Multi-author Review
Signaling in the chemosensory systems

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Signaling in chemosensory systems

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The sensory systems are the devices with which we perceive the external world. Unlike most animals, humans primarily rely on vision and audition [1]. The relevance of these senses for human life seems to have driven intense research into the elucidation of visual and auditory perception, leaving the understanding of the more primitive chemical senses behind. However, during the last 2 decades enormous progress has been made in the field of olfaction [2], which, for instance, is visible in the award of the Nobel Prize in Physiology or Medicine to Linda Buck and Richard Axel in 2004 [3]. Also, taste research caught up with the advance in other sensory systems through dramatic developments during the last couple of years [4]. These advances have been inspired by the discovery of the genes encoding the chemosensory receptors of the olfactory and taste systems and the experimental tools that were based on them in conjunction with advanced physiological methods [5, 6]. Although far from being complete, to date we have a fairly comprehensive view about how chemicals interact with their receptors to initiate signal transduction in the sensory cells. We are about to understand how chemical information is encoded and processed [2, 4], whereas it is the challenge for the next decade to uncover how sensory information triggers a behavioral output. The 25th Blankenese Conference, held in May 2005, acknowledged the aforementioned progress by choosing 'signaling in sensory systems' as the meeting's topic. The present multi-author review was written by distinguished meeting delegates who contributed significantly to the recent progress and intends to highlight some of the recent advances that have been achieved in the field of the chemical senses.

A fact that sometimes escapes our attention is that the mammalian olfactory system is not a uniform organ but a highly substructured system consisting of the main olfactory epithelium and the vomeronasal organ, both of which can be further subdivided into functionally distinct entities. In the first review, Heinz Breer and his colleagues nicely illustrate the anatomical and functional organization of the mammalian chemosensory system. Based on data obtained through *in situ* hybridization, immunohistochemistry and transgenic expression of marker enzymes, these authors point out that different olfactory subcompartments contain distinct cell types that use different receptors and transduction mechanisms as well as projection sites into different brain regions. They relate the morphological properties to the known or putative functional roles of the respective olfactory subsystem. The article by Frank Zufall and associates builds on the roles that the main olfactory and the vomeronasal subsystems play in detecting chemical cues and regulating chemosensory-dependent behaviors. The authors abandon the long-held view that the former detects volatiles, whereas the latter recognizes nonvolatile pheromones. Rather, they present a model that involves parallel processing of partially overlapping sets of social signals to regulate, in a complementary manner, mammalian social behavior in both systems.

Olfactory perception is based on complex molecular mechanisms that involve hundreds of receptors to detect and discriminate thousands of odors. Idan Menashe and Doron Lancet explain how the G-protein-coupled olfactory receptors work and how they generate unique combinatorial codes for the detection of odor stimuli [7]. They move on to show that olfactory receptors can differ largely in their affinities for odorants, with the implication that only a few have biological significance for the detection of a given odor, and that only the receptors with the strongest affinity determine odor detection and recognition threshold concentrations. Next, they summarize human olfactory diversity at the level of phenotypically detectable specific and general anosmia. These are paral-

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leled by the existence of ~600 nonsynonymous single-nucleotide polymorphisms (SNPs) in the olfactory receptor gene repertoire [8]. Based on these observations, the authors offer a molecular basis for perceptual diversity in the human population.

In marked contrast to the olfactory system, the gustatory system has little discriminative power. Sapid stimuli come as five basic tastes, sweet, umami, bitter, salty and sour. Taste stimuli are detected by assemblies of ~100 cells that form well-known specialized morphological structures, the taste buds, which are located in the chemosensory papillae on the tongue. However, we know astonishingly little about the precise function of these small chemosensory organs. Their characterization has largely relied on cytological and ultrastructural data. The review by Stephen Roper takes us into these structures and points out that modern immunohistochemistry has refined our knowledge about the functional identity of taste bud cells. In his article, Roper describes the location of synapses and how this might affect signal processing in the taste bud. Finally, he discusses how action potentials are generated in, and which neurotransmitters are released from, taste bud cells. Recent progress also enabled deep insight into the molecular and cellular basis of sweet, umami, and bitter taste. Maik Behrens and Wolfgang Meyerhof update our current view of human bitter taste, but referring wherever appropriate to discoveries that have been made in rodents. These authors describe the molecular architecture and evolution of the family of mammalian bitter taste receptor genes, which comprise ~25 members in humans [9], as well as nutritional implications. They further discuss the oral expression patterns of the bitter taste receptors and their signal transduction pathways. These data, together with observations made in transgenic mice, suggest that bitter taste in the periphery is encoded independently from other taste modalities by a separate population of taste receptor cells predetermined to transmit aversive stimuli [10]. Like olfactory receptor genes, bitter taste receptor genes are highly polymorphic, showing numerous nonsynonymous SNPs [11]. Bitter taste receptor haplotypes determine our ability to taste certain thioamides [12, 13] and are likely to account for many more perceptual differences in the human population.

It is interesting to see that principles known from the mammalian chemosensory systems also apply to the worm *Caenorhabditis elegans*. Already in this simple organism a distinction can be made between olfaction and taste, and attraction and aversion can be behaviorally identified [14]. Notably, the worm avoids compounds that we perceive as bitter [15]. Carmela Bergamasco and Paolo Bazzicalupo introduce to us the organization of chemical sensitivity at the cellular and molecular level. A surprising peculiarity of this animal is its large repertoire of ~1300–1700 chemosensory receptors highlighting the animal's dependence on chemical cues. The experimental versatility of this animal model enabled researchers to determine the precise role of signaling molecules or pathways in individual neurons and how they are required for a particular biological response. Furthermore, neuronal modulation apparently allows the worms to cope with a continuously changing environment. This tight linkage of the biochemical function of signaling molecules with the activity of identified neurons that trigger definite behaviors is unprecedented in mammals to date. In this sense chemosensory research in *C. elegans* is highly relevant for research in mammals and defines the goals to be reached in the years to come. It certainly will present an ideal topic for a future Blankenese Conference.

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