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VIEWPOINT

Stem Cell Biology and Gene Therapy

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It is difficult to articulate the extent to which our understanding of stem cells has evolved. For some time, it has been known that development and tissue renewal require populations of pluripotent progenitor cells that are competent to proliferate and pursue stringently regulated programs of gene expression to support emergence of differentiated cells with specialized structural and functional phenotypes. However, recent indications of stem cell plasticity have extended the boundaries for mechanistically integrating regulatory cues that mediate biological control of differentiation as well as options for gene therapy and tissue engineering.

The impact of stem cells on discovery of fundamental regulatory pathways and clinical applications are far-reaching. New dimensions to in vivo and ex vivo cell isolation, fractionation, characterization, and propagation of stem cells have emerged. Novel approaches for gene transduction have been required. And, complex ethical as well as regulatory/legal issues have necessitated resolution. Stem cell research and therapeutic applications have impacted a broad segment of people who infrequently share similar concerns. Scientists, ethicists, legislators, health care providers, community leaders, academic institutions, the biotechnology and pharmaceutical industries, the judicial system, and regulatory agencies are evaluating the rules that govern developments and application in this rapidly progressing field. The implications of discovery as well as the extent of restriction or permissiveness for translation of research findings to biological applications can significantly influence options for laboratory investigation, clinical practices, and science policy.

It is unrealistic to comprehensively address the issues that are encompassed by stem cell biology and gene therapy in an encapsulated manner. Rather, we have focused on several key issues that are central to the field which reflect current knowledge, practice, and policies as well as those that can be anticipated.

The origins and properties of stem cells are being actively investigated. The ontogeny and anatomical distribution of primitive progenitor cells remain biologically relevant and open-ended questions. The articles by Jackson et al. (pp 1–6), Phinney (pp 7–12), Triffitt (pp 13–19), and Ballas et al. (pp 20–28) provide valuable insight into our current knowledge of the structural and functional properties of embryonic and postnatal stem cells.

Progress in stem cell biology and gene therapy has been and will continue to be linked with capabilities to modulate stem cell proliferation, differentiation, and tissue targeting. Advances in gene transfer are pivotal for strategies that will augment therapeutic potential. Moore (pp 29–38), Srivastava (pp 39–45), and Medin and Fowler (pp 46–54) highlight recently developed options for propagation and genetic modification of stem cells.

Clinical applications of stem cells and tissue targeted gene therapy are reviewed in the articles by Becker (pp 55–64), Yeung and Chung (pp 65–72), Devine (pp 73–79), O'Brien et al. (pp 80–87), Schwarzenberger and Kolls (pp 88–95), and Tse and Egalka (pp 96–103). Properties of mesenchymal and muscle derived stem cells are assessed. Stem cell plasticity and use of tissue-specific and/or tumor restrictive gene promoters for delivery of therapeutic agents to sites of tumor metastasis are reviewed. The article by Gee (pp 104–112) addresses risk assessment and the necessary safeguards for new dimensions of treatment that are based on cellular and gene therapy.

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There is an ever-increasing repertoire of cellular, biochemical, and molecular mechanisms that are viable for translation to cell and gene-based therapeutic applications. The challenge is to enhance our capabilities to rectify aberrant gene expression without compromising fidelity of regulatory parameters that are requisite for the establishment and maintenance of cell, tissue, and organ function.