The Rise of Stem Cell Therapies in Mexico:  
Inadequate Regulation or Unsuccessful Oversight?

Surgimiento de Terapias con Células Troncales en México:  
¿Regulación Inadecuada o Supervisión Inefectiva?

O surgimento de terapias com células estaminais no México:  
regulamentação desadequada ou insucesso na supervisão?

Abstract

Mexico has emerged as one of the favoured places for medical tourists to obtain unapproved stem cell therapies, which are commonly hazardous, yet easily available. This paper explores the regulatory landscape under which these therapies have arisen, which has led to a flourishing stem cell tourism phenomenon. It also illustrates that even though there are relevant regulatory provisions and a governmental agency to oversee biomedical research, so far the ineffective enforcement of these legal mechanisms has allowed the spread of untested stem cell therapies, which lack adequate evidence of quality, safety and efficacy. Two stem cell providers are examined as case studies in order to illustrate the main challenges represented by their operation. It is suggested that the ineffective enforcement of available legal provisions broadly applicable to stem cell therapies may jeopardise the establishment of public trust in this emerging field.

Key words: stem cell tourism, regulation, ethical oversight, cell-based therapies, Mexico.

Resumen

México se ha posicionado como un lugar clave para aquéllos que buscan obtener terapias con células troncales, las cuales representan graves riesgos para la salud. Este artículo explora el régimen regulatorio en el cual estas terapias han surgido, mismo que ha permitido la prosperidad del turismo médico con células troncales en el país. También, se demuestra que los instrumentos regulatorios existentes, así como las autoridades gubernamentales responsables de aplicar la legislación son inefectivos y han permitido la expansión de estas terapias, de las cuales no se ha probado calidad, seguridad y eficacia. Dos proveedores de terapias con células madre son objeto de estudio con el propósito de ilustrar los desafíos que representa el funcionamiento de los mismos. Finalmente, se argumenta que la inefectiva aplicación de las provisiones legales existentes, pone en riesgo la integridad de la investigación con células madre.

Palabras clave: turismo médico de células troncales, regulación, supervisión ética, terapias celulares, México.

Sumário

O México emergiu como um dos destinos privilegiados para turistas médicos procurando terapias com células tronco não aprovadas, que são geralmente perigosas, mas facilmente disponíveis. Este artigo explora o quadro legal em que estas terapias têm surgido, o qual levou a um florescimento do fenômeno do turismo de células estaminais no país. Ele também ilustra que, embora existam disposições regulamentares e uma agência governamental para supervisionar a investigação biomédica, até agora, a execução ineficaz destes mecanismos legais

* PhD candidate in Bioethics and Medical Jurisprudence PhD candidate in Bioethics and Medical Law in the Institute of Ethics, Science and Innovation (iSEI) and the Centre for Social Ethics and Policy (CSEP) in the School of Law of the University of Manchester. She is Lecturer in the School of Law of the Autonomous University of Nayarit, Mexico. This paper will be presented in the 19th World Congress on Medical Law in Brazil, 7-10 August 2012. The study was funded by the generous support of the ‘excellence grant’ from the Mexican Council for Science and Technology (CONACYT) and the Trust of the Autonomous University of Nayarit (UAN). The author would like to specially thank Dr. David Gurnham, Dr. Sarah Devaney, Dr. Barry Lyons, Dr. Sheelagh McGuiness and Dr. Marleen Eijkholt for their helpful comments on earlier drafts; all opinions and errors are the author’s sole responsibility. E-mail: maria.medina@uan.edu.mx, marichuymedina@gmail.com.
permitiu a disseminação de terapias com células estaminais não testadas, sem provas adequadas de qualidade, segurança e eficácia. São analisados dos casos de tratamento com células estaminais, para ilustrar os principais desafios representados pelas respectivas técnicas. Sugere-se que a ineficácia de disposições legais disponíveis amplamente aplicáveis às terapias com células estaminais pode comprometer o estabelecimento da confiança pública nesta área emergente.

Palavras-chave: turismo de células estaminais, regulação, supervisão ética, terapias baseadas em células, México.

Introduction

The continuous progress of the clinical side of stem cell (SC) science has become difficult both to ignore and to govern. Indeed, it has surpassed the capacity of governments across the globe to create effective legal control over novel SC therapies (Kiatponsan and Sipp, 2009). Equally, many of those therapies being offered are made available without scientific evidence to support their safety, efficacy and quality (Regenberg et al., 2009). As a result of the globalisation of healthcare, a relatively new industry has appeared in the international arena: medical tourism (Reisman, 2010; Hopkins et al., 2010). Medical tourism is a profitable facet of tourism in Mexico, with the result that the country has become a popular destination for medical amenities (OECD, 2010; Bookman and Bookman, 2007). Travel across jurisdictions by people seeking unregulated SC therapies is a subcategory of medical tourism, generally denoted ‘SC tourism’ (Zarzeczny and Caulfield, 2010).

