References

[1] Ibarra-Soria, X., Levitin, M. O. & Logan, D. W. The genomic basis of vomeronasal-mediated behaviour. *Mamm Genome* **25**, 75–86 (2014).

[2] Mombaerts, P. Genes and ligands for odorant, vomeronasal and taste receptors. *Nat Rev Neurosci* **5**, 263–278 (2004).

[3] Breer, H., Fleischer, J. & Strotmann, J. The sense of smell: multiple olfactory subsystems. *Cellular and Molecular Life Sciences CMLS* **63**, 1465–1475 (2006).

[4] Brennan, P. A. & Zufall, F. Pheromonal communication in vertebrates. *Nature* **444**, 308–315 (2006).

[5] Touhara, K. & Vosshall, L. B. Sensing odorants and pheromones with chemosensory receptors. *Annual Review of Physiology* **71**, 307–332 (2009).

[6] Firestein, S. How the olfactory system makes sense of scents. *Nature* **413**, 211–218 (2001).

[7] Bushdid, C., Magnasco, M. O., Vosshall, L. B. & Keller, A. Humans can discriminate more than 1 trillion olfactory stimuli. *Science* **343**, 1370–1372 (2014).

[8] Gerkin, R. C. & Castro, J. B. The number of olfactory stimuli that humans can discriminate is still unknown. *Elife* **4** (2015).

[9] Meister, M. On the dimensionality of odor space. *Elife* **4** (2015).

[10] Wyatt, T. D. *Pheromones and Animal Behaviour: Communication by Smell and Taste* (Cambridge University Press, 2003).

[11] Dulac, C. & Torello, A. T. Molecular detection of pheromone signals in mammals: from genes to behaviour. *Nat Rev Neurosci* **4**, 551–562 (2003).

[12] Spehr, M. *et al.* Parallel processing of social signals by the mammalian main and accessory olfactory systems. *Cell Mol Life Sci* **63**, 1476–1484 (2006).

[13] Morrison, E. E. & Costanzo, R. M. Morphology of olfactory epithelium in humans and other vertebrates. *Microscopy Research and Technique* **23**, 49–61 (1992).

[14] Hopkins, A. E. The olfactory receptors in vertebrates. *The Journal of Comparative Neurology* **41**, 253–289 (1926).

[15] Frisch, D. Ultrastructure of mouse olfactory mucosa. *American Journal of Anatomy* **121**, 87–119 (1967).

[16] Lancet, D. Vertebrate olfactory reception. *Annual Review of Neuroscience* **9**, 329–355 (1986).

[17] Moulton, D. G. & Beidler, L. M. Structure and function in the peripheral olfactory system. *Physiological Reviews* **47**, 1–52 (1967).

[18] Strotmann, J. *et al.* Olfactory neurones expressing distinct odorant receptor subtypes are spatially segregated in the nasal neuroepithelium. *Cell and Tissue Research* **276**, 429–438 (1994).

[19] Caggiano, M., Kauer, J. S. & Hunter, D. D. Globose basal cells are neuronal progenitors in the olfactory epithelium: A lineage analysis using a replication-incompetent retrovirus. *Neuron* **13**, 339 – 352 (1994).

[20] Leung, C. T., Coulombe, P. A. & Reed, R. R. Contribution of olfactory neural stem cells to tissue maintenance and regeneration. *Nature neuroscience* **10**, 720–726 (2007).

[21] Calof, A. L. & Chikaraishi, D. M. Analysis of neurogenesis in a mammalian neuroepithelium: Proliferation and differentiation of an olfactory neuron precursor in vitro. *Neuron* **3**, 115 – 127 (1989).

[22] Mackay-Sim, A. Stem cells and their niche in the adult olfactory mucosa. *Arch Ital Biol* **148**, 47–58 (2010).

[23] Kawagishi, K. *et al.* Stereological quantification of olfactory receptor neurons in mice. *Neuroscience* **272**, 29 – 33 (2014).

[24] Nagashima, A. & Touhara, K. Enzymatic conversion of odorants in nasal mucus affects olfactory glomerular activation patterns and odor perception. *J Neurosci* **30**, 16391–16398 (2010).

[25] Mori, K. & Sakano, H. How is the olfactory map formed and interpreted in the mammalian brain? *Annu Rev Neurosci* **34**, 467–499 (2011).

[26] Hinds, J. W., Hinds, P. L. & McNelly, N. A. An autoradiographic study of the mouse olfactory epithelium: evidence for long-lived receptors. *Anat Rec* **210**, 375–383 (1984).

[27] Graziadei, P. P. & Graziadei, G. A. Neurogenesis and neuron regeneration in the olfactory system of mammals. i. morphological aspects of differentiation and structural organization of the olfactory sensory neurons. *J Neurocytol* **8**, 1–18 (1979).

[28] Mackay-Sim, A. & Kittel, P. Cell dynamics in the adult mouse olfactory epithelium: a quantitative autoradiographic study. *J Neurosci* **11**, 979–984 (1991).

[29] Mackay-Sim, A. & Kittel, P. W. On the life span of olfactory receptor neurons. *Eur J Neurosci* **3**, 209–215 (1991).

[30] Kondo, K. *et al.* Age-related changes in cell dynamics of the postnatal mouse olfactory neuroepithelium: cell proliferation, neuronal differentiation, and cell death. *J Comp Neurol* **518**, 1962–1975 (2010).

[31] Diaz, D. *et al.* The olfactory system as a puzzle: playing with its pieces. *Anat Rec (Hoboken)* **296**, 1383–1400 (2013).

[32] Brann, J. H. & Firestein, S. A lifetime of neurogenesis in the olfactory system. *Frontiers in Neuroscience* **8** (2014).

[33] Murray, R. C. & Calof, A. L. Neuronal regeneration: lessons from the olfactory system. *Semin Cell Dev Biol* **10**, 421–431 (1999).

[34] Pace, U., Hanski, E., Salomon, Y. & Lancet, D. Odorant-sensitive adenylate cyclase may mediate olfactory reception. *Nature* **316**, 255–258 (1985).

[35] Sklar, P. B., Anholt, R. R. & Snyder, S. H. The odorant-sensitive adenylate cyclase of olfactory receptor cells. differential stimulation by distinct classes of odorants. *Journal of Biological Chemistry* **261**, 15538–43 (1986).

[36] Boekhoff, I., Tareilus, E., Strotmann, J. & Breer, H. Rapid activation of alternative second messenger pathways in olfactory cilia from rats by different odorants. *The EMBO journal* **9**, 2453–2458 (1990).

[37] Breer, H., Boekhoff, I. & Tareilus, E. Rapid kinetics of second messenger formation in olfactory transduction. *Nature* **345**, 65–68 (1990).

[38] Nakamura, T. & Gold, G. H. A cyclic nucleotide-gated conductance in olfactory receptor cilia. *Nature* **325**, 442–444 (1987).

[39] Dhallan, R. S., Yau, K.-W., Schrader, K. A. & Reed, R. R. Primary structure and functional expression of a cyclic nucleotide-activated channel from olfactory neurons. *Nature* **347**, 184–187 (1990).

[40] Kleene, S. & Gesteland, R. Calcium-activated chloride conductance in frog olfactory cilia. *The Journal of Neuroscience* **11**, 3624–3629 (1991).

[41] Kleene, S. J. Origin of the chloride current in olfactory transduction. *Neuron* **11**, 123–132 (1993).

[42] Lowe, G. & Gold, G. H. Nonlinear amplification by calcium-dependent chloride channels in olfactory receptor cells. *Nature* **366**, 283–286 (1993).

[43] Kurahashi, T. & Yau, K. W. Co-existence of cationic and chloride components in odorant-induced current of vertebrate olfactory receptor cells. *Nature* **363**, 71–74 (1993).

[44] Jones, D. & Reed, R. Golf: an olfactory neuron specific-g protein involved in odorant signal transduction. *Science* **244**, 790–795 (1989).

[45] Wong, S. T. *et al.* Disruption of the type {III} adenylyl cyclase gene leads to peripheral and behavioral anosmia in transgenic mice. *Neuron* **27**, 487 – 497 (2000).

[46] Stephan, A. B. *et al.* Ano2 is the cilial calcium-activated chloride channel that may mediate olfactory amplification. *Proceedings of the National Academy of Sciences* **106**, 11776–11781 (2009).

[47] Kaupp, U. B. Olfactory signalling in vertebrates and insects: differences and commonalities. *Nat Rev Neurosci* **11**, 188–200 (2010).

[48] Brunet, L. J., Gold, G. H. & Ngai, J. General anosmia caused by a targeted disruption of the mouse olfactory cyclic nucleotide-gated cation channel. *Neuron* **17**, 681 – 693 (1996).

