Genetics and ethics: a possible and necessary dialogue

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Abstract Genetics and ethics have had numerous convergences and divergences over time. From Darwin through the Asilomar Conference and the Universal Declaration on the Human Genome and Human Rights, much has been achieved, but much still remains to be done. The use of biological materials that are already being stored and the adequacy of new technologies, such as clustered regularly interspaced short palindromic repeats (CRISPR), are some of the current challenges of this possible and necessary interaction. This paper will discuss some ethical aspects involved in current genetics.

Keywords Genetics · Ethics · Bioethics · CRISPR · Biobank · Indigenous populations

A story in progress

Charles Darwin's work *On the origin of species* (Darwin 1859) elicited a tremendous shock by presenting a new perspective on integrating life. This change in understanding from obscure and dogmatic ideas intensified the debate between new knowledge and ancient traditions (Lucas 1979). Scholars reflected on how to overcome this, as for example, Thomas Huxley with his conference on science, religion, and

education (Huxley 2009). Huxley made a comprehensive approach to these three aspects, without prejudices. Applying the biological knowledge generated by Darwin to explain social aspects, as in the case of Eugenia (Galton 1869), only increased the need for this reflection. During the same period, Gregor Mendel proposed his work (Mendel 1866), which made no further contributions to the discussion, perhaps because his focus was on plants.

In the 20th century, some social applications of the theory of evolution were negative (Stoddard 1920), whereas others were positive (Moreno 1934). The first one used genetics arguments to justify racism (Stoddard 1920), while the second integrated genetics with social perspectives (Moreno 1934).

The further development of genetics, which was already understood as a new area of scientific knowledge, extended many aspects of hereditary mechanisms, such as the understanding of DNA's structure. In the late 1960s, however, the possibility of changing this structure with the emergence of what was then called *genetic engineering* generated new questions.

When this DNA alteration was possible, researchers were surprised by the mechanism they now had at their disposal and the risks associated with this manipulation. Led mainly by Paul Berg and David Baltimore, a group of scientists from a committee of the US National Academy of Sciences proposed a voluntary moratorium on research in this new area (Berg et al. 1974). Some months later, the results of the International Conference on Recombinant DNA Molecules, held at Asilomar, California, were published (Berg et al. 1975). The Asilomar conference was attended by 140 scientists (mostly biologists, as well as medical doctors, and lawyers) and 16 journalists. This conference was a milestone in the history of science, because scientists self-reflected on their own practices. The Asilomar document is a precursor of the precautionary principle, which originated in the thoughts of Albert Schweitzer (Schweitzer 1999), and was first used in the

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1980s (Raffensperger and Tickner 1999). The precautionary principle states that any risk of serious or irreversible damage requires taking measures to prevent its occurrence.

The challenges of research on human subjects had been discussed in light of the abuses committed during World War II, especially with the development of the Nuremberg Code in 1947 (Trials of war criminal before the Nuremberg Military Tribunals 1949). This document contains a requirement that all participants authorize, through informed consent, their inclusion in research projects. Numerous other documents incorporated this requirement, such as the Declaration of Helsinki of the World Medical Association (WMA), in 1964.

In order to transform words into action, WMA proposed a second version of the Declaration of Helsinki, in 1975, which proposed, among other things, creating research ethics committees that would review all research projects involving human subjects (WMA 1964). The core of this proposal is not new; Thomas Percival, in 1803, had already proposed that all new innovative applications in health first be discussed with other, more experienced, professionals (Percival 1987). In 1976, the National Institutes of Health created, with the same purpose, the first committee on recombinant DNA, based on proposals made at the Asilomar conference (Hutt 1978).

Regulatory aspects

This reflection on the appropriateness of genetics research, by both scientists and society as a whole, generated the need for rules to guide scientific activity. In the USA, in 1978, the Belmont Report (Ethical Principles and Guidelines for the Protection of Human Subjects of Research), established by The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, laid the foundation for the current ethical and regulatory system for research (USA Government 1978). Many other countries all around the world made efforts in the same direction. In Brazil, the first standards for health research were established in 1988 (Brasil 1988). Later, in Europe, the Oviedo Convention on Human Rights and Biomedicine was approved (Council of Europe 1997). It is important to note that neither of these documents, the Belmont Report, Brazilian regulatory statement, or Oviedo Convention, mentioned genetics research.

In 1996, Brazil established the new Guidelines for Research Involving Human Subjects, the Resolution CNS 196/96 (Brasil 1996). This regulatory document established eight special research areas that required local and national approval for their execution. Research in human genetics was the first special thematic area included in the document. Another special area in genetics was, specifically, cooperative research between researchers from Brazil and indigenous populations (Brasil 1996). Later, more detailed and specific rules for these three special areas were also published (Brasil 1999; 2000;

2004). Other documents also had repercussions for research in human genetics, such as those relating to storage of biological material (Brasil 2011).

The combination of review directives, regulatory aspects, and ethical reflections on medical genetics research had different effects. Some committees had more familiarity with these topics because, in some cases, there was already an institutional culture of the ethical appropriateness of research, and the researchers were recognized as qualified in their respective areas of scientific expertise. In these institutions, genetic research projects submitted for evaluation by the research ethics committee had procedures similar to any other projects. However, if an institution was not familiar with a research area, or if the ethics committee did not include researchers in the field of genetics, the review process was slow and often conducted without a proper understanding of the purpose and suitability of the research. This example from Brazil can also be applied to other Latin American countries (Lemke et al. 2010).

Genetics, research, and ethics as keywords

In order to find similarities and differences between genetics research and ethics between international and Latin American scientific literature, a search was conducted using PubMed (US National Library of Medicine 2015) and SciELO (SciELO—Scientific Electronic Library Online 2015) databases, through January 2015. In the SciELO database, only Latin American countries were selected.

