Patentability of human genes: the conceptual differences between the industrialised and Latin American countries

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Abstract The patenting of human genes has generated considerable controversy, both in the doctrinal field and in the legal and administrative. In the core countries, particularly the USA and the European Union, a favourable criterion to patentability has been increasing, contrasting with the criteria adopted by Latin American countries, which almost unanimously banned the patentability of genes and gene sequences. This issue not only has legal connotations, but also ethical issues come into play. Particularly in the USA, the recent decision of the Supreme Court in the *Myriad* case is part of a pro-patent movement, even when its superficial reading seems to be oriented in the opposite direction. In the European Union, the criterion that favours human intervention, whatever its gravitation in the results, tips the balance in favour of patentability.

Introduction

The purpose of this study is to crystallise the differences between legal regulations and case law in the USA and the European Union, on the one hand, and the Latin American countries, on the other, with regard to the patentability of genes and sequences of human genes.

These differences are based on the existence of conflicting legal and ethical criteria.

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Currently, patent law is set to the economic policy of the states. It is difficult, if not impossible, to reconcile points of view that enable to make their contents universal.

The subject under discussion

When the Human Genome Project set out to sequence the whole human genome, it rapidly became apparent that the information obtained could have a significant market value. To make this information freely available to anyone who wanted to use it would mean giving up an important “business opportunity”.

The possibility of commercialising the human genome was rejected by scientists at the meeting held in Bermuda in February 1996, during which they assumed two commitments (Marshall 2001):

- (1) to share the results of sequencing “as soon as possible”, whenever the stretch of DNA sequenced exceeded a thousand base pairs, and
- (2) to send this information within 24 h to the public database GenBank.

The battle for the patenting of human genetic material began in July 1991, the date on which the National Institute of Health (NIH) filed a claim in the US Patent Office (US Patent and Trademark Office-USPTO) to patent the partial sequences of 337 genes. This caused a significant reaction in the scientific world (Leslie 1991).

In February 1992, new patents for 2375 expressed sequence tags (ESTs) were claimed but the USPTO rejected the request. An appeal was lodged against that decision, and the NIH again requested patents for 4448 ESTs (Correa and Bergel 2013).

According to the work of Thomas and collaborators, between 1981 and 1985, 1175 patents were granted for sequences of human DNA (Thomas et al. 1996).

Thereafter, the rate of growth of applications increased exponentially. Already in 1998, Heller and Eisenberg warned about the disadvantages likely to result from the rights more and more genes and DNA sequences being held privately. This proliferation of owners of the output of genomic research—according to the authors—would make it hard to assemble the necessary property rights for the protection and development of an innovation (Heller and Eisenberg 1998).

In 2001, the Director of Biotechnology at the USPTO found that, since 1980, more than 20,000 patents had been granted, on genes or other related molecules, and that around 25,000 applications were pending (Coriat and Orsi 2005).

By 1997, there were conflicts among some “genomic companies”, which foreshadowed future disputes between companies that sequenced a gene and those who linked it to a disease or a biological function. Thus, for example, the conflict that arose between Millennium and Hoffman La Roche, on the one hand, and Progenitor, on the other, regarding the leptin receptor gene (Eisenberg 1997).

Biotechnology’s own problems were overwhelmed with the arrival of genomics. With the progress of research aimed at unravelling genetic information, through cloning and sequencing procedures in the field of molecular biology, the issue of patents acquired a great relevance, while, at the same time, great efforts were needed to systematise the making of decisions and distinctions in this area.

Today, genes and gene sequences are patented as “products”. However, the truth is that what is being patented has not so much been produced but rather discovered, and exists “human genetic information”. This should force another approach in the field of intellectual property, considering the ethical, social and scientific issues this matter raises, along with the technical and legal criteria proper to this branch of law. The eminent French researcher, Axel Kahn, pointed this out clearly, when he stated that talking about marketing or patents on genes really means that we are talking about “genetic information” (Kahn 2000).

Expecting to find solutions based on traditional patterns forced continuous change on the concept of intellectual property rights; its lack of convincing coherence put the general system in crisis. The socio-political and not exclusively “technical” nature of patent law in the biotechnology field is revealed in the different “policy” adopted by the patent offices in Europe and the USA.

