



Europäische Akademie

zur Erforschung von Folgen wissenschaftlich-technischer Entwicklungen
Bad Neuenahr-Ahrweiler GmbH

Direktor:
Professor Dr. Carl Friedrich Gethmann

Newsletter

Akademie-Brief ▪ No. 25 (April 2001)

Editorial

The Europäische Akademie publishes the results of its project groups in its book series. In addition, these results are presented at special events to the public. Since the Federal Government's move to Berlin the presentations have been held at different locations in the capital. E.g., the study on "Environmental Standards" was presented at the "Berliner Medienclub", "Xenotransplantation" at the new building of the "Landesvertretung" Rheinland-Pfalz. The presentations are meant to combine the tasks of science with the public's legitimate demands for information.

The studies should illustrate that the scientific community takes on the responsibility for problems arising in the context of scientific work: those problems are dealt with in an interdisciplinary manner and the results of the combined reflections are discussed with the public. In this way science is able to meet the public and scientific demands in an effective way. The presentations consist of a welcoming speech held by representatives of the Europäische Akademie's partners and a summary of the concerned topic by members of the project group followed by a discussion. Apart from relevant scientific communities the representatives of appropriate business research companies are addressees of the lectures. Most of all, representatives of society in its political organisation, Members of Parliament and ministry officials are addressed. Furthermore, journalists who transport news into the "real" public are an important target group.

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Focus

Stem Cell Therapy. The Potential Importance of Research into "Therapeutic Cloning", Embryonic Stem Cells and Adult Stem Cells

Robin Lovell-Badge

We have now become very used to the idea of organ transplants in medicine, for a wide range of problems from cataracts to kidney or heart failure. However, we are also all aware of the frequency with which they fail. Immune rejection is one of the most common causes of graft or transplant failure. There is also a serious shortage of donors. Both problems could be solved if autologous grafts are performed, taking tissue from one part of the body to repair another. But there are relatively few cases where this can be done at present – skin grafts for burns victims, or valves from leg veins used to repair heart valves. Rather than using whole organs or tissues, an alternative would be to isolate and use special cells called stem cells.

The idea behind stem cell therapy, is to isolate such cells that have been lost, multiply them *in vitro* and then use them to replace damaged tissue. Many more types of disease could be treated in this way than with conventional organ transplants, as often it is one cell type that has gone wrong rather than the whole organ. It may also be particularly suitable for chronic debilitating diseases, such as Parkinson's, Multiple Sclerosis and diabetes, as well as for cases of acute trauma, such as cardiac infarction or spinal cord injury.

However, it may be too difficult to isolate the appropriate stem cells from the affected tissue in the patient or they may not be able to grow well enough *in vitro* to give sufficient numbers of cells for therapy. But there are potential solutions to this problem. Contrary to former suppositions, recent work has shown that it is possible for one type of stem

cell to change into another in some circumstances. For example, for a blood stem cell to give nerves. This might allow patient-specific stem cell therapy, where stem cells from one part of the body are used to repair damage to another. Alternatively, we could use special stem cells known as Embryonic Stem cells or ES cells. These are derived from early "blastocyst" stage preimplantation embryos (about 5 days old in humans).

In mouse models it has been shown that ES cells are both immortal and "pluripotent", i.e. they can essentially be grown indefinitely, in very large numbers, while retaining the ability to give rise to all cell types of the body. Many of these cell types, e.g. nerve cells, muscle cells, cells that form blood vessels, pancreatic islet cells, etc. can differentiate not only *in vivo*, after reintroduction of the ES cells back into an early embryo, but also *in vitro*. The latter is very impor-

tant and would be essential if the cells are to be used for therapies. The more specialised cells that have differentiated *in vitro* can be grafted back into animals, where they have been shown to, at least partially, correct a range of diseases, including mouse models of Parkinson's and diabetes.

