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# Stem Cell Research in the Nordic Countries

Science, Ethics, Public Debate and Law

NORDFORSK POLICY BRIEFS 2007-2

September 2007  
For NordForsk by the Nordic Committee on Bioethics



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STEM CELL RESEARCH IN THE NORDIC COUNTRIES  
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## TABLE OF CONTENTS

### I.

<b>1</b>	<b>Introduktion på svenska</b>	<b>6</b>
<b>2</b>	<b>Stamcellsforskning – den nordiska dimensionen</b>	<b>8</b>

### II.

<b>1</b>	<b>Introduction</b>	<b>12</b>
<b>2</b>	<b>Stem cell research – from basic biology to therapeutic applications</b>	<b>14</b>
2.1	Stem cells and their potential	14
2.2	Embryonic stem cells	15
2.3	Somatic stem cells	15
2.4	Somatic cell nuclear transfer	16
2.5	Promises and pitfalls in stem cell research and therapy	16
<b>3</b>	<b>Stem cell research in the Nordic countries</b>	<b>17</b>
3.1	Denmark	17
3.2	Finland	18
3.3	Iceland	18
3.4	Norway	19
3.5	Sweden	19
3.6	Funding of stem cell research	20
<b>4</b>	<b>Commercialisation of stem cell research</b>	<b>21</b>
4.1	Stem cells as products	21
4.2	Patent law and national legislation	22
4.3	Conclusion	23
<b>5</b>	<b>Ethical issues related to stem cell research</b>	<b>26</b>
5.1	What are the issues?	26
	Promises and overselling	27
	How many embryos are needed?	27
	Advantages and disadvantages of different sources of stem cells	28
	Ethics and language	28
5.2	How to deal with the moral status of embryos	29
5.3	The moral status of the embryo	31
	Somatic cell nuclear transfer and reproductive cloning	32
	Chimeras	33
	Christian religion and the moral status of the embryo	34
5.4	How to live with disagreement on the moral status of embryos	35
5.5	Proper treatment of the donors	36
	Aborted fetuses	36
	Surplus embryos	37
	Unfertilized eggs	37
	Bone marrow (and other sources of stem cells from adult human beings)	37
5.6	A just use of resources	38
5.7	Access and patenting	38
	Patenting	39
5.8	Concluding remarks	39

<b>6 Debate and communication</b>	<b>40</b>
6.1 Policy-making and democracy	40
6.2 Communication	40
6.3 The debate in the Nordic Countries	41
Denmark	41
Finland	41
Iceland	41
Norway	42
Sweden	42
6.4 Concluding remarks	44
<b>7 Legislation on stem cell research in the Nordic countries</b>	<b>46</b>
7.1 Introduction	46
7.2 The international context of legislation on stem cell research	47
United Nations	47
The Council of Europe	47
The European Union	48
7.3 Evolution of legislation on stem cell research in the Nordic countries	50
Denmark	50
Finland	50
Iceland	53
Norway	54
Sweden	55
7.4 Regulation of stem cell research from a global viewpoint	58
Europe	58
Germany	58
The United Kingdom	59
USA	60
Singapore	60
7.5 Conclusions	61
<b>8. Stem cell research – the Nordic dimension</b>	<b>62</b>
<b>Further reading</b>	<b>66</b>
<b>Working group members</b>	<b>67</b>
<b>External experts</b>	<b>67</b>
<b>References</b>	<b>68</b>

# 1. Introduktion

Stamcellsforskningen har under detta årtionde ökat snabbt och de vetenskapliga framstegen har lett till hopp om nya behandlingsmetoder för allvarliga och obotliga sjukdomar. Forskningen har också lett till ökade möjligheter till ekonomisk nytta. Samtidigt har etiska frågor rörande ursprunget till vissa stamceller, mänskliga embryon, gett upphov till livliga diskussioner bland forskare, etiker, professionella inom hälsovården, patientorganisationer och allmänheten. Finansiärer, beslutsfattare och lagstiftare har också svarat på den snabba vetenskapliga utvecklingen.

