



OPINION

The stem cell regulatory environment in South Africa – cause for concern

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Every innovation in medicine is met with a mixture of excitement, expectation and a certain degree of apprehension. Nowhere is this more apparent than in the field of cell-based therapy, i.e. the application of cells to patients, locally or systemically, for therapeutic purposes. Excitement and expectation are generated by the many preclinical and early clinical studies that continue to reveal the enormous potential of regenerative medicine. The recent successful implantation of a large airway, engineered *ex vivo* from a donor trachea, into a patient as a replacement for a stenosed left main bronchus (post-tuberculosis), is a case in point.¹ Likewise, reports of dramatic functional improvement in children with cerebral palsy treated with autologous cord-blood stem cells at Duke University warrant our serious consideration.² And this is just the beginning. It is believed that cell-based therapy will have a significant positive impact on virtually every organ system in the body, and that the extent of this impact is limited only by the limits of our scientific creativity.

However, these innovations come with numerous complex and challenging moral and ethical issues, including for example those surrounding embryonic stem cells, stem cell banking and the ethics of cloning (therapeutic versus reproductive). And of course, patient safety needs to be ensured.

In order to ensure that cost-effective therapeutic benefit and patient safety are well balanced, many elements need to be in place. Among these is an appropriate regulatory environment in which all activities involving cell therapy are governed by an appropriate set of rules and guidelines. Several important reasons follow:

1. Work involving material that will be (re)introduced into patients must be conducted under strictly controlled and accredited conditions of sterility to ensure that the unintended transfer into patients of harmful material (infectious and otherwise) is avoided.
2. Preclinical studies and well-controlled clinical trials need to have been conducted before introduction of cells into patients to ensure that the purported therapeutic effect is real and that there are no serious side-effects.
3. The absence of regulations permits (and even encourages) the emergence of medically unsound and unethical practices that may be associated with the exploitation of emotionally vulnerable patients.
4. The absence of regulations dissuades the transfer of intellectual property and foreign investment into South Africa because of the fear of an unknown legislative environment that may impact negatively on activities that have taken considerable time and resources to establish, when the regulations do come into play.

With regard to human tissues in general, and stem cells in particular, South Africa is currently operating in a regulatory vacuum in which the rules and guidelines are fragmentary. For example, those that dictate how we should conduct research on stem cells are incomplete. Likewise, issues relating to whether or not stem cells should be stored, and whether or not businesses should operate on a 'for-profit' or 'not-for-profit' basis, have not been fully debated. Nor have the complex issues surrounding the creation and use of embryonic stem cells or cloning. The current situation is therefore critically fragile and specific legislation is sorely lacking.

The National Health Act (No. 61 of 2003) (NHA), which replaced an outdated set of acts previously in force, was published 6 years ago. Chapter 8 of the NHA, which deals with the 'Control of use of blood, blood products, tissue and gametes in humans', has to date not been promulgated (with the exception of Section 53, which deals with the establishment of a blood transfusion service, and which was enacted on 30 June 2008). This means that we have to fall back on the Human Tissue Act (No. 65 of 1983), which was published at a time at which many of the complex and controversial issues that require carefully balanced rules and guidelines were not yet part of the scientific landscape.

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No specific regulations dealing with activities involving human stem cells have yet been formalised by the Department of Health to support the relevant Act(s) addressing this subject. It must be noted, however, that over the last few years the Department has published several sets of draft regulations dealing with human tissues including stem cells, gametes, *in vitro* fertilisation, DNA, etc. However, none of these regulations are currently in force.

The absence of regulations exposes South Africans to several potential problems. First, the absence of clear guidelines that ensure patient safety impacts negatively on patient outcomes. In addition to the more obvious issue of infection (transfer of infectious agents in transplanted material), the long-term consequences that could result from transplantation of material, the biological activity of which has not been adequately studied, need to be borne in mind. A recent report on a boy with ataxia telangiectasia who developed a multifocal brain tumour following treatment with human fetal neural stem cells (administered via intracerebellar and intrathecal injection) is a case in point.³

