

## MEDICINE

# Monitoring and Regulating Offshore Stem Cell Clinics

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Traveling to another country in the hope of finding a stem cell–based treatment for a disease—“stem cell tourism”—has been the object of intense scrutiny in recent years, following reports of charlatany, baseless claims, and adverse medical events (1). Providers of stem cell–based interventions vary widely in their assertions about the conditions that can be treated, the degree of improvement, and the cell types and protocols used (2), but there are many advertisements for medical procedures that have never been proven efficacious in appropriately designed clinical trials. To date, proven therapeutic applications for stem cells have been mainly for blood and immunological disorders. The scientific community and advocacy groups have begun to respond by formulating guidelines for physicians and scientists engaged in the clinical translation of stem cell research (3) and lists of questions for prospective patients to ask when considering an experimental stem cell treatment (3, 4). Inaction and occasional complicity on the part of the government and medical establishment in some countries, however, have made enforcement, self-policing, and the maintenance of patient trust problematic.

Controversies involving unverified medical treatments are not a new thing, but the adoption of protective laws and their vigorous enforcement has enabled many countries, including the United States, to rein in claims

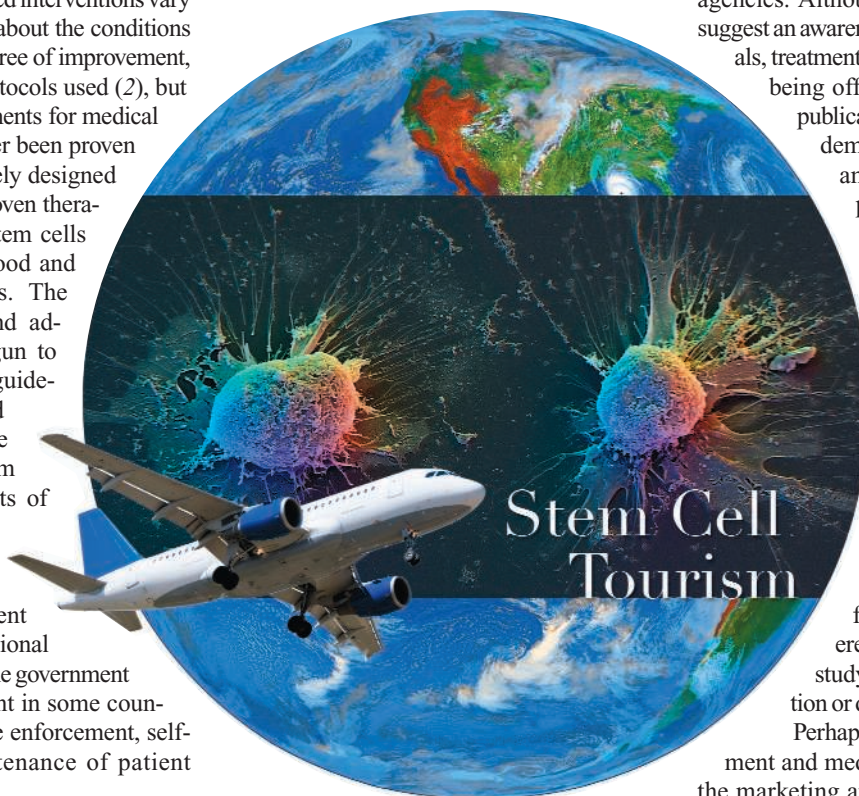
that can legally be made by providers or to relegate them to operating outside of their borders. The possibility of operating extraterritorially has meant that unapproved treatments could be had by those willing to travel abroad, but in the great majority of instances, this has

Unverified medical treatments based on stem cells are proliferating and need oversight.

Netherlands (9), and Ireland (10); others have been forced out of business (11) or prevented from opening by negative publicity (12, 13).