Human ES cells have been available for about three years and they clearly share many of the properties of those from mice. So, could we use human ES cell lines to develop cell-based therapies? It would seem likely, except for the big problem of immune rejection. The few lines that have been established so far would not overcome this problem. One possibility is to have available many lines, perhaps a bank of 100 or even 1000, which would be tissue-typed, so that a close enough match would be available for most patients and for most types of therapy. But this would still require the use of immunosuppressive drugs to prevent rejection of grafted cells. These have consequences that would need to be weighed against the likely benefit of the therapy.

The ideal option would be to isolate ES cells from the patient, but of course the right cell type to do this only exists within the very early embryo. What if we could reverse the normal direction of differentiation and obtain suitable stem cells from an adult cell? The nuclear transfer or cloning techniques, which gave rise to Dolly, showed that it is indeed possible to reprogramme the nucleus of an adult cell. Beside reproductive aims, which will not be discussed here, this has led to the notion of cell-nuclear replacement or "therapeutic cloning".

The unfertilised egg has a large amount of cytoplasm that contains the factors that normally reprogramme an incoming sperm nucleus into one appropriate for an early embryo. It also turns out that this cytoplasm can reprogramme an adult cell nucleus, essentially tricking it into behaving like a nucleus of a one-cell embryo. So, by removing the oocyte's own nucleus and replacing it with that of an adult donor cell, it is possible to obtain an embryo. This is the nuclear transfer technology that could in theory be used to derive human ES cells for patient-specific therapeutic purposes.

In principle, a biopsy would be taken from the patient and an adult cell reprogrammed by nuclear transfer into an unfertilised egg. The resulting early embryo would be cultured *in vitro* to the blastocyst stage, the inner cells isolated and used to derive ES cells. These would have the same genetic make-up

as the patient. We could then apply techniques to direct these to form the relevant cell type to cure the patient. If there is a genetic cause to the disease it may be possible to correct the genetic defect in the stem cells, prior to grafting the cells back into the patient.

So, we have two potential strategies for patient-specific stem cell therapy: adult stem cells or ES cells derived by cell-nuclear replacement. There appear to be more ethical concerns about the latter, so it is worth comparing the two and looking at some of the factors that we need to consider before we can attempt to do stem cell therapy.

Adult stem cells are often very rare and inaccessible, for example, blood stem cells are present at very low numbers in blood (about 1 in 10,000,000) and while more frequent in bone marrow, they are still rare. Cord blood, obtained from the umbilicus at birth is another source of blood stem cells, but these need to be banked and stored in anticipation of any disease and there is no indication that they can give rise to cells other than those typical of the haematopoietic system. Grafts of pancreatic islets have been shown to work to treat diabetes, but for each patient there is a requirement for multiple donors and aggressive immunosuppression. With respect to neurons and glia, stem cells do exist in the brain and spinal cord, but these central nervous system or CNS stem cells are rare and tend to be in regions that are difficult to access safely. For many other adult cell types we do not know where the stem cells are or if they even exist. For example, no one has identified those for the lining of the lung, needed in cases of Cystic Fibrosis, emphysema or after inhalation burns. On the other hand, we know that ES cells are able to give rise to all cells of the lung in chimaeric mice, so it is likely that conditions could be found to obtain them *in vitro*.

To make human ES cells, we need to consider either the use of spare embryos from IVF programmes or the use of nuclear transfer to reprogramme an adult cell. Some people consider the use of spare embryos left over from IVF programmes to derive ES cell lines as unacceptable. However, the cell nuclear replacement technique ("therapeutic cloning") uses unfertilised eggs. These are not given the same moral value and, especially as their genetic material is removed and replaced with an adult cell nucleus, the ES cell line could be considered just as an extension of the adult.

It is often difficult to isolate pure populations of stem cells from adult tissues, they tend to grow poorly and they often

have a limited lifespan. Therefore it may be difficult to obtain sufficient numbers for therapy, moreover, it can be much harder to select desired properties from cells that grow slowly. There is also a risk that mutation occurring *in vitro* may result in faster growing cells, which will take over the culture. These may have changed in other properties, such that they will no longer be suitable for therapy and indeed they may no longer be safe to use.