[49] Baker, H. *et al.* Targeted deletion of a cyclic nucleotide-gated channel subunit (ocnc1): Biochemical and morphological consequences in adult mice. *The Journal of Neuroscience* **19**, 9313–9321 (1999).

[50] Belluscio, L., Gold, G. H., Nemes, A. & Axel, R. Mice deficient in golf are anosmic. *Neuron* **20**, 69–81 (1998).

[51] Logan, D. W. *et al.* Learned recognition of maternal signature odors mediates the first suckling episode in mice. *Curr Biol* **22**, 1998–2007 (2012).

[52] Buck, L. & Axel, R. A novel multigene family may encode odorant receptors: A molecular basis for odor recognition. *Cell* **65**, 175 – 187 (1991).

[53] Imai, T. & Sakano, H. Odorant receptor gene choice and axonal projection in the mouse olfactory system. *Results Probl Cell Differ* **47**, 57–75 (2009).

[54] Glusman, G., Yanai, I., Rubin, I. & Lancet, D. The complete human olfactory subgenome. *Genome Research* **11**, 685–702 (2001).

[55] Zhang, X. & Firestein, S. The olfactory receptor gene superfamily of the mouse. *Nature neuroscience* **5**, 124–133 (2002).

[56] Young, J. M. *et al.* Different evolutionary processes shaped the mouse and human olfactory receptor gene families. *Human Molecular Genetics* **11**, 535–546 (2002).

[57] Godfrey, P. A., Malnic, B. & Buck, L. B. The mouse olfactory receptor gene family. *Proceedings of the National Academy of Sciences of the United States of America* **101**, 2156–2161 (2004).

[58] Zhang, X., Zhang, X. & Firestein, S. Comparative genomics of odorant and pheromone receptor genes in rodents. *Genomics* **89**, 441 – 450 (2007).

[59] Freitag, J., Krieger, J., Strotmann, J. & Breer, H. Two classes of olfactory receptors in xenopus laevis. *Neuron* **15**, 1383 – 1392 (1995).

[60] Mombaerts, P. Axonal wiring in the mouse olfactory system. *Annu Rev Cell Dev Biol* **22**, 713–737 (2006).

[61] Sullivan, S. L., Adamson, M. C., Ressler, K. J., Kozak, C. A. & Buck, L. B. The chromosomal distribution of mouse odorant receptor genes. *Proceedings of the National Academy of Sciences of the United States of America* **93**, 884–888 (1996).

[62] Young, J. M. *et al.* Odorant receptor expressed sequence tags demonstrate olfactory expression of over 400 genes, extensive alternate splicing and unequal expression levels. *Genome Biol* **4**, R71 (2003).

[63] Mombaerts, P. Molecular biology of odorant receptors in vertebrates. *Annual Review of Neuroscience* **22**, 487–509 (1999).

[64] Liu, A. H., Zhang, X., Stolovitzky, G. A., Califano, A. & Firestein, S. J. Motif-based construction of a functional map for mammalian olfactory receptors. *Genomics* **81**, 443 – 456 (2003).

[65] Young, J. M. & Trask, B. J. V2r gene families degenerated in primates, dog and cow, but expanded in opossum. *Trends Genet* **23**, 212–5 (2007).

[66] Ressler, K. J., Sullivan, S. L. & Buck, L. B. A zonal organization of odorant receptor gene expression in the olfactory epithelium. *Cell* **73**, 597 – 609 (1993).

[67] Vassar, R., Ngai, J. & Axel, R. Spatial segregation of odorant receptor expression in the mammalian olfactory epithelium. *Cell* **74**, 309 – 318 (1993).

[68] Kubick, S., Strotmann, J., Andreini, I. & Breer, H. Subfamily of olfactory receptors characterized by unique structural features and expression patterns. *Journal of Neurochemistry* **69**, 465–475 (1997).

[69] Malnic, B., Hirono, J., Sato, T. & Buck, L. B. Combinatorial receptor codes for odors. *Cell* **96**, 713 – 723 (1999).

[70] Strotmann, J. *et al.* Local permutations in the glomerular array of the mouse olfactory bulb. *The Journal of Neuroscience* **20**, 6927–6938 (2000).

[71] Serizawa, S. *et al.* Mutually exclusive expression of odorant receptor transgenes. *Nat Neurosci* **3**, 687–693 (2000).

[72] Chess, A., Simon, I., Cedar, H. & Axel, R. Allelic inactivation regulates olfactory receptor gene expression. *Cell* **78**, 823 – 834 (1994).

[73] Ishii, T. *et al.* Monoallelic expression of the odourant receptor gene and axonal projection of olfactory sensory neurones. *Genes Cells* **6**, 71–78 (2001).

[74] Mombaerts, P. Odorant receptor gene choice in olfactory sensory neurons: the one receptor–one neuron hypothesis revisited. *Current Opinion in Neurobiology* **14**, 31 – 36 (2004).

[75] Strotmann, J., Wanner, L., Helfrich, T., Beck, A. & Breer, H. Rostro-caudal patterning of receptor-expressing olfactory neurones in the rat nasal cavity. *Cell and Tissue Research* **278**, 11–20 (1994).

[76] Tsuboi, A., Miyazaki, T., Imai, T. & Sakano, H. Olfactory sensory neurons expressing class i odorant receptors converge their axons on an antero-dorsal domain of the olfactory bulb in the mouse. *European Journal of Neuroscience* **23**, 1436–1444 (2006).

[77] Scott, J. W. & Brierley, T. A functional map in rat olfactory epithelium. *Chem Senses* **24**, 679–690 (1999).

[78] Miyamichi, K., Serizawa, S., Kimura, H. M. & Sakano, H. Continuous and overlapping expression domains of odorant receptor genes in the olfactory epithelium determine the dorsal/ventral positioning of glomeruli in the olfactory bulb. *The Journal of Neuroscience* **25**, 3586–3592 (2005).

[79] Ressler, K. J., Sullivan, S. L. & Buck, L. B. Information coding in the olfactory system: Evidence for a stereotyped and highly organized epitope map in the olfactory bulb. *Cell* **79**, 1245 – 1255 (1994).

[80] Feinstein, P. & Mombaerts, P. A contextual model for axonal sorting into glomeruli in the mouse olfactory system. *Cell* **117**, 817–831 (2004).

[81] Vassar, R. *et al.* Topographic organization of sensory projections to the olfactory bulb. *Cell* **79**, 981–991 (1994).

[82] Schaefer, M. L., Finger, T. E. & Restrepo, D. Variability of position of the p2 glomerulus within a map of the mouse olfactory bulb. *J Comp Neurol* **436**, 351–362 (2001).

[83] DeMaria, S. & Ngai, J. The cell biology of smell. *J Cell Biol* **191**, 443–452 (2010).

[84] Mombaerts, P. *et al.* Visualizing an olfactory sensory map. *Cell* **87**, 675 – 686 (1996).

[85] Feinstein, P., Bozza, T., Rodriguez, I., Vassalli, A. & Mombaerts, P. Axon guidance of mouse olfactory sensory neurons by odorant receptors and the beta2 adrenergic receptor. *Cell* **117**, 833–846 (2004).

[86] Wang, H. W., Wysocki, C. J. & Gold, G. H. Induction of olfactory receptor sensitivity in mice. *Science* **260**, 998–1000 (1993).

[87] Zhang, J., Huang, G., Dewan, A., Feinstein, P. & Bozza, T. Uncoupling stimulus specificity and glomerular position in the mouse olfactory system. *Mol Cell Neurosci* **51**, 79–88 (2012).

[88] Vassalli, A., Rothman, A., Feinstein, P., Zapotocky, M. & Mombaerts, P. Minigenes impart odorant receptor-specific axon guidance in the olfactory bulb. *Neuron* **35**, 681–696 (2002).

[89] Cho, J. H., Lépine, M., Andrews, W., Parnavelas, J. & Cloutier, J.-F. Requirement for slit-1 and robo-2 in zonal segregation of olfactory sensory neuron axons in the main olfactory bulb. *The Journal of Neuroscience* **27**, 9094–9104 (2007).

[90] Takeuchi, H. *et al.* Sequential arrival and graded secretion of sema3f by olfactory neuron axons specify map topography at the bulb. *Cell* **141**, 1056 – 1067 (2010).

[91] Bozza, T. *et al.* Mapping of class i and class ii odorant receptors to glomerular domains by two distinct types of olfactory sensory neurons in the mouse. *Neuron* **61**, 220–233 (2009).

[92] Imai, T., Suzuki, M. & Sakano, H. Odorant receptor derived camp signals direct axonal targeting. *Science* **314**, 657–661 (2006).