Mexico is positioned along with China, Costa Rica, India and Thailand as a country with a flourishing SC tourism industry (Kiatponsan and Sipp, 2009a; Lau et al., 2008). The growth of the SC tourism industry has been fuelled by the ever-increasing demand from desperate patients, who will engage in any type of therapy available in the SC marketplace (Levine, 2010). This phenomenon is also encouraged by media hyperbole, which exaggerates claims about the actual or known therapeutic value of SCs (Zarzeczny et al., 2009); thus taking advantage of the naive optimism of patients suffering from debilitating and degenerative diseases (Qiu, 2009).

This paper aims to shed light on the regulatory landscape under which these therapies have arisen, which has led to a flourishing SC tourism phenomenon in the country. It is organised as follows: first, a general overview of the global rise of the SC tourism phenomenon is presented. This is followed by an outline of the current regulatory regime and the national authority responsible for overseeing biomedical research in Mexico. It demonstrates that the existing legal provisions are not rigorously applied by the relevant public agency. SC therapy providers are scrutinised as case studies in order to elucidate the legal and ethical challenges that governmental authorities face in effectively overseeing and monitoring the emergence of these therapies.¹ I argue that the absence of targeted regulation and ineffective law enforcement relating to SCs and clinical applications may jeopardise the establishment in Mexico of public trust in this emerging field. Adequate regulation and effective law enforcement will ensure the safety and well-being of those seeking SC treatments, while also facilitating innovative biomedical research and promoting responsible medical practices.

1. The boom in stem cell tourism: cause for concern

Across the world, patients are crossing national borders seeking unregulated SC treatments (Sipp, 2011); in a few cases, these are presented and marketed in conjunction with complementary and alternative medicine (Sipp, 2011a). The lax regulatory regime existing in many countries worldwide, as is the case in Mexico, may compromise not only patients’ safety but also progress and trust in scientific research. ¹ The empirical enquiry to collect the data used in this paper was undertaken during the period 2010-2012. A detailed internet data gathering was conducted, using the Google® search engine in order to identify SC therapies marketed on the web in the Mexican context. Data was also retrieved from www.clinicaltrials.gov. Official notes to corroborate the information gathered were also obtained through an online public request submitted to the Mexican government’s portal for transparency and access to information (IFAI): www.informex.org.mx.
SC science (Cohen, 2010). Therefore, adequate regulatory regimes are needed in order to guarantee sufficient protection of patients and research subjects enrolled in SC science activities and clinical applications (Cohen 2010a).

International scientific organisations have expressed concerns about the expansion of unproven SC treatments, which are largely marketed through the Internet (Taylor et al., 2010). For example, the International Society for Stem Cell Research (ISSCR) has published Guidelines for the Conduct of Human Embryonic Stem Cell Research (2006) and Guidelines for the Clinical Transplantation of Stem Cells (2008); it has also produced a Patients Handbook on Stem Cell Therapies (2008) (see Hyun et al., 2008; Daley et al., 2007). Furthermore, academics have urged caution and expressed concerns about the absence of an international moral consensus or agreed guidelines to regulate these practices (Gunter et al., 2010). In the years to come, SC tourism will continue to expand and will be poorly regulated on an international scale (DeRenzo, 2011). The regulatory issues become more complex when medical groups have vested interests in ensuring that for-profit SC medical applications proceed with minimal government surveillance (Lysaght and Campbell, 2011).

Since very few SC clinical trials have taken place thus far, there is no conclusive scientific evidence of the effectiveness and safety of SC treatments (Steinhoff, 2011; Taupin, 2010). For instance, authorisation to conduct the first human embryonic stem cell (hESC) clinical trial in the United Kingdom (UK) occurred only recently (Gretchten, 2011). In the United States (US), clinical trials using induced pluripotent stem cell (iPSC) have also commenced (Trounson, 2009). The US-based Geron company conducted phase I clinical trial in which hESCs were used to treat spinal cord injuries, yet it has dropped out these trials (Baker, 2011). In Europe, similarly, the biotech company ReNeuron has obtained approval to conduct the first clinical trial of the use of genetically engineered neural SCs to treat neuron disease (Mack, 2011). SC clinical trials should be approached with caution, since research carried out using hESCs and iPSCs have indicated a high risk of forming malignant teratomas (tumours) (Sugarman and Sipp, 2011: 127).

While global SC tourism has flourished due to the media hype and enthusiasm for innovative SC science (Braude et al., 2005); this growth should spur governments to enhance policies, education and communication between physicians and patients (Master and Resnik, 2011). Countries which have taken a strong stand on the SC tourism phenomenon and unproven treatment enterprises include Costa Rica (Joseph, 2011), while Germany and China are in the process of reforming its legislation (Tuffs, 2010; Durfee and Huang, 2011). In Mexico, most SC therapies are commercialised in private facilities and applied outside controlled clinical trials or official monitoring (Ryan, 2010). There is no clear evidence of whether there is a comparison between a control group of patients or attempts to evaluate the possibility of a placebo effect; nor is there any proof that providers are complying with international scientific and ethical standards. The false claims associated with unregulated SC therapies generate serious ethical and legal concerns and can potentially harm patients financially and physically (Lodi et al., 2011). This situation also creates false expectations among desperate SC tourists (e.g. terminally and chronically ill patients), potentially worsening their suffering and putting their health at serious risk (Caplan and Levine, 2010).

