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## PRESIDENTIAL SYMPOSIUM

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# Why Have Neurogenesis in Adult Olfactory Systems? The Presidential Symposium at the 2006 AChemS Conference

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The topic of the Presidential Symposium at the 28th Annual Meeting of the Association for Chemoreception Sciences, on 29 April 2006, was “Why Have Neurogenesis in Adult Olfactory Systems?” This introductory paper plus the following 3 papers arose from the science presented in that symposium.

Cell proliferation has long been known to occur in adult animals. It occurs in many tissues, including the epidermis and intestinal lining wherein it functions in the turnover and repair of tissue normally exposed to harsh environments. For many years, cell proliferation was thought to be absent from the nervous system of adult animals. This was the prevailing dogma until the 1960s, when radiolabeled molecules became more available for biological studies. This included tritiated thymidine, which could be used to label cells in the S-phase of the cell cycle. This provided a convenient and reliable marker of cells replicating their DNA and, at least in many cases, thus in the process of mitosis. This methodology allowed for claims of neurogenesis in brains of adult rodents in the 1960s by Altman and colleagues (e.g., Altman and Das 1966; Altman 1969). The claims were received with a mixture of skepticism, enthusiasm, and indifference, and they were not fully appreciated until later studies using the same and new techniques replicated and extended their findings. Now, with nonradio-labeled markers of DNA replication such as bromodeoxyuridine and antibodies for molecules specifically expressed in different phases of the cell cycle, identifying cell division in tissues is relatively simple and commonplace and has led to demonstrations of neurogenesis in the brains of adult animals representing an impressive phylogenetic range.

Although adult neurogenesis is phylogenetically widespread in the brains of adult vertebrates, including representatives of the major classes of vertebrates—elasmobranchs, teleosts, amphibians, reptiles, birds, and mammals—it is limited to very few brain regions. The 2 vertebrate brain regions most

recognized as sites of adult neurogenesis are the subventricular zone/olfactory bulb and the dentate gyrus of the hippocampus. Other areas in the adult mammalian brain, including the cortex, have been reported to undergo neurogenesis, but this topic is being debated.

Adult neurogenesis occurs in other animal groups in addition to the vertebrates, most notably in some insects and crustaceans. In these groups as in the vertebrates, adult neurogenesis occurs only in limited parts of the nervous system and often associated with olfaction. In insects, it occurs in the mushroom bodies, which are large neuropils containing intrinsic interneurons called Kenyon cells. Kenyon cells are higher order multimodal integrators that receive their most prominent input from the antennal lobes, which are the insect's primary olfactory neuropils. In crustaceans, adult neurogenesis principally occurs in 2 parts of the brain: the olfactory lobes and the optic lobes. Neurogenesis occurs not only in the brain but also in the peripheral olfactory systems of many animals, including vertebrates, crustaceans, and snails.

A focus of research on adult neurogenesis is elucidating the cellular and molecular mechanisms of cell birth and migration (e.g., Merkle and Alvarez-Buylla 2006; Sawamoto et al. 2006). Receiving much less attention has been the “function” of olfactory neurogenesis in adults. Adult neurogenesis is certainly not limited to the olfactory system, but if adult neurogenesis occurs in a species, it is likely to occur in the olfactory pathway. Why is this so? What is different about olfaction that makes adult neurogenesis so prevalent? This led me to organize the 2006 AChemS Presidential Symposium on the topic, Why have adult olfactory neurogenesis?

