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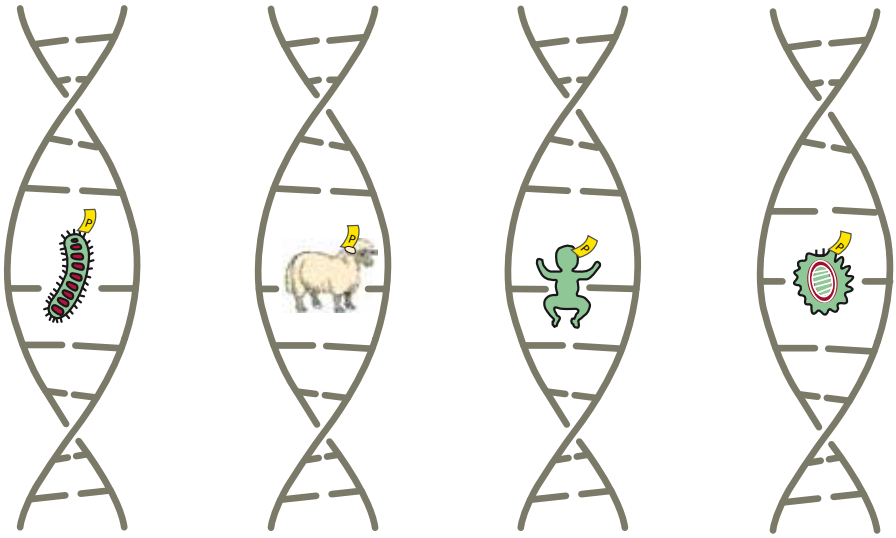

Blacklist of European Biotech Patents 2009–2011

A Testbiotech Report by
Christoph Then & Ruth Tippe

In collaboration with
"Kein Patent auf Leben!"

November 2011

KEIN PATENT AUF LEBEN

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1. Summary and introduction

The EU Patent Directive "Legal Protection of Biotechnological Inventions" (98/44 EC) allows to grant patents on living beings and their genetic information. Since its adoption in 1998, the European Patent Office (EPO) has granted several thousand patents covering, for example, human gene sequences, genetically engineered laboratory animals and genetically engineered plants. Many of these patents are problematic from an ethical perspective, and some of them even violate current patent law. In many cases, the patents cover discoveries rather than true inventions, and very often, the extremely broad claims are in sharp contrast to the disclosed technical contribution.

The legal regulations are inadequate and their implementation by EPO is, in most cases, based on a biased interpretation in favour of industry. For example, Art. 53B prohibits patents on plant varieties, but current legal practise is completely undermining this article. Art. 53A excludes patents perceived to be contrary to public order and morality. However, the EPO only very rarely applies this article.

The Patent Office and political decision makers have failed to define and implement legal borders within patent law so that they adequately meet the current challenges emerging from modern bio-technologies. The existing problems are not just about individual cases. They also call into question the justification of patent law in general and its role in civil society. There are some very basic ethical questions about our relationship with living beings, and whether plants and animals can be regarded as human inventions. Modern patent law is seeing a major change in its paradigm. Many such patents are not concerned with the protection of inventions, but the monopolisation of resources. There is an urgent need to revise patent law to serve the needs of civil society and not just the interests of the patent holder. The most appropriate solution is to exclude patents on genetic resources and living beings as requested by many stakeholders but not foreseen by European law.

The "Black List" of granted European patents gives ten examples (listed according the date they were granted) awarded by the EPO in the years 2009–2011, all of which highlight the urgent need for political action on adopting patent laws tailored to the current challenges presented by biotechnology. Most of the research and analysis on the patents was carried out by the initiative "No Patents on Life!" in cooperation with the non-profit organisation, Testbiotech. Amongst the examples are patents on human germ cells (oocytes and sperm cells) and a patent on chimpanzees genetically engineered to suffer from epilepsy.

Furthermore, this paper includes a statistical overview of the number of patent applications and granted European patents in the field of biotechnology.

2. Blacklist of granted European patents

Human oocytes, EP1794287 (Merck-Serono)

Patent holder: Merck-Serono, Germany
Date granted: 22.07.2009

Content:
The patent covers not only a process for treating human oocytes (egg cells), but also usage in the context of in-vitro fertilisation. The way in which the patent was granted gives Merck an exclusive right to work with these cells that de facto implies a monopoly right to the oocytes themselves. Claim 8 of the patent as granted reads:

> *"A method of in-vitro fertilization comprising producing a mature oocyte (…) and treating the mature oocyte with sperm."*

Analysis:
The patent violates current European patent law since the law states that "the human body, at the various stages of its formation and development (…) cannot constitute patentable inventions." (Art. 5 of Directive 98/44 EC). Recital 16 of EU Directive 98/44 further explains that germ cells (sperms and oocytes) are also covered by this exclusion.

This patent (at least indirectly) gives Merck-Serono a monopoly right to certain human oocytes and it is therefore unacceptable from the perspective of human dignity. Testbiotech filed an opposition to the patent in 2010.

This patent is not the only one in this category granted in Europe: In 2003, Vitrolife (Sweden) was granted a patent on frozen human embryos and oocytes (EP 1121015). In 2005, XY (US) was awarded a patent on human sperm (EP 1257168). Merck-Serono has had a patent on human sperm since 2003 (EP 1196153). In 2011, Ovasort (UK) was awarded a patent on human sperm (EP 1263521). By granting these kinds of patents, the EPO is encouraging the commercial exploitation of the human body.

Chimpanzees suffering from epilepsy, EP 1852505 (Bionomics)

Patent holder: Bionomics Ltd, Australia
Date granted: 31.03.2010

Content:
The patent holder investigated the genetic conditions of a larger group of patients suffering from epilepsy. Claims cover the gene sequences it discovered, and potential new methods of diagnosis and therapy.