These offices, which, together with the Japanese, handle virtually all patent applications in the world, issued a joint communiqué, in 1998. This established a set of unifying criteria on the central theme of the validity of patents: “the purified natural products should not be considered natural

products or simple discoveries, as they do not exist naturally in isolation” (Nuffield Council on Bioethics 2000).

This statement implied holding that the simple isolation of natural substance rendered it “appropriable” through intellectual property rights.

When subsequently the battle began for the patentability of genes and, thus, for the genetic information they contain, this criterion was imposed in the offices mentioned above; DNA sequences isolated from their environment became patentable, as long as this was deemed to constitute an “industrial product” and not merely a natural substance.

We will analyse now the main arguments drawn upon to justify the patenting of products or, indeed, of human genes.

The “invention” of genetic sequence

In order not to undermine the policies followed by the patent offices from the countries mentioned, it was necessary to broaden the concept of invention to include the isolation of a genetic sequence from its natural environment or reproducing it through a technical procedure.

This broader definition of invention now stretches to include the idea of “human intervention in nature” and not only inventions as usually understood.

The USPTO believes that obtaining genetic information encoded in a DNA sequence does not involve the acquisition of a simple scientific knowledge about a natural phenomenon (discovery). The operation involves—according to the office—creating an artificial molecule, which includes genetic information similar to the information contained in a gene. Therefore, the genetic information is, according to this view, part of an invention, a new molecule obtained with human intervention and that can be patented as such. In a proper environment, using the machinery of a living cell, the program carrying the gene could be read and executed. In this sense, the gene is compared to any means of information support (magnetic stripe, computer discs, videotapes, etc.) (Sterckx 1999).

This line of reasoning comes from maintaining that, as long as “something” is within the human body, it is a natural element and should not be considered patentable. When that something is isolated from the human body, however, it can be protected by a patent, even when its information is identical to that of a natural element, since the process used is technical. These arguments fall short, in my opinion, of really persuading or convincing, because the simple fact that an element has been isolated from the human body through technical means does not change its “nature”.

For USPTO, as well as for the European Patent Office (EPO) and the Japanese office, without the isolation and cloning of a gene, it is not possible to identify its base sequence, which leads to the claim that we are in the presence of an invention and not a mere discovery.

This scheme of creation of a new molecule is termed an invention although, in the end, it contains only the genetic information that was there initially. I submit that it is not possible to transform a discovery into an invention with the sole purpose of gaining the concession of a patent.

Regardless of the difficulties of a discovery, the bottom line is that the operator has not modified the content of the genetic information and has only made possible—recurring to techniques used for some time and that are in the public domain—to attain knowledge of something that was there already.

As was pointed by the Nuffield Council on Bioethics, the hypothesis that the isolation and cloning involved in a discovery produce new molecules of a type not produced naturally is questionable. The fact that genes are essentially genetic information makes the subject of their patentability very different from that involving the isolation of other chemical components (Nuffield Council on Bioethics 2000).

The sequence of the genome—says Sulston—is a discovery, not an invention. Just like a mountain or a river, it is a natural object that was already there, if not before us, at least before we had consciousness of its existence (Sulston and Ferry 2003).

The applicability of criteria for chemical compounds as ground for patentability

The doctrine elaborated by the patent offices from central countries was devised specifically so as to justify the patentability of genes, as a response to the interests of industry. To argue thus case, the attempt was made to establish the equivalence of DNA and other chemical molecules.

An USPTO publication explains the “reasons” for such equivalence: “if genes are treated in the same way as other chemical compounds, then progress will be stimulated since the original inventor will be able to recover investigation expenses, other investigators will be stimulated to invent from the first patent and that new chemical compound will be accessible for future generations of researchers. The gene will be a new “matter compound” susceptible of being patented.” (USA Federal Register 2001).

This stance was upheld by John D. Dall—at the time Director of Biotechnology of the USPTO—in these terms: “genes are complex organic molecules and when isolated and purified from where they reside, they may be patented as chemical compounds” (USA Federal Register 2001).

According to these criteria, a patent over a new “chemical compound”—the gene—covers any use, whether or not discovered by the owner. Barton criticises this principle, saying it is not clear how wise it is to apply legal principles of chemical compounds to genetics. In this line of argument, he points out that the present knowledge of science is that a gene can encode more than one protein, possibly through different mechanisms

of RNA transcription and splicing into messenger RNA (mRNA). In this case, the different proteins for which the gene is coding are not chemically identical. From this, we can conclude that the discovery of a gene and the protein(s) which it encodes should not give rights over other proteins encoded by the same DNA sequence (Barton 2002).