With respect to the range of cell types that a given adult stem cell can give rise to, clearly they can all give rise to the specialised cells that reflect their normal function *in vivo*, i.e. if they had been left in the organ to which they belong. CNS stem cells can therefore give rise to both nerves and to several types of support cell. However, amongst these two classes of cells there is a large, very diverse range of cell types. In many experiments that have been done so far using adult CNS stem cells, the precise identity of the neurons has not been ascertained. Indeed, some evidence suggests that stem cells isolated from one part of the CNS may only be able to give rise to neurons typical of that region of the CNS. If we have to be even more precise about the source from which they are obtained, this raises further difficulties that will have to be overcome before we can contemplate using adult stem cells for therapy.

Though the finding that some adult stem cell types have a wider potential than previously thought is exciting from a fundamental scientific point of view, up till now we know almost nothing about the process that allows this, nor enough about how to direct the stem cells to change into any other particular cell type *in vitro*. In contrast, ES cells can be purified very easily, they grow very well in culture and they are essentially immortal. There is good evidence that the reprogramming by the cell-nuclear replacement ("cloning") technique also rejuvenates the adult cell nucleus. We know that ES cells can give rise to any cell type within the body, so potentially they can be used to treat any disease. In addition, we already know how to select particular cell types from differentiating mouse ES cells in a controlled manner.

It is obviously very important to know that any cells used for transplant are safe, free from contamination (pathogens and other cell types) and that they have the desired properties. For ES cells, it is normal to give rise to many cell types. However, for an adult stem cell to change its fate it has to undergo an abnormal process and we need to know that

this is not so abnormal as to be dangerous. Nevertheless, for either approach, many more animal models will be required and we need to define appropriate ways of conducting clinical trials in humans.

From all the criteria above, it seems that therapeutic approaches arising from ES cells are likely to lead to successful cures for a far greater range of affected tissue types and far sooner than will be possible with adult stem cells. However, uses for adult stem cells may well be found for some specific conditions. My personal view is that we are dealing with a question of potential risk versus likely benefits, where the potential benefits of ES cells are definitely worth pursuing. Moreover, it is better that this type of work is permitted in the context of a well regulated and controlled system, such as that already in place in the UK, where the science can proceed in step with ethical issues, rather than in many countries around the world that have little or no regulation.

This paper is the shortened text of an article Professor Dr. Robin Lovell-Badge wrote for the Grey Series No. 24 on "Embryo Experimentation in Europe" (see below) of the Europäische Akademie.

Professor Dr. Lovell-Badge is working at the Division of Developmental Genetics, MRC National Institute for Medical Research, The Ridge-way, Mill Hill, London NW7 1AA, UK.

He is member of the project group "Embryo Experimentation in Europe" initiated by the Europäische Akademie.

Working groups

Climate Prediction and Precautions

The most recent progress meeting on 21 February and 9 March 2001 was on the identification of elements of rational climate politics and the final reading of several manuscript sections. According to the state of work the project group decided to end up with its regular meetings in summer 2001. Therefore, a final report could be expected at the end of 2001.

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News in Brief

POIESIS & PRAXIS

The editor of POIESIS & PRAXIS – International Journal of Science and Technology Assessment – invites papers to be submitted for this new periodical. The peer-reviewed journal will present full-length papers, short discussion notes and occasional papers concerning the various topics of ethics in the context of technological advancements and technology assessment. Book reviews of relevance are welcome too.

Please send the papers to Georg Kamp (managing editor) at the Europäische Akademie's address or by e-Mail to: PoesisAndPraxis@DLR.de

"On the uniqueness of humankind – Über die Sonderstellung des Menschen"

This year's spring symposium "On the uniqueness of humankind" took place from 28 to 30 March 2001 in Bad Neuenahr-Ahrweiler. It was organised in co-operation with the Medical Society of Gießen. After a keynote address by H.-R. Duncker on "Man as a biological and cultural being", the theoretical thematic and practical concept of the *Sonderstellung* of the human being was examined in three sessions against the background of the present day knowledge in biosciences, philosophy, sociology and jurisprudence. Differences between humans and non-human animals and machines were discussed. The sections were chaired by G. Vowinkel, F. Thiele and M. Gutmann. Participants came from Austria, Great Britain, Honduras, The Netherlands, Latvia, Poland, Russia, Switzerland, USA and Germany.