Using a combination of the keywords “research”, “genetics”, and “ethics”, it was possible to identify 7276 papers published in PubMed and 18 in SciELO using all three keywords in the same article.

Two important issues were also evaluated, as subsets, in the same papers: “informed consent” and “indigenous populations”. In PubMed, 391 (5.4 %) papers also investigated indigenous populations; in the SciELO database, there were no references found when using the same selection criteria by keyword. When the keywords were changed to include “informed consent”, 1254 (17.2 %) references in PubMed and 2 (11.1 %) in SciELO were found. The two papers in SciELO were very specific—one commented on forensic aspects and the other on prenatal genetic screening.

These data reveal that more scientific information about these topics is necessary, in order to provide a useful background for reflection on important ethical issues. It is, in fact, rather difficult to believe that there were so few publications on these relevant topics in the SciELO database. These findings, especially in SciELO, could be explained by the selection of keywords by the authors.

Ethical reflections and research in genetics

The concept of dangerous knowledge, proposed by Van Renselaer Potter, refers to knowledge that accumulates more rapidly than the wisdom required to use it (Potter 1971). This concept had already been linked to genetics research even before the Asilomar conference, at the beginning of the 1970s, in an article published in *Time magazine* entitled “Man into superman: the promise and peril of the new genetics” (Paoletti 1974). Recognizing research in genetics as a source of dangerous knowledge does not entail avoiding or proscribing it. On the contrary, recognizing the potential for dangerous knowledge entails the need for extended discussion on the various aspects of research, including ethical, legal, and social issues (ELSI). This was, perhaps, one of the great legacies of the Human Genome Project (HGP), which included ELSI as a part of the project (Knoppers et al. 1996). As a result, a document was published containing proposed guidelines for research on the human genome (Human Genome Organization, HUGO 1996).

In the same period, UNESCO asked the International Bioethics Committee (IBC) to draw up a document on genetics and human rights (Lenoir 1997). This was released as the UNESCO’s Universal Declaration on the Human Genome and Human Rights (UNESCO 1997).

Despite all of these advances, many ethical, legal, and social issues still deserve to be reflected on in genetic research, such as the use and storage of biological material and precaution in the use of new technologies.

Currently, there are adequate standards for storage of biological material (Dietrickx and Borry 2009); however, many researchers have large biological collections in different countries associated with old research projects, which were planned and conducted before the current regulatory system was proposed. Using biological material, which the UNESCO Declaration considers to be a heritage of humanity (UNESCO 1997), should be discussed to cover all interests associated with it. Stored biological materials have an inestimable scientific value because they are evidence of conditions that often no longer exist, but when they come from traditional populations, such as indigenous groups, other social and historical issues must be factored in to the discussion. The most important is to identify solutions that align the different perspectives in order to preserve both biological and social memory. Novel ethical solutions should be used rather than simply applying currently prevailing guidelines to situations of the past. Joint and unprejudiced decisions that include all parties are essential for identifying suitable solutions. Reflections are important in this techno-science era, especially when a new technology is introduced and applied to genetic research without major studies about ethical and social issues. One of the key issues is the irreversibility of the actions involved and the introduction of new features into the gene pool. One of these new techniques is

CRISPR (clustered regularly interspaced short palindromic repeats), which is used to edit portions of the genome. From its introduction in 2002 (Jansen et al. 2002) to the present, more than 1300 papers have been published using this technique. In 2012, CRISPR was used to reprogram specific DNA targets (Jinek et al. 2012), leading to new possibilities to generate and introduce synthetic genes using different DNAs, including those of animal species that resemble humans (Niu et al. 2014).

CRISPR is a good example of the concepts of dangerous knowledge, precautionary principle, and techno-science. Many other aspects involving individuals, society, and nature could be involved, such as human dignity, justice, respect of persons, and retrospective and prospective responsibility.

The rapid development of scientific knowledge and immediate implementation of new technologies made it difficult to identify what is technology and what is science. This idea had already been proposed in the 1980s, under the name of techno-science (Hottois 1984; Latour 1987), when scientific knowledge was generated and applied too quickly; it is worth noting that more than 1000 articles were published on CRISPR, from 2012 to 2014. The lack of reflection associated with the use of this technique is evidenced by the lack of publications that address it. Despite the many scientific and technological advances associated with CRISPR, there are only two papers in PubMed with both keywords: CRISPR and ethics. Both are comments: one addressing the issue of gene patents (Webber 2014) and the other discusses the issues involved in the trans-humanism associated with the use of this technology (Nau 2014).

Finally, the precautionary principle is an important approach to this issue, because CRISPR meets the criteria for potentially serious and unpredictable risks, if measures are not implemented to prevent those risks before there is real damage. Although it is much more risky than DNA fragmentation, which led to the Asilomar Conference, or the Human Genome Project, which proposed reflecting on ELSI associated with mapping the human genome, CRISPR has been increasingly used, but without adequate reflection on its many implications. CRISPR is thus one of the most important challenges presented by ethics and genetic research.

Final considerations

One of the major contributions of modernity was to put forth a reflection on what is universal and individual, abstract and concrete, and objective and subjective (Münch 2001). Genetics deals with all of those aspects.

Much more than fearing genetic advances, or questioning the need for ethical reflection on research to implement these advances in society, it is essential to rescue and update ethical *zeitgeist* of the 1970s.

The complex interaction between genetics and ethics demonstrates the need for an interdisciplinary approach to assess

the adequacy of genetic practices and the ethical reflections about them.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by the author.

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