[93] Connelly, T., Savigner, A. & Ma, M. Spontaneous and sensory-evoked activity in mouse olfactory sensory neurons with defined odorant receptors. *J Neurophysiol* **110**, 55–62 (2013).

[94] Col, J. A. D., Matsuo, T., Storm, D. R. & Rodriguez, I. Adenylyl cyclase-dependent axonal targeting in the olfactory system. *Development* **134**, 2481–2489 (2007).

[95] Imai, T. *et al.* Pre-target axon sorting establishes the neural map topography. *Science* **325**, 585–590 (2009).

[96] Zou, D.-J. *et al.* Postnatal refinement of peripheral olfactory projections. *Science* **304**, 1976–1979 (2004).

[97] Serizawa, S. *et al.* A neuronal identity code for the odorant receptor-specific and activity-dependent axon sorting. *Cell* **127**, 1057 – 1069 (2006).

[98] Liberles, S. D. & Buck, L. B. A second class of chemosensory receptors in the olfactory epithelium. *Nature* **442**, 645–650 (2006).

[99] Johnson, M. A. *et al.* Neurons expressing trace amine-associated receptors project to discrete glomeruli and constitute an olfactory subsystem. *Proceedings of the National Academy of Sciences* **109**, 13410–13415 (2012).

[100] Dewan, A., Pacifico, R., Zhan, R., Rinberg, D. & Bozza, T. Non-redundant coding of aversive odours in the main olfactory pathway. *Nature* **497**, 486–489 (2013).

[101] Pacifico, R., Dewan, A., Cawley, D., Guo, C. & Bozza, T. An olfactory subsystem that mediates high-sensitivity detection of volatile amines. *Cell Reports* **2**, 76 – 88 (2012).

[102] Liberles, S. D. Trace amine-associated receptors: ligands, neural circuits, and behaviors. *Curr Opin Neurobiol* **34C**, 1–7 (2015).

[103] Ferrero, D. M. *et al.* Detection and avoidance of a carnivore odor by prey. *Proceedings of the National Academy of Sciences* **108**, 11235–11240 (2011).

[104] Zhang, J., Pacifico, R., Cawley, D., Feinstein, P. & Bozza, T. Ultrasensitive detection of amines by a trace amine-associated receptor. *The Journal of Neuroscience* **33**, 3228–3239 (2013).

[105] Li, Q. *et al.* Synchronous evolution of an odor biosynthesis pathway and behavioral response. *Current Biology* **23**, 11 – 20 (2013).

[106] Fulle, H. J. *et al.* A receptor guanylyl cyclase expressed specifically in olfactory sensory neurons. *Proc Natl Acad Sci U S A* **92**, 3571–3575 (1995).

[107] Juilfs, D. M. *et al.* A subset of olfactory neurons that selectively express cgmp-stimulated phosphodiesterase (pde2) and guanylyl cyclase-d define a unique olfactory signal transduction pathway. *Proc Natl Acad Sci U S A* **94**, 3388–3395 (1997).

[108] Meyer, M. R., Angele, A., Kremmer, E., Kaupp, U. B. & Muller, F. A cgmp-signaling pathway in a subset of olfactory sensory neurons. *Proceedings of the National Academy of Sciences of the United States of America* **97**, 10595–10600 (2000).

[109] Hu, J. *et al.* Detection of near-atmospheric concentrations of co2 by an olfactory subsystem in the mouse. *Science* **317**, 953–957 (2007).

[110] Sun, L. *et al.* Guanylyl cyclase-d in the olfactory co2 neurons is activated by bicarbonate. *Proceedings of the National Academy of Sciences* **106**, 2041–2046 (2009).

[111] Galef, B. G. & Wigmore, S. W. Transfer of information concerning distant foods: A laboratory investigation of the 'information-centre' hypothesis. *Animal Behaviour* **31**, 748 – 758 (1983).

[112] Munger, S. D. *et al.* An olfactory subsystem that detects carbon disulfide and mediates food-related social learning. *Current biology : CB* **20**, 1438–1444 (2010).

[113] Leinders-Zufall, T. *et al.* Contribution of the receptor guanylyl cyclase gc-d to chemosensory function in the olfactory epithelium. *Proceedings of the National Academy of Sciences* **104**, 14507–14512 (2007).

[114] Arakawa, H., Kelliher, K. R., Zufall, F. & Munger, S. D. The receptor guanylyl cyclase type d (gc-d) ligand uroguanylin promotes the acquisition of food preferences in mice. *Chemical Senses* **38**, 391–397 (2013).

[115] Døving, K. B. & Trotier, D. Structure and function of the vomeronasal organ. *The Journal of Experimental Biology* **201**, 2913–2925 (1998).

[116] Keverne, E. B. The vomeronasal organ. *Science* **286**, 716–720 (1999).

[117] Berghard, A. & Buck, L. Sensory transduction in vomeronasal neurons: evidence for g alpha o, g alpha i2, and adenylyl cyclase ii as major components of a pheromone signaling cascade. *The Journal of Neuroscience* **16**, 909–918 (1996).

[118] Norlin, E., Gussing, F. & Berghard, A. Vomeronasal phenotype and behavioral alterations in g(alpha)i2 mutant mice. *Current Biology* **13**, 1214 – 1219 (2003).

[119] Rudolph, U. *et al.* Ulcerative colitis and adenocarcinoma of the colon in g[alpha]i2-deficient mice. *Nat Genet* **10**, 143–150 (1995).

[120] Chamero, P. *et al.* G protein g(alpha)o is essential for vomeronasal function and aggressive behavior in mice. *Proc Natl Acad Sci U S A* **108**, 12898–903 (2011).

[121] Liman, E. R., Corey, D. P. & Dulac, C. Trp2: A candidate transduction channel for mammalian pheromone sensory signaling. *Proceedings of the National Academy of Sciences* **96**, 5791–5796 (1999).

[122] Menco, B. P. M., Carr, V. M., Ezeh, P. I., Liman, E. R. & Yankova, M. P. Ultrastructural localization of g-proteins and the channel protein trp2 to microvilli of rat vomeronasal receptor cells. *The Journal of Comparative Neurology* **438**, 468–489 (2001).

[123] Leypold, B. G. *et al.* Altered sexual and social behaviors in trp2 mutant mice. *Proceedings of the National Academy of Sciences* **99**, 6376–6381 (2002).

[124] Stowers, L., Holy, T. E., Meister, M., Dulac, C. & Koentges, G. Loss of sex discrimination and male-male aggression in mice deficient for trp2. *Science* **295**, 1493–1500 (2002).

[125] Yang, C. & Delay, R. J. Calcium-activated chloride current amplifies the response to urine in mouse vomeronasal sensory neurons. *The Journal of General Physiology* **135**, 3–13 (2010).

[126] Kim, S., Ma, L. & Yu, C. R. Requirement of calcium-activated chloride channels in the activation of mouse vomeronasal neurons. *Nat Commun* **2**, 365 (2011).

[127] Hasen, N. S. & Gammie, S. C. Trpc2-deficient lactating mice exhibit altered brain and behavioral responses to bedding stimuli. *Behavioural Brain Research* **217**, 347 – 353 (2011).

[128] Kimchi, T., Xu, J. & Dulac, C. A functional circuit underlying male sexual behaviour in the female mouse brain. *Nature* **448**, 1009–1014 (2007).

[129] Ben-Shaul, Y., Katz, L. C., Mooney, R. & Dulac, C. In vivo vomeronasal stimulation reveals sensory encoding of conspecific and allospecific cues by the mouse accessory olfactory bulb. *Proceedings of the National Academy of Sciences* **107**, 5172–5177 (2010).

[130] Papes, F., Logan, D. W. & Stowers, L. The vomeronasal organ mediates interspecies defensive behaviors through detection of protein pheromone homologs. *Cell* **141**, 692–703 (2010).

[131] Omura, M. & Mombaerts, P. Trpc2-expressing sensory neurons in the main olfactory epithelium of the mouse. *Cell Reports* **8**, 583–595 (2014).

[132] Dulac, C. & Axel, R. A novel family of genes encoding putative pheromone receptors in mammals. *Cell* **83**, 195–206 (1995).

[133] Herrada, G. & Dulac, C. A novel family of putative pheromone receptors in mammals with a topographically organized and sexually dimorphic distribution. *Cell* **90**, 763–73 (1997).

[134] Matsunami, H. & Buck, L. B. A multigene family encoding a diverse array of putative pheromone receptors in mammals. *Cell* **90**, 775–84 (1997).

[135] Ryba, N. J. & Tirindelli, R. A new multigene family of putative pheromone receptors. *Neuron* **19**, 371–9 (1997).

[136] Young, J. M., Massa, H. F., Hsu, L. & Trask, B. J. Extreme variability among mammalian v1r gene families. *Genome Res* **20**, 10–8 (2010).

