nature REVIEWS
NEUROSCIENCE
July 2003 Vol 4 No 7
REVIEW

Nature Reviews Neuroscience **4**, 551 -562 (2003); doi:10.1038/nrn1140

MOLECULAR DETECTION OF PHEROMONE SIGNALS IN MAMMALS: FROM GENES TO BEHAVIOUR

Catherine Dulac & A. Thomas Torello about the authors

Preface

The instinctive and species-specific behavioural response of animals to pheromones has intrigued biologists for a long time. Recent molecular and electrophysiological approaches have provided new insights into the mechanisms of pheromone detection in rodents and into the sensory coding of pheromone signals that lead to gender discrimination and aggressive behaviour.

Summary

- Pheromones are species- and gender-specific chemical cues that provide information about the social and sexual status of an animal. Pheromones are used by most species, from single-cell organisms to mammals, although their use in humans and other higher primates is disputed.
- In mammals, pheromones are detected by the vomeronasal organ (VNO) — a bilaterally symmetrical, cylindrical organ encased in a bony capsule on the anterior nasal septum. VNO neurons send a single unbranched axon to the accessory olfactory bulb (AOB), which in turn sends projections to the vomeronasal amygdala.
- Compounds with pheromonal activity have been purified from urine and anogenital gland secretions. Urine contains high levels of major urinary proteins, which seem to deliver small volatile molecules to chemosensory receptor neurons. Analysis of hamster vaginal secretions led to the identification of the protein aphrodisin, which elicits copulatory behaviours in male hamsters.
- In the mouse and rat, two large families of pheromone receptors — the V1Rs and the V2Rs — have been characterized. These receptor families are expressed in molecularly distinct and topographically segregated regions of the VNO neuroepithelium.
- It was recently shown that there is a functional association between the V2Rs, the M10 and M1 families of non-classical major histocompatibility complex molecules and β2-microglobulin (β2m). M10 and β2m form a complex with V2R that is localized to the dendritic tips of VNO neurons at the site of pheromone detection, and they are thought to be involved in pheromone-receptor trafficking.
- The cation channel Trp2 is highly expressed in VNO neurons, and it seems to be involved in the transduction of pheromone signals. G-protein activation by vomeronasal G-protein-coupled receptors triggers a phospholipase C-dependent cascade, which in turn activates Trp2.

- Electrophysiological recordings showed that subsets of VNO neurons are activated selectively by either male or female urine, whereas the response of others was independent of the sex of the donor animal, and might instead provide information about other characteristics of the donor.
- Neurons that express a given vomeronasal receptor project to multiple glomeruli that occupy spatially conserved regions within the AOB. In the main olfactory system, glomeruli are composed of fibres from neurons that express the same receptor, but glomeruli in the AOB seem to receive inputs from several receptor types. The divergent pattern of glomerular position in the AOB could be rendered convergent at the level of mitral cells, which might transmit information from a single receptor type to higher brain centres.
- Genetic ablation of *Trp2* markedly impairs the sensory activation of VNO neurons by urine pheromones, and in addition, *Trp2*$^{-/-}$ male mice seem to be unable to recognize the sexual identity of their conspecifics. These data contradict the established idea that VNO activity is required for the initiation of male–female mating behaviour, and instead they imply a crucial role in ensuring sex discrimination.

back to top