

International

One step forward, two steps back: examining stem-cell patenting

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Superman actor Christopher Reeve broke his spine after falling from a horse and never regained the use of his lower limbs. Until his death, he vocally supported research into stem cells for the treatment of various neurological diseases. Since the early 1990s advances in stem-cell technology have raised hopes for new approaches to the treatment of serious, previously untreatable diseases. In particular, progress has been made towards promising treatments for diabetes, heart disease and neurological diseases such as Parkinson's.

However, where scientists, doctors and patients envision new curative treatments, others see stem-cell technology as an offence to natural life, and the use of such technology has led to debate over whether it is ethically acceptable to use material derived from human embryos. Critics frequently raise moral concerns based on religious or ethical grounds. In Europe, the debate has been heated and attitudes to stem-cell research vary widely between member states due to differences in religion and culture. In some places, notably the United Kingdom and Scandinavia, research using embryonic stem cells is allowed and even encouraged, whereas in others (in particular, Catholic countries), such research is banned or severely restricted.

As has been seen in other technical areas, debate relating to controversial scientific methods transfers to the IP field, giving rise to discussions about whether it should be possible to patent such methods. The background for this is usually that laypeople and politicians often misunderstand the patent

system, seeing patents as providing a right to exploit the technique protected by the patent, rather than being aware of the real effect of a patent as a monopoly right to prohibit all but the patent holder from exploiting it.

Patents and morals

As with other medicines, patents are the key to protecting the large investments required to develop basic research into whether embryonic stem cells can be used to benefit patients. There is a long and expensive path from the first promising results obtained in the laboratory to offering patients an actual treatment. Without the prospect of patent protection, investment is difficult to attract.

Patents related to medicines as well as uses of biological material, such as cells, are generally patentable in Europe; however, a basic exception to such patentability is that European patents cannot be granted on inventions which are contrary to morality. 'Morality' is a difficult standard to work with, since the concept of morality varies between individuals and from country to country – particularly in Europe, where religious and moral standards differ between the northern and southern states.

The European Patent Office (EPO) grants patents that are enforceable in 38 European countries. It is an independent organisation with its own appeal body and is unrelated to the European Union, even though there is a significant overlap in member states. The EPO has the difficult task of determining whether inventions based on the use of embryonic stem cells are contrary to morality.

Throughout the 1990s, when there was much debate over whether research into and patenting of embryonic stem cells, the

European Union set down common rules for research in the biotechnical field by issuing the EU Directive on the Legal Protection of Biotechnological Inventions (98/44/EC).

The Biotech Directive provides that the use of human embryos for industrial or commercial purposes is unpatentable. As an EU directive, it must be implemented in the laws of all EU member states and questions on its interpretation may be referred to the European Court of Justice (ECJ).

The EPO, although not automatically bound by EU directives, decided to adopt the wording of the Biotech Directive into the regulations of the European Patent Convention; however, the EPO is now bound by ECJ decisions.

Stem cells

Before going into detail regarding the patent protection of stem cells, it is important to understand the scientific basis. Broadly speaking, there are two types of stem cell: embryonic stem cells and somatic stem cells. Whereas embryonic stem cells are pluripotent and can differentiate into any kind of cell type, somatic stem cells are more limited in their abilities. For example, in principle, skin stem cells can evolve only into skin cells and blood stem cells can evolve only into blood cells. Embryonic stem cells are typically derived from fertilised eggs (eg, left over from *in vitro* fertilisation). The original stem cells may be cultivated *in vitro* generating further stem cells or precursor cells, and making stem-cell lines available. Stem cells can also be prepared from a non-fertilised human ovum stimulated by a process known as parthenogenesis. Such ovum behaves like an embryo in the early stages of cell division, but cannot develop into a human foetus.

ECJ view

The ECJ investigated the boundaries for the patent protection of inventions relating to embryonic stem cells in a case dealing with Professor Brüstle's German patent on neural precursor cells. The patent covered neural precursor cells prepared from embryonic stem cells, and described the use of such cells in the treatment of severe neural deficiencies such as Parkinson's, Huntington's and Alzheimer's diseases. The patent did not cover the embryonic

stem cells *per se* or the use thereof, and as such the patent did not fall under the exceptions to patentability set out in the Biotech Directive. In spite of this, in its 2011 decision the ECJ found that even if the invention did not relate directly to the use of human embryos, any invention relating to materials or methods requiring the prior destruction of human embryos or their use as base material could not be patented. The court defined the term 'human embryo' very broadly to encompass any fertilised human ovum, as well as unfertilised human ova stimulated by parthenogenesis, although the latter have no potential to develop into a foetus or ultimately a child.