Mexico is a convenient healthcare service destination for medical tourists from nearby countries (mostly Mexican-American (Hispanic) and US citizens) (Connell, 2011). Arguably, the main reasons for these patients seeking treatment abroad are

---

2 The ISSCR issued recommendations online, such as the ‘Top 10 stem cell treatment facts’ as part of the advice provided to people thinking of travelling for SC-based therapies; see www.closerlookatstemcell.org accessed 6 July 2012.

3 iPSCs appear to have the renewing potentiality of hESCs, yet this is still to be scientifically corroborated (see Takahashi et al., 2007; Yu et al., 2007).

4 For example, it is not clear whether private SC clinics follow international legal instruments that are established to ensure best practices in clinical research (e.g. the Helsinki Declaration — last reviewed in 2008), the International Ethical Guidelines for Biomedical Research Involving Human Subjects (1993, revised 2002) adopted by the World Health Organization or the International Conference on Harmonization for Good Clinical Practices (1990).
geographic proximity, affordable costs, rapid access and the availability of SC therapies that are not approved in their home countries. Although many issues of regulatory harmonisation, safety and security have yet to be resolved since the adoption by Canada, Mexico and the US of the North American Free Trade Agreement (NAFTA, 1994), trade in healthcare goods and services has increased remarkably, mainly across the northern border regions of Mexico (Judkins, 2007; Horton and Cole, 2011). In this context of free trade in medical goods and services, many private facilities have emerged as a common US source of medical services, including experimental SC therapies (see Dalstrom, 2011). Certainly, SC tourists may expose themselves to severe health risks when undertaking unregulated but easily available SC therapies (Cohen, 2012). In addition, due to the lack of harmonised practices, prospective medical tourists may need to sacrifice legal remedies which are otherwise available in their home countries (Cortez, 2010).

2. The need for a change in Mexico’s existing biomedical regulatory landscape

The lack of specific legislation overseeing SC science in Mexico can be explained in terms of the extensive dispute about the moral status of the embryo which has hampered the adoption of adequate governance in this field (Medina-Arellano, 2012). There is a need for an in-depth revision of the existing regulatory regime to identify improvements in its scope and create targeted regulation of SC science. This should be accompanied by tougher measures of compliance to be implemented by the relevant regulatory agency, since the enforcement of existing rules has been negligible to date.

2.1. Overview of biomedical legislation

In Mexico, the legal framework that delineates public policies and norms regulating the constitutionally sanctioned right to healthcare protection is the General Health Act (GHA, 1982). The GHA stipulates that the Ministry of Health shall create the necessary public policies on health, granting statutory power to create and issue administrative official norms (NOMs)\(^5\). The GHA sets forth the following associated secondary regulations: the Biomedical Research Regulation (1987), which stipulates the conditions required to perform clinical trials on human subjects, including research involving the use of human organs, tissues and derivatives; and the Sanitary Disposal of Human Organs, Tissues and Cadavers Regulation (1985), hereinafter referred to as the Tissue Regulation, which provides general rules concerning the removal, utilisation and transplantation of organs and tissues, including their components and derivatives from living and deceased individuals. However, it is not clear whether its scope extends to the regulation of adult SCs derived from tissues for therapeutic and research purposes. The Tissue Regulation explicitly incorporates neither substantial nor procedural rules for the use of tissues or cells, nor any criteria to establish what activities utilising this human raw material are permitted.

The overall legal provisions that apply to cells within the existing federal health regulations are wide in scope, but certain descriptions may be applicable to SCs, since these are classified according to their plasticity (Panno, 2005). For instance, Article 314, Section I of Chapter XIV “Donation, transplantation and end of life” of the GHA specifies that “germinal cells are those male and female gametes able to give rise to an embryo.” However, the definition of germinal cells or gametes is very specific and refers to the category of cells that may give rise to an entire living human, whereas a broader understanding of SCs indicates that “stem cells are those that have the capacity to self-renew (make more stem cells by cell division) as well as to differentiate into mature, specialized cells” (ISSCR, 2008). As regards a definition of tissues, section XIII provides that a tissue is a “morphological entity composed of a group of cells of

\(^5\) NOMs are administrative rules that are issued to provide parameters or apply particular norms to further regulate general provisions (see Signet, 1997).
identical nature, which are regularly ordered and perform the same role” (GHA).

The above provisions do not offer a generic definition of cells, or more precisely of SCs. However, the references found within the GHA in relation to human tissues and cells are fairly general. By applying a purposive approach to interpretation of the law, it is plausible to infer that the definition of tissues found in the legislation ought to be interpreted as including cells, in fulfilling the purposes of the GHA and the associated secondary Tissue Regulation, Article 1 of which establishes that its object is to regulate the use of human organs, tissues and their components (cells), derivatives and products. This interpretation is corroborated by the content of the provisions of the GHA, Article 341, which states that blood, the bloodstream and its derivatives, making explicit reference to haematopoietic stem cells (HSCs), shall be considered tissues (GHA). As mentioned earlier and as is shown in what follows, the GHA and related secondary regulations are broadly framed, with the result that the authorities find themselves helpless in overseeing this area, given the complete lack of precision regarding what is allowed and prohibited in research and therapeutic settings involving the utilisation of human biological material such as tissues, cells and their derivatives.

