Focus of the PhD-Project (Prof. Dr. Frank Zufall)

Molecular mechanisms of odor sensing in the mouse

The peripheral olfactory system in mice consists of several subsystems including the main olfactory epithelium (MOE), the vomeronasal organ (VNO), the Grueneberg ganglion and the septal organ of Masera. Each of these subsystems projects to different parts of the brain, detects a specific set of chemosensory signals, employs distinct signaling pathways, and controls distinct behavioral repertoires. A main focus of this work is the analysis of chemo-electrical signaling pathways of the olfactory and vomeronasal sensory neurons. The ion channels and second messenger pathways that contribute to the activation, adaptation and propagation of odor- and pheromone-induced electrical signals are incompletely understood. It appears that these mechanisms are highly different between olfactory subsystems. These questions are investigated in the native olfactory system of wildtype or gene-targeted mice by using a wide variety of methodological approaches, from high-resolution electrophysiological and imaging techniques in acute tissue slices to in vivo analysis in behaving mice. A long-term goal of this work is to understand the cellular, molecular and behavioral mechanisms that underlie mammalian chemical communication.

Methods:

State-of-the-art electrophysiological recording of neural activity in brain slices and intact mouse preparations; high resolution Ca^{2+} imaging in neuronal compartments, genetic deletion of target molecules; anatomical, molecular and genetic analysis of knockout mice; high-throughput expression systems; disease models

Selected publications:

Del Punta K, Leinders-Zufall T, Rodriguez I, Jukam D, Wysocki CJ, Ogawa S, Zufall F and Mombaerts P (2002) Deficient pheromone responses in mice lacking a cluster of vomeronasal receptor genes. *Nature* **419**, 70-74.

Leypold BG, Yu CR, Leinders-Zufall T, Kim MM, Zufall F and Axel R (2002) Altered sexual and social behaviors in trp2 mutant mice. *Proc Natl Acad Sci USA* **99**, 6376-6381.

Kelliher KR, Ziesmann J, Munger SD, Reed RR and Zufall F (2003) Importance of the CNGA4 channel gene for odor discrimination and adaptation in behaving mice. *Proc Natl Acad Sci USA* **100**, 4299-4304.

Lucas P, Ukhanov K, Leinders-Zufall T and Zufall F (2003) A diacylglycerol-gated cation channel in vomeronasal neuron dendrites is impaired in TRPC2 mutant mice: mechanism of pheromone transduction. *Neuron* **40**, 551-561.

Leinders-Zufall T, Brennan P, Widmayer P, Chandramani S. P, Maul-Pavicic A, Jager M, Li XH, Breer H, Zufall F and Boehm T (2004) MHC class I peptides as chemosensory signals in the vomeronasal organ. *Science* **306**, 1033-1037.

Brennan PA and Zufall F (2006) Pheromonal communication in vertebrates. *Nature* **444**, 308-315.

Spehr M, Kelliher KR, Li XH, Boehm T, Leinders-Zufall T and Zufall F (2006) Essential role of the main olfactory system in social recognition of major histocompatibility complex peptide ligands. *J Neurosci* **26**, 1961-1970.

Leinders-Zufall T, Cockerham RE, Michalakis S, Biel M, Garbers DL, Reed RR, Zufall F and Munger SD (2007) Contribution of the receptor guanylyl cyclase GC-D to chemosensory function in the olfactory epithelium. *Proc Natl Acad Sci USA* **104**, 14507-14512.

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Munger SD, Leinders-Zufall T and Zufall F (2009) Subsystem organization of the mammalian sense of smell. *Annu Rev Physiol* **71**, 115-140.

Spehr J, Hagendorf S, Weiss J, Spehr M, Leinders-Zufall T and Zufall F (2009) Ca^{2+}-calmodulin feedback mediates sensory adaptation and inhibits pheromone-sensitive ion channels in the vomeronasal organ. *J Neurosci* **29**, 2125-2135.

Munger SD, Leinders-Zufall T, McDougall LM, Cockerham RE, Schmid A, Wandernoth P, Wennemuth G, Biel M, Zufall F and Kelliher KR (2010) An olfactory subsystem that detects carbon disulfide and mediates food-related social learning. *Curr Biol* **20**, 1438-1444.

Schmid A, Pyrski M, Biel M, Leinders-Zufall T and Zufall F (2010) Grueneberg ganglion neurons are finely tuned cold sensors. *J Neurosci* **30**, 7563-7568.

Chamero P, Katsoulidou V, Hendrix P, Bufe B, Roberts R, Matsunami H, Abramowitz J, Birnbaumer L, Zufall F and Leinders-Zufall T (2011) G protein Gαo is essential for vomeronasal function and aggressive behavior in mice. *Proc Natl Acad Sci USA* **108**, 12898-12903.

Weiss J, Pyrski M, Jacobi E, Bufe B, Willnecker V, Schick B, Zizzari P, Gossage SJ, Greer CA, Leinders-Zufall T, Woods CG, Wood JN and Zufall F (2011) Loss-of-function mutations in sodium channel Nav1.7 cause anosmia. *Nature* **472**, 186-190.