FEATURES

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Neural Development in Human Embryonic Stem Cells

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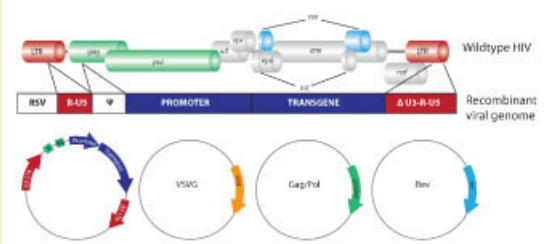
The derivation of neural lineages from human embryonic stem cells (hESCs) *in vitro* is based largely on exposure of hESCs to exogenous signals and substrates, designed to mimic conditions in the developing embryo. However, selection of specific lineages and the discovery of gene function in human neural development may be enhanced by the ability to intrinsically regulate gene expression. Dottori et al. review the induction and differentiation of neural lineages from hESC and describe the modification of these cells by recombinant lentiviral vectors. Recombinant lentiviral vectors provide an efficient method to stably introduce genes into hESC and their differentiating derivatives. Developments in lentiviral technology to enhance transduction efficiency and in the regulation of transgene expression have paralleled advances in understanding hESC biology. The potential applications of lentiviral vectors for hESC remain to be fully explored. Dottori et al. describe new uses of lentiviral vectors in hESC cells and derivatives for library screening in drug development and the use of zinc finger nucleases for gene editing. Additionally, the emerging field of optogenetics, a method revolutionizing neuroscience, is described for its potential in hESC cell research.



Mesenchymal Stem Cells: Agents of Immune Modulation

Karen English and Bernard P. Mahon

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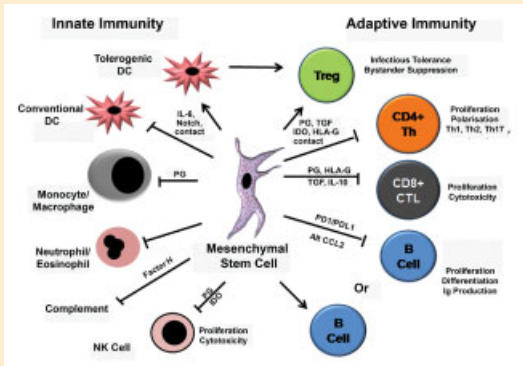
Adult mesenchymal stem or stromal cells (MSC) modulate and suppress innate and adaptive immune responses. This provides an opportunity to use tissue mis-matched/allogeneic MSC therapies against currently untreatable diseases. The nature of this immune privilege is explored in the context of recent literature by English and Mahon in this issue. The authors focus on the mechanistic basis of immune modulation and the abilty of MSC to induce regulatory T cells and tolerogenic dendritic cells. Two insights make this review a significant contribution to our understanding of the topic. The authors resolve conflicting data by suggesting that allogeneic MSC are plastic, responding to different local signals and exerting different effects on immune effector mechanisms. This will be a key issue for developing novel MSC therapies. The second insight is perhaps more significant; the authors examine the evidence for and against the immune privileged status of allogeneic MSC *in vivo*. This timely assessment is an important antidote to the more fanciful claims made for MSC as "cure-alls". MSC are not immunologically inert, retain some immunogenicity and in some, but not all, disease settings this limits therapeutic efficacy. Ultimately successful allogeneic MSC therapies will rely on such improved understanding of these parameters.



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Cytotoxic Immunotherapy for Cancer

Laura K. Aguilar, Brian W. Guzik, and Estuardo Aguilar-Cordova

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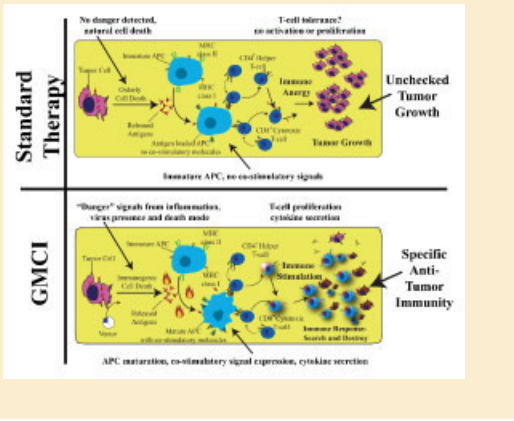

With the recent approval of the first immunotherapies for treating cancer, the field of tumor immunology has finally started to deliver results. It has been known for many years that the immune system plays a critical role in preventing tumor development, yet must be regulated to prevent autoimmunity. Critical to success for immunotherapy has been a better understanding of the complex molecular and cellular interactions that maintain the balance between immune activation, suppression and ignorance. Another critical component has been a better understanding of cancers' immune evasion techniques. A polyclonal response to tumor antigens is necessary to maintain a specific, yet broad, response that is not easily evaded by tumors. Cytotoxic immunotherapy, described by Aguilar et al in this issue, is an approach which accomplishes this using a viral vector to create an in situ vaccine that is personalized to the patient's own tumor. Evidence supports both innate and adaptive immune stimulation leading to activation of antigen presenting cells, including dendritic cells, and antigen-specific T cells. Preclinical data demonstrated synergy with standard cancer therapies including radiation, surgery and some chemotherapy agents. Clinical success will come from using basic science to drive clinical development strategies.

Cardiomyogenic MicroRNA Expression and iPSCs

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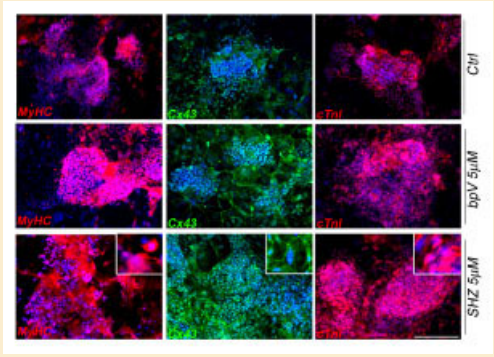

In the quest for heart cell therapies and *in vitro* disease modeling, cardiomyocyte differentiation of induced pluripotent stem cells (iPSCs) is prompting an extensive research effort. iPSCs are generated from somatic cells, thus sharing the genotype of the donor, and are spontaneously prone to form beating cardiac foci. Recently, small chemical compounds are being investigated as non-immunogenic tools to enhance a specific commitment in stem cells. Quattrocelli et al analyzed the effects of sulfonyl-hydrazone-1 (SHZ) and bis-peroxo-vanadium (bpV) on cell viability and yield efficiency during iPSC differentiation towards beating foci and single cardiomyocytes. Results showed that SHZ had more beneficial effects than bpV on cardiac foci specification and Cx43^{+} cardiomyocyte yield. In addition, SHZ significantly increased the expression of early and late cardiac-specific microRNAs, namely *miR-1*, *miR-133a* and *miR-208a*. Investigating the effects on cell viability - a recurrent issue in chemically conditioned differentiation of stem cells - experiments showed that bpV and high SHZ concentrations can activate Casp3 and induce apoptosis in differentiating iPSCs. Evidence indicates that small chemical compounds provide valid tools for enhancing specific gene/microRNA expression promoting cardiac differentiation in iPSCs, although dosage optimization is critical to maintain balance between differentiation rate and cell survival.