Successful clinics that remain in business are sometimes supported by local medical associations, governments, and regulatory agencies. Although the company Web sites suggest an awareness of the need for clinical trials, treatments costing \$20,000 or more are being offered in the absence of prior publication of peer-reviewed studies demonstrating efficacy. For example, TheraVita has an impressive list of Thai physicians, including the current presidents of the Thai Heart Association and the Thai Atherosclerosis Society (14), and recognition from the Davos-based World Economic Forum as a 2006 Technology Pioneer (15). However, the peer-reviewed article listed by the company as “accreditation” for its therapeutic regime of adult stem cell therapy for heart disease was considered by the authors to be a safety study and did not use randomization or double-blind controls (16, 17).

Perhaps as important as the government and medical establishment links are the marketing and patient recruitment strategies used by these companies. A number of companies, such as NuTech Mediworld, a human embryonic stem cell clinic, and Medra, Inc. ([www.medra.com/](http://www.medra.com/)), which uses human fetal cells, have enjoyed publicity in the form of published interviews, blogs, or YouTube videos describing subjective patient experiences following treatment (18, 19). TheraVita, and its associated companies VesCell ([www.vescell.com/](http://www.vescell.com/)) and Regenocyte ([www.regenocyte.com/](http://www.regenocyte.com/)), use online patient testimonials (14), blogging activity (20), and patient recruitment seminars held within the United States (21). Beike Biotechnology and other China-based treatment centers have a vocal proponent in the *China Stem Cells News*’ Web site ([www.stemcellschina.com/](http://www.stemcellschina.com/)), which serves as an online portal highlighting



meant to countries not known as leaders in biomedical research (e.g., despite more than 30 years of legal actions in the United States against purveyors of laetrile, a discredited cancer remedy, it remains readily available in places such as Mexico and the Bahamas).

The debate over human embryonic stem cell research in the United States under the George W. Bush administration not only opened the door to increased investment into stem cell research and its applications by Asian countries (5–7), but may have also distracted regulatory attention from the growing problem of unsubstantiated therapeutic claims involving adult stem cells. Nonetheless, several stem cell clinics have been closed by law enforcement or regulatory agencies in the United States (8), the

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news and treatment experiences from local and foreign patients. The site lists dozens of subjective accounts of “successful” (typically defined as “some improvement”) outcomes in people suffering conditions including autism, epilepsy, and stroke and includes a contact form for those with treatment inquiries.

Major research nations have also seen the appearance of stem cell clinics and therapeutics companies. Companies in Japan advertise stem cell-based treatments for conditions such as diabetes, Alzheimer’s disease, and spinal cord injury (22–25). The X-cell Center ([www.xcell-center.com/](http://www.xcell-center.com/)) in Cologne, Germany, offers to treat ailments ranging from erectile dysfunction to amyotrophic lateral sclerosis (ALS). Adult stem cells as a treatment modality have been championed with particular fervor by numerous groups in the United States, which commonly cite lists of many conditions that have been treated with adult cells (26, 27). Such catalogs may introduce doubts and misunderstandings about the current state of the science.

Companies such as Medra, Stemedica ([www.stemedica.com/](http://www.stemedica.com/)), Stem Cell Biotherapy ([www.stemcellbiotherapy.com/cn/index.php/lang/en](http://www.stemcellbiotherapy.com/cn/index.php/lang/en)), and Regenocyte have taken advantage of the resulting confusion and have occupied the current international regulatory vacuum. For example, Stem Cell Biotherapy and Regenocyte advertise procedures unavailable in the United States and arrange for patients to be sent to affiliated hospitals in other parts of the world. Of these, Medra became particularly notorious for the extraordinary claims made by its founder, psychiatrist William Rader, who has refused to share information on cell lines and techniques he claims can be used for treatment of conditions including spinal cord injury and Down syndrome (28).

There are several effective measures to prevent companies from going too far in their business practices. In the United States, the Food and Drug Administration provides clear rules governing the purity, potency, and quality of medical products (including stem cells) (29); the Federal Trade Commission oversees truth in advertising (30). Similar laws and authorities are in place in the European Union, and Thailand is now making moves to regulate stem cell therapies more tightly. A committee convened by the Thai Medical Council, which governs practice by licensed physicians, has drafted recommendations that call for stricter oversight of procedures involving stem cells in conditions other than blood disorders (31). These only came following a period of confusion as stem cells were seen as neither drug nor typical medical treatment, which put them for a time outside the

purview of both the medical and drug-regulatory authorities. Such researcher-led efforts are to be encouraged and promulgated to regulatory agencies in other Asian countries as effective means of protecting patients as well as the national reputation.

