BIOETHICS NEWS

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Reports

The ethics of synthetic biology

The aim of synthetic biology is to produce new biological systems that can be used to improve those currently existing, or to create new ones.

Some ethical concerns raised by these new biological techniques have been recently addressed in a special edition of Bioethics (Bioethics; number 8; pp ii-iii-2013).

The ethical debate on synthetic biology has taken a different route to discussions on gene therapy, since in the latter the ethical problems basically arose due to objective failures in the technique itself, even resulting in the deaths of some patients.

In synthetic biology, these types of regrettable accidents have not (yet) occurred, so the ethical reflection turns more naturally to examining the techniques themselves and their possible applications in more depth.

As discussed in an Editorial in the Bioethics issue cited, "despite the interest that it arouses, the technique of synthetic biology is still a young field, as a recent consultation in PubMed detected fewer than 100 entries using the search term "synthetic biology, DNA and ethics"".

Some consider that this lack of ethical references is because this new biological field does not present any major ethical problems, but it is more likely that profound reflection on the topic has not yet commenced.

One issue that was raised on the ethics of synthetic biology is whether a moratorium should be proposed for this type of research, as has occurred in other scientific areas (Asilomar, for example), especially as concerns the safety of the techniques. This seems reasonably assured however, so the ethical problems may arise more around "social justice and biodiversity".

With respect to humans, synthetic biology may provide objective breakthroughs in the treatment of various diseases, the development of new drugs and vaccines, facilitate tissue regeneration or even the production of completely synthetic cells.

Therefore, the possibility of generating new biological systems, which do not presently exist in nature, or reconstructing or modifying others that do not exist right now, may result in bioethical problems on the moral status of life, reflection on the risk/benefit of new technologies and the implications that these could have for future generations.

To delve a little deeper into these questions, a major European project was conducted between 2009 and 2012 under the European Commission´s Seventh Framework Programme: Synthetic Biology for Human Health: the Ethical and Legal Issues (SYBHEL)" (Sybhel.org).

This project set out to evaluate the ethics of synthetic biology, its possible impact on human health, to suggest recommendations on the regulation and commercial aspects of synthetic biology as applied to human health and especially to determine the policies that should govern this new scientific field.

Within this general framework, specific aspects considered were the relationship between synthetic biology and the philosophical and ethical issues that

may arise around the concept of life.

In the Bioethics issue cited above, various specialists addressed some of the topics to which we have referred, particularly how synthetic biology could affect biodiversity, since on producing new forms of life, the number of species that currently exist could increase; they also evaluated how the production of new organisms could affect the concepts of health and disease, to what extent synthetic biology could affect social justice, and even whether synthetic biology could be a mistake in itself, due to the difficulty in establishing general ethical rules and the advisability of case-by-case assessment.

In any case, as stated in the Editorial of the aforementioned Bioethics issue discussed "Synthetic Biology is a promising technology that raises new ethical and philosophical issues", but which may also open great new opportunities for improving human life.

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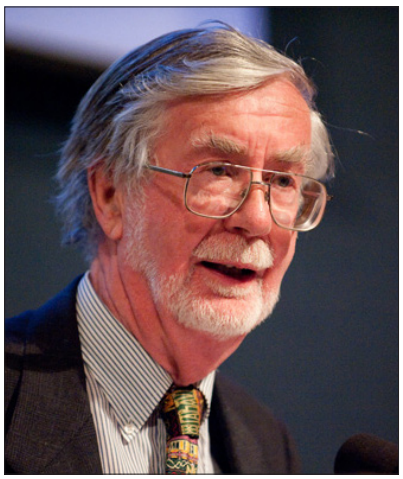
Is it advisable for nuns to take contraceptives as preventive treatment to reduce the risk of uterine or ovarian cancer?

A lively debate on this subject has been recently published in the Los Angeles Times, following an opinion piece authored by Malcolm Potts[1], professor of Obstetrics and Gynaecology at Berkeley University in California (U.S.) (published 30-I-2014) and a group of readers who responded to his comments in the same newspaper a few days later (6-II-2014).

In the article, Potts openly criticised the opposition shown by a group of nuns from the state of Colorado (U.S.) to comply with President Obama's governmental precept referring to the mandatory funding of contraceptive methods by companies for their employees.



Malcolm Potts

Potts maintains that it is advisable for the nuns themselves (who for conscientious reasons object to encouraging the use of these methods among contracted staff) to use it as a way of reducing the risk of certain types of reproductive cancers.

