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Molecular Basis of Olfaction

In late 2013, I began to approach leading researchers to contribute chapters for *Molecular Basis of Olfaction* to be published by Academic Press in February 2015. Olfaction research is a dynamic area with relevance across many applications from medicine to explosives-detection. In this volume I am attempting to obtain material covering the molecular mechanisms involved in olfaction of vertebrates and insects. Additionally, because olfaction is less well characterised for invertebrates, but far more sensitive and biologically important than for most vertebrates, I have sought chapters on ways the molecular characterization is being applied to broad research questions such as blocking of host-finding by insect disease vectors.

Contributing authors come from research groups in China, USA, France, Germany, Sweden & New Zealand.

Chapter List

1. Mammalian olfactory receptors, odorant binding proteins, and odorant ligands: molecular mechanisms, 3D-modeling, and activity relationships
Marie-Annick Persuy, Guenhaël Sanz, Anne Tromelin, Thierry Thomas-Danguin, Jean-François Gibrat & Edith Pajot-Augy

2. Olfactory signaling in insects
Dieter Wicher

3. Advances in high-throughput identification and characterisation of olfactory receptors in insects
Nicolas Montagné, Arthur de Fouchier, Richard D. Newcomb & Emmanuelle Jacquin-Joly

4. Olfactory disruption: towards controlling important insect vectors of disease
Jackson T. Sparks & Joseph Clifton Dickens

5. Pheromone reception in moths: from molecules to behaviors
Guirong Wang, Jin Zhang & William Walker

Preface

Smell is a potent wizard that transports you across thousands of miles and all the years you have lived.
Helen Keller

This poignant quotation by Helen Keller speaks to the evocative nature of olfaction for humans. Beyond being simply an important diagnostic mechanism for interpreting the environment, olfaction can often recall old memories or stir complex emotions. In my home country of Australia there are stories of soldiers returning from battle in World War II by ship and realising that they were nearing their homeland prior to sighting it, simply from the characteristic smell of the oil-laden *Eucalyptus* trees that dominate much of the Australian landscape. These weary combatants were not just detecting trees but imbibing their loved ones, their childhoods, their hopes and their loss.

Coming from Helen Keller, this quote also subtly hints at the key role olfaction plays when sight is not the primary sense used for navigation. This is actually the case for most of the animals on earth; huge numbers of species of invertebrates use olfaction as their key method of assessing their environment and detecting food, mates, hosts, predators etc. In creatures such as insects, olfaction-related cognition is much simpler than for humans, however, it is known to be important in individual learning, in parasitic wasps for example. Olfaction is so important to insects that they have evolved extremely sensitive olfactory receptors (ORs) to detect low concentrations (sometimes nanomloar and below) of volatile compounds; these receptors largely reside in their antennae but do occur elsewhere. The olfactory sensitivity of insects helps make them formidable evolutionary competitors but is also exploited by humans to disrupt insect behaviour (e.g., pheromone disruption of moth pests and pheromone trapping).

Olfaction has attracted significant scientific interest for many years. In 1937, Japanese researchers utilised electrodes to measure the negative electrical potential generated across olfactory epithelium of dogs, caused by olfactory stimulation. This technique was adapted for study of frogs and rabbits in 1956 and given the name electro-olfactography; it has since been widely utilised for study of olfaction in mammals. In 1957, the technique was adapted to insects and named electro-antennography, and in 1959 the first insect pheromones were characterised from the silk moth, *Bombyx mori*. While electrophysiological techniques such as these were used successfully for decades and could be used to detect the presence and degree of olfactory stimulation by various compounds, they were unable to decipher the molecular basis of olfaction.

However, around the same time in 1953, Watson and Crick published the structure of DNA. This was a seminal moment in science and was built on by others to produce great advances in our understanding of molecular biology and in the power of the techniques available to study it. Then in 1991, Richard Axel and Linda Buck discovered that vertebrate ORs were a subclass of the well-known G Protein-coupled Receptor (GPCR) family of proteins. This discovery (which was subsequently recognised with a Nobel Prize in 2004) combined with advances in DNA/RNA sequencing technologies and bioinformatics, led to the elucidation of OR repertoires of a range of vertebrate species and of associated molecular signalling processes. The first vertebrate receptor to be de-orphaned (have its cognate ligands characterised) was OR17 from the rat in 1998, which was shown to react to C_7-C_{10} saturated aldehydes.

Because insects also express many GPCRs including homologs of human proteins (e.g., serotonin and histamine receptors), it was expected that invertebrate ORs would be readily isolated through homology searches. While this was true for the nematode *Caenorhabditis elegans*, it took until 1999 for the first insect OR to be identified from the vinegar fly (*Drosophila melanogaster*) using unbiased approaches. This is because insect ORs aren't GPCRs but an unrelated group of receptor proteins with a similar tertiary structure. Being different to classic GPCRs, the signalling mechanisms have also proven to be different in insects, such as the existence of a highly conserved universal chaperone protein, and the activation of both metabotropic and ionotropic signalling cascades (first reported in 2008).

The purpose of this volume is to summarise the latest understanding of molecular mechanisms of olfaction in vertebrates and insects. I have chosen to focus most chapters on insects for several reasons. First, molecular biology of insect olfaction is still an evolving paradigm compared to that of vertebrate olfaction which is relatively well characterised. Secondly, insects are a megadiverse group that interact with varying levels of specificity, with virtually all other land organisms and therefore as a group have a huge array of ORs that detect countless volatile compounds, many important to humans. This is of great interest in terms of studying general biology but insect ORs also show huge promise in many applications such as pest/disease management and biosensing. Lastly, a lean towards insects gives a point of differentiation with other works on olfaction that have traditionally focussed on mammals, of which there are relatively few species.

This first edition of *Molecular Basis of Olfaction* is designed to provide insight into key areas of olfaction research, and is intended for use by researchers, teachers, students, molecular biologists, and biologists in general. Leading researchers from China, United States of America, France, Germany, Sweden and New Zealand have contributed the chapters presented here, and I take this opportunity to sincerely thank all authors for their effort and expertise.

Chapter One by Persuy and co-workers from France, summarises our knowledge of molecular mechanisms of odorant detection in mammals and includes 3D modelling of mammalian ORs, and relationships between receptor structure and activity. In Chapter Two, Dieter Wicher (Max Plank Institute for Chemical Ecology) discusses cellular signalling in various types of olfactory neurons in insects. Chapter Three by Montagné et al., provides an insight into the latest advances in isolating and characterising insect ORs, including the use of transcriptomics. The final two chapters focus on specific areas of insect olfaction research of importance to humans. Chapter Four by Sparks, Bohbot and Dickens (USA Department of Agriculture) discusses disruption of olfaction in insect vectors of human disease such as mosquitoes and tse tse fly. The last chapter (by Zhang and colleagues) summarises knowledge of one of the great olfactory phenomena in biology, pheromone detection by moths, and the events leading from antennal detection of a pheromone to neural processing and resultant behaviours.

I anticipate that future editions of this volume will update these summaries as well as expanding the focus of the current edition.

Richard Glatz
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Kangaroo Island, Australia