Media reports can also play an important role. An *L.A. Times* feature on Biomark International (32) raised public doubts about the company. A series of BBC documentaries revealed a trade in which human fetuses from the Ukraine were sold to stem cell tourism clinics in the Caribbean, which resulted in the closing of at least one major clinic, the Institute for Regenerative Medicine in Barbados, owing to loss of its clients (11). To ensure the truly global dissemination of guidelines and patient information regarding stem cell-based clinical applications, the international research community, represented by organizations such as the International Society for Stem Cell Research, could provide local language translations or summaries of relevant documents and could use their members to distribute them to the press and government authorities. The World Health Organization could also contribute by releasing a consensus position on the clinical application of stem cell research.

Patient advocacy groups have begun to compile useful resources of physicians and hospitals offering stem cell procedures for conditions such as ALS (33). Although these serve only as anecdotal evidence, they tend to offer more balanced accounts, citing both positive and negative experiences, and may help to flag especially flagrant violators of patient trust. Stem cell and regenerative medicine research organizations might likewise consider steps toward identifying and dealing with members who have commercialized unproven treatments prematurely. Educational alliances between basic research, clinical, and patients groups, such as the Coalition for the Advancement of Medical Research, might prove to be an effective measure against the more egregious claims.

To ensure that the potential of stem cell research has the chance to develop unhampered by tragedy or fraud, members of the research community must work together to lobby their own local authorities to put proper regulations in place and must accept as their duty following the hard road to the truth, not the most expedient or profitable one. Given the current limits of international law and scientific diplomacy, a global ban on unapproved treatments seems unlikely to succeed, so for now, each government must take great care when granting funds and recognition to programs that fall short of ethical or professional standards. And ultimately, those who look to stem cells with hope for cures must also share

in the obligation to protect this nascent field by becoming not only patient advocates, but also advocates of patience.