[137] Rodriguez, I., Del Punta, K., Rothman, A., Ishii, T. & Mombaerts, P. Multiple new and isolated families within the mouse superfamily of v1r vomeronasal receptors. *Nature neuroscience* **5**, 134–140 (2002).

[138] Zhang, X., Rodriguez, I., Mombaerts, P. & Firestein, S. Odorant and vomeronasal receptor genes in two mouse genome assemblies. *Genomics* **83**, 802–11 (2004).

[139] Leinders-Zufall, T. *et al.* Ultrasensitive pheromone detection by mammalian vomeronasal neurons. *Nature* **405**, 792–796 (2000).

[140] Boschat, C. *et al.* Pheromone detection mediated by a v1r vomeronasal receptor. *Nat Neurosci* **5**, 1261–2 (2002).

[141] Isogai, Y. *et al.* Molecular organization of vomeronasal chemoreception. *Nature* **478**, 241–245 (2011).

[142] Nodari, F. *et al.* Sulfated steroids as natural ligands of mouse pheromone-sensing neurons. *J Neurosci* **28**, 6407–18 (2008).

[143] Del Punta, K. *et al.* Deficient pheromone responses in mice lacking a cluster of vomeronasal receptor genes. *Nature* **419**, 70–4 (2002).

[144] Dulac, C. & Wagner, S. Genetic analysis of brain circuits underlying pheromone signaling. *Annual Review of Genetics* **40**, 449–467 (2006).

[145] Chamero, P., Leinders-Zufall, T. & Zufall, F. From genes to social communication: molecular sensing by the vomeronasal organ. *Trends Neurosci* **35**, 597–606 (2012).

[146] Yang, H., Shi, P., Zhang, Y. P. & Zhang, J. Composition and evolution of the v2r vomeronasal receptor gene repertoire in mice and rats. *Genomics* **86**, 306–15 (2005).

[147] Ishii, T. & Mombaerts, P. Coordinated coexpression of two vomeronasal receptor v2r genes per neuron in the mouse. *Mol Cell Neurosci* **46**, 397–408 (2011).

[148] Martini, S., Silvotti, L., Shirazi, A., Ryba, N. J. & Tirindelli, R. Co-expression of putative pheromone receptors in the sensory neurons of the vomeronasal organ. *J Neurosci* **21**, 843–8 (2001).

[149] Silvotti, L., Moiani, A., Gatti, R. & Tirindelli, R. Combinatorial co-expression of pheromone receptors, v2rs. *J Neurochem* **103**, 1753–63 (2007).

[150] Ishii, T., Hirota, J. & Mombaerts, P. Combinatorial coexpression of neural and immune multigene families in mouse vomeronasal sensory neurons. *Curr Biol* **13**, 394–400 (2003).

[151] Loconto, J. *et al.* Functional expression of murine v2r pheromone receptors involves selective association with the m10 and m1 families of mhc class ib molecules. *Cell* **112**, 607–18 (2003).

[152] Leinders-Zufall, T. *et al.* Mhc class i peptides as chemosensory signals in the vomeronasal organ. *Science* **306**, 1033–1037 (2004).

[153] Leinders-Zufall, T., Ishii, T., Mombaerts, P., Zufall, F. & Boehm, T. Structural requirements for the activation of vomeronasal sensory neurons by mhc peptides. *Nature neuroscience* **12**, 1551–1558 (2009).

[154] Bruce, H. An exteroceptive block to pregnancy in the mouse. *Nature* **184** (1959).

[155] Wyatt, T. D. Pheromones and signature mixtures: defining species-wide signals and variable cues for identity in both invertebrates and vertebrates. *Journal of Comparative Physiology A* **196**, 685–700 (2010).

[156] Chamero, P. *et al.* Identification of protein pheromones that promote aggressive behaviour. *Nature* **450**, 899–902 (2007).

[157] Haga, S. *et al.* The male mouse pheromone esp1 enhances female sexual receptive behaviour through a specific vomeronasal receptor. *Nature* **466**, 118–22 (2010).

[158] Hurst, J. L. *et al.* Individual recognition in mice mediated by major urinary proteins. *Nature* **414**, 631–4 (2001).

[159] Roberts, S. *et al.* Darcin: a male pheromone that stimulates female memory and sexual attraction to an individual male's odour. *BMC biology* **8**, 75 (2010).

[160] Liberles, S. D. *et al.* Formyl peptide receptors are candidate chemosensory receptors in the vomeronasal organ. *Proc Natl Acad Sci U S A* **106**, 9842–7 (2009).

[161] Riviere, S., Challet, L., Fluegge, D., Spehr, M. & Rodriguez, I. Formyl peptide receptor-like proteins are a novel family of vomeronasal chemosensors. *Nature* **459**, 574–7 (2009).

[162] Bufe, B., Schumann, T. & Zufall, F. Formyl peptide receptors from immune and vomeronasal system exhibit distinct agonist properties. *Journal of Biological Chemistry* **287**, 33644–33655 (2012).

[163] Yang, H. & Shi, P. Molecular and evolutionary analyses of formyl peptide receptors suggest the absence of vno-specific fprs in primates. *J Genet Genomics* **37**, 771–8 (2010).

[164] Ma, M. *et al.* Olfactory signal transduction in the mouse septal organ. *The Journal of Neuroscience* **23**, 317–324 (2003).

[165] Giannetti, N., Saucier, D. & Astic, L. Organization of the septal organ projection to the main olfactory bulb in adult and newborn rats. *J Comp Neurol* **323**, 288–298 (1992).

[166] Kaluza, J. F., Gussing, F., Bohm, S., Breer, H. & Strotmann, J. Olfactory receptors in the mouse septal organ. *Journal of Neuroscience Research* **76**, 442–452 (2004).

[167] Tian, H. & Ma, M. Molecular organization of the olfactory septal organ. *The Journal of Neuroscience* **24**, 8383–8390 (2004).

[168] Ma, M. Encoding olfactory signals via multiple chemosensory systems. *Crit Rev Biochem Mol Biol* **42**, 463–480 (2007).

[169] Levai, O. & Strotmann, J. Projection pattern of nerve fibers from the septal organ: Dii-tracing studies with transgenic omp mice. *Histochemistry and Cell Biology* **120**, 483–492 (2003).

[170] Storan, M. J. & Key, B. Septal organ of gruneberg is part of the olfactory system. *J Comp Neurol* **494**, 834–844 (2006).

[171] Fuss, S. H., Omura, M. & Mombaerts, P. The grueneberg ganglion of the mouse projects axons to glomeruli in the olfactory bulb. *Eur J Neurosci* **22**, 2649–2654 (2005).

[172] Fleischer, J., Hass, N., Schwarzenbacher, K., Besser, S. & Breer, H. A novel population of neuronal cells expressing the olfactory marker protein (omp) in the anterior/dorsal region of the nasal cavity. *Histochem Cell Biol* **125**, 337–349 (2006).

[173] Brechbuhl, J., Klaey, M. & Broillet, M.-C. Grueneberg ganglion cells mediate alarm pheromone detection in mice. *Science* **321**, 1092–1095 (2008).

[174] Liu, C. Y., Fraser, S. E. & Koos, D. S. Grueneberg ganglion olfactory subsystem employs a cgmp signaling pathway. *J Comp Neurol* **516**, 36–48 (2009).

[175] Fleischer, J., Schwarzenbacher, K., Besser, S., Hass, N. & Breer, H. Olfactory receptors and signalling elements in the grueneberg ganglion. *J Neurochem* **98**, 543–554 (2006).

[176] Fleischer, J., Schwarzenbacher, K. & Breer, H. Expression of trace amine–associated receptors in the grueneberg ganglion. *Chemical Senses* **32**, 623–631 (2007).

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

[178] Chao, Y.-C. *et al.* Receptor guanylyl cyclase-g is a novel thermosensory protein activated by cool temperatures. *EMBO J* **34**, 294–306 (2015).

[179] Serizawa, S., Miyamichi, K. & Sakano, H. One neuron-one receptor rule in the mouse olfactory system. *Trends in Genetics* **20**, 648 – 653 (2004).

[180] Eggan, K. *et al.* Mice cloned from olfactory sensory neurons. *Nature* **428**, 44–49 (2004).

[181] Li, J., Ishii, T., Feinstein, P. & Mombaerts, P. Odorant receptor gene choice is reset by nuclear transfer from mouse olfactory sensory neurons. *Nature* **428**, 393–399 (2004).

[182] Serizawa, S. *et al.* Negative feedback regulation ensures the one receptor-one olfactory neuron rule in mouse. *Science* **302**, 2088–2094 (2003).