The author states that, in populations of women who have had few or no pregnancies, on having had more ovulatory menstrual cycles (he says that women who have had several children with long periods of breastfeeding may have had no more than 40 ovulatory cycles in their fertile lifetime, compared to the 400 that may have occurred in childless women), the risk of suffering ovarian or uterine cancer is significantly increased.

Potts is an advocate for the right to abortion, and was the first health director of the influential American Planned Parenthood Federation, which provides family planning services.

The author began by presenting scientific information (biased, as we will now explain) to then move on to a crushing moral evaluation of the Magisterium of the Church on contraceptive methods and human sexuality.

Nevertheless, we must ask ourselves if Potts' statements are true with respect to the indisputable benefits of oral contraceptives in childless women to reduce their risk of cancer.

In a reply to the article author[2], Dr. Rebecca Peck, professor at Daytona Beach University in Florida (U.S.), countered that the statements made by Potts were true, but only in part. According to Peck, ovarian and uterine cancers are much less common than breast cancer. Uterine cancer has an estimated prevalence of 1 in 19 women throughout their lifetime, and 1 in 72 women in the case of ovarian cancer. However, breast cancer appears in 1 in 8 women.

To back up his statement, Potts cited the National Cancer Institute, the leading U.S. agency for cancer research. However, what he did not consider is that the same agency reported that, unlike the case of uterine and ovarian cancers, the risk of breast, cervical and liver cancer is increased with the use of oral contraceptives[3,4]. Breast cancer is more common in women

who started using oral contraceptives in adolescence.

In women with no children and who therefore have not breastfed, the prevalence of breast cancer is higher than in mothers who have breastfed. Thus, the use of oral contraceptives in this case, as in the case of the nuns, would increase this risk even further.

It should also be taken into consideration that oral contraceptives can predispose women to thromboembolic problems. In this respect, we have recently published a paper in the journal American Journal of Obstetrics and Gynecology[5] on this topic, and there are related reports in the document archives of the Bioethics Observatory website[6].

From our point of view, we believe that the medical risk/benefit balance does not support the preventive use of contraceptives in celibate women, such as the nuns referred to in this article, to reduce the risk of uterine and ovarian cancer. In the end of course, this must be subject to the will of potential users, provided that they have been medically well-advised.

What seems clearer is that, if they are certainly not going to have sex, morally there is no major issue for them to take oral contraceptives for medical purposes, as long as the drugs used are virtually one hundred percent contraceptive.

Justo Aznar and Julio Tudela

References

[1]http://www.latimes.com/opinion/commentary/la-oe-potts-catholic-nuns-birth-control-20140130,0,4138959.story#axzz-2ru1N9l27

[2] http://www.catholicnewsagency.com/news/la-editorial-wrong-on-birth-control-catholic-women-charge/

[3] http://www.cancer.gov/cancertopics/factsheet/Risk/oral-contraceptives

[4] Burkman R, Schlesselman JJ, Zieman M. Safety concerns and health benefits associated with oral contraception. American Journal of Obstetrics and Gynecology 2004; 190(4 Suppl):S5–22

[5] Aznar J, Cerdá G. Factor V Leiden carriers taking oral contraceptives have an increased risk of thrombosis. American Journal of Obstetrics and Gynecology. 2013;209(2):156

[6] http://www.observatoriobioetica.com/pp/10-1.html#5

Summary: It has sometimes been proposed that it would be advisable for nuns to use contraceptives to reduce the risk of certain types of reproductive cancers. This report states that this is not easy to sustain for medical reasons, although there are no ethical drawbacks if the drugs used act by a virtually contraceptive mechanism.

Description: Use of contraceptives in nuns to prevent reproductive cancers.

News

Embryos with two mothers and one father

The exchange of genetic material between oocytes and embryos offers a new reproductive option for the prevention of mitochondrial diseases. It has been found that mitochondrial dysfunction could be a cause of major diseases that can affect various organs. Tissues with high energy demands, such as the brain, heart, muscles and central nervous system, are severely weakened when there are mitochondrial abnormalities. Mitochondrial diseases can be due to mutations in mitochondrial DNA or in the nuclear genes involved in mitochondrial function.

There is currently no effective treatment for patients with mitochondrial diseases, so great emphasis is being put on preventing the transmission of these conditions.

One new possibility in this respect is cloning using nuclear transfer between oocytes, which essentially consists of extracting the nucleus of the oocyte from a woman who has abnormal mitochondria and transferring it to another oocyte of a healthy woman, in whom the nucleus has already been extracted. In this way, a new oocyte is obtained with the mitochondria from the oocyte of the healthy woman and the nucleus of the affected woman. This new oocyte can be fertilised with sperm from a healthy donor, so that a blastocyst would be obtained that was unaf-

fected by the mitochondrial disease suffered by the patient (Fertil Steril 101; 31-35, 2014).