Further, genetically engineered laboratory animals were patented to serve as a test system for developing new pharmaceuticals. Claim 33 lists the relevant animals as follows:

> *"rats, mice, hamsters, guinea pigs, rabbits, dogs, cats, goats, sheep, pigs and non-human primates such as monkeys and chimpanzees ."*

Analysis:
European animal welfare legislation places several restrictions on the use of mammals in animal experiments. The protection of human primates and great apes falls under strict international

regulations and is only allowed in rare cases within the European Union.[1] The intention of this paper in this regard is not to decide whether animal experiments, and particularly experiments with great apes, are required to develop new drugs to treat epilepsy. However, it is beyond any doubt that it is desirable to avoid these kinds of experiments.

It is beyond of the intention of this paper to decide in this context if animal experiments or even experiments with great apes are needed to develop new drugs to treat epilepsy. However, it is beyond any doubt that it is desirable to avoid these kinds of experiments.

Granting patents on non-human primates and other mammals that are genetically engineered to suffer from epilepsy allows economic interests to emerge to produce and market as many animals as possible during the lifetime of the patent. Instead of dealing with legal exceptions restricted by ethical concerns (e.g. animal experiments), society will now be faced with animal models viewed as products that can be marketed to maximise profits. The animals will be turned into economic commodities devoid of their own intrinsic value. These patents are a turning point in the relationship between humans and animals, and, as such, raise deep concerns.

European patent law allows the patenting of animals that are likely to suffer if substantial medical benefit can be expected (Art. 6 of Directive 98/44 EC). However, judgements on medical benefit can hardly be made at the date of patent examination. Thus, this directive is inadequate to prevent needless animal suffering to further the economic interests of a patent holder.

Current legal regulations are substantially influenced by the decision in the so-called oncomouse case, which was the first such patent to be granted in the US and Europe (EP 0169672). The argument for granting this patent was that it would help to develop new cancer treatments and there would be a reduction in animal experiments. Both these expectations have failed to materialise. The animals never played a role in the development of new drugs and the number of animal experiments has even increased during the last few years. In the light of this development, a legal prohibition of patents on animals would be most effective in this context.

Regarding the human gene sequences which are claimed as inventions, the patent holders mention that "informed consent was obtained from each individual for blood collection and its use in subsequent experimental procedures". However, it is not clear if consent was really obtained for filing patents on the relevant genetic conditions of these patients (for general discussion see EP 1090117).

Human gene sequences for diagnosis of cancer, EP 1090117 (Novartis)

Patent holder: Novartis USA/ Switzerland
Date granted: 07.04.2010

Content:
Novartis discovered several mis-regulated gene sequences in the tissue and blood samples of a family with a predisposition to pancreatic cancer. These gene sequences, as well as procedures for diagnosis and treatment of cancer in pancreatic cells, were patented.

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1 Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes, Official Journal of the European Union L 276/33, 20.10.2010

Analysis:
Patents on human genes are controversial for several reasons. Ultimately, these patents are not concerned with inventions but with genetic resources, which might be important for the diagnosis and treatment of severe health disorders. Monopolising the gene sequences hampers research and development in many cases. Several investigations and publications conclude that these patents are in conflict with the interests of doctors and patients rather than being beneficial. For example, a UK Human Genetics Commission report (2011) summarises the following widespread concerns, which were brought up during an experts´ conference in October 2010:[2]

1. *"Research and development (R&D) costs for genetic tests are relatively small and do not justify patent rights;*
2. *The proliferation of patents may hinder test development;*
3. *Research may be prevented by inadequate exemptions from patent infringement for researchers;*
4. *Monopoly service provision may drive up the price of tests, increasing healthcare costs and/or hindering patient access to tests;*
5. *The quality of testing (and thus patient care) may be affected when only one company is conducting testing."*

The EPO systematically sets aside all consequences of gene patents during their examination of the relevant applications. In this case, the EPO did not even ask if Novartis had gained informed consent of the patients participating in their research, before filing this patent. In other cases when oppositions were filed, the EPO did not give any consideration to the interests of the patients concerned.

The so-called Breast Cancer (BRCA) gene sequences are a quite well known example and highlight the negative impact of these patents. These gene sequences were patented by Myriad in the US, Canada and Europe (EP 0705902, EP 0705903), despite the fact that patient groups representing the interests of women concerned about this genetic predisposition explicitly spoke out against it. Consequently, many laboratories and clinical institutions that offered even better or cheaper tests for the diagnosis of hereditary breast cancer, had to stop their services. Ultimately, patients can be trapped by these kinds of patents, and taken hostage by the economic interests of the patent holder: Without a license, no other company can offer therapies or diagnosis developed on the basis of the patented gene sequences. By reserving their claims within the human genome, companies such as Myriad and Novartis are giving more weight to their own economic interest than to the interests of the patients concerned. All in all a legal prohibition on the patenting of gene sequences would be a necessary and adequate consequence.

2 Intellectual Property and DNA Diagnostics, A report of a seminar on the impact of DNA patents on diagnostic innovation by the Human Genetics Commission, October 2010, http://www.hgc.gov.uk/UploadDocs/DocPub/Document/IP%20and%20DNA%20Diagnostics%202010%20final.pdf

Genetic selection of athletic performance, EP 1546403 (Genetic Technologies)

Patent Holder: Genetic Technologies Ltd, Australia
Date granted: 17.11.2010

Content:

The patent holder developed a process for selecting potential elite athletes. For this purpose blood samples were analysed from several hundred elite athletes (50 of the athletes had competed in Olympic Games), from blood donors, from children, from members of the Zulu population, from Australian aborigines and from adults participating in a talent-identification programme at the Australian Institute of Sport.

The patent covers methods to predict athletic performance in a human individual and to optimise training programmes. The gene selection targets young individuals who can be trained in professional programmes to become elite athletes.