#### References and Notes

1. N. Amariglio *et al.*, *PLoS Med.* **6**, e29 (2009).
2. D. Lau *et al.*, *Cell Stem Cell* **3**, 591 (2008).
3. International Society for Stem Cell Research, *Guidelines for the Clinical Translation of Stem Cells* (ISSCR, Deerfield, IL, 4 December 2008); [www.isscr.org/clinical%5Ftrans/](http://www.isscr.org/clinical%5Ftrans/).
4. Juvenile Diabetes Research Foundation International, *Participating in a Clinical Trial*; [www.jdrf.org/index.cfm?fuseaction=home.viewPage&page\\_id=91EC2BF7-1321-C844-134D2E25FB931863](http://www.jdrf.org/index.cfm?fuseaction=home.viewPage&page_id=91EC2BF7-1321-C844-134D2E25FB931863).
5. B. Einhorn, J. Veale, M. Kripalani, *Business Week*, 10 January 2005, p. 34; [www.businessweek.com/magazine/content/05\\_02/b3915052.htm](http://www.businessweek.com/magazine/content/05_02/b3915052.htm).
6. J. Du *et al.*, *Stem Cell Mission to China, Singapore and South Korea* (for the U.K. Department of Trade and Industry, Pera Innovation, London, 2005); [www.oti.globalwatchonline.com/online\\_pdfs/36206MR.pdf](http://www.oti.globalwatchonline.com/online_pdfs/36206MR.pdf).
7. D. Sipp, *Stem Cell Report* **2**, 62 (2007).
8. M. Enserink, *Science* **313**, 160 (2006).
9. The Netherlands Health Care Inspectorate, Utrecht, 3 October 2006; [www.igz.nl/uk/files/379598](http://www.igz.nl/uk/files/379598).
10. S. Boseley, *Guardian*, 1 May 2006; [www.guardian.co.uk/society/2006/may/01/health.medicinelandhealth](http://www.guardian.co.uk/society/2006/may/01/health.medicinelandhealth).
11. S. Price, *Nation News* (Barbados), 26 November 2007; <http://web.archive.org/web/20080128173958/http://www.nationnews.com/story/315095110731643.php>.
12. “Stem cell firm drops Bermuda from website,” *Royal Gazette*, 18 August 2008; [www.theroyalgazette.com/siftology.royalgazette/Article/article.jsp?sectionId=60&articleId=7d8893730030003](http://www.theroyalgazette.com/siftology.royalgazette/Article/article.jsp?sectionId=60&articleId=7d8893730030003).
13. M. Ebbin, *Bermuda Sun*, 14 September 2007; [www.bermudasun.bm/main.asp?SectionID=24&SubSectionID=270&ArticleID=34993](http://www.bermudasun.bm/main.asp?SectionID=24&SubSectionID=270&ArticleID=34993).
14. TheraVita, [www.vescell.com/stem-cells-treating-physicians.php](http://www.vescell.com/stem-cells-treating-physicians.php).
15. World Economic Forum, [www.weforum.org/en/Communities/Technology%20Pioneers/SelectedTechPioneers/2006TechPioneers/index.htm](http://www.weforum.org/en/Communities/Technology%20Pioneers/SelectedTechPioneers/2006TechPioneers/index.htm).
16. Y. Porat *et al.*, *Br. J. Haematol.* **135**, 703 (2006).
17. K. V. Arom, P. Ruengsakulrach, V. Jotisakulratana, *Asian Cardiovasc. Thorac. Ann.* **16**, 143 (2008).
18. A. Boxel, <http://amandaboxel.wordpress.com/>.
19. R. Kilgore, <http://jp.youtube.com/watch?v=kbozmOL1kSY>.
20. J. Steele, *VesCell Adult Stem Cell Therapy Blog*, 19 December 2007; <http://stem-cell-therapy.blogspot.com/2007/12/new-adult-stem-cell-blog.html>.
21. Regenocyte, <http://stem-cell-therapy.blogspot.com>.
22. Elixcell, [www.elixcell.com/](http://www.elixcell.com/).
23. Rejuvacell, <http://rejuvacell-inc.com/Our%20Group.htm>.
24. Stem Cell Sciences, [www.stemcellsciences.com/](http://www.stemcellsciences.com/).
25. Nichi-In Center for Regenerative Medicine, [www.nichiin.org/](http://www.nichiin.org/).
26. D. Prentice, in *Monitoring Stem Cell Research: A Report of the President’s Council on Bioethics* (President’s Council on Bioethics, Washington, DC, 2004), Appendix K.
27. Repair Stem Cell Institute, [www.repairstemcells.org/DiseaseTreated.php](http://www.repairstemcells.org/DiseaseTreated.php).
28. D. Ono, KABC-TV news, Los Angeles, 2007; <http://abclocal.go.com/kabc/story?section=news/local&id=5283114>.
29. D. G. Halme, D. A. Kessler, *N. Engl. J. Med.* **355**, 1730 (2006).
30. U.S. Federal Trade Commission, *Frequently Asked Advertising Questions: A Guide for Small Businesses*; [www.ftc.gov/bcp/edu/pubs/business/advbus35.shtm](http://www.ftc.gov/bcp/edu/pubs/business/advbus35.shtm).
31. Editorial, *Bangkok Post*, 22 June 2008; [www.bangkokpost.com/220608\\_Perspective/22Jun2008\\_pers007.php](http://www.bangkokpost.com/220608_Perspective/22Jun2008_pers007.php).
32. A. Zaremba, *Los Angeles Times*, 20 February 2005; [www.latimes.com/features/health/medicine/lasci-stemcells20feb20,1,3062179.full.story](http://www.latimes.com/features/health/medicine/lasci-stemcells20feb20,1,3062179.full.story).
33. S. Byer, B. Byer, ALS Worldwide, Madison, WI; [www.alsworldwide.net](http://www.alsworldwide.net).

10.1126/science.1168451