Contributions: K. O. Hondrich: "The human: between having a world and being an existence of man"; C. F. Gethmann: "Die praktische Sonderstellung des Menschen"; "Die Sonderstellung des Menschen im Verfassungsrecht", R. Müller-Terpitz; contributions will be published in the academy's book series.

Welcome

Friederike Wütscher is the successor of Dagmar Uhl, M. A.; since the beginning of march she is responsible for public relations and printing at the Europäische Akademie.

Book Series

The ninth volume of the Europäische Akademie's book series "Wissenschaftsethik und Technikfolgenbeurteilung" was published recently:

G. Banse, C. J. Langenbach, P. Machleidt (Eds.): *Towards the Information Society. The Case of Central and Eastern European Countries*. Reihe Wissenschaftsethik und Technikfolgenbeurteilung, Band 9, Springer, Berlin 2000

Graue Reihe

Nr. 20 Genetische Diagnostik und Versicherungsschutz; Felix Thiele (Hrsg.); 2., unveränderte Aufl. 2/01

Nr. 24 Embryo Experimentation in Europe. Bio-medical, Legal and Philosophical Aspects; Minou Bernadette Friele (ed.); 2/01

These editions of the "Graue Reihe" ("Grey Series") can be ordered free of charge at the Europäische Akademie. Further titles (No. 1-24) are also available – please contact the Europäische Akademie:
Europaeische.Akademie@DLR.de

Lectures

Carl Friedrich Gethmann:

30.3.01 „Die praktische Sonderstellung des ‚Menschen‘“, International Conference on the Uniqueness of Humankind – Über die Sonderstellung des Menschen, Europäische Akademie Bad Neuenahr-Ahrweiler

4.4.01 „Ethische Probleme der nuklearen Endlagerung“, Tagung „Ethische Aspekte der Endlagerung“, Gesellschaft für Anlagen- und Reaktorsicherheit, Köln

Michael Decker:

15.3.01 „Der interdisziplinäre Experten-Diskurs. Ein Selbstläufer?“, Workshop „Diskursiv vernetzte Technikfolgenabschätzung – Ihre Formen, Funktionen und Probleme“, Kulturwissenschaftliches Institut Essen

Ulrich Rehberg:

15.1.01 „Gesellschaftliche Aspekte des Naturschutzes in Verdichtungsräumen und die Methodik ihrer Erforschung“, Eidgenössische Forschungsanstalt Wald, Schnee und Landschaft, Abteilung Landschaft und Gesellschaft, Birmensdorf, Schweiz

Felix Thiele:

14.3.01 "Ethical Problems of Genetic Testing – an Example", Kamingsgespräch "Pharmacogenetics – risks and changes of individualized medicine and genetic testing", Schering AG, Berlin

8.3.01 „Zukunftsforum Bio- und Gentechnologie“, Podiumsdiskussion 3. Biotechnologietage Bielefeld, Universität Bielefeld



New Publications

M. B. Friele: „Moralische Komplizität in der medizinischen Forschung und Praxis“, in: U. Wiesing, A. Simon, D. v. Engelhardt (Hrsg.): *Ethik in der medizinischen Forschung*. Schattauer, Stuttgart 2000

C. F. Gethmann (Hrsg.): *Philosophie und Technik*. Fink, München 2000 (mit A. Gethmann-Siefert)

C. F. Gethmann: „Ethische Probleme der Verteilungsgerechtigkeit beim Handeln unter Risiko“, in: C. F. Gethmann, A. Gethmann-Siefert (Hrsg.): *Philosophie und Technik*. Fink, München 2000, 61-74

C. F. Gethmann: „Bemannte Raumfahrt als Kulturaufgabe“, in: C. F. Gethmann, A. Gethmann-Siefert (Hrsg.): *Philosophie und Technik*, Fink, München 2000, 163-176