Analysis:

This patent is the cause of several ethical problems. There is the question of whether those individuals who gave blood samples (such as the participants at Olympic Games) had consented to their blood being used for commercial purposes, and for a patent application. It is possible that the human rights of the athletes and the other individuals who gave their blood samples for other purposes, have been violated by this patent. For example, the blood of "71 healthy children participating in an unrelated study" was used to perform the relevant tests. The EPO did not examine these problems. The question of whether informed consent is necessary to apply for a patent has been discussed for years. So far, this has not resulted in particular regulations within patent law that could protect patients and other individuals against uninformed or even unwanted commercial usage of their genomic data. This case and others show the need for regulation.

Furthermore, when analysing this case, it has to be taken into account that after granting patents like this, the patent becomes an incentive to market the product as fast as possible (within the lifetime of the patent), and with the highest possible profits. Lobbyists may even apply pressure to allow testing in new areas, or even to support large scale testing.

There may be some sound reasons to conduct these tests if they involve independent experts to ensure the application of appropriate scientific criteria. However, the EPO have not defined or restricted commercial usage (for example, they could reduce the incentive for unwanted commercialisation by specifying the purpose of the gene selection within the claims). The range of possible usages is broad and can cause considerable ethical concerns. For example, the test could be used to select embryos during in-vitro fertilisation, or it might be used to choose a partner for reproduction. The usage of these tests during childhood or in schools can create a high level of (social, mental, psychological) stress in terms of what pupils deemed to have the "right" genetic conditions might be expected to achieve. Ultimately, the pressure to market relevant products may lead to a form of eugenic selection for athletes. The wording of the patent description shows that some of these concerns are founded in reality, especially as the patent holder actually draws some parallels between the breeding of race horses and the selection of human athletes:

"The information generated from such screenings would save the breeders and investors of horses (camels, dogs) a tremendous amount of time and money as well as identify the potential ability of an animal at an early stage of development. As with humans, the information generated from genotypic screening of a horse as well as other parameters (bloodlines etc.) may help to identify a potential elite athlete and/or design a better training regiment for a specific animal (e.g., a polo pony)." (page 7 of the patent)

The EPO did not consider any ethical problems during its examination. To ignore "public order" and "morality" (wording of Article 53a, EPC) so completely in this case, does not only draw attention to a deficit of the patent law. It also shows that the EPO has a problem with understanding its own responsibility. Very generally, the EPO rejects the examination of questions to do with the impact of granted patents, and leaves these questions to be dealt with in legal regulations outside patent law.

Melons, EP 1962578 (Monsanto)

Patent holder: Monsanto, USA
Date granted: 04.05.2011

Content and analyses:
This is a patent on melons derived from conventional breeding.

Further information at www.no-patents-on-seeds.org

Patent on bread, beer and fuels, EP 1370674 (Verenium)

Patent holder: Verenium Corporation, USA
Date granted: 18.05.2011

Content:
Microorganisms that produce enzymes (for degrading starch, amylases) and are active even under extreme conditions (such as very high or low temperatures) were collected from various locations (such as hot springs or particular marine regions). The gene sequences for these enzymes were re-synthesized in the lab and partially engineered according to economic criteria. The patent covers the gene sequences and the enzymes and processes in their production. In addition, a broad range of products were patented such as baked goods, beverages, textiles, paper, feed and production of fuels (from lignocellulosic fibres) which could be produced with the help of these enzymes.

Analysis:
Verenium emerged from a fusion that included Diversa. As a company, Diversa had focussed on bio-prospecting. It collected micro-organisms with a potential economic value on a global scale. This led to several comprehensive patent applications being filed which claimed enzymes isolated from those microorganisms, which might be used for various technical purposes (WO 2006096527, WO 2007055735, WO 2007092314). Diversa was exposed by several stakeholders for conducting biopiracy. The patent as granted is also based on bio-prospecting. The description of the patent states:

"Such enzymes may function at temperatures above 100oC in terrestrial hot springs and deep sea thermal vents, at temperatures below 0oC in arctic waters, in the saturated salt environment of the Dead Sea, at pH values around 0 in coal deposits and geothermal sulfur rich springs, or at pH values greater than 11 in sewage sludge."

The EPO did not ask any questions about the origin of the various gene sequences. The obligations under the Convention of Biological Diversity (CBD) are especially relevant in this context. If genetic resources are exploited, the Convention requests prior informed consent and that benefits are shared with the countries of origin.

Furthermore, the extremely broad claims are putting the legitimacy of current patent law into question. If the production of an enzyme is enough to claim, for example, a patent on bread, these kinds of patents can be abused to take control of large parts food production. There is no balance between the technical contribution of the patent and the scope of the patent.

Basically, the worrying developments exposed in this case are caused by a lack of legal prohibition pertinent to the patenting of gene sequences and microorganisms.

Mater Protein, EP 1328545 (government of the USA)

Patent holder: US Dept. Health and Human Services, USA
Date granted: 22.06.2011

Content:
US researchers discovered a gene sequence active in oocytes producing a protein that is crucial for fertility in mice. The patent holder named it "Mater Protein". Female animals in which this gene sequence is not active do not reproduce. Similarities in humans are probable. The patent describes several methods of influencing fertility by using the gene sequence and compounds such as proteins or antibodies. It covers the gene sequence, the protein, the antibodies and methods to influence fertility.

Analysis:
Patenting of human gene sequences is controversial. In many cases, research and development are massively hampered by these patent monopolies and, in general, these patents are far more concerned with discoveries and basic biological resources than with true technical inventions.

The EPO has already granted thousands of patents on human genes on the basis of EU Directive 98/44 EC. It is often enough to isolate the gene sequences and to describe a possible technical function to get such a patent. In the case of the "Mater Protein", the relevant gene sequence was simply detected. What is described is a genetic condition common to humans and animals that is crucial for their reproduction. By granting this patent, the genetic heritage becomes the intellectual property of a US agency. Beyond the question of the particular impact of a patent, this case touches on the very basic question of whether (human) genes can be seen as property, or whether the genome must be seen as a common heritage of mankind.

