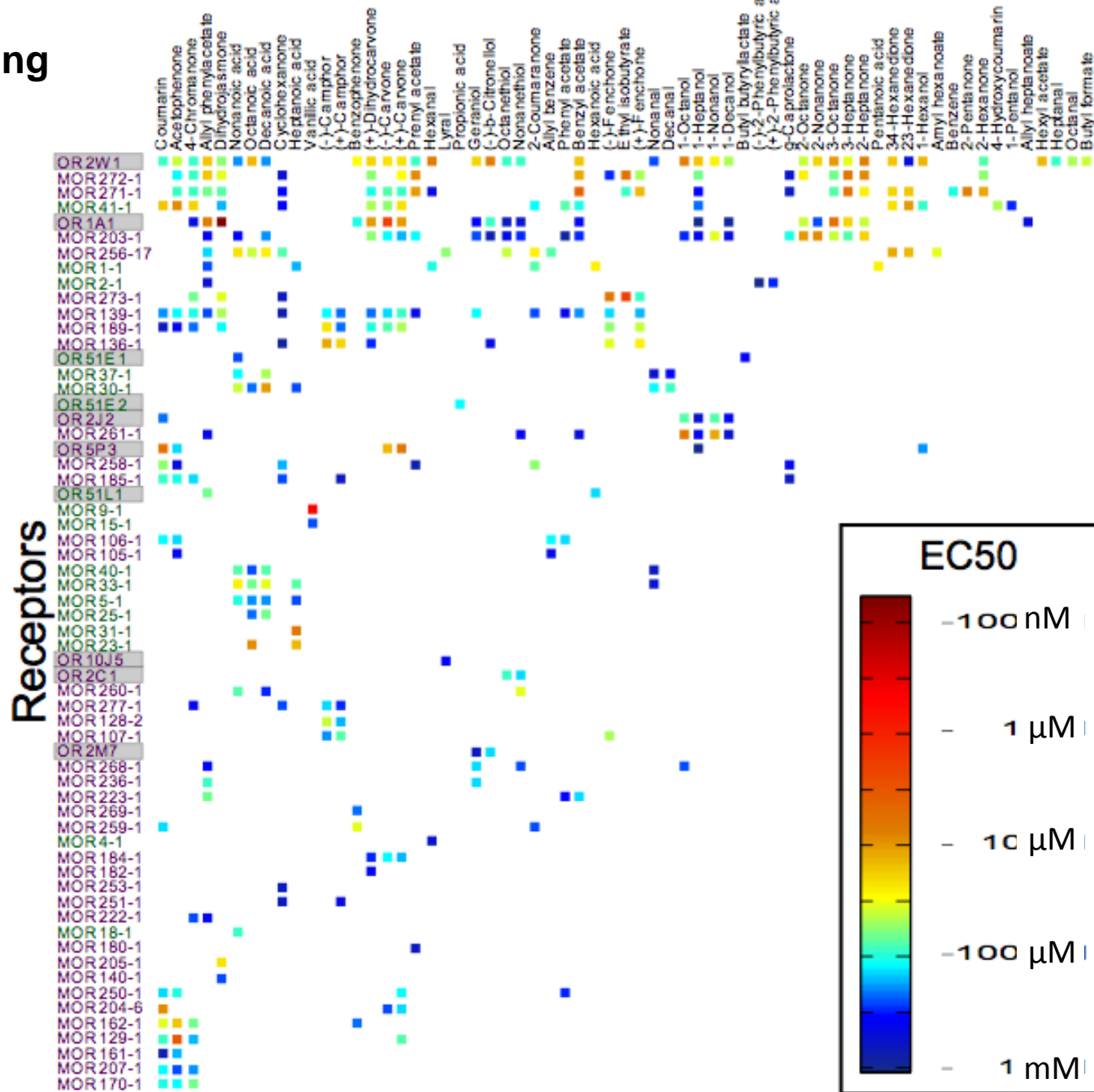
Cell Surface Expression



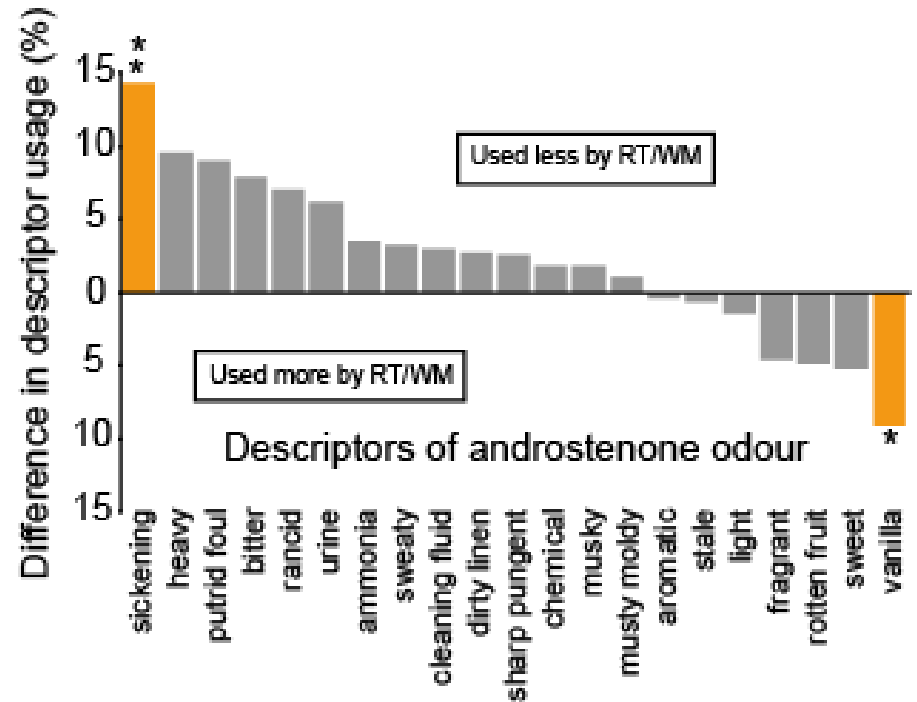
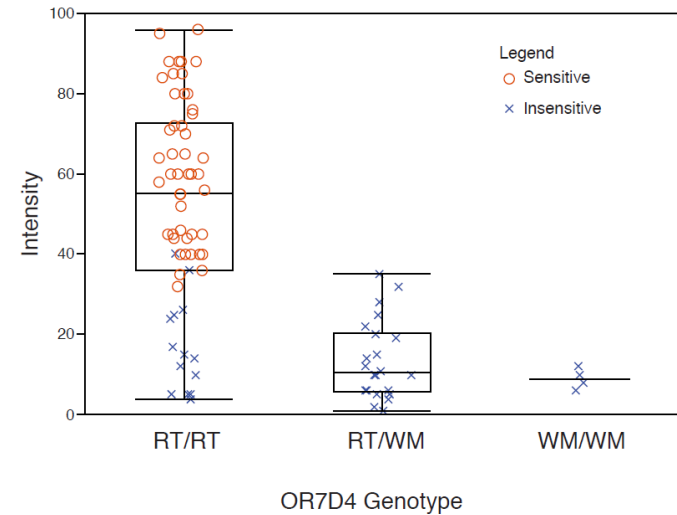
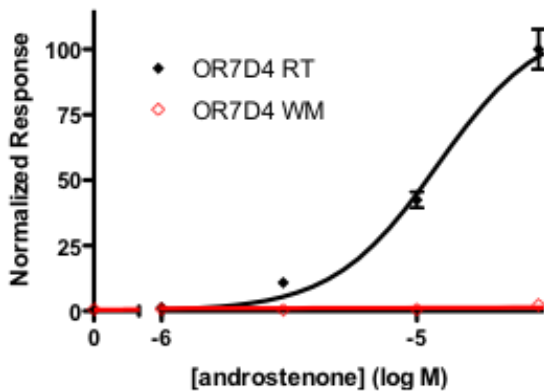
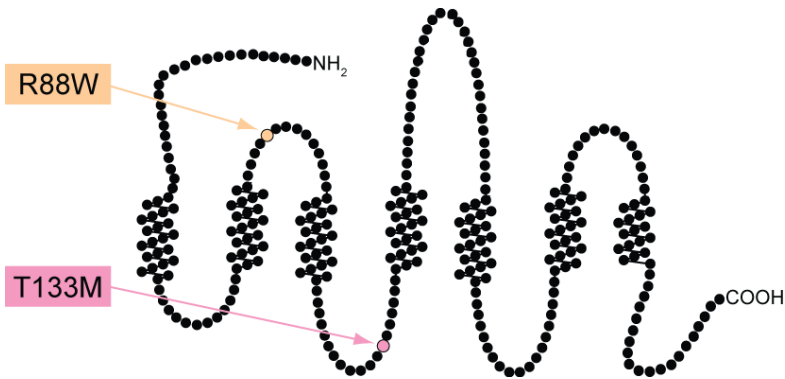
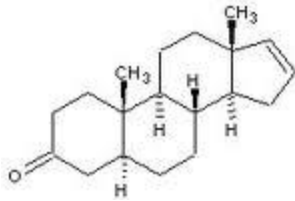
Large-scale
in vitro
screening

with
human
and
mouse
ORs

Odorants

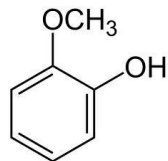
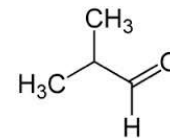
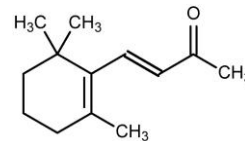
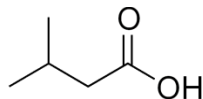
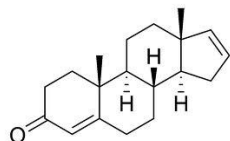
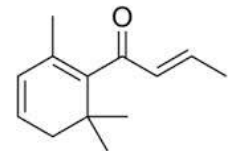
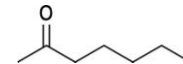
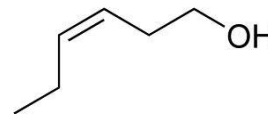
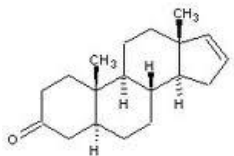


OR functional variation affects odor perception in humans



Individual OR genes and odor perception

OR	variant type	odor	natural source	reference
OR7D4	missense	androstenone androstadienone	pork	Keller et al., 07 Lunde et al., 12
OR11H7P	segregated pseudogene	isovaleric acid		Menashe et al., 07
OR cluster			urine after eating asparagus	Eriksson et al., 10
OR cluster			soapy flavor of cilantro	Eriksson et al., 12
OR2J3	missense	cis-3-hexen-1-ol		McRae et al, 12
OR5A1	missense	beta-ionone	juice	Jaegar et al., 13
OR cluster		2-heptanone		McRae et al., 13
OR cluster		isobutyraldehyde		McRae et al., 13
OR cluster		beta-damascenone		McRae et al., 13
OR10G4	missense	guaiacol		Mainland et al.,



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Sandeepa Dey

Hanyi Zhuang

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Peter Dong

Linda Liu

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Zoya Qureshy

Rich Roberts

Akemi Toyama

Yoshi Ishimaru

Momo Kubota

Qiuyi Chi

Felix Hsu

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