The First Journal on Human Gene Therapy Celebrates its 25th Anniversary

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THIS STORY BEGAN IN 1990 when a handful of scientists working in the nascent field of gene therapy came together with a young, forward-thinking publishing company run by Mary Ann Liebert to launch a provocative new journal. At the time, the science of gene therapy was thin but the expectation of its broad-based clinical success was very thick. In the inaugural issue of *Human Gene Therapy*, then Editor-In-Chief French Anderson stated that “We plan for *Human Gene Therapy* to evolve with this major new frontier and to document the progress and the setbacks as we go.” (Anderson, 1990).

The Journal indeed stayed true to this mission during its rich and storied history. *Human Gene Therapy* played a major role in publishing the translational science behind the first clinical trials of *in vivo* and *ex vivo* gene therapy. The debate over these trials was as much about the ethics and public policy of gene therapy in humans as it was about the science; *Human Gene Therapy* served as a public forum to present these complex issues. The formative stages of gene therapy are chronicled almost verbatim in the early issues of the Journal.

Human Gene Therapy expanded with the exponential growth of the field and served as a venue for publishing outstanding preclinical science as stakeholders went back to the bench after some setbacks in the clinic. As you know, the gene therapy community “stayed the course.” With a strong foundation of science and technology, we are now seeing a crescendo of good news through successful clinical trial results to exciting new directions. To keep in step with this new era, we created two sibling journals: *Human Gene Therapy Methods* (Wilson, 2011), to provide a venue for publishing the technology that will enable the field to succeed, and *Human Gene Therapy Clinical Development* (Wilson, 2012), to capture important research on the regulatory and translational sciences. Establishing a new journal in 2013 brought us full circle to the early days of *Human Gene Therapy*, which also focused on key translational issues albeit under very different circumstances. No longer are we striving for clinical success; current efforts attempt to leverage recent clinical successes across a broader array of diseases and facilitate access and distribution to patients.

The incredible impact of *Human Gene Therapy* on the field was recognized in 2009 by The National Libraries Association, which identified the Journal as “One of the 100 Most Influential Biomedical and Life Science Journals of the Last 100 Years.” The role *Human Gene Therapy* played in documenting the story of Glybera, the first commercially

approved gene therapy product in the West, illustrates how broad and substantive this impact has been. Glybera is an adeno-associated virus type 1–based product that was approved by the European Medicines Agency in 2012 for use in patients with a rare form of high triglycerides due to a deficiency of lipoprotein lipase. Virtually every milestone involved in the development of this product was published in one of the *Human Gene Therapy* journals, including the two proof-of-concept preclinical studies in mouse and feline models of the disease that provided the rationale to progress to the clinic (Ross *et al.*, 2004, 2006), the investigational new drug–enabling safety studies and initial characterization of potential human subjects (Rip *et al.*, 2005), the safety and molecular analyses of the phase 2 clinical trials (Ferreira *et al.*, 2013), and an extensive review of the regulatory approval of the product (Bryant *et al.*, 2013).

We plan to celebrate our silver anniversary in several ways, beginning with the recognition of pioneering gene therapy scientists. A blue ribbon panel of investigators was convened to identify 12 individuals who have made seminal contributions to the field in the context of a career that has consistently contributed to cell and gene therapy research for an extended period of time. The committee, which was chaired by Dr. Mary Collins, defined a seminal contribution as a groundbreaking clinical study or a basic/technical advance that has substantially influenced the direction and/or trajectory of translational research. In some instances, the Pioneer Award was shared among several scientists whose seminal work within a programmatic area could not be fairly singled out. Each pioneer will contribute a perspective piece on their career and future directions for the field in one of the 2014 issues of *Human Gene Therapy*. The composition of the Pioneer Series Award Selection Committee and the pioneer awardees can be found on pages iv–v of this issue.

This issue of *Human Gene Therapy* was designed to capture the exciting scientific developments of the field as well as celebrate its rich tradition of discussing key ethical and policy issues. In addition to a number of first-rate peer-reviewed articles, we feature a series of articles from key stakeholders regarding the Recombinant DNA Advisory Committee (RAC), which is an organization that has provided leadership and governance for gene therapy research in the United States. This series of articles coincides with the recent deliberations of the Institute of Medicine (IOM), which convened a committee to evaluate the role of the RAC in gene therapy research going forward; their recommendations will be published in a report entitled,

“Oversight and Review of Clinical Gene Transfer Protocols: Assessing the Role of the Recombinant DNA Advisory Committee” by Koehler *et al.* (2014). We lead off our coverage of this debate with an article by Nelson Wivel—director of the NIH Office of Recombinant DNA Activities from 1986–1996—that chronicles the history of the RAC. Testimonies provided by several participants of the IOM committee are published in this issue, as is a commentary by bioethicist Arthur Caplan concerning the IOM’s recommendations.

The occasion of our silver anniversary provides an opportunity to reflect on the last 25 years. What strikes me is the resolve and commitment of a community of stakeholders who believed that gene therapy would eventually succeed. Patients with otherwise incurable diseases are benefiting from gene therapy, which is the true cause of celebration. However, we have only scratched the surface of the true clinical potential of the field. We need more science and improved technology. We need to establish business models that will support the commercial development of this so-called disruptive technology. We look forward to the day when gene therapy will no longer be described as experimental or emerging or disruptive but just standard of medical care. *Human Gene Therapy* and its sibling journals will continue to progress to support this evolution and achieve this goal.

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