The granting of these patents means that a shift in paradigm is taking place in patent law. Patents are no longer a tool to protect inventions, but are becoming an instrument to grab and misappropriate basic resources. Companies, and in this case even the government of the USA, are using patent law in a global run to gain monopolies on the genome of micro-organisms, plants, animals and humans.

Greek Mountain Tea, EP2229950 (IBAM)

Patent holder: IBAM, Germany
Date granted: 22.06.2011

Content:
The German patent holders described how "Greek" Mountain Tea (that is also grown and harvested in other Mediterranean countries) interacts with the central nervous system. They announced that the tea preparations could be used to treat Attention Deficit Hyperactivity Disorder (ADHS). Sideritis is the botanical name of the plants and encompasses about 100 species, although the patent is not restricted to any particular species. The patent covers the plants as well as the extracts from the plants for the treatment of ADHS.

Analysis:
The claims cover the plants and their use in tea preparations. This is something that has been known in traditional medicine for more than 2000 years. Plants grow wild in Mediterranean countries such as Turkey, Spain, Portugal, Italy and Greek. They are described as having both sedative and stimulative effects.

It is possible to get a patent on naturally occurring compounds if they are shown to have unexpected, inventive usages. One of the best known examples in patent law is the isolation of a compound from death cap mushrooms that can help to treat poisoning from this fungus.

However, in the case of the Mountain Tea, no particular compounds were isolated, but the patent was granted on the whole plants as they are used in tea. The patent covers previously described effects of the plants on the nervous system as a sedative and relaxant, that can at the same time, also be a stimulant. The patent should be considered to be more of a delusion than an invention, since it is largely based on traditional knowledge and also uses the research of other scientists. For example, in Turkey there has, for several years, been ongoing systematic research to identify compounds in the Mountain Tea.

Good to know that in this specific case it might become difficult to implement the patent if its users are sufficiently well informed. If the plants are collected or bought as tea, they should be freely available for all purposes, even for the treatment of ADHS. The patent should only be valid if, for example, ADHS treatment is stated on the packaging. As a result, the same tea can be patented in one case, and in another it is not, without any difference between the plants.

Plants with stress resistance, EP 1616013 (Bayer)

Patent holder: Bayer, Germany
Date granted: 27.07.2011

Content and analysis:
The patent covers plants with a higher stress resistance, with and without genetic engineering. For more information, please see: www.no-patents-on-seeds.org

Human sperm, EP 1263521 (Ovasort)

Patent holder: Ovasort Ltd, Cardiff, UK.
Date granted: 10.08.2011

Content:

The patent covers processes for in vitro fertilisation. The patent holder developed a method to select sperm cells that contain a female X-chromosome. To do this, sperm cells are separated by an electrical field. The claims cover not only the process of separation, but also the sperm (of humans and animals) as well the production of female animals with the selected sperm.

Analysis:

The patent violates current European patent law, which states, "the human body, at the various stages of its formation and development (…) cannot constitute patentable inventions." (Art. 5 of Directive 98/44 EC). Recital 16 of EU Directive 98/44 explains that germ cells (sperms and oocytes) are also covered by this exclusion.

This patent constitutes a monopoly right to human sperm cells and is therefore not acceptable from the perspective of human dignity. Furthermore, marketing under this patent might encourage sex selection in human embryos that can itself create huge ethical problems.

This patent is not the only one that has been granted in this category in Europe: In 2003, Vitrolife (Sweden) was awarded a patent on frozen human embryos and oocytes (EP 1121015). In 2005, XY (US) was awarded a patent on human sperm (EP 1257168). Merck-Serono holds a patent on the use of human oocytes, and in 2003, a patent on human sperm cells was granted to the same company (EP 1196153). By granting these kinds of patents, the EPO is encouraging the commercial exploitation of the human body.

A further problem that should not be overlooked has been caused by the claim covering the production of animals with the selected sperm. According to the "product by process" rule, this patent also covers the animals itself. This might have serious implications for agriculture and animal breeding. Thus patent violates Art. 53b, EPC, which excludes patents for breeding of plants and animals.

3. Overview of patent applications and granted European patents in the field of biotechnology

The "No Patents on Life!" initiative has collected the figures based on the European Patent Office database. The international classifications (IPC) used for the research are given for each figure.

Following categories are also used here:

- WO ... A: These applications are filed at the World Intellectual Property Organisation in Geneva (WIPO) and then transferred to various national or regional patent offices, who examine the applications and possibly grant the patents. Many of these applications are also transferred to the EPO.
- EP ... A: These patent applications are filed at the EPO, partially via WIPO, partially directly at the EPO.
- EP ... B: These patent are granted in Europe .

Currently, around 53,000 European patent applications in biotechnology have been filed, around 18,000 had been granted by the end of 2010.

These figures show that the number of patent applications in the field of biotechnology has been in decline during the last ten years. In contrast, the overall number of applications rose steadily until recently a plateau was reached. The decline is predominately in the numbers of patent applications on gene sequences, on pharmaceuticals (developed by genetic engineering) and on laboratory animals. In the context of plant breeding, gene diagnosis and stem cell research the decline is weaker, and there has even been a slight increase.

These figures reflect the considerable hype around patent applications in the fields of genetic engineering and biotechnology at the turn of the century. However, there was no steady trend in the development of new medications. In contrast, many gene diagnosis applications were developed, leading to an increase in the number of patents filed.

Relatively few products from the plant-gene-technology sector have actually been placed on the market in the last 20 years. Thus the figures on patent applications in this field only reflect technological developments to a limited extent. Instead, a large number of these applications are attributable to the intention to use patent law to gain control over genetic resources that are important for plant breeding and the future of world food security. Many critics see this development as blatant abuse of patent law (www.no-patents-on-seeds.org).