Nordisk kommitté för bioetik (NKB) har aktivt bidragit till debatten om stamcells- och embryoforskning. Kommittén arrangerade ett seminarium om etiska frågor i samband med forskning på stamceller från människor och publicerade en rapport år 2000. Stamcellsforskning och embryots moraliska status har även diskuterats vid andra tillfällen organiserade av NKB, en kurs i undervisning i bioetik i Hønefoss 2002, arrangerad i samarbete med NorFA, ett seminarium kallat Bioprofesi – etik och bioteknologi i framtiden i Köpenhamn 2004 och ett internationellt möte om preimplantatorisk genetisk diagnostik och embryourval i Reykjavik 2004. Det finns även en översikt över lagstiftningen om forskning på embryon, stamcellsforskning och kloning i publikationen “Lagstiftning om bioteknologi i Norden – en översikt” publicerad av kommittén 2003 och uppdaterad och utvidgad 2005.

Nordisk kommitté för bioetik åtog sig i december 2006 att göra denna rapport för NordForsk. NordForsk har stött stamcellsforskning genom ScanBalts stamcellsforskningsnätverk sedan 2005. Nätverket, som koordineras av Norge, har deltagare från Sverige, Danmark, Finland, Island, Estland, Litauen, Ryssland, Polen och Tyskland. Enligt sin strategi stöder NordForsk forskningssamarbete där det finns en gemensam nordisk styrka, vilket definitivt gäller stamcellsforskningen. En av utmaningarna är att kunna behandla de många etiskt känsliga frågorna med respekt och öppenhet. Ändamålet med denna rapport är att stärka det nordiska stamcellsforskningsamfundet och beslutsfattarna genom att lägga fram en gemensam nordisk kunskapsbas för att stöda välinformerat beslutsfattande i framtiden när det gäller dessa frågor.

En arbetsgrupp tillsattes bestående av experter inom olika områden från alla de nordiska länderna. Den bestod av professor Ingileif Jónsdóttir, immunolog (Island/NKB), ordförande, professor Vilhjálmur Árnason, filosof (Island/NKB), dr. Thórarinn Guðjónsson, stamcellsforskare (Island), professor Thomas G. Jensen, genetiker (Danmark/NKB), Ellen Knutsen Rydberg, senior rådgivare (Norge/NordForsk), dr. Salla Lötjönen, jurist (Finland/NKB), professor Anders Nordgren, filosof (Sverige), dr. Ulla Schmidt, teolog (Norge), dr. Thorvald Sirnes, sociolog (Norge), Heli Skottman, stamcellsforskare (Finland), Katarina Uddenberg, bioingenjör / business

development manager (Sverige) och professor Stellan Welin, filosof (Sverige). Dr. Jakob Elster, filosof (Norge) och Helena von Troil, mikrobiolog och vetenskapskommunikatör (Finland) och sekreterare för Nordisk kommitté för bioetik var arbetsgruppens sekreterare. Flera utomstående experter (se appendix) bidrog också till arbetet.

Arbetsgruppen höll fyra möten för att diskutera ämnet för rapporten, planera arbetet, föreslå och diskutera idéer samt diskutera olika utkast. Rapporten består av en introduktion till stamcells forskning och stamcells forskningen i Norden, kommersialisering, etik, debatt och kommunikation, lagstiftning och slutligen ett sammandrag som fokuserar på den nordiska dimensionen i stamcells forskning. De författare som anges skrev de olika kapitlen, men alla medlemmar av arbetsgruppen bidrog mycket till rapporten som helhet med sina idéer och sin expertis, genom att läsa och kommentera olika versioner av rapporten och delta aktivt i diskussionerna.

