Growth hormone precursor cells: identification, enrichment, transplantation and differentiation

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Growth hormone(GH) secreted by the somatotrope cells of the pituitary gland is critically essential throughout life, regulating growth, bone density, the cardiovascular system and the metabolism of proteins, carbohydrates and lipids. Deficiency in GH is a significant clinical problem that affects both adults and children. The current therapy of GH replacement by injection does not simulate the natural physiologically controlled release from somatotrope cells. Little is known on the mechanism and maintenance of correct somatotrope numbers in a normal pituitary gland. Interestingly the pituitary has an enormous capacity for the expansion and complete restoration of the GH secreting population. Past studies have implicated a resident stem/precursor-like cell, however, this cell type was never identified.

Recently our laboratory was the first to report the identification and characterisation of a resident pituitary precursor cell that shares characteristics with stem cells. This cell type is rare, has clonogenic properties forming a heterogeneous colony from a single cell, has high proliferative potential, expresses cell surface stem cell-related antigens and shows the capacity to differentiate into GH cells. We termed this cell type **P**ituitary **C**olony **F**orming **C**ell or PCFC. The expansion and differentiation characteristics of PCFCs make them ideal for potential use in a cell based therapy for GH deficiency.

We have developed a protocol to obtain highly enriched populations of PCFCs using a combination of cell surface antigen markers and the ability of PCFCs to import the fluorescent di-peptide β-Ala-Lys-Nε-7-amino-4-methylcoumarin-3-acetic acid (AMCA). To test PCFC potential *in vivo* we used a tissue engineering model specifically developed by our laboratory to grow transplanted tissue/cells for repair. This model involves a vascularized microchamber system in the mouse offering the advantage of circulating blood to supply the cells with nutrients to maintain survival. PCFCs implanted into the microchamber both survived and differentiated into GH cells *in vivo*. Our studies show that the PCFC microchamber system has the potential to be developed into a GH secreting organoid.