C. F. Gethmann, G. Kamp: „Gradierung und Diskontierung von Verbindlichkeiten bei der Langzeitverpflichtung“, in: D. Birnbacher, G. Brudermüller (Hrsg.): *Zukunftsverantwortung und Generationensolidarität*, Würzburg 2001, 137-153

G. Hanekamp: „Kulturalismus als enttäuschte Kennerschaft“, in: *Zeitschrift für Wirtschafts- und Unternehmensethik*, Nr. 1 2000, 336

G. Hanekamp: „Kulturalistische Unternehmensethik. Ein Programm“, in: *Zeit-*

schrift für Wirtschafts- und Unternehmensethik, Nr. 2 2001, 48

S. Lingner: „Gentechnische Anpassung an globale Erwärmung?“, Letter in: *Spektrum der Wissenschaft*, 3/2001, 8

E. Neumann-Held: "Can it be a 'sin' to understand disease? On 'genes' and 'eugenics' and an unconnected connection", in: *Medicine, Health Care and Philosophy*, Nr. 4 2001, 5-17

E. Neumann-Held: Guest-Editorial: "Organism – Historical and Philosophical Issues", in: *Theory in Bioscience*, vol. 119 (3, 4), 171-173 (with M. Gutmann and C. Rehmann-Sutter)

E. Neumann-Held: "The Theory of Organism and the Culturalist Foundation of Biology", in: *Theory in Bioscience*, vol. 119 (3, 4), 276-317 (with M. Gutmann)

U. Rehberg: „Integrativer Naturschutz als Beitrag zu einer nachhaltigen Landschaftsnutzung in Verdichtungsräumen“, in: Bundesamt für Naturschutz (Hrsg.), H. Korn, U. Feit (Bearb.): *Treffpunkt Biologische Vielfalt. Interdisziplinärer Forschungsaustausch im Rahmen des Übereinkommens über die biologische Vielfalt*, Bonn 2001

F. Thiele: „Humangenetische Diagnostik. Wissenschaftliche Grundlagen und gesellschaftliche Konsequenzen.“ Bericht über eine Arbeitsgruppe der Europäischen Akademie, in: *TA-Datenbank-Nachrichten*, Nr. 4, 9. Jg., Dezember 2000, 102-107

F. Thiele, C. R. Bartram: „Humangenetische Diagnostik. Wissenschaftliche Grundlagen und gesellschaftliche Konsequenzen“, in: *Management & Krankenhaus*, 1/2001, 26

F. Thiele, D. Uhl: „5 Jahre Europäische Akademie“, in: *TA-Datenbank-Nachrichten*, Nr. 4, 9. Jg., Dezember 2000, 98-100



Personalities



Dr. Miltos Liakopoulos studied Psychology in Athens (Deree College), Greece; he did his postgraduate studies in London (London School of Economics), UK, where he received a MSc and a PhD in Social Psychology with a thesis on the debate on biotechnology.

Since 1994 he has held various positions as researcher at the London School of Economics and the Science Museum, London, in European Commission concerted actions in the areas of Science & Technology as well as Biotechnology public perceptions and policy.

Since 2000 he has been an member of scientific staff at the European Academy, co-ordinating the project "Functional Foods in Europe"; his research interests are in the areas of science & technology perceptions and policy, impact of TA in policy, and ethics of science.

Publisher:	Europäische Akademie zur Erforschung von Folgen wissenschaftlich-technischer Entwicklungen Bad Neuenahr-Ahrweiler GmbH, Wilhelmstraße 56, D-53474 Bad Neuenahr-Ahrweiler e-mail: europaeische.akademie@dlr.de, Internet: www.europaeische-akademie-aw.de
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Print:	Warlich Druck GmbH, Bad Neuenahr-Ahrweiler ISSN 1432-0150, frequency of publication: 6 times per year, 2.500 copies, reproduction is permitted with reference to the source, please send two voucher copies.