Arbetsgruppen och Nordisk kommitté för bioetik hoppas att rapporten ger grundläggande fakta om stamcells forskning och en inblick i forskningen i Norden, kommersiella aspekter och etiska och juridiska frågeställningar samt debatt och kommunikation. Vi anser att det finns en klar nordisk dimension i stamcells forskningen och vi hoppas att den här rapporten ökar politikernas och andra beslutfattares intresse för stamcells forskning samt att den fungerar som grund för informerad diskussion. Med en stark koordinerad satsning kan de nordiska länderna fortsätta att spela en viktig roll i stamcells forskningen och dess övergång i produkter och behandlingsmetoder till nytta för alla medborgare.

På Nordisk kommitté för bioetik och arbetsgruppen för etik och stamcells forsknings vägnar

*Professor Ingileif Jónsdóttir*

## 2. Stamcellsforskning – den nordiska dimensionen

I alla de nordiska länderna förekommer stamcellsforskning av hög vetenskaplig standard i starkt nordiskt och internationellt samarbete. Den omfattar både grundforskning och tillämpad forskning på stamceller från embryon (embryonala stamceller) och somatiska stamceller från människor och djur. Alla större universitet i de nordiska länderna har stamcellsforskningsprogram eller -projekt och flera forskningscenter ägnar sig nästan enbart åt stamcellsforskning. I alla Nordens länder finns det privata företag som fokuserar i någon grad på stamcellsforskning och utnyttjandet av stamceller i forskning och utveckling av produkter och teknologi. Kliniska prövningar med användning av stamceller pågår åtminstone i Danmark, Finland och Sverige.

Olika forskningsgrupper inom den akademiska världen och industrin i Norden fokuserar på ett brett fält inom forskning och utveckling runt stamceller från embryon samt somatiska stamceller från olika vävnader. Forskningen gäller grundläggande vetenskapliga frågor i utvecklingsbiologi, blodcellsbildning, neurobiologi och cancerforskning, allt från specialisering av stamceller till olika typer av specialiserade celler, till högt tillämpad forskning i regenerativ medicin, olika typer av cellterapi och transplantation, konstruktion av vävnader (tissue engineering) och prövning av mediciner och andra bioaktiva molekyler.

Forskare är överens om att kunskap från forskning på stamceller från embryon bidrar till

framgångsrik forskning på somatiska stamceller och vice versa, och att forskning på stamceller från människor och stamceller från djur ökar kunskapen på bägge områden.

Forskningscenter i Danmark, Finland och Sverige framställer stamcellslinjer från mänskliga embryon och flera forskningsgrupper i Norden producerar stamcellslinjer från embryon av olika djurarter. Framställning av cellinjer från olika typer av somatiska stamceller är vanlig och sådana cellinjer används mycket i grundforskning. Man lägger också vikt på utveckling av teknologi i samband med isolering av stamceller, odling och specialisering. I detta mycket kompetitiva fält finns ett väl etablerat och fruktbart samarbete mellan olika grupper i de nordiska länderna. Detta, tillsammans med vetenskapligt mycket hög standard borde göra det möjligt för det nordiska forskningssamfundet att behålla en ledande roll i stamcellsforskning och -utveckling i framtiden.

Flera faktorer är viktiga för att de nordiska länderna skall kunna fortsätta att dra nytta av stamcellsforskning. Förutom hög vetenskaplig standard gäller det tillgång till forskningsmedel, investering i forskning och utveckling, bra utbildningssystem, internationellt samarbete och rörlighet för studenter, stödande lagstiftning, stark demokratisk tradition, positivt bioetiskt klimat och allmänhetens stöd.

Forskningsråden i alla de nordiska länderna stöder stamcellsforskning, och det gör även Nord-Forsk. Förutom offentligt stöd finns det många

privata fonder i Norden som stöder stamcells forskning, och vetenskapsmän från alla de nordiska länderna har fått forskningsmedel från mycket kompetitiva internationella program, så som den Europeiska Forskningsfonden och EU ramprogrammen för forskning och utveckling. Ett växande antal privata företag som är involverade i stamcells forskning visar att investerare tror på möjligheten att utnyttja stamcells forskning till produktutveckling och finansiell nytta.