The European Directive 98/44/EC¹

Following the model devised by the patent offices of these industrialised countries, the European Directive 98/44/EC—the most comprehensive document elaborated thus far on protection of biotechnology innovations—adopted the same approach as made clear in its article 3.2 (European Directive 98/44/EC).

It should be noted that this shift, with which a mere discovery can be considered a patentable invention, breaks with a long European tradition answerable to ethical, social and cultural principles and a commitment to clarity.

Article 5 of said Directive, in its sections 1 and 2, states clearly a new direction, accepted by countries of the European Union, regarding patentability of human genetic material (European Directive 98/44/EC).

After proclaiming in section 1 that the human body and its parts (including genetic sequences) may not be patented, in whole or in part, it establishes in section 2 the real that actually applies: “An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element”.

The contradiction between both sections is insurmountable and was the object of fierce criticism.

Jacques Testart, the prominent French scientist, ridiculed this legal argument: “As by definition any object of investigation must be isolated by technical means, it ends up authorising what was forbidden in its beginning”; adding “it starts by feigning prohibition to end up authorising it” (Testart 2002).

In the same vein as this critique, Sicard, at the time President of the French National Consultative Ethics Committee, expressed this view: it should be noted that we are in the presence of a fiction, since it is not possible to discover a gene without isolating it; adding that the concept of isolation has been formulated as a dangerous artifice designed to ensure that any gene of potential use can be patented as an object, rapidly and regardless of (Sicard 1998).

¹ The European Directive 98/44/EC, adopted by the European Council, governing the protection of biotechnological inventions, is mandatory for the countries of the European Union (EU).

The aforementioned directive was challenged by the Netherlands, with support from Italy and Norway, with the central reason that patentability of elements isolated from the human body, that is derived from section 2 of article 5, equates to the industrialisation of living human matter and is contrary to the dignity of the human being (Bergel 2007).

Regardless of the logical contradictions indicated in article 5, this rule was upheld by the Court of Justice of the European Union, 9 October 2001, which rejected the objections with unconvincing arguments that shed light on the complicated maze of interests at play in this subject.

The judgment of the Supreme Court of the USA

After several decisions of USPTO and of the specialised courts, the issue of patentability reached the US Supreme Court, which issued an important decision on 20 March 2013, ruling on a lawsuit of several petitioners against Myriad Genetics requesting the annulment of the patents granted in relation to genes *BRCA1* and *BRCA2* associated with breast and ovarian cancer (Supreme Court of the United States 2013).

The Court partially accepted the lawsuit stating the non-patentability of natural genes and simultaneously kept the patentability criteria in relation to complementary DNA (cDNA).

On the first issue, the Court stated “*Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes. The location and order of the nucleotides existed in nature before Myriad found them. Nor did Myriad create or alter the genetic structure of DNA. Instead, Myriad’s principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes within chromosomes 17 and 13*”.

The Court added that “*nor are Myriad’s claims saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a non-naturally occurring molecule. Myriad’s claims are simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from the isolation of a particular section of DNA. Instead, the claims understandably focus on the genetic information encoded in the BRCA1 and BRCA2 genes*”.

These arguments of the Court on the non-patentability of natural genes are clear and irrefutable, requiring no further comment.

With regard to the patentability of cDNA, the Court held that “*cDNA does not present the same obstacles to patentability as naturally occurring, isolated DNA segments. As already explained, creation of a cDNA sequence from mRNA results in an exons-only molecule that is not naturally occurring. Petitioners concede that cDNA differs from natural DNA in that “the non-coding regions have been removed”. They nevertheless argue that cDNA is not patent eligible because “the nucleotide sequence of cDNA is dictated by nature, not by the lab*

technician”. That may be so, but the lab technician unquestionably creates something new when cDNA is made. cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived. As a result, cDNA is not a “product of nature” and is patent eligible under 101, except insofar as very short series of DNA may have no intervening introns to remove when creating cDNA. In that situation, a short strand of cDNA may be indistinguishable from natural DNA” (Guo 2013).

