EDITORIAL

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Stem cell research: Regulating translational application

As the pace of translational stem cell research accelerates, researchers and governing bodies must work together to develop and implement rigorous ethical standards to guide the transition into the clinical sphere.

The field of stem cell research has entered an invigorating translational phase aiming to yield discoveries that will pave the way for regenerative medicine to cure diseases for which traditional methods have failed. Government agencies and charities are increasingly directing funding towards translational research in both the US and Europe. In the UK, the Medical Research Council has set up a translational stem cell research committee to fund research proposals with clear translational goals. In the US, the portfolio of the Californian Institute of Regenerative Medicine includes more than forty translational projects (see Comment by A. Trounson and N. D. DeWitt; *Nat. Cell Biol.* **14,** 331; 2012). The focus on applied stem cell research and the transition into stem-cell-based therapy in the clinic must be accompanied by the development of regulatory oversight of basic research with translational potential.

The capacity to reprogram human adult somatic cells into a pluripotent state or a different cell type has opened the door to the development and study of patient-specific cells. These cells not only provide a tool for researchers to understand more about the mechanistic basis of disease, but also offer the possibility of drug testing in a dish. Fundamentally, it is the responsibility of researchers to ensure that appropriate consent has been obtained from patients for the initial study and follow-up research, especially in cases involving genomic analysis that could potentially disclose sensitive information.

Although clinical trials using reprogrammed patient-specific cells are a long way off, other areas of stem cell research are closer to clinical application. The International Society for Stem Cell Research (ISSCR) has taken a strong lead in promoting stringent guidelines for translational stem cell research. In 2008, they produced a booklet for researchers and clinicians who are moving their research to the clinical phase, in which they called for rigorous standards and evaluation, a thorough informed consent process for patients involved in clinical trials, and transparency.

Few stem-cell-based treatments, such as bone marrow transplantations to treat blood-related disorders, have proven beneficial for patients in rigorous clinical trials and are now offered as treatments. Most other such therapies are in an experimental phase, and only a handful of clinical trial results have been published so far. In 2010, de Luca, Pellegrini and co-workers presented the results of their 10 year study using the human cornea, demonstrating the transplantation of limbal adult stem cells to restore retinal epithelium destroyed by burn (*New Engl. J. Med.* **363,** 147–55; 2010). Earlier this year, Lanza and colleagues reported no adverse effects when they transplanted retinal pigment epithelium cells derived from human embryonic stem cells into patients suffering from advanced stages of macular degeneration (*Lancet* **379,** 713–720; 2012).

Unfortunately, beyond such strictly regulated clinical trials (see www.clinicaltrials.gov), many treatments proposing to use stem cells (in particular, adult mesenchymal stem cells) to cure a range of ailments are being offered to patients around the world, with no clinical trial results to support their claims. The challenge for the field is to develop stringent rules in conjunction with government authorities, so that clinical trials are appropriately identified and regulated, and to remain vigilant about informing the public and the authorities in cases of non-compliance. The ISSCR has taken significant steps in this direction by developing a comprehensive resource for patients considering stem-cell-based therapies (www.closerlookatstemcells.org) and by encouraging their members to promote the dissemination of this information.

Governments have also taken note of this need. In January, China halted unapproved stem cell treatments and placed applications for new trials on hold until July 2012. In a press release from the ISSCR, Chinese stem cell researchers welcomed this measure and noted that it demonstrates that governing bodies are taking steps to put in place much-needed regulation at the same time as increasing their investment in stem cell research. Last year, the X-Cell Center in Germany closed after four years of proposing expensive treatments involving the injection of stem cells (derived from bone marrow) into various affected body parts of patients, a method radically different from using bone marrow transplantation to treat blood disorders. The closure of this clinic was a result of a change in European laws requiring that hospital doctors apply for European-Union-wide licenses to use innovative therapies such as stem-cell-based treatments, and of the active lobbying of German stem cell researchers belonging to the North Rhine Westphalia Stem Cells Network. The latter wrote an open letter against the activities of this clinic and directed patients to the ISSCR handbook on stem cell therapies.

However, some physicians seem to believe that full approval of a possible treatment by national organisations such as the Food and Drug Administration could take too long, or would not be necessary if patients are made aware of the risks involved and if a review panel has estimated their safety. Last year, the governor of Texas underwent an experimental stem cell treatment. In parallel, a change was proposed in Texas regulation that could allow experimental stem cell therapies to be made commercially available to patients. This triggered the reaction of ISSCR members, who stated that such changes would breach their guidelines for clinical trials involving stem cells.

Unapproved stem-cell-based therapies represent a danger for the patients and will ultimately be detrimental for the development of regenerative medicine. By taking responsibility and implementing regulatory oversight, researchers can enhance the move towards safe and effective translational applications.