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Developing Cell Carriers for Delivering Cells from the Laboratory to the Clinic – Clinical and Commercial Experiences

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Abstract

My group began culturing sheets of autologous keratinocytes for the treatment of burns patients in 1992, working with local burns surgeons in Sheffield (1). An analysis of the difficulties of producing these sheets so that their production matched the needs of the patients, led to the development of an alternative simpler technology for transferring cells from the laboratory to the clinic, that of using an engineered surface (plasma polymerised acrylic acid). This was commercialised through a University of Sheffield spin out company, CellTran Ltd. During the 8 years that CellTran ran, 2000-2008, it produced two products approved for clinical use for the treatment of patients with burns and chronic non-healing wounds – Myskin™, autologous keratinocytes on a carrier dressing, and Cryoskin, allogeneic keratinocytes available from frozen on a carrier dressing. We published a single blind study showing the efficacy of this cell therapy for the acceleration of healing of chronic non-healing neuropathic diabetic ulcers (2). MySkin™ has been commercially available in the UK since 2004 for NHS patients suffering from severe burns and chronic non-healing ulcers and is now produced by the company Regenerys Ltd.

The same approach of delivering cells on carrier dressings was then extended to developing surfaces for delivery of corneal epithelial cells (3) human melanocytes and keratinocytes (for the treatment of patients with vitiligo or hypopigmentation following burns injury) (4) and more recently for the delivery of bone marrow MSC cells for the treatment of chronic wounds (5,6).

The above approaches to delivering cells from the laboratory to patients who may be geographically distant from the cell culture facility require that cells can travel for several days and still be fit for purpose on their arrival. This is an important step in translating cell therapy to enable many patients to benefit from this therapy.

Beyond this in an international collaboration with India funded by the Wellcome Trust our group has developed a synthetic biodegradable carrier for assisting surgeons in cornea regeneration. Patients can lose the specialist limbal stem cells which provide the clear cornea for a variety of reasons – trauma, genetic diseases or immune conditions. Once these cells are lost the cells which rush in to cover the cornea are essentially scar tissue and this results in loss of vision for the patient. Currently some 12 specialist centres worldwide culture limbal epithelial stem cells in the laboratory (usually taking cells from the good eye to treat the opposite scarred eye when the condition is unilateral). To assist the cells to survive on the eyes, cells are transplanted back on human amniotic membrane. This is a donor human tissue with inherent risks of viral disease transmission and it's also variable and not everyone has access to amniotic membrane.

Our group has developed an electrospun biodegradable membrane made of polylactic acid and we have shown that it can be combined not only with cultured cells (expanded under clean room conditions) but also with small tissue explants held in place with fibrin glue. Both lead to regeneration of a multi-layered corneal epithelium in vitro. Working with our colleagues in India we have now obtained regulatory approval to do a first in man study in India taking small explants of the unaffected eye, placing these on the biodegradable membrane held in place with fibrin and putting the membrane on the eye.

So not only will the synthetic membrane be safer it offers the potential to greatly simplify the process of treating these patients , making the therapy much more accessible to ophthalmic centres worldwide without the need for specialist clean rooms for the culture of cells or access to tissue bank for amniotic membrane. This should allow the technology to become accessible to many more patients. (7)

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