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Review Series – Stem Cell Research

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Recent advances in stem cells and regenerative medicine

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There have been many recent advances in our understanding of stem cell biology, tissue regeneration and organ repair mechanisms. This is accompanied by a significant increase in the number of stem cell therapy, cell therapy and regenerative medicine studies being published. These studies range from basic studies in animal models to clinical trials. This increased potential for regenerative medicine is timely, given the increasing burden of chronic disease and disability. Although pharmaceutical approaches to chronic disease have been transformative, many diseases result in chronic organ and tissue damage that is unlikely to be solved through conventional pharmaceutical approaches. To tackle these chronic and important disabling conditions, it is likely that a new approach will be required which has been termed regenerative medicine. The broad approaches of regenerative medicine are: (i) to understand the intrinsic repair mechanisms within tissues to try and promote these to improve healthy regeneration and reduce pathological wound healing responses such as excessive scarring and (ii) develop cell therapies whereby exogenous cells can be transplanted into tissues to help repair the damaged tissue or organs. With an improved understanding of stem cell biology and tissue repair mechanisms there have also been rapid advances in the creation of artificial substrates or artificial niches for stem cells to grow upon. Stem cell niches within tissue are special environments defined by both the cellular and the extracellular environment in which stem cells reside. Stem cell niches help to tightly regulate the growth and differentiation of the stem cells into their daughter cells within tissue. In conditions of severe tissue damage, such as liver cirrhosis, the niche can become so abnormal that even transplanted cells cannot readily engraft and grow normally. In this situation strategies to improve the niche, for example, by reducing scarring are required to improve regeneration or allow successful cell therapy. It is also likely that artificial stem cell niches will be developed where stem cells can grow upon prior to transplantation of this composite graft. This does mean that regenerative medicine is a highly multidiscipline subject, requiring input from developmental biologists, stem cell biologists, experts in organ damage and inflammation and scarring, clinicians, experts in chemistry and the physical sciences and imaging expertise. Coordinating these efforts means that regenerative medicine may be best considered within the framework of large academic/medical institutes with access to many of these disciplines in one linked site. In the following review series we have some very interesting summaries of the state-of-the-art in the field of stem cell biology and regenerative medicine, written by researcher- active leaders in the field.

In the review by Muir *et al.*,[1] the current state of progress towards cell therapy for type I diabetes is explained. Here, the requirement is for functioning β cells that will produce appropriate levels of insulin in response to fluctuating blood sugar. The translational potential of this field is boosted by the ongoing clinical use of islet cell therapy. Here, islets are isolated from cadaveric donor pancreases and transplanted into recipient livers to treat hypoglycaemic unawareness in type I diabetes. As in many types of cell and organ transplantation there is a dearth of suitable donors. Stem cells are a potential source of therapeutic β cells that could overcome this issue. Muir *et al*. explains that two major sources of cells for islet stem cell therapy are pluripotent stem cells (induced pluripotent stem cells or embryonic stem cells) or transdifferentiated exocrine cells. These exocrine cells are currently discarded at

the time that islets are isolated from the donor pancreas prior to transplantation—making them a potentially abundant future source.

In the review by Dr Williams,[2] the basic biology underpinning neuronal regeneration and remyelination is described. Myelin protects neurons and the myelin sheaths are damaged in many diseases including multiple sclerosis, a major focus of Dr William's research. Myelinating oligodendrocytes are generated from their precursor cells—oligodendrocyte precursor cells (OPCs) and understanding their function is important for developing remyelination therapies. Strategies to improve remyelination are discussed including the promotion of OPC function, the transplantation of exogenous OPCs and the transplantation of cells with paracrine effects that can stimulate OPC mediated through myelination.

El-Jawhari *et al.*[3] discuss the prospects for use of mesenchymal stem cells (MSCs) in the treatment of rheumatoid arthritis. MSCs can be isolated from various tissues and have immunosuppressive properties when injected locally into damaged tissues or infused into subjects with inflammatory conditions. In response to inflammatory disease such as rheumatoid arthritis the stromal cells within joints begin to take on a more immuno-stimulatory role and this aspect is discussed by El-Jawhari *et al.* This finding makes these cells potential future targets for biological or other novel therapies.

Than *et al.* describe recent advances in stem cell therapy to promote liver regeneration.[4] The liver is a naturally regenerative organ and can efficiently regain its size and function when up to two-thirds of the liver has been removed. Presumably, this was understood by the Greek originators of the legend of Promethius who was punished by having his liver partly eaten every day by an eagle, only for it to regrow again overnight—ready for the next day's punishment. In a sense, this is what happens with chronic liver injury due to alcohol or viruses. Unfortunately, the liver often progressively scars with this injury and alongside this the regenerative capacity eventually fails. Than *et al.* outline the cell therapy approaches that have been taken in animal models and are now being tested in clinical trials that have the dual aim or reducing scaring and promoting regeneration.

The review by Succony *et al.*[5] highlights the darker side of stem cells, namely their potential for cancer development. This aspect is particularly highlighted with reference to the lung. Regeneration and cancer are 'biological cousins' and it is always worth considering the risk of promoting cancer through the promotion of tissue repair. On the other hand, by understanding the stem cell-like nature of cancer cells we can begin to design treatments that combat these features and hopefully have better efficacy and a lower risk of relapse.

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