By the end of 2010, thousands of patents on human gene sequences, plants and animals had been granted:

Gene sequences from human and animals:	3,700
Animals:	1,100
Plants:	1,800

Fig. 1: Overall number of patent applications and granted patents at the European Patent Office

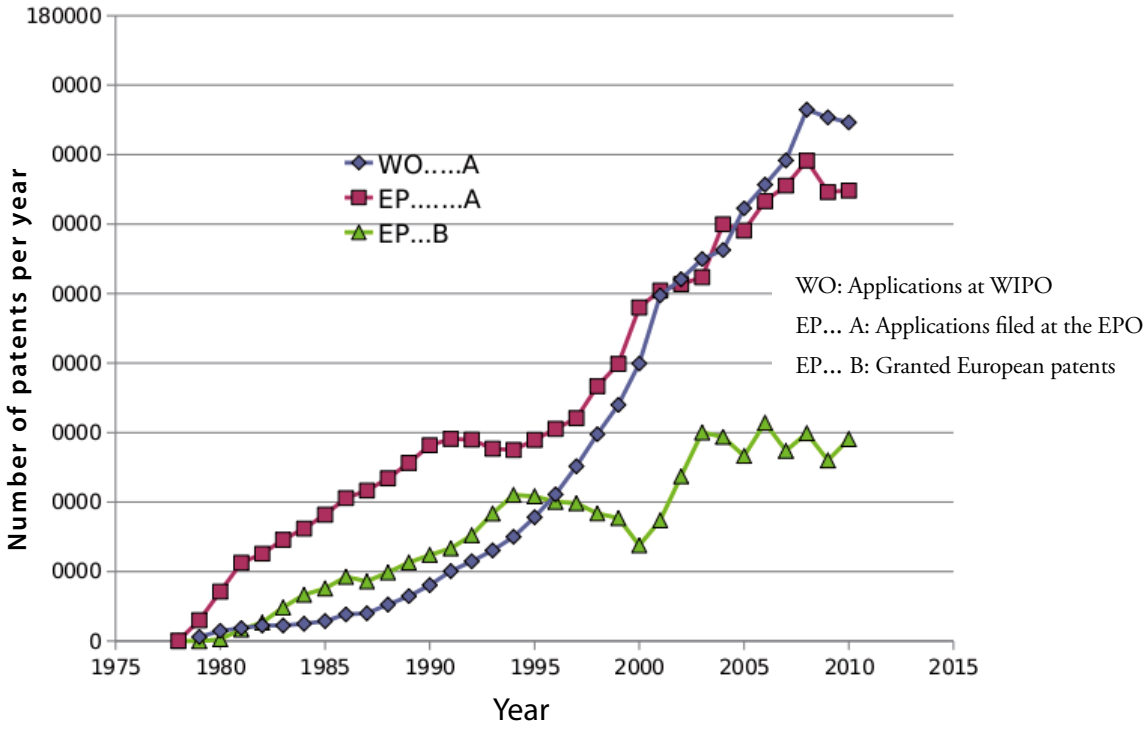


Fig. 2: Number of patent applications and granted patents at the European Patent Office in biotechnology

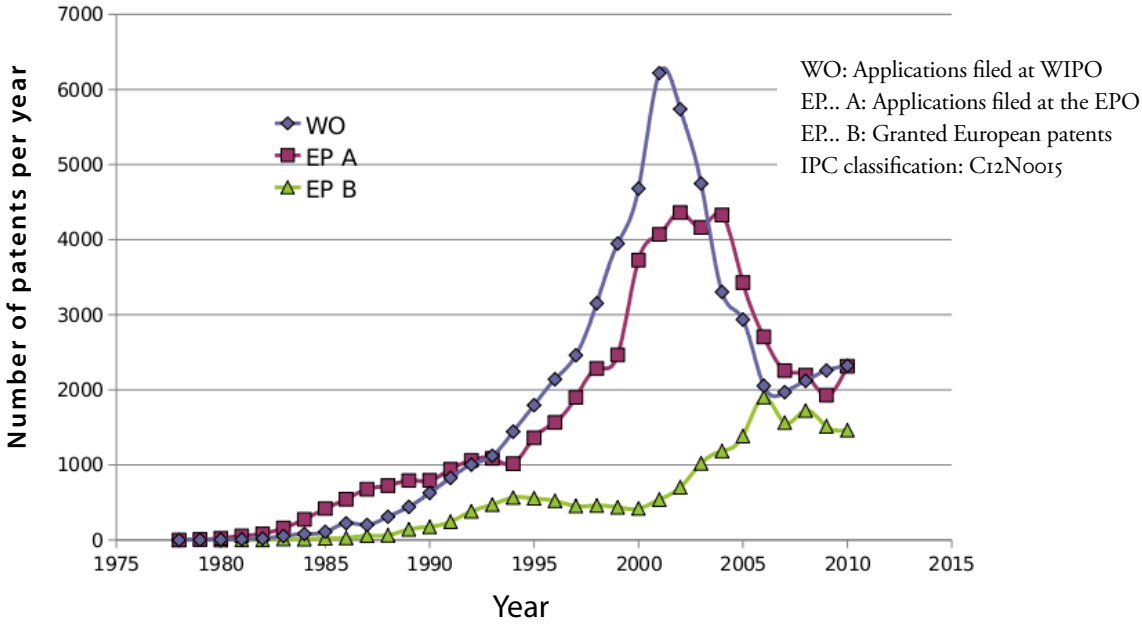


Fig. 3: Number of patent applications and granted patents at the European Patent Office on gene sequences of humans and animals