Second, the absence of a regulatory framework creates opportunities for the proliferation of undesirable practices and creates opportunities for individuals to move freely into areas and practices that are medically untested or frankly unsound. In a recent survey of 8 South African patients who received 'stem cell' therapy for spinal cord injury (one of whom subsequently developed the locked-in syndrome), the following facts emerged: (i) 5 of the 8 patients went overseas and 1 received cells from Germany in South Africa, at an average cost of R122 500 per treatment (excluding travel and accommodation costs for those who went overseas); (ii) 4 patients received rabbit stem cells, 1 received autologous stem cells, 1 received cells of unknown origin and the 2 that remained in South Africa received sheep stem cells; and (iii) the stem cells were injected subcutaneously, intramuscularly, intravenously, via lumbar puncture or into the subdural space during spinal surgery (Skeen and Pepper – unpublished paper presented at the 7th South African Symposium on Haematopoietic Stem Cell Transplantation, Johannesburg, 30 - 31 January 2009). The lack of regulations means that there is no check in place to prevent activities of this sort.

Third, local organisations and businesses wishing to enter the cell therapy field do so without knowing whether their operations will be impacted on negatively by legislation once this is formalised. Furthermore, the absence of regulations results in a lack of investment into activities associated directly or indirectly with cell therapy. This is because an unstable regulatory environment may have negative consequences on investment into the field with the publication of regulations that may be restrictive. Foreign investors who may wish to consider investing into South African cell therapy businesses will be dissuaded from so doing because they have no way of

knowing whether, when the regulations do come into effect, they will impact negatively on the activities into which the investors have put their money.

The enormous potential benefits that cell-based therapy has to offer to human health – and South African patients are no exception – are undisputed. The facilitation of research in cell-based therapy and the implementation of such therapies are therefore highly desirable. In order for this to occur, an appropriate regulatory environment is required. Without this, South Africans not only run the risk of being denied the fruits of cutting-edge research, but will also be exposed to unethical practices and financial exploitation (especially those who are emotionally vulnerable). From an economic point of view, and specifically from a biotech point of view, the absence of a regulatory environment that should provide comfort for potential investors is likely to put South Africa light-years behind in the development and use of new cell therapy products. The lack of movement in the development of appropriate legislation and the precarious situation that our country finds itself in by perpetuating an unregulated environment, point to an urgent need for open consultation between all relevant stakeholders.

Any discussion on cell therapy needs to take the following into consideration. An important distinction needs to be made between activities that involve altruistic donation of human material and those that result in commercial gain. Any commercial activity directly involving human material (including stem cells) that is provided on an altruistic basis by a voluntary donor should be run on a not-for-profit basis with publicly accessible accountability of how resources are managed. Other activities that involve human stem cells directly or indirectly and that are not based on the principle of an altruistic donation should be permitted to run on a for-profit basis. It is important to note that in accordance with the National Health Act, stem cells may not be sold or traded privately. Furthermore, payment in respect of the acquisition, supply, importation or export of stem cells may only be received by an authorised institution.

The development of relevant regulations to support the Human Tissues Act lies within the jurisdiction of the national Department of Health. Given the huge burden that infectious diseases place on our national resources (financial and human), it is understandable that priorities within the National Department of Health may not lie with the topic of this article. Chapter 8 of the NHA and the regulations pertaining thereto have been written and published, but not yet enacted. Given the long time delays between publication of the initial versions (upon which formal comments/submissions have already been made) and the present time, during which (i) the diverse stakeholders have had a chance to grow in their understanding of the cell-therapy field, and (ii) significant advances and new challenges have arisen, fresh debate is needed before re-



activating the legislative machine. Only after this has taken place will it be appropriate to revisit and revise the current documents. Once this has been done, it is sincerely hoped that the passage into formal legislation will be expedited.

1. Macchiarini P, Jungebluth P, Go T, *et al*. Clinical transplantation of a tissue-engineered airway. *Lancet* 2008; 372: 2023-2030.
2. Duke University School of Medicine, Department of Pediatrics. http://pediatrics.duke.edu/modules/dept_peds_annc/index.php?id=79 (accessed 13 May 2009).
3. Amariglio N, Hirshberg A, Scheithauer BW, *et al*. Donor-derived brain tumor following neural stem cell transplantation in an ataxia telangiectasia patient. *PLoS Med* 6(2): e1000029. doi:10.1371/journal.pmed.1000029.