The ECJ's decision was interpreted by patent practitioners and scientists in Europe as severely limiting access in Europe to the patent protection of inventions that even remotely relate to embryonic stem cells.

The corresponding European patent was recently revoked on formalistic grounds. The decision has now been appealed and it will be interesting to see whether the EPO Boards of Appeal follow the ECJ's very stringent interpretation. Unfortunately, at the earliest, a final decision will be issued just a few years before expiry of the patent.

View of EPO Enlarged Board of Appeal

The EPO Enlarged Board of Appeal has also considered the extent to which methods employing the use of stem cells can be patented in Europe. The Wisconsin Alumni Research Foundation (WARF) filed an application for a patent directed to a cell culture containing embryonic stem cells. In contrast to Brüstle's invention, this patent was aimed directly at the embryonic stem cells. When the WARF patent application was filed, the only method to obtain embryonic stem cells was by destruction of the embryo, and on that basis the Enlarged Board of Appeal found the patent to be invalid. The board's view was that a product that could be prepared only by methods involving the destruction of embryos could not be patented.

Technology overtakes

At a time when the outlook for the patenting of embryonic stem cells was pessimistic, technology evolved and obviated the need

for embryonic stem cells derived directly from fertilised human eggs or embryos in a manner leading to the destruction of the embryo. For several years it has been possible to obtain pluripotent stem cells from human embryos using single-cell biopsy without destroying the embryos or interfering with their developmental potential. Thus, obtaining stem cells in this manner does not conflict with the Biotech Directive, even when using the broad definitions given by the ECJ. In addition, embryonic stem-cell lines have been established and are available from cell collection.

Because embryonic stem cells can now be obtained by both methods requiring destruction of the embryo and non-destructive methods, the German Federal Court found Brüstle's patent to be valid insofar as it related to methods using embryonic stem cells prepared without destruction of human embryos. It seems that the EPO is also applying this line of reasoning. In July 2013 the EPO granted a patent on another of Brüstle's inventions directed to methods for preparing microglial precursor cells from human pluripotent stem cells (ie, an invention paralleling the first Brüstle case).

Furthermore, the UK courts have questioned whether it is reasonable to consider an unfertilised ovum to be a human embryo. Even though an unfertilised ovum can be manipulated to behave similarly to an embryo in the early stages, it cannot then develop into a viable foetus. The UK High Court has made a new referral to the ECJ in order to clarify this question, but a final decision is some years away.

Somatic stem cells

Whereas there has been lively debate over the patentability of embryonic stem cells, the picture regarding somatic stem cells is much clearer. The Biotech Directive specifically allows patent protection of isolated elements from the human body, and thus somatic stem cells and uses thereof can be protected by patents. The use of somatic stem cells also does not raise the same ethical and religious concerns as the use of embryonic stem cells, because somatic stem cells can be obtained from adult humans without the need to destroy embryos.

Technically, somatic stem cells offer the advantage that a patient's own cells can be used, and therefore the challenges posed by adverse immune reactions are reduced. Promising results using somatic stem cells have already been obtained.

Outlook

Whether the destruction of human embryos is required to operate an invention is the main factor when deciding whether an invention in the stem-cell area can be protected by a patent in Europe. Methods involving the use of material generated in a way that destroys human embryos cannot be patented, whereas methods using cells obtained by non-destructive methods are patentable. The relevant case law has been developed over the past 15 years since the passage of the Biotech Directive in 1998, and the pendulum has swung back and forth between the allowance and the rejection of embryonic stem-cell patenting. Today, the case law appears to be maturing into an understanding that uses of embryonic stem cells as such are not by definition unpatentable; rather, they are unpatentable only if embryos are destroyed in the generation of the stem cells.

Therefore, parties interested in seeking a patent involving embryonic stem cells should take precautions when drafting the patent text – it may be relevant to include in the patent text that the material has been obtained without destroying embryos in the process of collecting the cells. **iam**

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