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Narratives, uncertainty and subjectivity in the context of regenerative medicine

Narrativas, incertidumbre y subjetividad en los contextos de la medicina regenerativa

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Abstract

The emergence of bio-economies and debates about what biomaterials can be used in stem cell research are shaping subjectivities and identities in biomedicine today. Narratives of neoliberal nation-states often emphasise the idea that responsibility for health problems lies directly with the citizenry, while social safety nets are increasingly reduced. This creates a sense of security for citizens by endorsing certain therapeutic promises that semiotically disconnect the material conditions of uncertainty in which these cell therapy technologies are developed. In this respect, the study of the discursive practices associated with these technologies introduces a new performative understanding of the concept of health in regenerative medicine.

Resumen

La aparición de las bioeconomías y las deliberaciones sobre qué biomateriales son adecuados para la investigación con células troncales están moldeando las percepciones y las identidades en el campo de la biomedicina en la actualidad. Las narrativas de los estados-nación con enfoque neoliberal a menudo enfatizan la idea de que la responsabilidad de los problemas de salud recae directamente en la ciudadanía, al mismo tiempo que se reducen las redes de seguridad social. Esto crea una sensación de seguridad ciudadana al respaldar ciertas promesas terapéuticas que separan simbólicamente las condiciones materiales inciertas en las que se desarrollan estas tecnologías de terapia celular. En este contexto, el análisis de las prácticas discursivas asociadas a estas tecnologías aporta una nueva comprensión sobre cómo se construye la noción de salud en el ámbito de la medicina regenerativa.

Bioeconomy: regenerative medicine versus pharmaceutical subjugation

The 2019 Biomass R&D Board document introduces the concept of the bioeconomy as a revolution that enables sustainable scientific and technological development [1]. From an American perspective, talking about the bioeconomy means treating agricultural biotechnologies as drivers of sustainable development. This idea is reflected in the most widely accepted definition of the bioeconomy to date, proposed by the OECD in 2006, which describes it as "the set of economic activities of a society that harnesses the latent value in biological products and processes to generate new growth and benefits for its citizens and nations" [2]. However, biomedicine is also included in the first European documents as an essential component of the bio-economy [3]. In particular, they emphasise the importance of coordinating the governance of the bioeconomy between science, technology, policy, regulation, markets and civil society.

The long-term study on the bioeconomy, The Bioeconomy to 2030: Designing a Policy Agenda, notes that "at a time when governments are facing rising healthcare costs, it is difficult to justify the high cost of many biomedical technologies without tangible results and improvements in patient health". [4]. In this sense, although we can talk about bioeconomies in the agricultural bioeconomy and the bioeconomy of assisted reproduction once they are on the market, in the pharmaceutical industry only 16% of new products have their origin in biotechnology. since 1987, and pharmacogenetics has not yet managed to establish itself in clinical practice [1].

In this context, regenerative medicine is emerging as an innovative biomedical paradigm that represents a new approach to the study and treatment of disease, particularly degenerative disease. Furthermore, it appears to offer a type of revolutionary medicine that focuses on actual regeneration and healing, as opposed to the mere treatment of symptoms that characterises drug regimens. This new vision of regenerative medicine has the potential to drive innovation, create new industries and markets, and improve national economic competitiveness [5,6].

The high hopes and expectations of various stakeholders, such as patients, investors, policymakers, as well as biomedical communities and companies that see the clinical and commercial potential of regenerative medicine, have created strong pressure to accelerate their clinical and commercial development, despite the level of uncertainty in the field [7,8]. Not only do these therapies face challenges in entering the clinic, but they also face notably divergent views on which innovation pathways are desirable or not, which has led to conflict both within and outside the biomedical community, including the challenges presented by the COVID-19 pandemic worldwide.

