

## Editorial

### Stem Cell Based Therapy for Autoimmunity

The immune system is challenged with the task of protecting us from unknown foreign pathogens such as viruses and bacteria. This is achieved through a complex system of physical, soluble and cellular factors that can be roughly divided into innate and adaptive immune systems. An underlying feature that enables recognition and responses to unknown targets is the generation of antigen receptors on lymphocytes through the process of random gene recombination. However, a consequence of this is the generation of self-reactive receptors capable of responding to self-antigens and causing pathology. Although a number of mechanisms such as clonal deletion and regulation have evolved to eliminate or counter the action of these self-reactive clones, self-reactive clones still exist and cause pathology. Five to six percent of the population suffers from autoimmunity, with over 60 different types of autoimmune diseases described, including the more readily recognised diseases such type 1 diabetes, multiple sclerosis, rheumatoid arthritis and systemic lupus erythematosus to name a few [1]. While different in clinical symptoms and pathology, an underlying similarity of autoimmune diseases is a chronic adaptive immune response to self-tissues that ultimately leads to clinical illness. At present, the standard treatment for autoimmunity involves immunosuppressive agents designed to dampen the immune response but this is often associated with unwanted side effects such as increased susceptibility to infection. As yet, a cure has not been described and thus a challenge for the medical and clinical research communities is devising treatments and strategies that are specific for autoimmune diseases and do not render the recipient immune-compromised. This quest is the goal of many approaches that include the use and manipulation of stem cells. In this series of reviews, we focus on the use of haematopoietic and mesenchymal stem cells in the treatment of autoimmune disease, highlighting the promises, potential and challenges that lie ahead.

While the immunological importance of the bone marrow compartment has been known for half a century, it is only in the past 15 years or so that the strategy of bone marrow or haematopoietic stem cell transfer (HSCT) to specifically treat autoimmunity has been trialed in humans. In the first series of papers, three leading groups in the field of HSCT review and provide their experience in clinical trials in treating three quite different autoimmune diseases. Delemarre *et al.* [2] targets the chronic joint disease known as juvenile idiopathic arthritis, Couri and Voltarelli [3] address type 1 diabetes, an autoimmune disease that destroys the insulin secreting cells of the pancreas, and lastly Milanetti and colleagues [4] review the extensive studies they and others have generated in treating systemic sclerosis. While much still need to be learnt about the mechanism(s) involved with the beneficial effects observed in many patients treated with autologous HSCT and why some relapse, this general strategy is proving to be very exciting and providing the first glimpse of potentially long-term medication free remission. As mentioned, our understanding of the mechanisms associated with the benefits associated with HSCT is not complete and whether many mechanisms may in fact be in action. Focusing on type 1 diabetes, LoCascio and colleagues [5] explore various mechanisms associated with immune tolerance that may be involved or associated with HSCT as a treatment. It has been shown in a number of settings that driving the ectopic expression of autoantigens can promote immune tolerance. This theme forms the basis of studies describe by Scott [6] and Chan *et al.* [7] that show manipulating the haematopoietic stem cell system through retroviral transduction can promote autoantigen specific tolerance and suppress disease expression. The generation of tolerogenic B cells is a particular focus of the work by Scott with a historical journey describing the genesis of this research direction. It is of particular interest that this strategy has been used in a number of disease models, suggesting that the underlying mechanism involved is applicable across different antigens and disease settings. In contrast, our studies in the mouse model of experimental autoimmune encephalomyelitis (EAE) are of importance, reflecting current human trials and relapse rates that are still an issue. We have found that while HSCT alone can promote remission, it does not impart immune tolerance and thus whether this translates to the current human experience is of particular relevance. The final group of reviews highlights the potential role of mesenchymal stem cells in treating autoimmunity. Only recently their potential as a therapeutic agent has been identified, and in the context of autoimmunity it is their immunomodulatory features which are of most interest. EAE as a model for multiple sclerosis is a popular model to examine the role of mesenchymal stem cells. Payne and colleagues [8] present a comprehensive overview of MS and EAE and how mesenchymal stem cells may have a role in disease treatment. Many of these themes are discussed in more detail by Kassiss *et al.* [9] which examines the immunomodulatory influences of MSCs on various immune functions. Last but not least, Uccelli *et al.* [10], present their view on the controversial topic of MSC transdifferentiation into neural cells and their importance in the broader area of MSCs as a therapeutic agent to treat MS.

I am grateful to the editors of *Current Stem Cell Research & Therapy* for the opportunity to participate in this special issue of CSCRT and highlight the potential of stem cells in the treatment of autoimmunity. I believe this series of reviews will not only provide a valuable reference point for researchers and students in the field of autoimmunity and tolerance but also to those with a wider interest in stem cell biology and eager to learn how stem cells may provide avenues for therapies in diverse disease settings.

#### REFERENCES

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