Although the technical application of this technique appears a long way away, because as we know, human cloning has yet to be achieved, it has been proposed from various research fields related with assisted procreation.

Moreover, the major ethical difficulties entailed in this technique should not be forgotten, since in addition to those of human cloning, it would have those derived from the production of embryos, which if viable (which is doubtful) would have two mothers and one father.

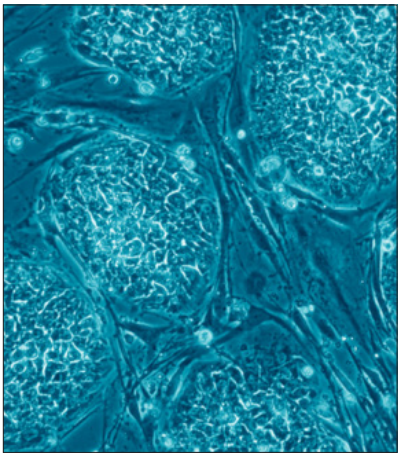
Summary: Nuclear transfer between oocytes enables a hybrid to be created from the oocyte of a woman with mitochondrial disease and another from a healthy one. The hybrid can then be fertilised, thus avoiding the possibility of transmitting mitochondrial diseases. This technique is still a hypothetical possibility for reproductive purposes, in addition to entailing major ethical problems.

Description: Embryos with two mothers and one father

Signs of aging in the embryo

The process by which cells cease multiplying is known as senescence. In 1961, biologists Hayflick and Moorehead cryoconserved human foetal cells, and found that these divide around 50 times and then simply stop doing so, as occurs in the human body.

In fact, senescent cells are involved in many of the signs of aging: wrinkled skin, cataracts and arthritic joints, which are produced by the effect of an increase in these cells. On the contrary, it has been found that by decreasing senescent cells in mice, signs of rejuvenation can be detected in these animals.



Considering that in all research, senescent cells have been found only in old or damaged tissues, the last place one would expect to find them would be at the very beginning of life, in the embryo. Now however, three scientific teams have reported that they have observed the same phenomenon at this point.

For the first time, senescent cells have been found in embryos, and scientists have presented proof that senescence is crucial for their proper development.

This discovery raises the possibility that the start and end of life are intimately connected. In order for life to have a good start, senescent cells are needed, i.e. youth needs a little bit of old age.

Scott Lowe, an expert in senescence at Memorial Sloan-Kettering Cancer Center, who did not participate in the research, has lauded the studies, which point to the unexpected role of old age, and predicted that it would provoke a spirited debate between developmental biologists, who study how embryos are formed. “They are going to love or hate this discovery”, said Lowe.

Although senescence can be a powerful defence against cancer, by stopping cell multiplication, this is at a high cost, since although tumour processes can be prevented, an increasing number of senescent cells accumulate, with a resulting increase in

In the middle of the last decade (2000), William Keyes, a biologist at Cold Spring Harbor Laboratory in Long Island, studied the way in which senescence leads to aging based on genetic experiments with mice; he did not find any evidence that the DNA in senescent cells in embryos was affected. After transferring to the Center for Genomic Regulation in Spain, he decided to continue his research on how normal cells started to become senescent, proposing the hypothesis that they do so in response to signals from neighbouring cells.

Once an embryonic cell becomes senescent, it does two things that all senescent cells do: it stops dividing and it secretes a type of chemical cocktail, which may stimulate inflammation.

New experiments suggest that this substance plays a different role in the embryo than in the adult body. It may act as a signal sent to other cells to become different tissues. It could also tell the tissues to grow at different rates into different shapes.

Keyes suspects that the role of senescent cells

could be crucial to the proper development of the embryo. Consequently, any action in senescent cells could have serious consequences for embryonic life (The New York Times, 21 November 2013).

Summary: Senescence is a process present in aging cells. Now, for the first time, senescent cells have been found in embryos, which seems to be important for normal embryonic development.

Description: Signs of senescence are detected in embryos

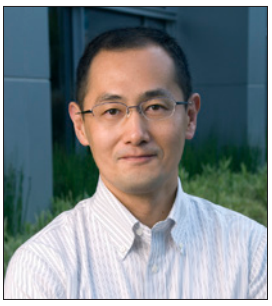
In Brief

01 Interference in the use of contraceptives in HIV positive women

The use of contraceptives in HIV positive women who are receiving antiretroviral therapy could be problematic, since antiretroviral therapy may reduce the efficacy of contraceptives in preventing unwanted pregnancy, while oral contraceptives may increase the toxicity of antiretroviral therapy (British Medical Journal 2013; 347: f6695).

