PATENTABILITY OF STEM CELLS

The View of the European Group of Ethics

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Ethical dimension in European Patent law

Until now 24 European states have joined the European Patent Convention (EPC) of 1973. The EPC considers some moral criteria in convention with the patentability of inventions, explicitly by Article 53 (a) that excludes inventions from patenting the expectation or publication of which would be contrary to "public" or „morality". The question, whether a patented invention is in line with Article 53(a) was more than once the object of proceedings before the EPO. Famous cases were e.g. „Oncomouse" of Harvard [1], concerning a transgenic animal, or "PGS" concerning a transgenic plant. Recently, a new technology is faced with the „morality" requirement of Article 53(a), namely stem cell research.

The EU Biotech Directive and New Rule 23

In the EU the growing need for a harmonization in the field of biotechnological inventions was seen. The development of the EU Biotech Directive started in 1988 and ended in 1998 with the approval of the EU Directive 90/44/EC [3] by the European Parliament. Two main opinions by the ethical commission called GAEIB [4] escorted the Directive: There should be no ethical objection to patents for biotechnological inventions per se. Furthermore, guidance should be given to which extent inventions involving elements of human origin should be patentable. The Implementation of the Directive into the EPC in Rule 23 took place in 1999 including following items among others: Explicitly excluded from patentability are processes for cloning human beings, for modifying the germ line genetic identity of human beings and uses of human embryos for industrial or commercial purposes (Rule 23d, EPC). An element isolated from the human body may constitute a patentable invention only if it is produced by means of a technical process, and is not the result of pure discovery (see Rule 23e, EPC).

GAIEB emphasized the opinion that only new, essentially changed elements of the human body can be patentable. The ethical aspect regarding the patentability in this field mainly considers as to whether there is a therapeutic benefit and a scientific progress [5].

Human stem cells

Undifferentiated cells, with the capability of dividing more or less non-limited and to develop more or less in a non-limited number of different cells, are called stem cells.

The characteristics of these stem cells has created various and completely new ideas in the field of medical treatment especially when one thinks of degenerative diseases or injuries. Main diseases of interest include diseases of neurological origin like Alzheimer, Paraplegia or Parkinson and of pancreas tissues such as diabetes. Stem cells also could be used for the toxicological testing of candidate drugs, what is termed „cell based drug screening".

One can distinguish between adult, embryonic and foetal stem cells or in other words between multipotent and pluripotent stem cells. Adult stem cells (ASZ) are multipotent, i.e. they can proliferate a

limited time period and can be differentiated to a limited number of cell types. Embryonic stem cells (ESZ) are derived e.g. from inner mass of a dead embryo in the blastocyte state, e.g. produced by in vitro fertilisation or somatic cell nuclear transfer. They are termed pluripotent as they are presumed to develop into any cell type and proliferate more or less „for ever“. They are not totipotent as the embryonic growth of such cells is no longer possible. Foetal stem cells (FSZ) are multipotent, if they are derived from the umbilical cord blood, but pluripotent if they are isolated from germ cells of an aborted 8-11 weeks old foetus. Human embryonic stem cells have so far been isolated or cultivated in the USA, Australia, India, Singapore, the UK, Sweden and Israel.

Worldwide the number of applied patents for stem cells was increased to approximately 2000 patents to the end of 2001, one quarter thereof for embryonic

stem cells. Taking into account multiple filings of patents in different jurisdictions, the total number of different patents is considerably lower. Approximately a third of all patents have been granted.

Patent claims have been directed to processes like isolation, selection and cultivation of stem cells, to cloning techniques for deriving stem cells from embryos, and to methods for treating patients using stem cells or differentiated cell tissue derived from stem cells [6]. Product claims usually include stem cells, stem cell lines, differentiated stem cells and genetically modified stem cells. Patents on such stem cells have already been granted in USA and – to the best of our knowledge – one in Europe. Key patents on embryonic stem cells are US 6.200.806 [7] or US 6.090.622 [8].

In Europe the one patent concerning human embryonic stem cells is the so-called „Edinburgh patent“[9]. In the meantime this case was debated at first instance before an Opposition Division. In the oral proceedings held in Munich in July 2002 the Opposition Division took the view that the granted patent failed to comply with the requirements of Article 83 and Article 53(a) in conjunction with Rule 23d(c) of the European Patent Convention (EPC). Article 83 stipulates that the invention must be disclosed in a manner sufficiently clear and complete for it to be carried out by a skilled person in the relevant field. Rule 23d(c) provides that uses of human embryos for industrial and commercial purposes are excluded from patentability. This decision underlies the review by a Board of Appeal at the EPO in the case of initiated Appeal Proceedings. The public attention drawn to the Edinburgh patent less concerned the stem cell issue itself than the question, how far methods for the cloning of humans using stem cells were protected by said patent. As the Opposition Division already pointed out in the communication published on April 14, 2000, the cloning of people had never been object of the patent. However, intervention into the germ-line of humans had been part of said patent. But this intervention had been excluded voluntarily by the patentee already before the end of the opposition period.

Recommendations of the EGE

Towards the issue of the patentability of stem cells the ethics-commission of the EU (EGE [10]) has released the opinion No 16 dated May 7, 2002 including the following items:

1. Isolated **stem cells**, which have not been modified, do not - as product - fulfil the legal requirements for patentability, especially with regard to industrial applications.

2. When unmodified **stem cell lines** are established, they can hardly be considered as a patentable product. Such unmodified stem cell lines do not have indeed a specific use but a very large range of potential undescribed uses. Therefore, to patent such unmodified stem cell lines would also lead to too broad patents.

3. Therefore, only stem cell lines, which have been modified by in vitro treatments or genetically modified so that they have acquired characteristics for specific industrial application, shall fulfil the legal requirements for patentability.

4. As to the patentability of processes involving human stem cells, whatever their source, there is no specific ethical obstacle, in so far as they fulfil the requirements of patentability (novelty, inventive step and industrial application).

Furthermore, the EGE suggests that applicants should declare which is the source of the stem cells decribed in a patent application. When the donated cells may become part of a patent application, donors should be informed of the possibility of patenting and they shall be entitled to refuse such use. It is finally the opinion of the EGE that patents shall only be granted, when the patent claim refers to a specific and a sufficiently accurately described stem cell line and its industrial application. To summarize, protection of any kind of stem cells appears to be possible at least via a process of preparing same.

[1] T 19/90
[2] T 356/93
[3] Directive on the legal protection of biotechnological inventions
[4] GAEIB: Group of Advisers on the Ethical Implications of Biotechnology to the European Commission
[5] Opinion on Ethical Aspects of Patenting Inventions involving Human Stem Cells
[6] Opinion on Ethical Aspects of Patenting Inventions involving Human Stem Cells, Opinion No 16 (Luxembourg Office for Official Publications of the European Communities, 2002), p. 11
[7] „Primate Embryonic Stem Cells“ von Thomson
[8] „Human Embryonic Pluripotent Germ Cells“ von Gearhart und Shamblott
[9] EP-B1-0695351
[10] EGE: European Group of Ethics in Science and New Technologies