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ABSTRACTS

List of Abstracts of the Seventeenth Annual Meeting of the European Chemoreception Research Organisation

Plenary Opening Lecture

1. Deconstructing Smell

L.B. Buck

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We have explored how mammals detect odorants and pheromones and how the brain translates those chemicals into diverse perceptions and instinctive behaviors. We found that odorants are detected in the nasal olfactory epithelium (OE) by ~1000 different odorant receptors (ORs), whereas pheromones are detected in the vomeronasal organ (VNO) by two smaller receptor families. Our studies showed that ORs are used combinatorially to encode odor identities. Exploring the patterning of OR inputs, we found that each sensory neuron in the OE expresses a single type of OR and that neurons with the same OR are scattered in one zone but synapse in a stereotyped fashion in OR-specific glomeruli in the olfactory bulb. At the next level, the olfactory cortex, we discovered another stereotyped map of OR inputs but here signals from different ORs are targeted to partially overlapping clusters of neurons and single neurons receive combinatorial OR inputs. By comparing responses to binary odorant mixtures versus their components, we found evidence that the cortical neurons act as coincidence detectors whose activation requires combinatorial OR inputs, thus providing an initial step in the reconstruction of an odor image from its deconstructed features. To explore how pheromones alter reproductive physiology and behavior, we made mice expressing a transneuronal tracer in gonadotropin releasing hormone (GNRH) neurons. These studies revealed that GNRH neurons receive pheromone signals from the OE as well as the VNO. We recently discovered a second class of chemosensory receptors in the OE, called TAARs, that recognizes at least one pheromone and may also be involved in the detection of other social cues by the OE.

Panel Discussión 1: Human Pheromones?

2. Human Pheromones?

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The question whether humans communicate chemosensorily is still under debate. While some authors argue that meaningful communication in humans is not mediated by chemical cues, others are convinced about the existence of such communication. In the round table discussion, these controversial points of view will be focused. Especially, it will be questioned weather the term ''pheromone'' is useful in investigating human chemosensory communication. If pheromones are considered to exist, they should bear some special features and these need to be specified. First, what is the chemical nature of pheromones: Are they expected to consist out of few or multiple substances, and are these substances olfactorily perceivable or not? Second, do humans have to have a special organ (e.g. the vomeronasal organ) in order to be able to respond to pheromones? Third, what kind of responses are pheromones considered to elicit? Does the perceiver respond behaviourally and/or physiologically, and is this response associated with cognitive changes? Fourth, does the communication have to contribute to the evolutionary fitness of the signal-sender and/or the perceiver? Finally, the assumed features of putative human pheromones form the basic methodological conditions for pheromone studies in humans: Namely, what kind of substances should be investigated, what kind of responses should be measured, and does the investigation need to be framed by a theory of evolutionary meaning?

3. A Putative Human Pheromone Induces Changes in Cortisol, Positive Mood, Physiology, and Sexual Arousal

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Pheromones are species-specific chemosignals. A hallmark of pheromonal communication is the ability of the chemosignal to modify endocrine state in conspecifics. While clear in many species, whether humans communicate with pheromones remains highly controversial. Here we found that merely a few sniffs of androstadienone, a molecule present in the saliva, semen, and sweat of men, significantly increased the sexual arousal, physiological reactivity, and critically, levels of the hormone cortisol in women. That a single molecule emitted by men is capable of stereotypically modifying mood, physiological arousal, and endocrine state in women qualifies this molecule as a human pheromone.

Invited Lecture

4. Gastronomy in the XXI Century: From Chemistry to Physics

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A review was undertaken of epistemology applied to gastronomy, defining the external sensorial stimulation by food and its cerebral

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32. Olfactory-Like Cells in the Cribriform Mesenchyme: A Possible Role in Axonal Wiring

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Olfactory receptors (ORs) are supposed to render chemosensory neurons in nasal epithelia responsive to odorants and pheromones. During prenatal development, some OR subtypes are also found to be expressed in cells located in the cribriform mesenchyme between the olfactory epithelium and the telencephalon. Monitoring the onset and time course of expression revealed that the ôextraepithelialô expression of olfactory receptors in the cribriform mesenchyme begins very early and is transient: in a time window between embryonic stages E10.25 and E14.0. In situ hybridization experiments have shown that most of the receptor subtypes were expressed in rather small cell populations, except receptor subtype mOR256-17, which was found in a significantly larger portion of extraepithelial cells. These cells in the cribriform mesenchyme also expressed key elements of olfactory neurons, including the olfactory marker protein OMP, the G protein Golf and adenylyl cyclase III. Upon visualization by specific antibodies, these cells turned out to have long protrusions extending along the surface of nerve fascicles. They are often located at bifurcations where two small axon fascicles merge to form a stronger bundle. In this region, olfactory nerve fascicles coalesce forming a coherent nerve. Within the compact nerve bundle, a population of axons visualized by OR-specific antibodies was no longer distributed evenly but rather was segregated within the nerve. These findings suggest that OR proteins in the membrane of olfactory cells in the cribriform mesenchyme and of axonal processes may be intimately involved in critical processes, such as sorting and fasciculation of outgrowing axons, which are fundamental for initiating and establishing the precise wiring of the olfactory system.