[183] Fuss, S. H., Omura, M. & Mombaerts, P. Local and cis effects of the h element on expression of odorant receptor genes in mouse. *Cell* **130**, 373–384 (2007).

[184] Nishizumi, H., Kumasaka, K., Inoue, N., Nakashima, A. & Sakano, H. Deletion of the core-h region in mice abolishes the expression of three proximal odorant receptor genes in cis. *Proc Natl Acad Sci U S A* **104**, 20067–20072 (2007).

[185] Lomvardas, S. *et al.* Interchromosomal interactions and olfactory receptor choice. *Cell* **126**, 403–413 (2006).

[186] Khan, M., Vaes, E. & Mombaerts, P. Regulation of the probability of mouse odorant receptor gene choice. *Cell* **147**, 907–921 (2011).

[187] Markenscoff-Papadimitriou, E. *et al.* Enhancer interaction networks as a means for singular olfactory receptor expression. *Cell* **159**, 543–557 (2014).

[188] Vassalli, A., Feinstein, P. & Mombaerts, P. Homeodomain binding motifs modulate the probability of odorant receptor gene choice in transgenic mice. *Mol Cell Neurosci* **46**, 381–396 (2011).

[189] Zhang, Y.-Q., Breer, H. & Strotmann, J. Promotor elements governing the clustered expression pattern of odorant receptor genes. *Mol Cell Neurosci* **36**, 95–107 (2007).

[190] Rothman, A., Feinstein, P., Hirota, J. & Mombaerts, P. The promoter of the mouse odorant receptor gene m71. *Mol Cell Neurosci* **28**, 535–546 (2005).

[191] Hoppe, R., Breer, H. & Strotmann, J. Promoter motifs of olfactory receptor genes expressed in distinct topographic patterns. *Genomics* **87**, 711 – 723 (2006).

[192] Michaloski, J. S., Galante, P. A. F. & Malnic, B. Identification of potential regulatory motifs in odorant receptor genes by analysis of promoter sequences. *Genome Res* **16**, 1091–1098 (2006).

[193] Plessy, C. *et al.* Promoter architecture of mouse olfactory receptor genes. *Genome Res* **22**, 486–497 (2012).

[194] Clowney, E. J. *et al.* High-throughput mapping of the promoters of the mouse olfactory receptor genes reveals a new type of mammalian promoter and provides insight into olfactory receptor gene regulation. *Genome Res* **21**, 1249–1259 (2011).

[195] Young, J. M., Luche, R. M. & Trask, B. J. Rigorous and thorough bioinformatic analyses of olfactory receptor promoters confirm enrichment of o/e and homeodomain binding sites but reveal no new common motifs. *BMC Genomics* **12**, 561 (2011).

[196] Hirota, J. & Mombaerts, P. The lim-homeodomain protein lhx2 is required for complete development of mouse olfactory sensory neurons. *Proc Natl Acad Sci U S A* **101**, 8751–8755 (2004).

[197] Kolterud, A., Alenius, M., Carlsson, L. & Bohm, S. The lim homeobox gene lhx2 is required for olfactory sensory neuron identity. *Development* **131**, 5319–5326 (2004).

[198] Hirota, J., Omura, M. & Mombaerts, P. Differential impact of lhx2 deficiency on expression of class i and class ii odorant receptor genes in mouse. *Mol Cell Neurosci* **34**, 679–688 (2007).

[199] McIntyre, J. C., Bose, S. C., Stromberg, A. J. & McClintock, T. S. Emx2 stimulates odorant receptor gene expression. *Chem Senses* **33**, 825–837 (2008).

[200] Nguyen, M. Q., Zhou, Z., Marks, C. A., Ryba, N. J. P. & Belluscio, L. Prominent roles for odorant receptor coding sequences in allelic exclusion. *Cell* **131**, 1009–1017 (2007).

[201] Fleischmann, A., Abdus-Saboor, I., Sayed, A. & Shykind, B. Functional interrogation of an odorant receptor locus reveals multiple axes of transcriptional regulation. *PLoS Biol* **11**, e1001568 (2013).

[202] McClintock, T. S. Achieving singularity in mammalian odorant receptor gene choice. *Chemical Senses* **35**, 447–457 (2010).

[203] Magklara, A. *et al.* An epigenetic signature for monoallelic olfactory receptor expression. *Cell* **145**, 555–570 (2011).

[204] Clowney, E. J. *et al.* Nuclear aggregation of olfactory receptor genes governs their monogenic expression. *Cell* **151**, 724–737 (2012).

[205] Lyons, D. B. *et al.* An epigenetic trap stabilizes singular olfactory receptor expression. *Cell* **154**, 325–336 (2013).

[206] Lewcock, J. W. & Reed, R. R. A feedback mechanism regulates monoallelic odorant receptor expression. *Proc Natl Acad Sci U S A* **101**, 1069–1074 (2004).

[207] Shykind, B. M. *et al.* Gene switching and the stability of odorant receptor gene choice. *Cell* **117**, 801 – 815 (2004).

[208] Strotmann, J., Bader, A., Luche, H., Fehling, H. J. & Breer, H. The patch-like pattern of or37 receptors is formed by turning off gene expression in non-appropriate areas. *Molecular and Cellular Neuroscience* **41**, 474 – 485 (2009).

[209] Dalton, R. P., Lyons, D. B. & Lomvardas, S. Co-opting the unfolded protein response to elicit olfactory receptor feedback. *Cell* **155**, 321–332 (2013).

[210] Rodriguez, I. Singular expression of olfactory receptor genes. *Cell* **155**, 274 – 277 (2013).

[211] Tan, L., Zong, C. & Xie, X. S. Rare event of histone demethylation can initiate singular gene expression of olfactory receptors. *Proceedings of the National Academy of Sciences* **110**, 21148–21152 (2013).

[212] Zhao, H. *et al.* Functional expression of a mammalian odorant receptor. *Science* **279**, 237–242 (1998).

[213] Sato, T., Hirono, J., Tonoike, M. & Takebayashi, M. Tuning specificities to aliphatic odorants in mouse olfactory receptor neurons and their local distribution. *J Neurophysiol* **72**, 2980–2989 (1994).

[214] Duchamp-Viret, P., Chaput, M. A. & Duchamp, A. Odor response properties of rat olfactory receptor neurons. *Science* **284**, 2171–2174 (1999).

[215] Kajiya, K. *et al.* Molecular bases of odor discrimination: Reconstitution of olfactory receptors that recognize overlapping sets of odorants. *The Journal of Neuroscience* **21**, 6018–6025 (2001).

[216] Bozza, T., Feinstein, P., Zheng, C. & Mombaerts, P. Odorant receptor expression defines functional units in the mouse olfactory system. *J Neurosci* **22**, 3033–3043 (2002).

[217] Rubin, B. D. & Katz, L. C. Optical imaging of odorant representations in the mammalian olfactory bulb. *Neuron* **23**, 499–511 (1999).

[218] Ma, M. & Shepherd, G. M. Functional mosaic organization of mouse olfactory receptor neurons. *Proc Natl Acad Sci U S A* **97**, 12869–12874 (2000).

[219] Belluscio, L., Lodovichi, C., Feinstein, P., Mombaerts, P. & Katz, L. C. Odorant receptors instruct functional circuitry in the mouse olfactory bulb. *Nature* **419**, 296–300 (2002).

[220] Araneda, R. C., Kini, A. D. & Firestein, S. The molecular receptive range of an odorant receptor. *Nat Neurosci* **3**, 1248–1255 (2000).

[221] Katada, S., Hirokawa, T., Oka, Y., Suwa, M. & Touhara, K. Structural basis for a broad but selective ligand spectrum of a mouse olfactory receptor: Mapping the odorant-binding site. *The Journal of Neuroscience* **25**, 1806–1815 (2005).

[222] Araneda, R. C., Peterlin, Z., Zhang, X., Chesler, A. & Firestein, S. A pharmacological profile of the aldehyde receptor repertoire in rat olfactory epithelium. *The Journal of Physiology* **555**, 743–756 (2004).

[223] Nara, K., Saraiva, L. R., Ye, X. & Buck, L. B. A large-scale analysis of odor coding in the olfactory epithelium. *J Neurosci* **31**, 9179–9191 (2011).

[224] Krautwurst, D., Yau, K. W. & Reed, R. R. Identification of ligands for olfactory receptors by functional expression of a receptor library. *Cell* **95**, 917–926 (1998).

[225] Rubin, B. D. & Katz, L. C. Spatial coding of enantiomers in the rat olfactory bulb. *Nat Neurosci* **4**, 355–356 (2001).

[226] Hamana, H., Hirono, J., Kizumi, M. & Sato, T. Sensitivity-dependent hierarchical receptor codes for odors. *Chemical Senses* **28**, 87–104 (2003).