In this regard, it should be noted that scientists who want a clean copy of a gene, then, can intercept the mRNA transcript and figure out what it says. Then, they can even use the mRNA to create complementary DNA, which has the same sequence. The cDNA—as Jeff Guo states—is what our DNA would look like if it were purged of all introns. But it does not exist naturally because our bodies like to keep our DNA safely locked away. So, cDNA is an artificial creation, even though it contains the same data as the mRNA, which is a natural creation (Guo 2013).

That is a fine distinction, but it was good enough for the Supreme Court, which notes that “the lab technician unquestionably creates something new when cDNA is made”. Because cDNA is something human-made and unnatural, it is therefore patentable. Of course, the Court was ruling on a very narrow part of patent law, which says that “products of nature” cannot be patented. Someone could still argue that cDNA fails the “obviousness” test, as the body does all the work to remove introns, the researcher just copies it back into a DNA form.

Consequently, the difference between natural DNA and cDNA is the fact of having a “gross” composite versus a clean one; however, both contain exactly the same genetic information.

The “laboratory technician”, mentioned in the Court’s verdict, who obtained the cDNA did not create anything. Despite the complexity of this developmental process and the time it takes, it is merely a non-creative laboratory work. This is unquestionably a great distance from being a “creation” that could lead to any “patentable invention”.

The Court used half a page—in my opinion, without success—to demonstrate the patentability of cDNA. Three main arguments were used:

- the laboratory technician creates something new by obtaining cDNA;
- cDNA conserves the natural DNA exons but is different from the DNA from which it comes; and
- as a result, cDNA is not a product of nature and is therefore patentable according to article 101.

The referred verdict reaffirms policies followed by the patent offices of industrialised countries (USPTO, EU, Japan Patent Office (JPO)) related to human genes patentability.

Indeed, after exhibiting powerful arguments to deny the patentability of natural DNA, it adds marginal reasons to authorise this action for cDNA.

In the first case, patentability could only be sustained from a perspective that ignores any distinction between invention and discovery. It would have been very unfortunate for an institution like the US Supreme Court to consider reasons to justify this. They preferred—on this occasion—to base the first part of the verdict with strong observations, and finally to resolve the main issue in a “fast” way.

The second issue is the most relevant one regarding practical situations, considering that the majority of patentability requests refer to cDNA.

The Court distances itself from the first arguments used to justify the patentability of cDNA.

Regardless of the specific issue for which it was called, the doctrine of the Court can be invoked by other courts in patent offices to cases where the man made a contribution on a pre-existent matter of nature—however minimal—becoming his intervention in the central matter that justifies the patent.

This key criterion could now extend to cover all laboratory work so that no distinction would remain between science and technology, thereby allowing the appropriation of nature through legal gadgets.

The position of Latin American countries

In contrast to the US and EU criteria, Latin American countries oppose the patentability of human genes. This is reflected in their industrial property laws and patent offices.

The position of Latin American countries is in better harmony with the central principles of patent rights. Although the agreement on trade-related aspects of intellectual property rights (TRIPS)—the broadest and deepest instrument ever subscribed regarding industrial property rights—does not define what should be considered an invention, because its article 27.1 refers only to the so-called objective patentability requirements; the matter was not simply ignored or relegated to a dangerous vagueness.

The difference between invention and discovery is still fully valid in patent right. It is not just a legal or technical issue, as it also recognises deep ethical and political implications.

Discovery means the revelation of something that pre-existed but which had not attained any public visibility of awareness.

On the other hand, invention implies an act of human creation directed to solve a technical issue. Dal Paz and Borges Barbosa clearly state: “an invention should be technical in its object, application and result to be patentable” (Dal Paz and Borges Barbosa 2008).

Regarding genetic elements, and despite the complexity of the task it entails, a technician merely reveals something that

pre-existed. The genetic information possessed by the natural material is exactly the same as that which will result in the patent.

Maria J. Amstalden Sanpaio and Marcia de Miranda Santos reveal this difference: “the USPTO approves patents requests for genetic markers EST’s and SNP’s (single nucleotide polymorphisms) existing in the DNA of organisms. SNP’s are indeed constructions existing in nature and are discovered, not invented by researchers. So it is valid to ask where we should set the limit to determine the appropriation of genome” (Dal Paz and Borges Barbosa 2008).