33. Functional Properties of Immature Dopaminergic Neurons in the Adult Mammalian Olfactory Bulb

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A significant fraction of the cells generated in the subventricular zone (SVZ) and added in adulthood to the olfactory bulb (OB) is constituted by dopaminergic (DA) neurons. In the mammalian OB, besides mature DA neurons, confined to glomerular layer (GL), cells in which the transcription of the tyrosine hydroxylase (TH) gene occurs in the absence of significant translational activity are present in the mitral cell and in the external plexiform layers (ML and EPL). It has been proposed that these are cells recently migrated to the OB from the SVZ, and committed to become DA but not yet entirely differentiated. Using a transgenic animal model expressing GFP under TH promoter we have studied the functional properties of these cells (TH-GFP) with the patch-clamp technique in thin slices. TH-GFP cells in the EPL are autorhythmic, as are mature DA neurons, whereas TH-GFP cells in the ML are not. The pacemakers are a T-type Ca-current and a persistent Na current, the same as for mature DA neurons. The cells in the EPL are synaptically connected to the olfactory nerve, whereas those in the ML are not. Finally, the progressive maturation of the voltage-dependent currents has been described. Our interpretation of these observatio ns is that TH-GFP cells outside the GL are immature DA neurons recently migrated to the OB from the SVZ, which disrupt their migration at the level of the ML, and send a dendritic process towards the GL trying to establish a synaptic contact. Only when/if this attempt succeeds, the TH-GFP cells receive some kind of consensus signal from the GL allowing them to fulfill their differentiation towards the DA phenotype and to complete their migration on the way to their final destination crossing the EPL.

34. Matrix Metalloproteinases (MMPs) in Primary Olfactory Pathway Formation

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The topography of olfactory sensory neuron (OSN) axonal projections from olfactory epithelium (OE) to olfactory bulb (OB) is an essential determinant of odor coding. The mechanisms subserving the sorting and targeting of axons are complex but it is widely accepted that ORs are necessary, but not sufficient to account for the specificity of targeting. During the earliest stages of olfactory pathway formation, OSN axons extend through the mesenchyme and associated ECM and contact the presumptive OB where they enter the CNS through fenestrations in the basement membrane and form a presumptive nerve layer. The MMPs are proteolytic enzymes that participate in ECM degradation and are implicated in the formation of connections in the developing CNS. I hypothesized that MMPs may be influencing OSN–ECM interactions by sculpting the ECM environment in the olfactory system (OS). There are at least 25 members of the MMP family and, collectively, these proteases can degrade all constituents of the ECM. To investigate whether MMPs are acting in the OS during development, I employed 2 approaches. First, an RT-PCR screen of MMP family members to profile gene expression at different developmental stages of olfactory development, beginning at E9 when OSN axons are first exiting the olfactory placode through early postnatal development. Second, in situ zymography is being used to detect and localize specific protease activities. Preliminary results demonstrate that a) select members of this family are active in the OS; b) there is differential gene expression between OE and OB; and c) protease activity is spatially localized within the OS. Thus, MMPs appear to have a role in olfactory pathway formation.

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35. Expression and Role of Complex Carbohydrates in Axon Guidance in the Olfactory System

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Primary sensory neurons in the vertebrate olfactory systems are characterised by the differential expression of distinct cell surface carbohydrates. We show here that the histo-blood groups Sda (or CT1 antigen) and H are expressed by primary sensory neurons in the olfactory system, while the blood group A carbohydrate is expressed by a subset of vomeronasal neurons only in the developing accessory olfactory system. We have used both loss-of-function and gain-of-function approaches to manipulate expression of these carbohydrates in the olfactory system. In null mutant mice lacking the alpha(1,2)fucosyltransferase FUT1, the blood group H and A carbohydrates were not expressed in the olfactory systems which