[227] Touhara, K. *et al.* Functional identification and reconstitution of an odorant receptor in single olfactory neurons. *Proceedings of the National Academy of Sciences* **96**, 4040–4045 (1999).

[228] Oka, Y. *et al.* Odorant receptor map in the mouse olfactory bulb: in vivo sensitivity and specificity of receptor-defined glomeruli. *Neuron* **52**, 857–869 (2006).

[229] Tsuboi, A. *et al.* Two highly homologous mouse odorant receptors encoded by tandemly-linked mor29a and mor29b genes respond differently to phenyl ethers. *Eur J Neurosci* **33**, 205–213 (2011).

[230] Peterlin, Z., Firestein, S. & Rogers, M. E. The state of the art of odorant receptor deorphanization: a report from the orphanage. *J Gen Physiol* **143**, 527–542 (2014).

[231] Shirasu, M. *et al.* Olfactory receptor and neural pathway responsible for highly selective sensing of musk odors. *Neuron* **81**, 165–178 (2014).

[232] McClintock, T. S. *et al.* In vivo identification of eugenol-responsive and muscone-responsive mouse odorant receptors. *J Neurosci* **34**, 15669–15678 (2014).

[233] Gaillard, I. *et al.* A single olfactory receptor specifically binds a set of odorant molecules. *Eur J Neurosci* **15**, 409–418 (2002).

[234] Lu, M., Echeverri, F. & Moyer, B. D. Endoplasmic reticulum retention, degradation, and aggregation of olfactory g-protein coupled receptors. *Traffic* **4**, 416–433 (2003).

[235] Saito, H., Kubota, M., Roberts, R. W., Chi, Q. & Matsunami, H. Rtp family members induce functional expression of mammalian odorant receptors. *Cell* **119**, 679 – 691 (2004).

[236] Zhuang, H. & Matsunami, H. Synergism of accessory factors in functional expression of mammalian odorant receptors. *Journal of Biological Chemistry* **282**, 15284–15293 (2007).

[237] Von Dannecker, L. E. C., Mercadante, A. F. & Malnic, B. Ric-8b, an olfactory putative gtp exchange factor, amplifies signal transduction through the olfactory-specific g-protein galpha-olf. *The Journal of Neuroscience* **25**, 3793–3800 (2005).

[238] Saito, H., Chi, Q., Zhuang, H., Matsunami, H. & Mainland, J. D. Odor coding by a mammalian receptor repertoire. *Sci Signal* **2**, ra9 (2009).

[239] Shepard, B. D., Natarajan, N., Protzko, R. J., Acres, O. W. & Pluznick, J. L. A cleavable n-terminal signal peptide promotes widespread olfactory receptor surface expression in hek293t cells. *PLoS One* **8**, e68758 (2013).

[240] Shirokova, E. *et al.* Identification of specific ligands for orphan olfactory receptors. g protein-dependent agonism and antagonism of odorants. *J Biol Chem* **280**, 11807–11815 (2005).

[241] Mainland, J. D. *et al.* The missense of smell: functional variability in the human odorant receptor repertoire. *Nat Neurosci* **17**, 114–120 (2014).

[242] Oka, Y., Omura, M., Kataoka, H. & Touhara, K. Olfactory receptor antagonism between odorants. *The EMBO journal* **23**, 120–126 (2004).

[243] Oka, Y., Nakamura, A., Watanabe, H. & Touhara, K. An odorant derivative as an antagonist for an olfactory receptor. *Chemical Senses* **29**, 815–822 (2004).

[244] Peterlin, Z. *et al.* The importance of odorant conformation to the binding and activation of a representative olfactory receptor. *Chemistry |& biology* **15**, 1317–1327 (2008).

[245] Zufall, F. & Leinders-Zufall, T. The cellular and molecular basis of odor adaptation. *Chemical Senses* **25**, 473–481 (2000).

[246] Bradley, J., Bonigk, W., Yau, K.-W. & Frings, S. Calmodulin permanently associates with rat olfactory cng channels under native conditions. *Nat Neurosci* **7**, 705–710 (2004).

[247] Bradley, J., Reuter, D. & Frings, S. Facilitation of calmodulin-mediated odor adaptation by camp-gated channel subunits. *Science* **294**, 2176–2178 (2001).

[248] Song, Y. *et al.* Olfactory cng channel desensitization by ca2+/cam via the b1b subunit affects response termination but not sensitivity to recurring stimulation. *Neuron* **58**, 374–386 (2008).

[249] Yan, C. *et al.* Molecular cloning and characterization of a calmodulin-dependent phosphodiesterase enriched in olfactory sensory neurons. *Proc Natl Acad Sci U S A* **92**, 9677–9681 (1995).

[250] Wei, J. *et al.* Phosphorylation and inhibition of olfactory adenylyl cyclase by cam kinase ii in neurons: a mechanism for attenuation of olfactory signals. *Neuron* **21**, 495–504 (1998).

[251] Leinders-Zufall, T., Ma, M. & Zufall, F. Impaired odor adaptation in olfactory receptor neurons after inhibition of ca2+/calmodulin kinase ii. *J Neurosci* **19**, RC19 (1999).

[252] Dawson, T. M. *et al.* Beta-adrenergic receptor kinase-2 and beta-arrestin-2 as mediators of odorant-induced desensitization. *Science* **259**, 825–829 (1993).

[253] Mashukova, A., Spehr, M., Hatt, H. & Neuhaus, E. M. Beta-arrestin2-mediated internalization of mammalian odorant receptors. *J Neurosci* **26**, 9902–9912 (2006).

[254] Boekhoff, I. *et al.* Olfactory desensitization requires membrane targeting of receptor kinase mediated by beta gamma-subunits of heterotrimeric g proteins. *J Biol Chem* **269**, 37–40 (1994).

[255] Nozawa, M., Kawahara, Y. & Nei, M. Genomic drift and copy number variation of sensory receptor genes in humans. *Proceedings of the National Academy of Sciences* **104**, 20421–20426 (2007).

[256] Hasin, Y. *et al.* High-resolution copy-number variation map reflects human olfactory receptor diversity and evolution. *PLoS Genet* **4**, e1000249 (2008).

[257] Waszak, S. M. *et al.* Systematic inference of copy-number genotypes from personal genome sequencing data reveals extensive olfactory receptor gene content diversity. *PLoS Comput Biol* **6**, e1000988 (2010).

[258] Menashe, I., Man, O., Lancet, D. & Gilad, Y. Different noses for different people. *Nat Genet* **34**, 143–144 (2003).

[259] Gilad, Y. & Lancet, D. Population differences in the human functional olfactory repertoire. *Mol Biol Evol* **20**, 307–314 (2003).

[260] Olender, T. *et al.* Personal receptor repertoires: olfaction as a model. *BMC Genomics* **13**, 414 (2012).

[261] Menashe, I. *et al.* Genetic elucidation of human hyperosmia to isovaleric acid. *PLoS Biol* **5**, e284 (2007).

[262] Wysocki, C. J., Whitney, G. & Tucker, D. Specific anosmia in the laboratory mouse. *Behav Genet* **7**, 171–188 (1977).

[263] Griff, I. C. & Reed, R. R. The genetic basis for specific anosmia to isovaleric acid in the mouse. *Cell* **83**, 407–414 (1995).

[264] Adipietro, K. A., Mainland, J. D. & Matsunami, H. Functional evolution of mammalian odorant receptors. *PLoS Genet* **8**, e1002821 (2012).

[265] Whissell-Buechy, D. & Amoore, J. E. Odour-blindness to musk: simple recessive inheritance. *Nature* **245**, 157–158 (1973).

[266] Jaeger, S. R. *et al.* A mendelian trait for olfactory sensitivity affects odor experience and food selection. *Current Biology* **23**, 1601 – 1605 (2013).

[267] McRae, J. F. *et al.* Genetic variation in the odorant receptor or2j3 is associated with the ability to detect the "grassy" smelling odor, cis-3-hexen-1-ol. *Chem Senses* **37**, 585–593 (2012).

[268] Lunde, K. *et al.* Genetic variation of an odorant receptor or7d4 and sensory perception of cooked meat containing androstenone. *PLoS One* **7**, e35259 (2012).

[269] Knaapila, A. *et al.* A genome-wide study on the perception of the odorants androstenone and galaxolide. *Chem Senses* **37**, 541–552 (2012).

[270] Keller, A., Zhuang, H., Chi, Q., Vosshall, L. B. & Matsunami, H. Genetic variation in a human odorant receptor alters odour perception. *Nature* **449**, 468–472 (2007).

[271] Logan, D. W. Do you smell what i smell? genetic variation in olfactory perception. *Biochem Soc Trans* **42**, 861–865 (2014).