Regenerative medicine faces several challenges, one of which is to establish itself as a real alternative to the innovation pathways that follow the research, development and commercialisation model of the pharmaceutical portfolio. In this sense, numerous stem cell therapy centres have emerged, offering experimental treatments, not only in terms of unproven therapies, but also in terms of socio-technical, legal and business models related to biomedical innovation. These pharmaceutical and biotechnology companies offer innovations of choice to informed customers seeking to meet their individual needs in a biotechnology market where the boundaries between public and private, nations and their laws, are increasingly blurred. This has given rise to forms of transnational biomedical tourism and the circulation of biomaterials that become commercial commodities available according to the purchasing power of potential customers [9].

Because of the proliferation of these experimental practices, legislators and professional societies have attempted to control the market for unregulated treatments, going so far as to include experimental stem cell-based therapies in the regulatory framework for pharmaceutical research and development. In other cases, patients have raised their voices in defence of regenerative medicine research against what they perceive as “pharmaceutical dominance” over their bodies and cells [10].

Emerging technologies such as regenerative medicine are leading to fundamental changes in healthcare systems and pose significant technological, regulatory and societal challenges. In order to analyse the tensions that arise between national organisations and regulations, as well as between user associations and their demands, we will focus on embryonic stem cell cell therapy and explore the levels of uncertainty in which these practices are being developed. In addition, we will examine the extent to which these practices can be considered as services and commercial spaces offered by biotechnology

companies in the field of regenerative health compared to traditional pharmacological contexts.

Invisibility of bodies

Sarah Franklin explores the relationship between in vitro fertilisation (IVF) technologies and stem cells through the concept of the "IVF interface - stem cells" [11]. Her research focuses on how stem cells have "dual reproductive value", either by regenerating tissues and cultures or by creating new organisms through assisted reproduction techniques. But this is just one example of the diversity of research addressing these issues.

Cyntia Cohen and Peter Cohen focus on analysing the "clinical research - innovative treatment - marketing" framework for these studies, in particular the phenomenon of stem cell tourism and legal loopholes at international level [12]. The bodies involved in cellular therapies with ES cells are mediated by cultural influences and inserted into networks where mechanisms of inclusion and exclusion can be identified [13]. It is important to highlight that some bodies are excluded from legal protection and relegated to spaces of exclusion and vulnerability.

ES cell harvesting technologies are used in the tissue economy [14] and the impact on women's bodies is often overlooked. As research into embryonic stem cell lines has increased, the shortage of oocytes has become an even more pressing issue, particularly in the context of IVF. This has led to the sale of eggs becoming a viable source of income for some women in precarious economic situations in Eastern Europe and other emerging economies. In these cases, women become sources of limited biomaterials that are not regenerated, and the harvesting of these biomaterials is associated with certain risks. In developing countries, these practices often involve openly transactional relationships in which women undergo risky procedures in exchange for modest fees. Women in South and East Asia and Eastern Europe may supplement their income by superovulating and selling eggs, or negotiate free IVF treatments in exchange for "donating" embryos for stem cell research [8,13].

Despite the existence of informed consent and women's agency in regulated contexts, the rhetoric around these practices often centres on concepts of altruism. Although women are the main tissue donors in the stem cell industry, the intellectual property rights derived from these samples do not belong to them, but to the laboratories. Furthermore, labelling an embryo as "surplus" is not easy for women undergoing IVF or clinical staff, but it has become an effective way of describing unimplanted embryos as a valuable surplus that should be donated to exploit their potential. socio-economic value. This terminology has a perlocutionary effect by ensuring that embryo donations come from women who feel a moral obligation to contribute to the regeneration of society. Thus, embryos, eggs, foetal material and umbilical cord blood have been configured through regulation and rhetoric as a form of wasted vitality if not destined for stem cell research. Each donor contributes to an imagined future community, supposedly healthier thanks to regenerative therapies, or to the future of her own children through a private autologous tissue bank.

Although the legal act of donation takes place after in vitro fertilisation (IVF), superovulation, termination of pregnancy or childbirth, the generation of these materials involves a complex interaction between the subjectivity of the woman, the trajectory of her reproductive biology, the social and biomedical technologies that regulate this trajectory, the regulatory framework that allows the request, information and mobilisation of maternal populations as donors, the technical repertoire of stem cell research that reorients the paths of maternal fertility development, embryogenesis, fetal development and the birth process. During this collaborative process, the donor is immersed in a variety of challenges such as compliance, self-care, medication management or risk. This bodily vulnerability and flexibility is technically and socially configured to meet the demands of stem cell research. Stem cells become real property and a product, and donation-based economies have never been sufficient to meet the clinical and research demand for tissues, which has always required less voluntary and more transactional forms of procurement.

