Current Progress in Stem Cell Technology: Realistic Opportunity for a New Frontier in Personalized Medicine

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Stem cells offer the potential of creating healthy tissues and organs using generic methods and a regenerating source. Some stem cells can be used to produce materials identical to patients' personal genetic profiles and tailored to individualized treatments. Stem cell technology may be applied to biomaterial development, disease models, regenerative medicine, and bioreactors. These and other applications will require understanding of the molecular mechanisms operating in stem cells, concurrent with advances in nanomaterials, animal and *in vitro* models, and tools to measure treatment parameters in patient-specific contexts at genetic, epigenetic and systems biology levels. Recent research has focused on inducing pluripotent stem cells from various somatic cell types, directing differentiation pathways, understanding the reprogramming process, improvement of reprogramming efficiency, and induction of pluripotency using methods that are minimally invasive to the genome.

This research has advanced the ability of stem cell technologies to facilitate bioengineering at multiple levels: engineering cells, tissues or organs, and entire organisms. To complement other presentations in this session on tissue/organ and biomaterial engineering, I will use examples from projects in our laboratory to illustrate techniques for manipulating the genes and molecular mechanisms within cells, and for altering the composition of an entire organism.

Cell engineering combines the manipulation of molecular biochemical mechanisms with cell culturing. For example, the transfer of DNA constructed to express a novel or pathological form of a gene into primary or cultured cells confers a new phenotype that has engineering utility. To create a large animal model for chronic myeloid leukemia, described below, we constructed the fused form of two genes that is often responsible for this cancer and transfected it within an expression vector into stem cells from human umbilical cord blood. In another example of cell engineering, the transfer of four master regulatory genes into differentiated cells causes reprogramming that induces pluripotency nearly indistinguishable from that of natural stem cells. We have improved the efficiency of this process by investigating alternative cell culture conditions, which led to the first cloned mouse derived entirely from a single induced pluripotent stem cell. While it is unethical and unnecessary to clone a human using this approach, the ability to collect a patient's own mature differentiated cells and induce pluripotency enables regenerative medicine by providing a source of stem cells that are easily accessible and entirely compatible with the individual's immune system.

Engineering of an organism may involve transplantation of an engineered tissue, or may occur directly from cellular engineering. To create our leukemia model, engineered human stem cells were injected in utero into fetal goats. The resulting animals carried human cells that had implanted and differentiated throughout the body, including the hematopoietic system, and exhibited the pre-leukemia phenotype that may be useful for studying the development of resistance to current therapeutic drugs.

These areas of bioengineering, combined with advances in synthetic biology, will lead to a variety of mechanisms for engineering life. Indeed, the construction of the first entirely synthetic, yet viable, genome was recently announced. The resulting abilities to model and treat disease, understand normal biology and its many variations, and tailor organisms for agricultural or other economic benefits will have profound effects. Such science must be accompanied by full dialog with society and careful consideration of ethical and legal issues.