Published in final edited form as:

Regen Med. 2013 March ; 8(2): 223–225. doi:10.2217/rme.13.1.

Call for fellowship programs in stem cell-based regenerative and cellular medicine: new stem cell training is essential for physicians

Paul S Knoepfler

Department of Cell Biology & Human Anatomy, School of Medicine, University of California, Tupper Hall 4303, Davis, CA 95616, USA and Institute for Regenerative Cures, University of California Davis School of Medicine, Sacramento, CA 95817, USA and Institute for Pediatric Regenerative Medicine, Shriners Hospital For Children Northern California, Sacramento, CA 95817, USA knoepfler@ucdavis.edu

Abstract

Stem cell-based regenerative and cellular medicine is an exciting, emerging area of medical practice. While bone marrow transplantation, a stem cell-based therapy, has been a part of medicine for decades, in recent years newer and more diverse forms of stem cell-based therapies are being used to treat a rapidly growing population of patients in the USA as well as worldwide. Nonetheless, to this author's knowledge, there is currently not a single academic medical fellowship training program in the USA that specifically prepares physicians for treating patients with stem cell-based therapies other than bone marrow or hematopoietic stem cell transplantation. An increasing number of physicians untrained in stem cell-based regenerative and cellular medicine are nonetheless transplanting stem cells into hundreds if not thousands of patients for a striking diversity of conditions. Furthermore, as stem cell technology advances, a growing number of physicians with academic affiliations may look to legitimately practice regenerative and cellular medicine. What little training that physicians can currently obtain must be found on an *ad hoc* basis. This article should act as a call for the development of formal academic medical fellowship programs to train physicians in the practice of cellular and regenerative medicine. The USA is used here as an example of a medical sphere in which it can be argued that such training would be helpful, however such programs would be quite helpful globally.

Keywords

cellular therapy; fellowship training; physician training; regenerative medicine; stem cells; US FDA

© 2013 Future Medicine Ltd

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

The problem: a critical physician training gap in a rapidly emerging field of medicine

The US FDA is increasingly taking regulatory action such as issuing warning letters to physicians and clinics in the new area of stem cell-based cellular and regenerative medicine, highlighting the problems associated with the lack of academic training and the increasing level of patient risk as perceived by the FDA. What are the risks that are associated with transplants of *in vitro* propagated stem cells into human patients? Stem cells propagated *in vitro* are known to change in ways that increase risk: to acquire mutations, often in oncogene-associated pathways; to spontaneously immortalize and escape senescence at a low, but potentially clinically significant rate; to be contaminated with xenoantigens that could potentially spark immune reactions, and to potentially be cross-contaminated with other cell types. For these and other reasons the FDA has defined *in vitro* propagated stem cells as drugs.

At this time, physicians conducting stem cell transplants (excluding bone marrow and hematopoietic stem cell transplantation) for patients are predominantly general and plastic surgeons as well as dermatologists, but other types of physicians are also getting involved, including internists. Primarily, these physicians are transplanting adult stem cells consisting of mesenchymal stem cells (MSCs) derived from adipose tissue or bone marrow. In certain scenarios, MSCs are infused intravenously, while other patients receive local injections in locations such as joints. The dominant institutional mechanism by which these physicians are transplanting stem cells is through relatively small, point-of-care for-profit clinics that lack academic affiliations. Hundreds of patients have already received stem cell transplants in the USA through such clinics, a fact that perhaps most physicians are unaware of today. However, it is important to stress that interest in cellular medicine amongst physicians is increasing in the academic sphere, including large teaching hospitals.

The legal definition of *in vitro* propagated stem cells as drugs by the FDA has been legally supported by a recent ruling in favor of the FDA in a federal court case between it and another stem cell clinic-related entity, Regenerative Sciences Inc. [1]. Regenerative Sciences Inc. had reportedly transplanted a propagated stem cell product into patients without filing an Investigational New Drug application with the FDA and without FDA approval, leading to an FDA injunction that spurred the court case [2]. While the actions of the FDA are entirely appropriate in my opinion, I would argue that a more effective approach to promoting compliance and uniformity in this new field is the implementation of physician training in an academic setting. Since state medical boards generally do not have policies or regulations on stem cell therapies, with a notable exception being the Texas State Medical Board [3,4], there is even greater ambiguity in the area of what should be defined as appropriate physician conduct related to stem cell transplantation.

