

Editorial

Satellite cells and Myoblast Transfer Therapy

This special issue of BAM (Volume 7, parts 3 & 4) arose from a Symposium on Myoblast Transplantation held as part of a 3rd International Congress of the Cell Transplant Society in Miami, Florida in late 1996 [Abstracts in *Cell Transplantation* 1996 5:5S-2]. This workshop marks a resurgence of interest in such cell therapy as a potential treatment for myopathies like the lethal childhood X-chromosome-linked, Duchenne Muscular Dystrophy (DMD). In DMD, defects in the protein product of the peccant gene, dystrophin, result in necrosis and replacement of skeletal muscles by fat and fibrous connective tissue which leads to death of boys usually around 20 years of age. Dystrophin was identified in 1987 and in 1989 the first Myoblast Transfer conference was held in New York to discuss a possible cell therapy aimed at replacing the missing gene product, dystrophin, by the introduction of normal donor myoblasts into the defective multinucleated myofibres of DMD boys [Proceedings in *Myoblast Transfer Therapy*, Eds. Eastwood AB, Karpatis G and Griggs R, 1990, Plenum Press]. Despite the lack of a strong experimental basis and reservations that extension to the clinical situation was premature, human trials were subsequently carried out. No effective replacement of the missing dystrophin was observed in the treated boys and, with one notable exception, most trials have been discontinued and myoblast transplantation deemed a failure. During this time, only a few groups continued with animal experiments aimed at clarifying the problems associated with myoblast therapy.

The papers in this volume demonstrate the continuing interest in myoblast therapy and provide a strong basis for developing strategies to overcome the problems that have now been identified. I thank the contributors for their enthusiastic response and the reviewers for their constructive comments which have made it a pleasure to edit this special issue. The papers are divided broadly into two groups: those that deal with the behaviour of the donor myoblasts (widely referred to as satellite cells in adult muscle) when their numbers are expanded under tissue culture conditions prior to injection into dystrophic host muscles, and those that focus on the host response to such transplanted muscle cells.

The opening papers report novel findings on the behaviour of myoblasts in tissue culture and provide insight into the failure of the clinical trials. They show that myoblasts can express new antigens when grown under certain tissue culture conditions so that autologous myoblasts will become immunogenic after transplantation; and describe the proliferative potential and senescence of human satellite cells in culture and a technique for extending their proliferative capacity. The next 2 papers discuss the influence of growth factors on the behaviour of satellite cells: from the roles of leukaemia inhibitory factor and various cytokines on the proliferation of primary myoblast cultures and in enhancing myoblast survival after injection *in vivo*, to the influence of fibroblast growth factor on satellite cells cultured on their parent myofibre. The source of myoblasts is the subject of the 2 final papers in this section: where the capacity of stem cells as a renewable source of mouse myoblasts is explored, and it is shown that skin fibroblasts might serve as an alternative supply of myoblasts for such cell transplantation.

In the next section, the immunological response of the host to injected myoblasts, ways of ablating this host response, and the controversial work of Peter Law are comprehensively reviewed. The host immune response is also the subject of the next paper where sliced muscle segments (instead of cultured myoblasts) are implanted and it is shown that immunomodulation of the host T cell response facilitates both the survival and movement of donor myoblasts from these grafts. Experiments demonstrating the developments in gene therapy and the benefits of combining this with cell therapy are critically discussed. The final papers explore functional aspects of dystrophic muscles: from the effective replacement of the dystrophin protein, to electrophysiological measurements of contractile properties and improvements in muscle strength.

I wish to dedicate this issue to the memory of Zoran Matejevic, a young man with DMD with whom I discussed Myoblast Transfer Therapy in 1989.

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