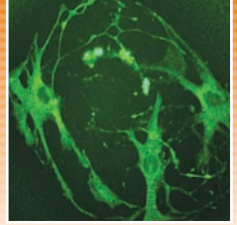
Neuroscience Research Unit



Adult Stem Cell Group

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BACKGROUND

Recent demonstrations isolating stem cells from the central nervous system, and the ability of nervous tissues to regenerate have given hope for the treatment of neurodegenerative diseases. The capacity of olfactory receptor neurons to regenerate from a pool of multipotent stem cells signalled this region of the nervous system as an important source of adult neural stem cells. While the regenerative capacity of the olfactory neuroepithelium has been well studied less is know about the molecular events controlling adult olfactory stem cell activity. Therefore, the aim of the research in the adult stem cell group is to isolate and characterise adult olfactory stem cells and examine the molecular mechanisms involved in olfactory stem cell proliferation and differentiation.

PROJECT 1

Isolation, identification and characterisation of olfactory stem cells

To isolate adult olfactory stem cells from the olfactory neuroepithelium to investigate the potential of these cells to proliferate and differentiate in culture. A major part of the project is to utilise our expertise in olfactory biology to isolate olfactory stem cells using flow cytometry. The identity of the olfactory stem cell is still unknown. We have developed culture methodology that has allowed us to isolate olfactory neurospheres from mice and demonstrated their proliferative and clonal capacity. With the use of extracellular markers to different populations of cells within the olfactory neuroepithelium, we will isolate homogeneous populations and study their capacity for proliferation and differentiation.

PROJECT 2

Differentiation of olfactory stem cells into neural cell types.

Characterisation of the ability of olfactory stem cells to proliferate and differentiate. BrdU incorporation experiments will be used to assess proliferation. Growth factor withdrawal followed by immunocyto-chemistry will be performed to determine the differentiation of the adult olfactory stem cells. A bank of antibody markers will be used to elucidate different neural cell types. For example, antibody markers of dopaminergic (dopamine ≤ hydroxylase (DBH); tyrosine hydroxylase (TH)) and cholingergic (choline acetyltransferase (ChAT)) neurons will be employed to determine the type of neurons differentiating from the neurospheres. There is a substantial amount of evidence suggesting that there are certain stem cell genes: Wnt-3a, Pax6 and Musashi-1 that are involved in cell fate determination. Examination of gene profiles by using RT-PCR will be used to determine if these genes are involved in cell fate determination of the adult olfactory stem cells.

Hearing Research Group

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BACKGROUND

Many forms of hearing loss result from damage to the sensory receptors for hearing, the hair cells in the inner ear. Hair cell degeneration can occur with exposure to loud noise, ageing, certain antibiotic treatments, and infection. Damaged hair cells are not replaced in humans, thus the hearing loss is permanent and irreversible. The long-term goal of our research is to investigate a potential treatment for the reversal or slowing of hearing loss in humans.

Stem cell-based treatments are currently being explored to treat hearing loss. Stem cells can repair tissues by replacing the damaged cells and/or by secreting factors that enhance the repair of native cells. Adult stem cells from the nasal lining, in particular, have practical and clinically relevant advantages for cell therapies. Our experiments in mice have shown that adult nasal stem cells can be induced to develop into hair cells. The next step is to investigate whether adult human olfactory stem cells to act as a source of new hair cells, a clinically relevant progression from animal studies. The research can provide original contributions for the understanding of adult human stem cells and, specifically, the potential of olfactory stem cells to act as a therapy for hearing loss.

A wide range of skills are available to students, including stem cell biology, electrophysiology, molecular biology, immunohistochemistry, cell culture, confocal microscopy (live cell imaging), and mouse behavioural hearing tests.

PROJECT 1

Using human adult olfactory stem cells for hearing repair

The specific aims of this study are 1) transform olfactory stem cells into auditory hair cells 2) inject stem cells into the inner ear and 3) test for hearing repair. There are several indicators to determine the success of the project. The transformation of stem cells into hair cells can be measured using specific and commercially available anatomical hair cell markers. The injection of stem cells into the inner ear is performed with established microsurgical techniques and testing for hearing repair is possible with a standard hearing test.

PROJECT 2

Testing functionality of stem-cell derived hair cells

If olfactory stem cells are to be used for hair cell replacement therapy, it is important to demonstrate that these stem cells can form functional hair cells. The aim of this project is to use electrophysiology to test whether stem cell-derived hair cells are physiologically functional. The application of electrophysiology to stem cell biology represents a powerful and under-explored research avenue. Whole cell recordings will be made from stem cell-derived hair cells in culture to characterise passive (capacitance, input resistance) and active membrane properties (potassium and calcium currents). These experiments will establish whether olfactory stem cells possess similar membrane properties as functional native hair cells.