Importantly, Article 327 of the GHA proscribes the commercial use of human organs, tissues and cells (GHA). Furthermore, Article 21 the Tissue Regulation establishes that the disposition of organs and tissues for therapeutic purposes shall be gratuitous; thus, Article 22 of the Tissue Regulation also stipulates that the commercialisation of organs and tissues is forbidden. Given that law proscribes the commercial transplantation or application of tissues and cells, public health centres authorised to store and transplant these raw biological material should operate under the principles of altruism, confidentiality, non-profit and solidarity, in accordance with Article 327 of the GHA (Canovas Pérez-Abreu and Dib-Kuri, 2007). Further, Article 323 stipulates that express written consent must be obtained from donors of human organs, tissues and cells (GHA). The associated Biomedical Research Regulation, in Articles 20 to 27, delineates broad parameters for obtaining consent from human research subjects, organ and tissue providers (also see Verastegui, 2006; López de la Peña, 1995).

2.2. Oversight Committees

The Ministry of Health, through an independent governmental authority called the Federal Commission for the Protection against Sanitary Risk (COFEPRIS) oversees clinical research in Mexico. Article 340 of the GHA establishes that COFEPRIS has the exclusive statutory competence to oversee the inspection, approval and authorisation of activities concerning the use, storage and transplantation of umbilical cord blood (UCB) and derived HSCs (see Sánchez Ramírez, 2009). However, there is an absence of legal guidelines for COFEPRIS to implement and enforce when evaluating, authorising and monitoring research and therapeutic activities involving human tissues and cells (Serrano-Delgado, 2009). Article 338 of the GHA establishes that the National Transplant Centre (CENATRA) has the authority to establish a registry of all allogeneic use and transplantations of human organs and tissues, being exclusively responsible for monitoring and applying this nationally (Dib-Kuri, 2005). However, CENATRA has no role in supervising the use or transplantation, whether for research or therapeutic purposes, of blood or any SCs derived from blood or human biological material (GHA).

According to Article 17 of the GHA, COFEPRIS is also responsible for enforcing clinical research rules in research and treatment settings. Significantly, it has the authority to control and oversee clinical trials and therapeutic activities involving human subjects and to monitor the development of new drugs, medicines and therapies entering the Mexican marketplace and their advertising, thus supervising, scrutinising and auditing healthcare establishments and issuing sanctions. Section VIII

---

6 In biological terms, tissues are conformed by cells and most SCs are derived from tissues; for example, human fat or adipose tissue is a rich source of somatic (adult) SCs (Zuk, 2002).

7 HSCs are those which have the ability to replicate into different types of blood cells and are successfully used to treat blood disorders (Appasani and Appasani, 2011: vii).

8 COFEPRIS can be regarded as the Mexican equivalent of the US FDA (see Gómez Dantés, 2011: S229).
of the same article (related to the provision of Article 340 GHA) establishes that COFEPRIS exerts control and vigilance over the disposal and transplantation of organs, tissues and cells of human beings. Further, Article 315 of the GHA provides that all establishments which perform activities involving the procurement, analysis, preparation and disposal of organs, tissues and cells shall obtain a licence and authorisation from COFEPRIS.

In accordance with the internal normative guidelines of COFEPRIS, which further regulate its licensing activities, Article 14, Section VIII stipulates that the commission shall:

“Approve, extend or cancel projects that involve the application of pharmaceutical drugs, supplies, medical devices, experimental activities or procedures in human beings aimed to pursue scientific knowledge, and with regard to which there is not enough scientific evidence to prove their preventive, therapeutic and regenerative efficiency” (COFEPRIS, 2004).

The assumption underlying the above provision is that current regulations stipulate no margin of discretion for physicians who are offering experimental therapies — in this case, using tissues and cells. Thus, given that COFEPRIS is responsible for the authorisation and licensing of the functioning of establishments which conduct medical procedures and clinical research involving human beings, all defined protocols must be submitted to, assessed by and approved by this agency before any medical or experimental activity is undertaken. Therefore, formal research protocols, clinical trials and experimental medical treatments being conducted in the country, must obtain an authorisation or licence, which should be registered with and monitored by COFEPRIS.

2.3. The Current State of Clinical Research

According to official notes obtained from COFEPRIS, to date it has authorised 369 healthcare establishments for the disposition of organs, tissues and cells, of which 206 are private and 103 are in the public healthcare sector (COFEPRIS, 2012). These healthcare centres not only collect and store tissues and cells, but also perform clinical trials and administer experimental medicine to human beings to treat diverse blood diseases such as acute limb ischemia, acute lymphoid and myeloid leukaemia, among other immune-system diseases (COFEPRIS, 2012).

It is relevant that in the official notes obtained from COFEPRIS, this regulatory authority highlighted the fact that it has authorised the research use in clinical trials of the following specific cells: germinal cells for assisted reproductive purposes, hematopoietic endothelial SCs, endothelial SCs, autologous mesenchymal SCs, neural SCs, autologous myoblast SCs, mesenchymal SCs derived from placentae and HSCs derived from BMW, UCB and the bloodstream (COFEPRIS, 2012). It thus specified that all licensed activities involving the employment of the above-listed cells are exclusively authorised for research purposes, since the use of these cells in advanced medical therapies, generalised treatments or standard medical treatments are not authorised by COFEPRIS at all.