There are many reasons why adult animals might have olfactory neurogenesis. Many animals have indeterminate growth such that they increase in size throughout their life. Olfactory neurogenesis allows their olfactory system to keep

pace with the increase in body surface. This effect, however, is not necessarily olfactory specific, as other parts of the body, including other sensory systems, may also expand with body size. A second reason for adult olfactory neurogenesis is that some animals respond to damage to or loss of the olfactory organ with regeneration and repair. Crustaceans are an excellent model of this. The olfactory organ is particularly susceptible to damage because its sensory function requires that it be intimately exposed to the external environment. Damage to and death of olfactory sensory neurons in such conditions are to be expected. So the continuous neurogenesis in the adult olfactory organ is likely to be an evolutionary adaptation to provide programmed replacement of cells to compensate for this cell damage and death. This continuous loss and addition of peripheral neurons could reasonably lead to a plasticity in olfactory central neural circuits that also includes adult neurogenesis. Third, given continuous olfactory neurogenesis, it would be functionally advantageous if the rate of birth and/or survival of new cells could be modulated by physiological conditions related to environmental richness, external stresses, internal state, learning, and others. Such plasticity in adult olfactory neurogenesis may have important functional implications—but it still may not completely explain why neurogenesis is common in olfaction but not other systems.

The 4 speakers in the symposium were invited to address the issue of why do adult nervous systems have neurogenesis. Their work covers key animal models of adult neurogenesis. Three of these presentations are represented as papers in this issue of *Chemical Senses* (Cayre et al. 2007; Gheusi and Lledo 2007; Schmidt 2007).

The symposium began with a presentation by Elizabeth Gould (Princeton University, Princeton, NJ) on “Adult neurogenesis in the mammalian brain.” This presentation provided a perspective on neurogenesis in nonolfactory regions of the mammalian brain, especially the hippocampus, but also other regions of the brain including the cortex. Dr Gould was unable to contribute a written paper to our proceedings.

Myriam Cayre (CNRS, Marseilles, France) presented work by her and colleagues on the regulation and function of adult neurogenesis using an insect model—the house cricket. Her main questions are what is the role of newborn neurons and how is adult neurogenesis regulated to enhance olfactory function? Neurogenesis in adult crickets occurs in a set of intrinsic interneurons in the mushroom bodies. This neurogenesis is regulated by internal cues such as morphogenetic hormones and by environmental cues such as the richness of the animal’s sensory environment and degree of sensory stimulation. These new cells can function by enhancing learning abilities of crickets. Her paper on this subject is Cayre et al. (2007).

Manfred Schmidt (Georgia State University, Atlanta, GA) reviewed work on the olfactory pathway of decapod crustaceans. In this model, adult neurogenesis occurs in both the peripheral and central olfactory pathways. A research focus

is the olfactory lobe, which has many structural and functional similarities to the comparable first synaptic relay in the brains of insects and mammals. Adult olfactory neurogenesis is phylogenetically broad in crustaceans and occurs in projection interneurons of the olfactory lobe. Schmidt described cellular mechanisms of neurogenesis, including precursor cells and a stem cell niche, and that internal and external factors can modulate neurogenesis. Schmidt presented a hypothesis as to why crustaceans have adult neurogenesis in the olfactory (and visual) pathways but not in some other pathways and concluded that this is related to the specific “topographic logic” of information processing in the olfactory lobe. His work is found in Schmidt (2007).

Pierre-Marie Lledo (Pasteur Institute, Paris, France) presented work in collaboration with Gilles Gheusi and colleagues on the mammalian olfactory system, focusing on the control of early events in olfactory processing by adult neurogenesis. He reviewed the production of new neurons, their integration into existing circuits in the olfactory bulb, and the functional roles of these new cells. Adult neurogenesis in the olfactory bulb is influenced by behaviors related to functions of the olfactory bulb, but the newly generated cells in turn influence those same behaviors. Lledo argued that adult olfactory neurogenesis in mammals is flexible and thus allows the brain to function in a way suited to the animal’s particular environment. The olfactory bulb is continually sculpted by the addition of new neurons and elimination of other neurons, such that the bulb’s networks are adaptive, which may be advantageous in learning. This work is published as Gheusi and Lledo (2007).

Collectively, these papers provide a summary of our current understanding of the function of olfactory neurogenesis in adult animals. More importantly, they offer ideas and speculations that will be helpful in future studies of why adult animals have olfactory neurogenesis.

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