The concept of "tissue" moves into a different epistemological space in which the potentiality of the germ cell is radically redefined. One of the key innovations of stem cell science is the reformulation of the previously orthodox notion of cellular potentiality. This applies to both somatic (non-reproductive) cells and germinal (reproductive) cells such as the egg or sperm. In both cases, the previous notion of potentiality limited the future possibilities of division and differentiation to the developing organism. Now a radically different, even incommensurable, range of possibilities is recognised in the same tissue. This not only reorganises the infrastructure of contemporary biomedicine around an economy of promise, potentiality and individualised expectation, but also

alters the temporality of the cell. According to this new understanding of bodily potentiality, the cell is no longer determined by its specific lineage or engaged in a pathway of differentiation and progressive loss of potential, but can instead enter a cycle of embryonic self-accumulation in which bodily potentiality can be regenerated indefinitely, regardless of the chronological trajectory of the organism.

Whereas reproductive medicine demands a literal work of reproduction of the female body, regenerative medicine focuses on the body's capacity for embryonic self-regeneration, prior to and independent of any developmental process. The very notion of the body's potentiality is being reconfigured in the biological sciences and their interactions with society.

The PRP Phenomenon: Drugs, Transplants and PRP

Once the stem cells have been obtained, they are grown in the laboratory and reprogrammed into different cell lineages of the organism. In the case of embryonic stem cells (ES cells), there are two major challenges in generating cell lines from them. On the one hand, it is necessary to achieve controlled differentiation of stem cells into specific cell lines. On the other hand, it is necessary to develop culture media that reproduce the conditions of the human body under GMP (Good Manufacturing Practices) standards, which are the standards for the proper manufacture and control of medicines.

To obtain stem cells with therapeutic potential in humans, it is essential to culture these cells in media that mimic the conditions of the human environment. These media must maintain the cells in their undifferentiated state and with pluripotent capacity. In addition, for their future use in therapies, culture media must be safe from possible contamination by infectious agents and provide a favourable environment for stem cell growth.

Initially, the first cell lines were generated using culture media containing components of animal origin, such as bovine serum, or on layers of non-human cells called "feeder cells", such as mouse fibroblasts, which served as a support for the growth of stem cells. However, these early media containing layers of animal origin carried the risk of transmitting retroviruses or other animal pathogens to the stem cells. To reduce this risk, the cells were subjected to multiple washes, which often damaged or destroyed the cells. Furthermore, in clinical practice, cells cultured in this way could trigger immunological reactions due to the presence of components of animal origin.

To overcome these challenges, human cells have been used to support the culture of embryonic stem cells. These human cells include placenta, endometrium, fibroblasts, fetal muscle, fetal skin and oviduct, which are used for both differentiation and culture maintenance. Other cells, such as bone marrow, skin and muscle, are used for culture maintenance only. Several research groups have attempted to define growth factors that maintain human cells and reduce exposure to animal products. Culture systems have been developed without the need for supporting cells, replacing them with synthetic matrices or components of the human extracellular matrix and supplementing them with growth factors.

The culture of embryonic stem cells presents a second critical challenge: achieving their controlled differentiation into specific cell lineages. This challenge lies in the limited understanding of the fundamental biology of stem cells and the need to elucidate the molecular mechanisms underlying differentiation processes. To achieve this goal, it is essential to gain a better understanding of the specific markers of stem cell pluripotency. These cells can be maintained in an undifferentiated state by adding differentiation regulatory proteins to the culture medium.

To date, a large number of cell lines have been established worldwide. A cell line is considered to be established when a progeny of viable cells has been obtained from stem cells and has maintained its phenotypic and genetic stability in culture. These cell lines must undergo rigorous quality control to ensure the absence of chromosomal problems, the ability to differentiate into the three basic cell lineages and the capacity for self-renewal. In addition, the traceability of these lines must be ensured.