As noted earlier, COFEPRIS has the duty to evaluate, approve and monitor biomedical research and experimental medical applications (Feinholz, 2009). This is troublesome, as it opens the door to potential conflicts of interest. It has been pointed out that COFEPRIS “requests ‘blind’ evaluations and leaves actual decision making to institutional research ethics committees (RECs) in the host organisations. The responsibility for ethically evaluating research protocols often falls upon ‘key’ persons: the dean of teaching programmes or the service head of the host organisation” (Santiago-Rodríguez, 2010: 590). Therefore, it is questionable whether RECs are independent evaluation bodies (Hernández, 2006). There is a risk of bias, since physicians are acting as judges and jury in the same (clinical) trial (Valdez-Martínez, 2005).

It is also documented that COFEPRIS is “poorly financed and empowered” (Santiago-Rodríguez, 2010: 591). For example, in relation to the oversight of clinical trials, empirical studies have revealed that “...COFEPRIS does not follow up on the success or failure of clinical trials’; the expectation is that firms would make any research results publicly available. The US FDA has pointed out to the COFEPRIS that the lack of monitoring is unacceptable; a minimal level of surveillance is
needed even if only on a random basis" (Santiago-Rodríguez, 2010: 590-1). Limited financial budgets, infrastructure and human resources inhibit its optimal regulatory performance in enforcing the available biomedical legal provisions and monitoring experimental medical activities (Santiago-Rodríguez, 2010). Certainly, COFEPRIS needs to be financially sound and staffed by highly qualified personnel in order to oversee effectively the experimental SC-based therapies which are now extensively commercialised across the country (Ryan, 2010).

According to Articles 41bis and 98 of the GHA, public and private healthcare centres in Mexico must establish RECs and bioethics committees in order to obtain official certification and to operate legally in the country, as well as to approve any research protocols for the conduct of investigations involving human beings.9 Thus, it is established as official public policy that conventional medical activities in Mexico must be based on evidence (Frenk, 2010). It is not clear whether there are set parameters that determine the guiding ethical principles to be followed by medical practitioners. The National Commission of Bioethics (Luengas et al., 2007) has issued recommendations (the implementation of which is voluntary, however) for the establishment of clinical RECs and bioethics committees, proposing as guiding ethical principles, at least in this context, those of beneficence, non-maleficence, autonomy and justice (Feinholz, 2009a). It is also worth noting that as of 2008, at least 83% of public healthcare centres in Mexico had failed to establish RECs.10 Furthermore, it has been shown that the existing RECs in public healthcare centres are more concerned with enacting bureaucratic procedures and improving training and research than with a commitment to the safety and adequate treatment of the subjects of clinical research (Santiago-Rodríguez, 2010).

While there are a few regulatory provisions and agencies overseeing biomedical activities, the level of surveillance of SC providers is still negligible. It is precisely the combination of two elements, the weak enforcement status of COFEPRIS and the absence of targeted regulation for the therapeutic use of tissues and cells, that may help us to understand the expansion of uncontrolled and unsafe SC therapies across the country. The existing inadequate regulatory regime and deficient surveillance potentially foster unethical behaviour prompted by economic and commercial interests. Under this lax ethical and legal regulatory system, there is an absence of compulsion for SC providers to disclose the actual risks represented by experimental SC therapies (Einsiedel and Adamson, 2012).

3. Case studies: translational stem cell science in Mexico

In this context, the field of SC science has not received particular attention and, in addition, the budget for biomedical activities has been reduced (Borbolla-Escoboza, 2010). Notwithstanding limited funding and the absence of governance in this area, various research projects involving SCs are currently being conducted in public national research centres (see Mayani, 2011). At the other end of the clinical spectrum, allogeneic and autologous transplantations of certain types of SCs which are harvested mainly from BMW, donated peripheral blood and UCB units are established practices to treat a variety of blood and immune system disorders in public healthcare institutions in Mexico (see Ruiz-Argüelles and Gómez-Almanguer 2008).

Most SC therapies available on the private market involve autologous adult SC transplantation and lack clinical evidence of their quality, efficacy and safety (MacReady, 2009). Patients are paying for expensive SC therapies in Mexico (Cyr anosky, 2012). Private hospitals providing SC therapies are not under stringent ethical and legal control. Examples from the case studies are SC injections extracted from patients’ own BMW and adipose tissues. As explained above, the regulatory system allows the storage of tissues and cells to be licensed by COFEPRIS, but the commercial use of...
human organs, tissues and cells is banned by the GHA and secondary regulation; thus, according to the official data obtained from COFEPRIS, there has to date been no authorisation of commercialised SC-based therapies as standard medical treatments or practices (COFEPRIS, 2012).