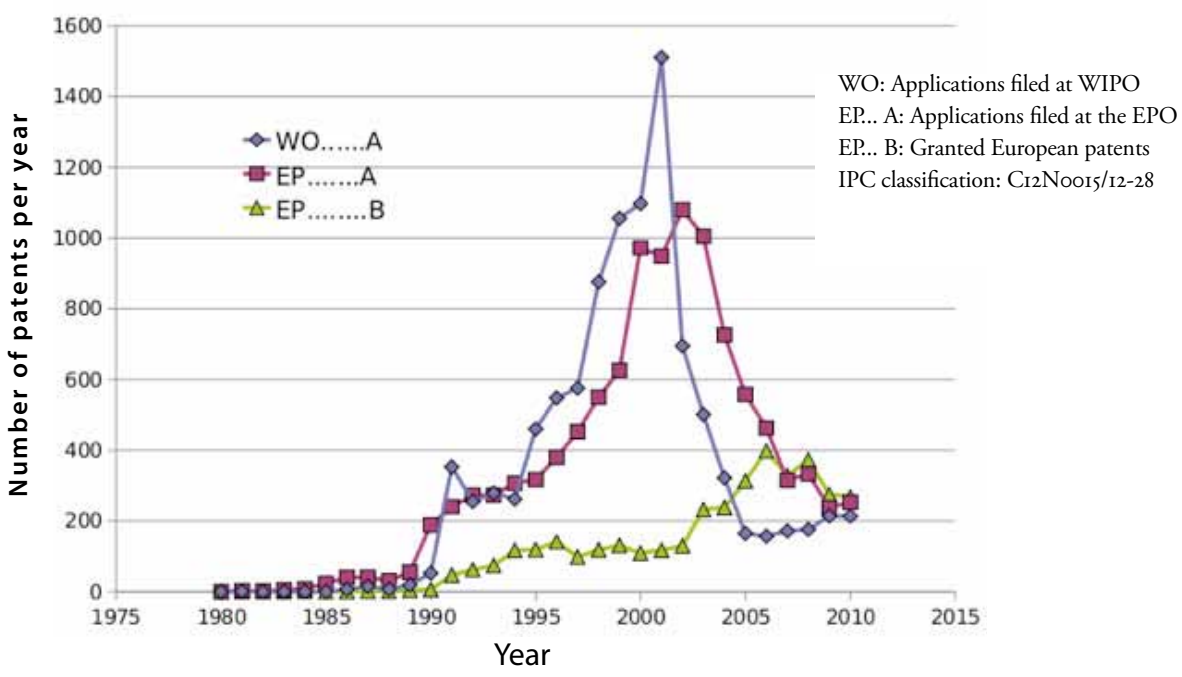


Fig. 4: Number of patent applications and granted patents at the European Patent Office on gene diagnosis

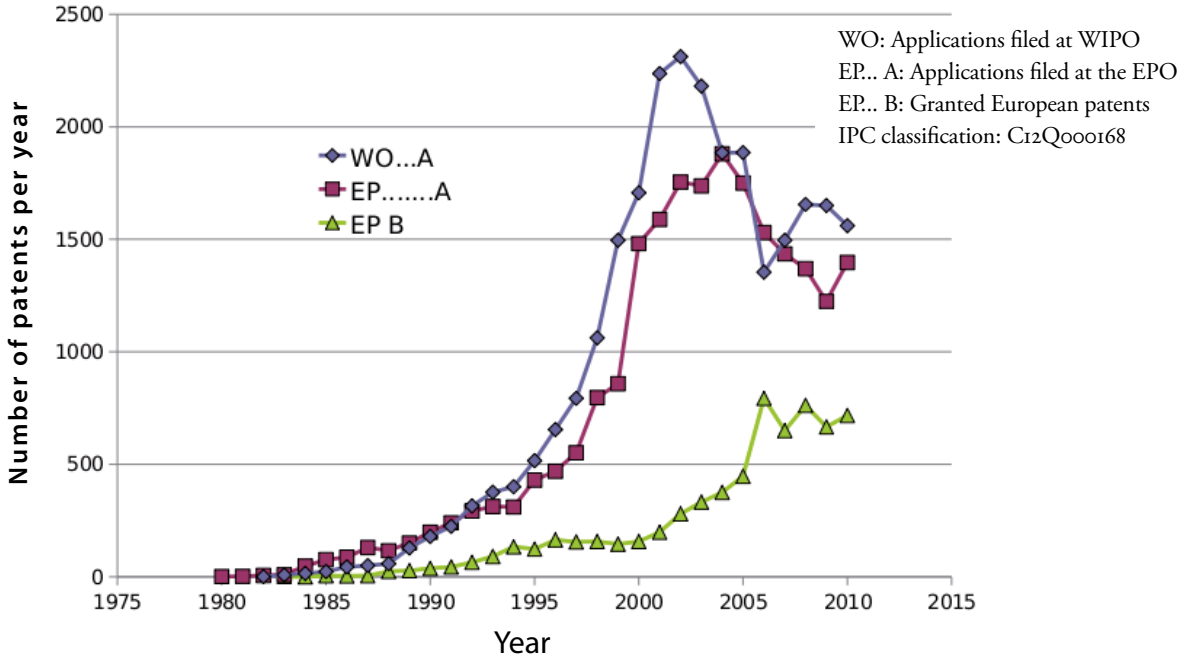


Fig. 5: Number of patent applications and granted patents at the European Patent Office on pharmaceuticals in general