While examining the region’s situation, we can point out Argentina’s patent law 24441, which established in its article 6 (g) that excludes from being regarded as an invention “any kind of living material and pre-existing substances of the nature”; while article 7 (b) specifies as non-patentable “biological and genetic elements existing in nature or their replicas issued from biological processes that are implicit in vegetal, animal and human reproduction”.

According to this, the exam guides from the INPI (Instituto Nacional de la Propiedad Industrial) establish that “substances that pre-exist in nature, even when purified, isolated or characterized, are not patentable” (art. 2.1.7.1).

Besides the legal interpretation, an ethical focus indicates that patenting simple discoveries of genetic material in the first steps of research, before any process of invention has occurred and before a true patent portfolio could be established, is designed with the unique and exclusive goal of blocking competition and ensuring a monopoly access to entire areas of knowledge, implying the abusive and distorted exercise of an industrial property right against weightier, more important social interests.

This position is based on ethical criteria that invalidate the patentability of human genes because of

- (a) injury human dignity;
- (b) the requirement that the human body and its parts must not be subject to commercial transactions;
- (c) the consideration of genetic information as the common heritage of humanity;
- (d) the opposition to respect for public order and morality; and
- (e) the opposition to the criterion of equity in distributing the fruits of scientific research (Correa and Bergel 2013).

In Brazil, article 10.I of patent law 9279/96 determines that a living being, the human body, the human genome, human genetic material and natural processes are not inventions.

Regarding the doctrine, just to mention a central opinion, Maria H Diniz expresses that the sequences of genetic material are not patentable because no inventive activity was involved in isolating the sequences or a gene (Freire de Sá and Oliveira Naves 2009).

In Mexico, article 19 of industrial property law establishes that discoveries revealing something that pre-existed in nature are not considered inventions.

In Ecuador, article 26 of law 2006-013 establishes areas of activity which must not be subject to commercial exploitation in order to protect morality, namely, the human body and its genetic identity, which are therefore not patentable.

In Chile, article 37 (f) of patent law 19039 establishes that the following are not considered inventions and therefore remain excluded from the protection of patent law: “parts of human beings as found in nature, natural biologic processes, or biologic material existing in nature, or the one that can be isolated, including the genome and germplasms”.

Dal Paz and Borges Barbosa (2008) reveal the effects deriving from conceptions accepted by each side (USA, Japan and the EU, on one side, and Latin America, on the other) regarding genes patentability. The polarisation of these concepts contrasts living elements (as found in nature) versus what is “manipulated by humans”.

As the rationality of rejecting the patentability of genes originates in the consideration that they are strictly part of living beings in nature, in the opposite vision, it is understood that genes do not exist as isolated units, being only recognisable through a scientific effort. It is human intellectual activity that justifies the protection of industrial property rights over these “discoveries” (Dal Paz and Borges Barbosa 2008).

In my opinion, the position of Latin American countries in prohibiting the patentability of genetic material is the one that best suits the past and current principles of patent law, allowing the free circulation of knowledge, which is a right of a deep historical and ethical value. However, circumstances external to the rights and wrongs of intellectual property rights seem to favour the patenting of genes, as advances in biotechnology and their economic impact dominate this field of activity.

Comparison of the systems

While comparing the observed criteria of the industrialised countries (USA, European Union and Japan) and the Latin American countries, we can extract the following conclusions:

- (a) In general, industrialised countries allow the patentability of genes and human gene sequences. Their patent offices have granted patents without serious deliberation.

In the European Union, an appeal against that decision was refused by the European Court of Justice.

In the USA, the recent judgment of the Supreme Court in essence maintains this position, since most of the genes to be patented have been in the form of cDNA, which is patentable according to that verdict.

- (b) Latin American countries refuse the possibility of patenting human genes and gene sequences in their legislations and operational guides of the industrial property offices.
- (c) The differences between systems reflect not only different legal interpretations (as the one between invention and discovery), but also imply an ethical difference. The main fact that genes and the genetic information they contain are part of the human body is ignored by industrialised countries, and therefore, they are subject to similar ethical limitations regarding appropriation and commercialisation.

Compliance with ethical standards I, Salvador Darío Bergel, hereby declare that this manuscript has not been submitted to any other journal. It has not either been published previously; no data have been fabricated or manipulated to support my conclusions, and no data, text, or theories by others are presented as if they were my own.

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