3.1. Stem cell therapy for Amyotrophic Lateral Sclerosis (ALS)

Arguably, Mexico is a pioneer in regenerative medicine (Editorial, 2008). However, it is uncertain whether this is subject to the requisite stringent oversight. Evidence to the contrary comes from the SC transplants performed at a private university medical facility, the San José Hospital (HSJ) of the Medical Technology School of Monterey (ITESM). This is one of the largest and most reputable private healthcare facilities in the country, globally renowned for its innovative high-tech medical care, clinical research and application of quality and safety standards (Vequist and Valdez, 2008). The HSJ is accredited by the relevant health authorities and has a licence from COFEPRIS to operate a healthcare establishment and a public biobank. However, it is not authorised to market SC therapies as generalised medical treatments (COFEPRIS, 2012).

Amyotrophic lateral sclerosis (ALS), which is also called Lou Gehrig’s disease, is a lethal neurodegenerative disorder which rapidly attacks the motor neuron cells of the brain and spinal cord and which later obstructs muscular functioning; an in-depth understanding of this illness has yet to be acquired (Sipp, 2011). Since 2006, the HSJ has conducted clinical trials to test SC-based therapies involving endoscopic injections of autologous somatic SCs, which are harvested from patient’s own circulating BMW blood and then injected into the frontal motor cortex (a region located in the front of brain) in order to treat ALS (Martínez et al., 2009). These interventions have been reported by the HSJ in peer-reviewed publications, which provide an account of its ALS treatment and outcomes. The HSJ has reported that its protocols and patient recruitment are reviewed and approved by its institutional REC, as described in its publication (Martínez et al., 2009). The informed consent of patients and families is also sought after the internal REC has granted permission to proceed.11 According to COFEPRIS’s official notes, this hospital has a registered REC and bioethics committee, in compliance with the requirement of Articles 41bis and 98 of the GHA (COFEPRIS, 2012). However, as noted in the overview of the current regulatory regime, there are as yet no clear and compulsory guidelines for the operation, functioning and integration of RECs in Mexico.

The data gathered for this study indicate that the HSJ makes no financial gain from these SC-based therapies, since the procedures are performed in a research setting. Although the hospital has complied with the existing legal requirements related to clinical trials, there are no clear rules to follow regarding the therapeutic use and transplantations of SCs. Notably, the scientific publication of the outcomes of this experimental SC therapy constitutes a positive feature in favour of the HSJ, since it shows its transparency in publishing its research results. In addition, the HSJ can be seen as seeking to maintain its medical prestige and trustworthiness by adopting a transparent operational approach through the disclosure of its results in a peer-reviewed scientific publication, notwithstanding the absence of comprehensive regulation of the therapeutic and research uses of tissues, cells and their derivatives (Sipp, 2011).

A growing body of non-governmental patient groups has scrutinised unregulated SC therapies marketed worldwide. For example, in the USA, the ALSUntangled group (ALSU) is a watchdog organisation which supports ALS patients in tracking and evaluating these SC-based therapies. The experiences reported to ALSU by patients who have undergone SC therapies at the HSJ, together with the findings of independent investigations conducted by ALSU, are published in the ALS Journal (Bedlack and Hardiman, 2009). The patients’ narratives indicate that they decided to undergo unregulated SC therapies because they had nothing to lose and all to gain (Gornall, 2010). The

11 According to article 19 of the 2008 amended Helsinki Declaration, there is a prospective obligation to register clinical trials on a public database before they are conducted. Further, article 30 provides the ethical duty to publish the outcomes of the research, whether positive or negative. At least this ethical obligation has been fulfilled by the HSJ’s team.
ALSU summary report about the HSJ procedures raised concerns regarding the lack of safety of the therapies and the failure to provide an objective appraisal of adverse outcomes (ALSUntangled, 2010). Furthermore, one in ten patients died within ten days of the transplant and a major exploration of the possible reasons was ignored (ALSUntangled, 2010). Nor was there any clear justification for transplanting or injecting SCs into the frontal cortex region of the brain, despite it being a procedure with the potential to affect cognitive function. Finally, the report states that the efficacy of the therapies was poorly communicated, that the standard cell dosage was not provided and that clinical tests were not randomised or blinded (ALSUntangled, 2010).

This case exemplifies the need to adopt adequate guidelines when conducting research and therapeutic applications of SC science by non-profit healthcare establishments. This should be accompanied by effective monitoring mechanisms to guarantee the proper implementation of established procedures and to overcome the current difficulties faced by COFEPRIS when overseeing emerging and innovative biomedical practices.

3.2. Stem cell-based heart repair therapy

The Mexican state of Baja California (BC) has traditionally occupied a niche as a destination for US citizens seeking easily accessible healthcare (Cortez, 2008). The geographical proximity of the border city of Tijuana to the US has led to this city having the largest number of private healthcare providers, with a substantial number of foreign patients being treated each year (Vargas Hernández, 2010). Among these private medical facilities is the Regenerative Medicine Institute of Hospital Angeles of Tijuana (referred to as the Angeles Regenerative Institute) (Grupo Angeles, 2010).12 According to the official notes obtained, Hospital Angeles of Tijuana runs an institutional REC and has a licence issued by COFEPRIS to bank germinal cells for reproductive purposes (COFEPRIS, 2012). COFEPRIS has only authorised the hospital to procure and use tissues and cells for therapeutic purposes. As earlier alluded to, COFEPRIS has authorised no public or private healthcare establishment to commercialise SC-based therapies as medicines, standard treatments or advanced therapies.