[272] Frumin, I., Sobel, N. & Gilad, Y. Does a unique olfactory genome imply a unique olfactory world? *Nat Neurosci* **17**, 6–8 (2014).

[273] Lledo, P.-M., Alonso, M. & Grubb, M. S. Adult neurogenesis and functional plasticity in neuronal circuits. *Nat Rev Neurosci* **7**, 179–193 (2006).

[274] Yamaguchi, M. & Mori, K. Critical period for sensory experience-dependent survival of newly generated granule cells in the adult mouse olfactory bulb. *Proc Natl Acad Sci U S A* **102**, 9697–9702 (2005).

[275] Rochefort, C., Gheusi, G., Vincent, J.-D. & Lledo, P.-M. Enriched odor exposure increases the number of newborn neurons in the adult olfactory bulb and improves odor memory. *J Neurosci* **22**, 2679–2689 (2002).

[276] Rochefort, C. & Lledo, P.-M. Short-term survival of newborn neurons in the adult olfactory bulb after exposure to a complex odor environment. *Eur J Neurosci* **22**, 2863–2870 (2005).

[277] Alonso, M. *et al.* Olfactory discrimination learning increases the survival of adult-born neurons in the olfactory bulb. *J Neurosci* **26**, 10508–10513 (2006).

[278] Woo, C. C., Hingco, E. E., Taylor, G. E. & Leon, M. Exposure to a broad range of odorants decreases cell mortality in the olfactory bulb. *Neuroreport* **17**, 817–821 (2006).

[279] Magavi, S. S. P., Mitchell, B. D., Szentirmai, O., Carter, B. S. & Macklis, J. D. Adult-born and preexisting olfactory granule neurons undergo distinct experience-dependent modifications of their olfactory responses in vivo. *J Neurosci* **25**, 10729–10739 (2005).

[280] Sultan, S. *et al.* Learning-dependent neurogenesis in the olfactory bulb determines long-term olfactory memory. *FASEB J* **24**, 2355–2363 (2010).

[281] Sultan, S., Rey, N., Sacquet, J., Mandairon, N. & Didier, A. Newborn neurons in the olfactory bulb selected for long-term survival through olfactory learning are prematurely suppressed when the olfactory memory is erased. *J Neurosci* **31**, 14893–14898 (2011).

[282] Mandairon, N., Stack, C., Kiselycznyk, C. & Linster, C. Enrichment to odors improves olfactory discrimination in adult rats. *Behav Neurosci* **120**, 173–179 (2006).

[283] Escanilla, O., Mandairon, N. & Linster, C. Odor-reward learning and enrichment have similar effects on odor perception. *Physiol Behav* **94**, 621–626 (2008).

[284] Veyrac, A. *et al.* Novelty determines the effects of olfactory enrichment on memory and neurogenesis through noradrenergic mechanisms. *Neuropsychopharmacology* **34**, 786–795 (2009).

[285] Gusmao, I. D. *et al.* Odor-enriched environment rescues long-term social memory, but does not improve olfaction in social isolated adult mice. *Behav Brain Res* **228**, 440–446 (2012).

[286] Watt, W. C. *et al.* Odorant stimulation enhances survival of olfactory sensory neurons via mapk and creb. *Neuron* **41**, 955–967 (2004).

[287] Kim, S. Y., Yoo, S.-J., Ronnett, G. V., Kim, E.-K. & Moon, C. Odorant stimulation promotes survival of rodent olfactory receptor neurons via pi3k/akt activation and bcl-2 expression. *Mol Cells* **38**, 535–539 (2015).

[288] François, A. *et al.* Early survival factor deprivation in the olfactory epithelium enhances activity-dependent survival. *Frontiers in Cellular Neuroscience* **7** (2013).

[289] Zhao, H. & Reed, R. R. X inactivation of the ocnc1 channel gene reveals a role for activity-dependent competition in the olfactory system. *Cell* **104**, 651–660 (2001).

[290] Zhao, S. *et al.* Activity-dependent modulation of odorant receptor gene expression in the mouse olfactory epithelium. *PLoS One* **8**, e69862 (2013).

[291] Coppola, D. M. & Waggener, C. T. The effects of unilateral naris occlusion on gene expression profiles in mouse olfactory mucosa. *J Mol Neurosci* **47**, 604–618 (2012).

[292] Santoro, S. W. & Dulac, C. The activity-dependent histone variant h2be modulates the life span of olfactory neurons. *Elife* **1**, e00070 (2012). NLM: Original DateCompleted: 20121217.

[293] Cavallin, M. A., Powell, K., Biju, K. C. & Fadool, D. A. State-dependent sculpting of olfactory sensory neurons is attributed to sensory enrichment, odor deprivation, and aging. *Neurosci Lett* **483**, 90–95 (2010).

[294] Cadiou, H. *et al.* Postnatal odorant exposure induces peripheral olfactory plasticity at the cellular level. *J Neurosci* **34**, 4857–4870 (2014).

[295] Ibarra-Soria, X., Levitin, M. O., Saraiva, L. R. & Logan, D. W. The olfactory transcriptomes of mice. *PLoS Genet* **10**, e1004593 (2014).

[296] Niimura, Y., Matsui, A. & Touhara, K. Extreme expansion of the olfactory receptor gene repertoire in african elephants and evolutionary dynamics of orthologous gene groups in 13 placental mammals. *Genome Res* **24**, 1485–1496 (2014).

[297] Spehr, M. *et al.* Identification of a testicular odorant receptor mediating human sperm chemotaxis. *Science* **299**, 2054–2058 (2003).

[298] Fukuda, N., Yomogida, K., Okabe, M. & Touhara, K. Functional characterization of a mouse testicular olfactory receptor and its role in chemosensing and in regulation of sperm motility. *J Cell Sci* **117**, 5835–5845 (2004).

[299] Zhang, X. *et al.* High-throughput microarray detection of olfactory receptor gene expression in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* **101**, 14168–14173 (2004).

[300] Zhang, X., Marcucci, F. & Firestein, S. High-throughput microarray detection of vomeronasal receptor gene expression in rodents. *Frontiers in Neuroscience* **4** (2010).

[301] Marioni, J. C., Mason, C. E., Mane, S. M., Stephens, M. & Gilad, Y. Rna-seq: An assessment of technical reproducibility and comparison with gene expression arrays. *Genome research* **18**, 1509–1517 (2008).

[302] Geiss, G. K. *et al.* Direct multiplexed measurement of gene expression with color-coded probe pairs. *Nat Biotechnol* **26**, 317–325 (2008).

[303] Mortazavi, A., Williams, B. A., McCue, K., Schaeffer, L. & Wold, B. Mapping and quantifying mammalian transcriptomes by rna-seq. *Nat Meth* **5**, 621–628 (2008).

[304] Khan, M., Vaes, E. & Mombaerts, P. Temporal patterns of odorant receptor gene expression in adult and aged mice. *Mol Cell Neurosci* **57**, 120–129 (2013).

[305] Hebenstreit, D. *et al.* Rna sequencing reveals two major classes of gene expression levels in metazoan cells. *Molecular systems biology* **7**, 497 (2011).

[306] Xie, S. Y., Feinstein, P. & Mombaerts, P. Characterization of a cluster comprising approximately 100 odorant receptor genes in mouse. *Mamm Genome* **11**, 1070–1078 (2000).

[307] Roberts, A., Pimentel, H., Trapnell, C. & Pachter, L. Identification of novel transcripts in annotated genomes using rna-seq. *Bioinformatics* **27**, 2325–2329 (2011).

[308] Saraiva, L. R. *et al.* Hierarchical deconstruction of mouse olfactory sensory neurons: from whole mucosa to single-cell rna-seq. *Sci Rep* **5**, 18178 (2015).

[309] Potter, S. M. *et al.* Structure and emergence of specific olfactory glomeruli in the mouse. *J Neurosci* **21**, 9713–9723 (2001).

[310] Keller, A. & Margolis, F. L. Immunological studies of the rat olfactory marker protein. *J Neurochem* **24**, 1101–1106 (1975).

[311] Monti-Graziadei, G. A., Margolis, F. L., Harding, J. W. & Graziadei, P. P. Immunocytochemistry of the olfactory marker protein. *J Histochem Cytochem* **25**, 1311–1316 (1977).

[312] Rodriguez-Gil, D. J. *et al.* Odorant receptors regulate the final glomerular coalescence of olfactory sensory neuron axons. *Proceedings of the National Academy of Sciences* **112**, 5821–5826 (2015).

[313] Buiakova, O. I. *et al.* Olfactory marker protein (omp) gene deletion causes altered physiological activity of olfactory sensory neurons. *Proc Natl Acad Sci U S A* **93**, 9858–9863 (1996).