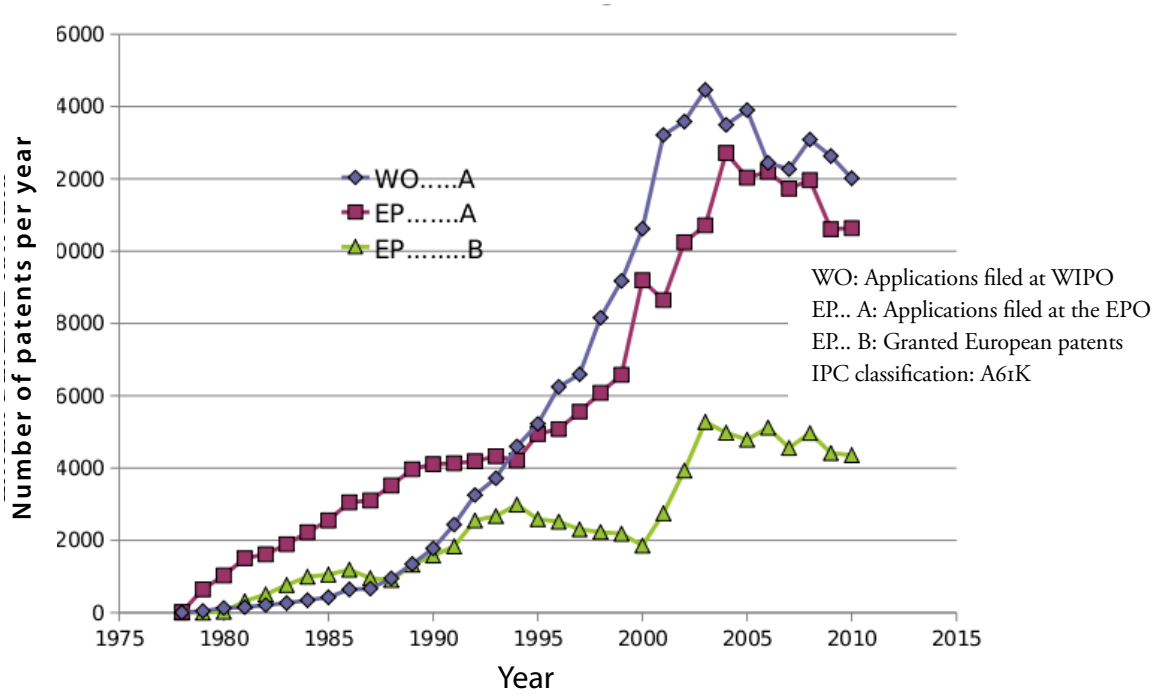


Fig. 6: Number of patent applications and granted patents at the European Patent Office on pharmaceuticals developed with the help of genetic engineering

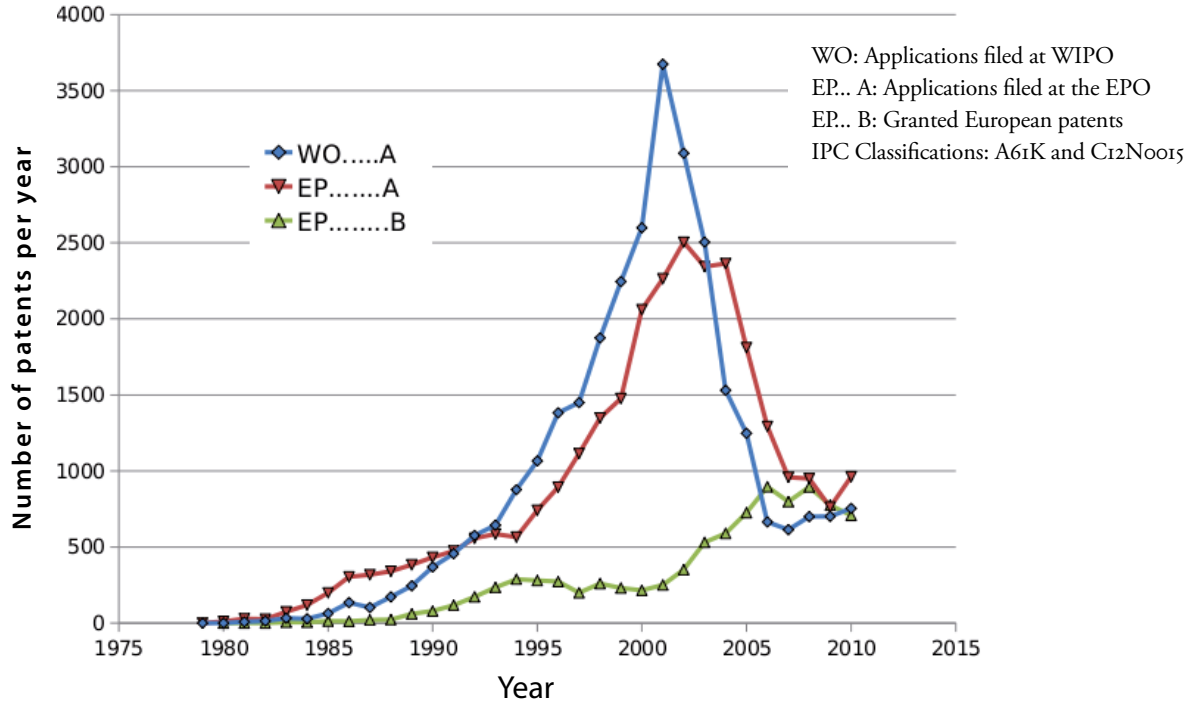
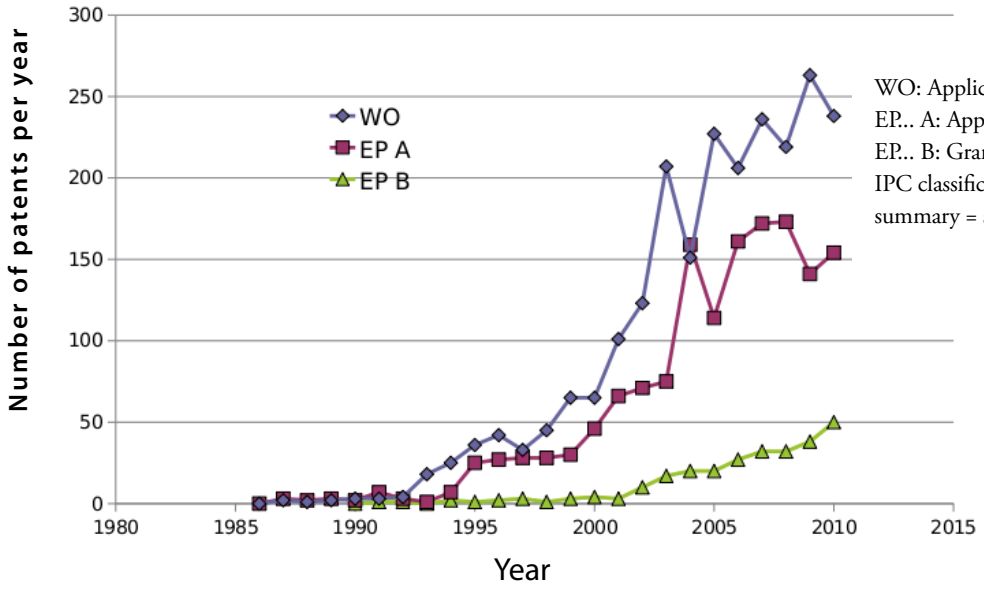
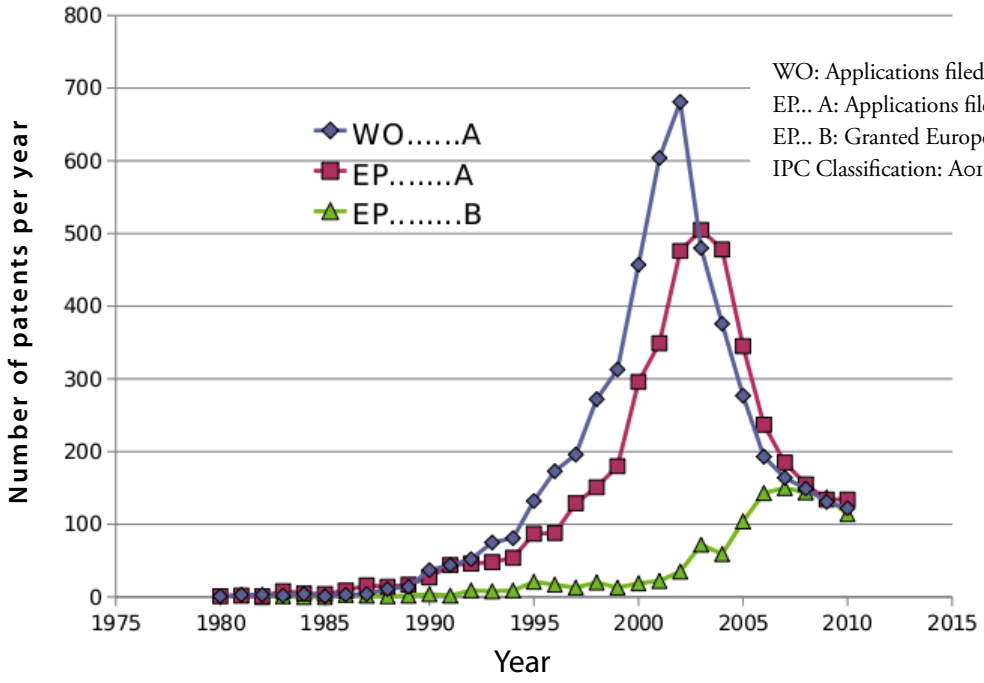