The Angeles Regenerative Institute offers an alternative to SC therapies not yet approved by the US FDA, as advertised on its website. It commercialises autologous adult SC-based therapies, consisting of the autologous transplantation of SCs harvested from patients’ adipose (fatty) tissue. These adipose SCs are obtained by liposuction, then re-injected, using a needle catheter, into the patient’s heart (Hotkar and Balinsky, 2011). According to the Angeles Regenerative Institute website, the aim of this SC therapy is to regenerate heart muscle tissue and to improve the working of the heart and the carrying of blood to it. In this case, the increased capacity of patients to walk longer distances allowed a heart functioning measure to assess the improvements following re-injection of patients’ SCs (Bioheart, 2010). To date, preclinical studies using adipose SCs have been conducted in animal models, while controlled testing of safety and efficacy in humans is still pending, since more pre-clinical studies are required in order to understand the mechanisms of differentiation of adipose SCs (Illouz and Aris, 2010).

According to the international clinicaltrials.gov database, the Angeles Regenerative Institute has been registered as conducting at least four clinical trials to test the safety and effects of autologous adipose-derived stromal cells delivered to patients with stroke, type II diabetes, diffuse lesions in the brain, renal failure and Parkinson’s disease. The status of these studies is given as “currently recruiting participants”. As previously indicated, according to the Mexican biomedical regulatory regime, non-profit experimental therapeutic activities are permissible provided that COFEPRIS grants authorisation. However, the Angeles Regenerative Institute not only conducts clinical trials, but

also commercialises these experimental autologous SC transplants as standard therapy. The hospital markets experimental SC-based therapies, meaning that research subjects undergoing experimental medical practices are being charged for their involvement, as if they were consuming proven medical treatments. This application of experimental SC therapies for financial gain carried out by this institute is in contravention of Article 327 of the GHA, which bans the commercialisation of tissues and cells, as well as of Articles 21 and 22 of the Tissue Regulation and the related provisions, which forbid the charging of patients who enter clinical trials or who receive therapy derived from tissues and cells.

In seeking to demonstrate a certain adherence to some guidelines, the Angeles Regenerative Institute website informs patients that it is certified by the International Cellular Medicine Society (ICMS, 2011). At the beginning of 2011, the ICMS accredited Angeles Regenerative Institute as the first private healthcare facility in Latin America where autologous adult SC transplants could be performed (ICMS, 2011a; 2011b). However, the reliability of the ICMS is highly contested, as its role as a private certifier of autologous SC-based treatments has raised concerns among the academic community and has been challenged by the FDA (Mitka, 2010). Hence, its legal status as an organisation legitimately entitled to certify SC medical practices is disputed. Some of the fundamental concerns about the ICMS are that it is not rigorous in certifying clinics, since sound scientific evidence or pre-clinical and clinical trial data are not required to obtain this certification for the later commercial application of SC-based therapies in humans (Editorial, 2010).

This case study demonstrates the lack of surveillance exercised by COFEPRIS. It is also asserted that the building of a substantial infrastructure of governance for SC science and its translation to the clinical setting are urgently needed, along with its effective oversight. Until now, physicians have taken advantage of the lack of SC-specific regulations; for example, failing to distinguish surgical interventions that may require rigorous clinical trials from those concerned solely with the practice of medicine or medical care. This is certainly problematic, since experimental SC therapies can be marketed and offered to the public without the close monitoring and security measures needed to prevent the generation of carcinogenic cells and infections, among many other precautions. Certainly, before SC therapies become easily available in the medical marketplace, it is essential that they undergo clinical trials. The clinical application of SC therapies is in its initial stages and conclusive evidence of quality, security and efficacy is not yet available, with the result that these interventions cannot be treated as simple medical activities with the frivolous SC treatment purveyor’s intention of gaining economic profit from desperate patients. This situation places patients in an extremely vulnerable position, which is aggravated when purveyors of SC therapies and clinics are certified by dubious private medical bodies.

As explored in previous sections, to date, the Ministry of Health has not issued targeted regulation or specific guidelines for the non-profit use of tissues and cells or derived biological raw material for research or therapeutic purposes. Ideally, the introduction of a NOM to standardise this area should specify the principal purposes to be licensed by the regulatory body, establish supervisory and compliance mechanisms, create criteria to identify deviations and overall guidelines to assure the quality and proper operation of clinical trials and any experimental therapeutic activity utilising tissues, cells and their derivatives, as well as assessing the introduction of SC therapies. The absence of more targeted regulations, official standards or guidelines makes it difficult for the supervisory authority to effectively implement the existing laws, which are broad and vague in relation to their ambit of regulation; therefore, legislation is inadequate and its enforcement dysfunctional.