The solution: a fellowship program in regenerative & cellular medicine

To address the education and training gaps in this new area of medicine, I propose the development of academic medical fellowship programs in stem cell-based regenerative and cellular medicine. The 1-year fellowship programs could, in terms of a training timeline for physicians, follow any number of residency training programs including surgery, internal medicine or hematology/oncology. The training program would be comprised of a curriculum (Box 1) including training in the following: regulatory issues such as FDA regulations; institutional review board issues; ethics; intensive cell biology coursework; preclinical studies, GMPs, MSC isolation and transplantation and emerging technologies such as induced pluripotent stem cells. A recent article by the California Institute for Regenerative Medicine [5] aims to educate physicians in how to work in collaboration with

the FDA, but intensive physician training is still needed. Physicians completing academic fellowships of this kind could be certified as Regenerative and Cellular Medicine Specialists. Some physicians are already using that term to describe themselves even in the absence of formal training.

How would such fellowship programs be established? Currently, the only academic fellowship program that includes training in cellular therapy is hematology/oncology (Hem/Onc). Specialists completing Hem/Onc training after an internal medicine residency are qualified to administer hematopoietic stem cell therapies to patients. Therefore, it seems logical that regenerative and cellular medicine fellowships could be best established in departments of internal medicine with guidance from the leaders of Hem/Onc programs. A growing number of institutions also have stem cell institutes, some even with GMP facilities, and the leadership of such centers as well as academic Stem Cell Research Oversight committees could also provide valuable training and input. The rapidly changing nature of stem cell biomedical research and large number of ongoing clinical trials necessitates that the proposed training program would evolve over time. Further, some aspects of training would be taught to fellows not as ‘established knowledge’, but rather as an evolving knowledge base, a context required for training in any kind of innovative medicine such as stem cells.

Conclusion

Stem cell-based regenerative and cellular medicine is rapidly expanding in terms of the number of physicians practicing under the title of ‘stem cell therapy’ or ‘regenerative medicine’, in the rapidly growing number of patients being treated, and in the number and variety of conditions being treated. The current lack of training for physicians in this area combined with the sharply increasing practice of regenerative and cellular medicine is a recipe for serious trouble manifesting in a number of ways, including potential harm to patients and largely avoidable, punitive conflicts between the FDA and physicians. The proposed solution is academically based fellowship training in cellular and regenerative medicine. While such fellowship training is not a panacea, it would improve the practice of regenerative and cellular medicine and hopefully obviate the need for regulatory action in some cases.

References

1. Cyranoski D. FDA’s claims over stem cells upheld. *Nature*. 2012; 488(7409):14. [PubMed: 22859178]
2. Cyranoski D. FDA challenges stem-cell clinic. *Nature*. 2010; 466(7309):909. [PubMed: 20725009]
3. DeFrancesco L. Texas legitimizes path around FDA oversight. *Nat. Biotechnol.* 2012; 30(5):379. [PubMed: 22565948]
4. Kaiser J. Stem cells. Texas Medical Board approves rules for controversial treatment. *Science*. 2012; 336(6079):284. [PubMed: 22517830]
5. Feigal EG, Tsokas K, Zhang J, Cromer MV, Whittlesey KJ, Werner MJ. Communications with the Food and Drug Administration on the development pathway for a cell-based therapy: why, what, when, and how? *Stem Cells Transl. Med.* 2012; 1(11):825–832. [PubMed: 23197694]

Box 1. Regenerative and cellular medicine fellowship training program curriculum

- Regulatory issues such as US FDA rules
- Institutional review board issues
- Ethics
- Intensive cell biology course
- Preclinical studies
- GMP standards
- Mesenchymal stem cell isolation and transplantation
- Emerging technologies:
  - Pluripotent stem cells
  - Transdifferentiation