Fig. 7: Number of patent applications and granted patents at the European Patent Office on stem cells



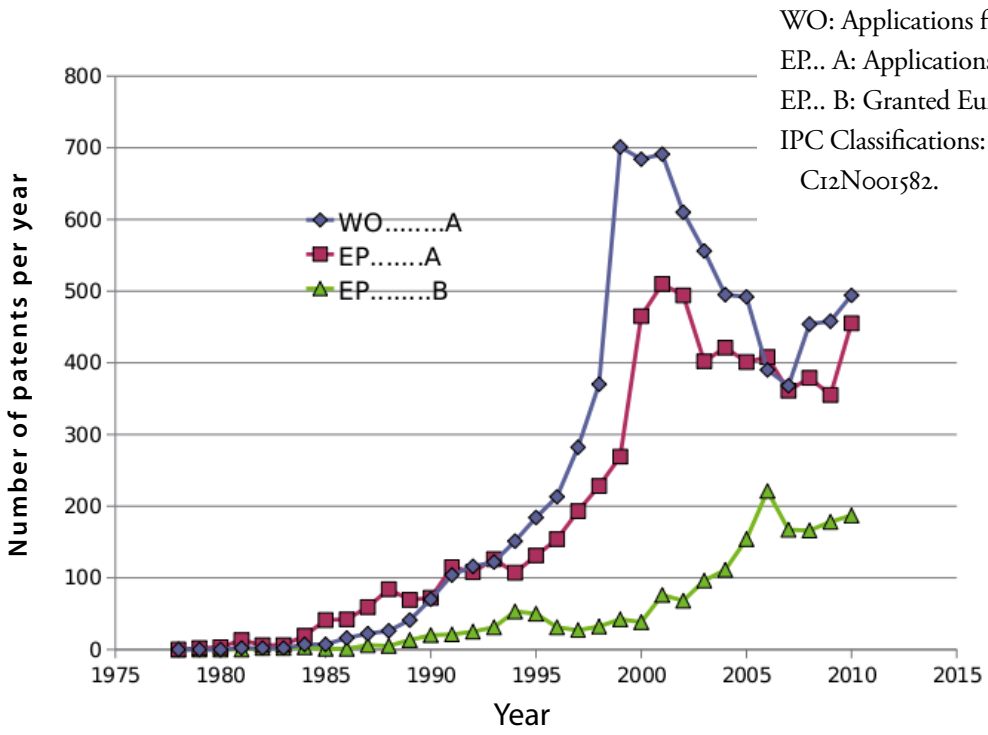
WO: Applications filed at WIPO
EP... A: Applications filed at the EPO
EP... B: Granted European patents
IPC classifications: C12N005 and engl. title or summary = stem or pluripotent

Fig. 8: Number of patent applications and granted patents at the European Patent Office on animals



WO: Applications filed at WIPO
EP... A: Applications filed at the EPO
EP... B: Granted European patents
IPC Classification: A01K0067

Fig. 9: Number of patent applications and granted patents at the European Patent Office on plants



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