Stem cell-based therapies are still at an early stage of development. A better understanding of cell biology and the overcoming of certain scientific and technical barriers are essential for the effective clinical application of research results. There are several levels of uncertainty associated with the translation of these technologies into clinical practice. These range from the need to achieve highly controlled differentiation of stem cells to the storage and transport of these cells in a way that preserves their viability. It also extends to the processing of the cells and their administration to the patient through carefully defined surgical protocols

that determine the most appropriate method of administration and the number of cells to be used. Currently, these uncertainties have been exacerbated by the emergence of COVID-19, as specified by Broxmeyer and Parker [15] in the context of haematopoietic cell therapies.

It is important to stress that the treatment of stem cells differs significantly depending on whether or not they are manipulated before being reintroduced into the patient. If the cells are manipulated in any way after they have been obtained and before they are reintroduced into the patient, they are considered to be medicinal products and as such must undergo all the requirements and controls necessary for their use in humans. In this case, the Spanish Agency for Medicines and Health Products (AEMPs) must authorise any clinical trial that may be carried out with this type of cell. On the other hand, if stem cells are not manipulated, they are not considered medicinal products and the authorisation of a potential clinical trial falls to the National Transplant Organisation.

The phenomenon known as PRP, or the use of platelet-rich plasma, is a clear example of the clinical need to offer regenerative products as alternatives to pharmacological ones. These alternatives appear to be safe and feasible and can complement other cellular therapies such as ES cells. The PRP technique is used in various medical disciplines, including sports medicine, orthopaedics, traumatology, dentistry and plastic surgery. It consists of centrifuging the patient's blood to obtain a platelet concentrate, which is then injected back into the body. This is done to stimulate the regeneration of damaged tissue.

As Cuende points out, it is essential to distinguish between the authorisation of a clinic to carry out processing methods for autologous biological products in regenerative medicine and the authorisation to use the product, either for research or as a product with proven efficacy and safety. in a broad sense [16]. In the case of PRPs, their regulation is the responsibility of the AEMPs, and the prescriber is responsible for monitoring regulation, traceability, pharmacovigilance and guaranteeing efficacy, even in the absence of high-quality clinical trials to support their use.

Conclusions

Regenerative medicine and the use of stem cells face a number of ethical, technical and regulatory challenges in their quest for clinical application. We begin this text with reference to the mechanisms of inclusion and exclusion that have been articulated in regenerative medicine [9]. We examine how the invisibility of women donors' bodies reinforces the possibility of conditions of vulnerability in the development of regenerative medicine. These mechanisms of exclusion can only take place under a neoliberal rhetorical framework that configures health as a private consumption option [17].

On the other hand, regenerative medicine is redefining the potential of cells by enabling unlimited regeneration. In the culture of embryonic stem cells, obstacles such as controlled differentiation and the search for suitable culture media need to be overcome. Although alternatives to media containing components of animal origin have been developed, such as synthetic matrices, challenges remain in terms of their composition and standardisation.

Controlled differentiation of stem cells can be achieved by eliminating maintenance factors or using specific growth factors. However, stem cell-based treatments are still in the early stages of development and face uncertainties that have been exacerbated by the COVID-19 pandemic.

The manipulation of stem cells prior to their introduction into patients has regulatory implications, and the approval of clinical trials depends on whether or not they are considered medicinal products. A prominent example is the use of platelet-rich plasma (PRP) in various medical disciplines, which requires specific regulation.

It is important to distinguish between the authorisation to process biological products and the authorisation to use them in patients, as is the case for regenerative therapies such as PRP and other similar therapies. In summary, regenerative medicine and stem cells face a number of multidisciplinary challenges on their way to clinical application, and innovative approaches are being explored to address these complexities.

Consent for publication

The author read and approved the final manuscript.

Competing interest

The author declare no conflict of interest. This document only reflects her point of view and not that of the institution to which she belongs.

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