Biomaterials in Regenerative Medicine: Promises and Progress

Ryan K. Roeder and John A. Nychka

The July 27, 1998 issue of *Business Week* featured a cover story on the business prospects for regenerative medicine entitled, “Biotech Bodies.”[1] The subtitle stated that, “Decades of research into tissue engineering are about to pay off as dozens of startups perfect living organs grown in the lab, not the body,” and it was further predicted that, “In the next 10 years, a veritable body shop of spare parts will wend its way from labs to patients.”[1] More than ten years have passed, along with significant investment of private and federal funding, and detractors can point to only a handful of commercialized tissue engineered products that have reached the clinic. However, upon first reading the *Business Week* feature story more than ten years ago, I was immediately reminded of high-temperature superconductors.

The May 11, 1987 issue of *Time* magazine featured an eerily similar cover story describing the technological revolution about to be unleashed by “the superconductivity revolution.”[2] Superconductivity was discovered by the Dutch physicist Heike Kamerlingh Onnes in 1911,[3] but was largely an esoteric science until the discovery of new enabling materials in 1986. Any materials scientist more than 35 years old will recall the genuine excitement at that time surrounding discoveries of high-temperature superconductivity in yttrium barium copper oxide (YBCO, 1986) and bismuth strontium calcium copper oxide (BSCCO, 1988) ceramics. Magnetic levitation (maglev) trains and efficient power transmission were all the buzz. Scientific discovery was, of course, separated from commercialization by significant hurdles in design, manufacturing, and economics. Twenty-five years later, there are three operational maglev trains globally. American Superconductor and Sumitomo Electric are beginning to install the first power transmission lines.[4]

So what does superconductivity have to do with regenerative medicine? More than one might first think. Consider the following comparisons and their potential implications:

Significant progress in the commercialization of technology utilizing high-temperature superconductors is arguably only happening now, 100 years after discovery of the phenomenon and 25 years after the discovery of enabling materials. While the concept of tissue engineering was formalized in 1987,[5] the roots of the science reach back to the first successes in tissue transplantation in the 1950s and 1960s. The point here is not to make foolish predictions for the future based on analogy, but to point out that any perceived lack of significant progress in commercialization of tissue engineering products should not yet be alarming from a historical perspective.

Unlike superconductors, one cannot point to a date like 1986 when enabling materials were discovered because the ideal biomaterial structure and properties for a tissue engineering scaffold is still very unsettled, likely to be different for every type of tissue to be engineered, and inherently complicated by biology. Nonetheless, scaffold biomaterials have been adopted from existing biomaterials (e.g., degradable sutures made from polylactide or polyglycolide) and the natural tissues themselves (e.g., collagen and calcium phosphates) with reasonable success. These existing biomaterials most likely constitute the enabling materials, but a key new discovery may yet be on the horizon.

The costs for commercializing high-temperature superconductors and tissue-engineered products are monumental. Construction costs for a maglev train are typically estimated to be on the order of \$100M/mile. A South Korean company recently ordered 3 million meters of power transmission cable from American Superconductor for “undisclosed terms.” In the United States, the regulatory pathway for a tissue engineered product involving biologics will typically require eight years and a \$50–300M investment, compared to “only” three years and \$5–20M for acellular devices comprised of materials previously used in approved devices.[6] Scott J. Hollister explains in this issue the regulatory, manufacturing, and clinical hurdles to translating scaffold therapies that are typically not well-recognized by academic researchers, and how these hurdles are poorly addressed by current federal funding initiatives. Thus, in both superconductors and regenerative medicine, we have technologically feasible progress slowed by prohibitive costs. Within medicine, this problem will almost certainly also lead to ethical dilemmas for healthcare access.

In summary, it appears that biomaterials and biomedical scientists will be wise to practice a “steady as she goes” mentality with a hopeful persistence balanced by a healthy dose of reality. The articles in this issue capture this mentality while highlighting key achievements and remaining challenges for biomaterials in regenerative medicine. The articles in this issue are also generally focused on scaffold biomaterials for skeletal tissues. These biases are not to detract from the importance of other applications in regen-

(Continued on page 55.)

Roeder *(Continued from page 50.)*

erative medicine, such as nanoparticles used for drug delivery, or other tissues, such as skin, nerves, blood vessels, etc.

We could not think of anyone more qualified to provide a big-picture perspective on the history and guiding principles for biomaterials in regenerative medicine than David F. Williams, who, in addition to numerous titles and distinctions, is the Editor-in-Chief for *Biomaterials,* which is the leading journal in the field. Next, Scott J. Hollister (University of Michigan) shares his expertise on the design and manufacturing challenges associated with multifunctional scaffold biomaterials, including a candid discussion of many of the aforementioned issues surrounding translation to commercially viable products. Gráinne M. Cunniffe and Fergal J. O'Brien (Trinity College, Dublin, Ireland) overview research specific to the structure and function of collagen scaffolds in orthopedic regenerative medicine. Andrew J. Steward, Yongxing Liu, and Diane R. Wagner (University of Notre Dame) then bring cell biology to the pages of *JOM* (what can be next?!) by introducing the fundamental science and engineering of cell attachment mechanisms to biomaterials, specifically for cartilage tissue engineering. We move from predominately "soft" materials to "hard" materials with a review of calcium phosphate scaffolds for bone repair by Jennifer H. Shepherd and Serena M. Best (University of Cambridge, U.K.). Finally, Susmita Bose et al. (Washington State University) further explore the use of calcium phosphate scaffolds, cements, and particles in drug delivery applications.

References

1. C. Arnst and C. Carey, "Biotech Bodies," *Business Week* (July 17, 1998).
2. M.D. Lemonick, "Science: Superconductors!," *Time* (May 11, 1987).
3. H.K. Onnes, *Commun. Phys. Lab. Univ. Leiden*, 124c (1911), p. 1.
4. J. Milton, *Nature News* (online) (October 8, 2010), doi:10.1038/news.2010.527.
5. J. Viola, B. Lal, and O. Grad, "The Emergence of Tissue Engineering as a Research Field" (National Science Foundation, Arlington, VA, 2003), *http://www.nsf.gov/pubs/2004/nsf0450/*.
6. A. Ratcliffe, *Tissue Engineering in Musculoskeletal Clinical Science,* ed. L.J. Sandell and A.J. Grodzinsky (Rosemont, IL: American Academy of Orthopaedic Surgeons, 2004), pp. 17–23.

Ryan K. Roeder is an associate professor in the Department of Aerospace and Mechanical Engineering, Bioengineering Graduate Program, University of Notre Dame, South Bend, Indiana and chair of the TMS Biomaterials Committee of the Structural Materials Division. John A. Nychka is with the Department of Chemical and Materials Engineering, University of Alberta, Edmonton, Canada, and vice chair of the Biomaterials Committee.