02 The technique for reprogramming adult cells has been improved.

One problem in reprogramming adult cells, using the technique proposed by Yamanaka in 2006, is that the percentage of cells reprogrammed is low, and not all are reprogrammed at the same time. Now, it appears that this problem has been resolved, after Israeli scientists developed a method that allows practically 100% of the cells to be reprogrammed within a week, and furthermore, all at the same time. In order to achieve this, they only had to silence a single gene, Mbd3, which is apparently responsible for counteracting pluripotence (Nature, DOI: 10.1038/nature 12587, 2013).



04 A technique to reduce the risk of infection by iPS cells when transplanted

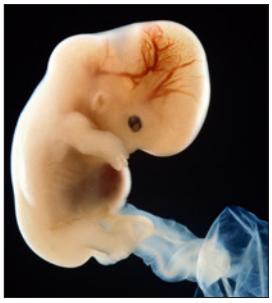
Another major advance in cell reprogramming and in obtaining iPS cells was achieved by researchers at Osaka and Kyoto universities, led by Masoto Nakagawa and Shinya Yamanaka, who succeeded in developing a method by which the cells generated have a lower risk of infection when transplanted. To achieve this, they used laminin-511, a synthetic protein (Scientific Reports online 8-I-2014).

05 Medical risks of in-vitro fertilisation

Children born using in-vitro fertilisation have double the risk of dying in the first 28 days after birth than those conceived naturally. They are also more likely to be premature and above all, have three times the likelihood of having low birth weight (PLOS ONE; 2014; 9, nº1, e80398, January 2014).

06 Alternative to the use of saviour siblings

One alternative to the creation and use of saviour siblings is the possibility of deriving cell lines from the embryos created (saviour embryos). Cells are then differentiated from them that can be transplanted to treat the sick sibling (Reproductive Biology online 20; 667-674, 2010). This new possibility would undoubtedly have similar ethical difficulties to the production of saviour siblings, if not more, since in this case, the saviour embryos produced would be destroyed to produce the required embryonic cell lines.



07 Regulation of genetic testing in the United States

According to a report by the Presidential Commission for the Study of Bioethical Issues in the United States, companies, clinicians and researchers must inform consumers, patients and study participants of incidental findings in relation to genetic tests and research trials that could affect their health. This report has been released by the Commission itself, as revealed in The Scientist (12 December 2013). Earlier that same year, the

American College of Medical Genetics and Genomics (ACMG) had made recommendations on the advisability of alerting patients about 57 genetic diseases that could be accidentally discovered after performing individual genome sequencing. The Presidential Commission has now indicated that the patient has the right to decide whether he or she wishes to know the result of that test. According to Commission member Stephen Hauser, incidental findings and the resulting problems are increasing in magnitude. People who undergo genetic test using whole-genome sequencing should be warned that "Each of us has scores of deleterious mutations in our genes and these will be picked up every time a whole-genome sequence is obtained". Clinicians and researchers must anticipate that there could be incidental findings in the tests and inform the patients and persons involved before the tests are carried out. The Commission also advocates shared decision-making. Another of the Commission's recommendations is the creation of disease-risk lists, about which clinicians involved in genetic counselling should be informed; patients should also be advised of their occasional finding in a genetic test and their right to know or not (http://bioethics.gov/node/3183).

08 Lacrimal and salivary glands have been created artificially

Last October, Nature Communications (DOI: 10.1038/ncomms.3497) published two studies describing the bioartificial creation of lacrimal and salivary glands. After their production, they were able to be transplanted in mice. Once transplanted, the organs created connected to the animals' nervous system and began to function. This is undoubtedly a new possibility for the treatment of various diseases, especially xerostomy, which is characterised by dry mouth.

09 HIV can be stored in certain human cells and remain active there

It is known that AIDS can be treated with new antiretroviral drugs, converting it from a fatal disease to a chronic one. However, the disease is not completely cured, although it is not known for certain why. In relation to this, on 12 January 2014, a group of American researchers published their findings (Nature Medicine, DOI: 10.1038/nm.3445) showing that the virus can hide in cells of the immune system, CD4+T cells, which can be used as reservoirs to keep these cells functioning for a long time, but dormant. Hence the disease cannot be completely cured, as the HIV remains in the patients' body, although inactive.