[314] Sammeta, N., Yu, T.-T., Bose, S. C. & McClintock, T. S. Mouse olfactory sensory neurons express 10,000 genes. *J Comp Neurol* **502**, 1138–1156 (2007).

[315] Nickell, M. D., Breheny, P., Stromberg, A. J. & McClintock, T. S. Genomics of mature and immature olfactory sensory neurons. *J Comp Neurol* **520**, 2608–2629 (2012).

[316] Stegle, O., Teichmann, S. A. & Marioni, J. C. Computational and analytical challenges in single-cell transcriptomics. *Nat Rev Genet* **16**, 133–145 (2015).

[317] Macosko, E. Z. *et al.* Highly parallel genome-wide expression profiling of individual cells using nanoliter droplets. *Cell* **161**, 1202–1214 (2015).

[318] Brennecke, P. *et al.* Accounting for technical noise in single-cell rna-seq experiments. *Nat Methods* **10**, 1093–1095 (2013).

[319] Mahata, B. *et al.* Single-cell rna sequencing reveals t helper cells synthesizing steroids de novo to contribute to immune homeostasis. *Cell Rep* **7**, 1130–1142 (2014).

[320] Buettner, F. *et al.* Computational analysis of cell-to-cell heterogeneity in single-cell rna-sequencing data reveals hidden subpopulations of cells. *Nat Biotechnol* **33**, 155–160 (2015).

[321] Keane, T. M. *et al.* Mouse genomic variation and its effect on phenotypes and gene regulation. *Nature* **477**, 289–294 (2011).

[322] Omura, M. & Mombaerts, P. Trpc2-expressing sensory neurons in the mouse main olfactory epithelium of type b express the soluble guanylate cyclase gucy1b2. *Molecular and cellular neurosciences* **65**, 114–124 (2015).

[323] Ferrero, D. M. *et al.* A juvenile mouse pheromone inhibits sexual behaviour through the vomeronasal system. *Nature* **502**, 368–371 (2013).

[324] Stowers, L. & Logan, D. W. Sexual dimorphism in olfactory signaling. *Curr Opin Neurobiol* **20**, 770–775 (2010).

[325] Bressel, O. C., Khan, M. & Mombaerts, P. Linear correlation between the number of olfactory sensory neurons expressing a given mouse odorant receptor gene and the total volume of the corresponding glomeruli in the olfactory bulb. *J Comp Neurol* (2015).

[326] Kwak, J. *et al.* Differential binding between volatile ligands and major urinary proteins due to genetic variation in mice. *Physiol Behav* **107**, 112–120 (2012).

[327] Yamaguchi, M. *et al.* Distinctive urinary odors governed by the major histocompatibility locus of the mouse. *Proc Natl Acad Sci U S A* **78**, 5817–5820 (1981).

[328] Goncalves, A. *et al.* Extensive compensatory cis-trans regulation in the evolution of mouse gene expression. *Genome Res* **22**, 2376–2384 (2012).

[329] Shiao, M.-S. *et al.* Transcriptomes of mouse olfactory epithelium reveal sexual differences in odorant detection. *Genome Biol Evol* **4**, 703–712 (2012).

[330] Kanageswaran, N. *et al.* Deep sequencing of the murine olfactory receptor neuron transcriptome. *PLoS One* **10**, e0113170 (2015).

[331] Shum, E. Y., Espinoza, J. L., Ramaiah, M. & Wilkinson, M. F. Identification of novel post-transcriptional features in olfactory receptor family mrnas. *Nucleic Acids Res* (2015).

[332] Kuhlmann, K. *et al.* The membrane proteome of sensory cilia to the depth of olfactory receptors. *Mol Cell Proteomics* **13**, 1828–1843 (2014).

[333] Kang, N. & Koo, J. Olfactory receptors in non-chemosensory tissues. *BMB Rep* **45**, 612–622 (2012).

[334] Griffin, C. A., Kafadar, K. A. & Pavlath, G. K. Mor23 promotes muscle regeneration and regulates cell adhesion and migration. *Dev Cell* **17**, 649–661 (2009).

[335] Braun, T., Voland, P., Kunz, L., Prinz, C. & Gratzl, M. Enterochromaffin cells of the human gut: sensors for spices and odorants. *Gastroenterology* **132**, 1890–1901 (2007).

[336] Wang, F., Kessels, H. W. & Hu, H. The mouse that roared: neural mechanisms of social hierarchy. *Trends Neurosci* **37**, 674–682 (2014).

[337] Dey, S. *et al.* Cyclic regulation of sensory perception by a female hormone alters behavior. *Cell* **161**, 1334–1344 (2015).

[338] Yang, H., Bell, T. A., Churchill, G. A. & Pardo-Manuel de Villena, F. On the subspecific origin of the laboratory mouse. *Nat Genet* **39**, 1100–1107 (2007).

[339] Jorde, L. B. & Wooding, S. P. Genetic variation, classification and 'race'. *Nat Genet* **36**, S28–33 (2004).

[340] Pezer, Z., Harr, B., Teschke, M., Babiker, H. & Tautz, D. Divergence patterns of genic copy number variation in natural populations of the house mouse (mus musculus domesticus) reveal three conserved genes with major population-specific expansions. *Genome Res* **25**, 1114–1124 (2015).

[341] Liu, K. J. *et al.* Interspecific introgressive origin of genomic diversity in the house mouse. *Proc Natl Acad Sci U S A* **112**, 196–201 (2015).

[342] Secundo, L. *et al.* Individual olfactory perception reveals meaningful nonolfactory genetic information. *Proc Natl Acad Sci U S A* **112**, 8750–8755 (2015).

[343] Fleischmann, A. *et al.* Mice with a "monoclonal nose": perturbations in an olfactory map impair odor discrimination. *Neuron* **60**, 1068–1081 (2008).

[344] von der Weid, B. *et al.* Large-scale transcriptional profiling of chemosensory neurons identifies receptor-ligand pairs in vivo. *Nat Neurosci* (2015).

[345] Jiang, Y. *et al.* Molecular profiling of activated olfactory neurons identifies odorant receptors for odors in vivo. *Nat Neurosci* (2015).

[346] Li, H. *et al.* The sequence alignment/map format and samtools. *Bioinformatics* **25**, 2078–2079 (2009).

[347] Dobin, A. *et al.* Star: ultrafast universal rna-seq aligner. *Bioinformatics* **29**, 15–21 (2013).

[348] Robinson, J. T. *et al.* Integrative genomics viewer. *Nat Biotechnol* **29**, 24–26 (2011).

[349] Thorvaldsdottir, H., Robinson, J. T. & Mesirov, J. P. Integrative genomics viewer (igv): high-performance genomics data visualization and exploration. *Brief Bioinform* **14**, 178–192 (2013).

[350] Anders, S., Pyl, P. T. & Huber, W. Htseq–a python framework to work with high-throughput sequencing data. *Bioinformatics* **31**, 166–169 (2015).

[351] Warnes, G. R. *et al.* *gplots: Various R Programming Tools for Plotting Data* (2015). R package version 2.17.0.

[352] Love, M. I., Huber, W. & Anders, S. Moderated estimation of fold change and dispersion for rna-seq data with deseq2. *Genome Biol* **15**, 550 (2014).

[353] Benaglia, T., Chauveau, D., Hunter, D. R. & Young, D. mixtools: An R package for analyzing finite mixture models. *Journal of Statistical Software* **32**, 1–29 (2009).

[354] Backes, C. *et al.* Genetrail–advanced gene set enrichment analysis. *Nucleic Acids Res* **35**, W186–92 (2007).

[355] Du, P., Kibbe, W. A. & Lin, S. M. lumi: a pipeline for processing illumina microarray. *Bioinformatics* **24**, 1547–1548 (2008).

[356] McLaren, W. *et al.* Deriving the consequences of genomic variants with the ensembl api and snp effect predictor. *Bioinformatics* **26**, 2069–2070 (2010).

[357] Langmead, B., Trapnell, C., Pop, M. & Salzberg, S. L. Ultrafast and memory-efficient alignment of short dna sequences to the human genome. *Genome Biol* **10**, R25 (2009).

[358] Quinlan, A. R. & Hall, I. M. Bedtools: a flexible suite of utilities for comparing genomic features. *Bioinformatics* **26**, 841–842 (2010).

[359] Munger, S. C. *et al.* Rna-seq alignment to individualized genomes improves transcript abundance estimates in multiparent populations. *Genetics* **198**, 59–73 (2014).

[360] Micallef, L. & Rodgers, P. eulerape: drawing area-proportional 3-venn diagrams using ellipses. *PLoS One* **9**, e101717 (2014).