---

13 The ICMS, a private, non-governmental organisation which has launched an SC accreditation programme that seeks to certify stem cell clinics and treatments mainly located and marketed outside the US. This organisation has been judicially challenged by the federal Food and Drug Administration (FDA) (see Cyranoski, 2010). In the US, under federal regulations, autologous adult SC therapies are considered to be highly manipulated biological medical products and are therefore categorised as medicines (Phinney, 2011), which require FDA approval before being marketed (Dolgin, 2010; Fink 2009). It is worth noting that the US Federal Bureau of Investigation had arrested four persons who offered unapproved SC treatments (see Furlow, 2012).
Conclusion

Experimental SC treatments are easily available and commercialised all over Mexico without appropriate legal monitoring. The GHA explicitly prohibits the commercial use of human tissues and cells and their derivatives; furthermore, any therapeutic procedures involving this human material must be gratuitous. The law also stipulates that healthcare providers must be licensed and authorised by COFEPRIS if they are to administer or conduct experimental medical procedures. However, no article in the legal system directly addresses the clinical application of SC-derived products, that is to say the use of either allogeneic or autologous SC transplantation in medical, experimental or therapeutic activities (e.g. the procurement, origin or derivation of SCs, patents, testing, scientific qualifications, follow-up and ethical monitoring of SC transplants and treatments).

The current norms, which are wide and vague in scope, are inadequate, since when they were enacted the legislators did not have in mind the current scientific developments, so legislation is outdated and enforcement is therefore dysfunctional (Feinholz, 2009). Hence, the problem in Mexico concerning the marketing of unsubstantiated SC treatments is not limited to the absence of targeted legal provisions, but extends to the enforcement of the existing rules, which has been negligible to date. There is a legal vacuum concerning the regulation of the allogeneic and autologous SC transplantation in medical, experimental or therapeutic activities (e.g. the procurement, origin or derivation of SCs, patents, testing, scientific qualifications, follow-up and ethical monitoring of SC transplants and treatments).

The current laissez-faire regime has allowed the spread of experimental SC therapies all over the country, putting at risk patients’ wellbeing and giving rise to significant ethical and legal challenges (Hyun, 2010). Although autologous adult SC transplantation presents less controversial ethical dilemmas and social concerns (since it does not involve embryo research), its unorthodox applicability imposes a burden on physicians, clinicians and practitioners to carefully measure the existing clinical risks involved, thus ensuring the safety and security of patients, while allowing progress and maintaining the best practices and reputation of this growing field (Herberts et al., 2011). The current inefficacy of available norms in dealing with the risks associated with the appearance of SC therapies in Mexico cannot prevail and their scope is bound to change. The effective governance of SC science applications is a “delicate balancing act between minimizing overregulation while still assuring adequate protection of research subjects” (Isasi and Knoppers, 2011).

The regulatory agency has failed to effectively monitor, supervise and sanction healthcare providers and purveyors of SC therapies that are clearly infringing the current legal provisions concerning the commercial use of tissues and cells. The ineffective enforcement of the law is partially explained by the current regulatory authorities being overstretched, underfunded and lacking compliance mechanisms (Santiago-Rodríguez, 2010), so that existing legal provisions are difficult to apply rigorously, a situation not helped by the lack of more targeted legislation to govern the SC science field as a whole. The unsuccessful supervision by COFEPRIS may be also attributed to a shortage of well-trained and experienced personnel to effectively monitor the emergence of experimental SC therapies and providers, as required. It is true that the enactment of targeted regulations alone cannot solve the problem, but if stringent rules for compliance are also promulgated, the law may cease to be a dead letter in this domain.

As provisional measures, the existing regulatory system should incorporate internationally accepted scientific guidelines and standards—for instance, those established by the ISSCR—and ensure that COFEPRIS enforces them effecti-
voly, in coordination with other relevant authorities (e.g. the Ministry of Tourism and medical tourism outsourcing agencies) until more sophisticated regulation is in place. Stronger regulatory agencies are crucial in order to implement international guidelines and standards in this area. This must be combined with the implementation of an adequate financial budget and trained personnel for the regulatory authority to efficiently monitor clinical trials and experimental medical practices, as well as to effectively enforce the legislative provisions adopted. Once COFEPRIS is better funded, a coordinated network, organised dialogue and interaction between relevant organisations and the head of this governmental authority would guarantee better surveillance of emerging SC therapies. Collaboration is crucial in order to disseminate accurate information among prospective SC tourists in relation to the current status of SC clinical applications in the country. This is necessary if the current government’s goal is the consolidation of Mexico as a reputable and secure place for medical tourism activities, ensuring the wellbeing and safety of those pursuing experimental SC therapies. There is no doubt that adequate mechanisms of compliance combined with more targeted regulatory provisions are necessary if Mexico is to invest seriously in trading its reputation as a medical destination for patients who are willing to undergo experimental therapies in the hope of alleviating their suffering.

Recibido: 16/7/2012
Aceptado: 7/11/2012

Bibliography


--- 2012. Official notes from COFEPRIS obtained through an online public request submitted to the Mexican government's portal for transparency and access to information: www.infomex.org.mx.


CONNELL J. 2011. Medical tourism. CABI, United Kingdom.


ISASI RM and KNOPPERS BM. 2011. From banking to international governance: fostering innovation in stem cell research. Stem Cells International.


TUFFS A. 2010. Stem cell treatment in Germany is under scrutiny after child's death. BMJ. No 341.