Användning av befruktade äggceller till forskning på stamcellslinjer från embryon är reglerad med lagar i alla de nordiska länderna, dock i olika sammanhang (d.v.s. konstgjord befruktning, bioteknologi, medicinsk forskning och genetisk integritet). Pågående och färska ändringar i lagstiftning som reglerar stamcells forskning i alla de nordiska länderna återspeglar ett svar på de snabba framstegen inom detta fält. Användning av somatiska stamceller för forskningsändamål är reglerat med lagstiftning om biomedicinsk forskning på människor eller klinisk forskning och med lagstiftning om samlingar av biologiskt material eller biobanker. Alla de nordiska länderna, utom Norge, har en relativt ny lagstiftning om klinisk forskning (från 1999 eller senare). Island, Norge och Sverige har specifika lagar om biobanker (från 2000 eller senare). Forskning på mänskliga embryon och stamceller från dessa berör grundläggande värderingar och fundamentala frågor om livets början och respekt för människovärdet. Därför har stamcells forskningen väckt lagstiftarens och allmänhetens intresse. Forskning på stamceller från mänskliga embryon har varit motivering till ändringar i gällande lagar i de nordiska länderna, precis som på andra håll i världen.

Det finns vissa skillnader mellan lagstiftningarna om forskning på mänskliga embryon och stamceller från dessa i de nordiska länderna. Sverige har en av världens mest liberala lagstiftningar som tillåter framställning av embryon för forskningsändamål genom konstgjord befruktning under mycket specifika förhållanden och efter strikt etisk utvärdering. I Norge har ett totalt förbud mot forskning på mänskliga embryon nyligen upphävts. Island tillåter forskning på mänskliga embryon för begränsat ändamål i samband med konstgjord befruktning. Ett lagförslag om ändringar av lagen om konst-

gjord befruktning lades fram i Althingi 2007, där vetenskapligt motiverad forskning på överlevna embryon skall tillåtas på samma sätt som redan är tillåtet i Danmark och Finland.

Sverige tillåter kärnöverföring för produktion av blastocyster för framställning av stamceller. Enligt förslaget till ändringar i lagstiftningen skall detta också tillåtas i Island. I alla de nordiska länderna är kloning för reproduktivt ändamål förbjuden.

I dagens marknadsekonomi är kommersialisering av stamcells forskning nödvändig för överföring av grundläggande kunskap till produkter så som nya diagnostiska tester, terapier och behandlingar. Lagstiftning om stamcells forskningen, inklusive patentering av forskningsresultat, är mycket viktig när det gäller tillämpad användning och kommersiella aspekter.

I Norden, som på annat håll, är revision av gällande lagar, för att tillåta stamcells forskning, knuten till hoppet om att forskningen kommer att öka vår kunskap om biologiska processer och sjukdomars patogenes och på så sätt bidra till utveckling av nya diagnostiska metoder och behandlingmöjligheter för allvarliga sjukdomar som i dag är obotliga. Men frågan om stamcells forskning, och i synnerhet forskning på stamceller från mänskliga embryon, gäller inte bara lagstiftning, utan är en mångfacetterad etisk frågeställning. Hoppet om framtida möjligheter till ökad förståelse av biologiska processer, samt utveckling av behandlingsmetoder för allvarliga sjukdomar, som idag inte kan botas är en mycket viktig etisk och moralisk fråga. En annan fråga är vad man får göra med mänskliga embryon och för vilka ändamål. Överlevna embryon förstörs när de används för framställning av stamcellslinjer, vilket väcker frågan om det är acceptabelt att förstöra embryon. Denna fråga behandlas på olika sätt i debatten kring forskning på stamceller från embryon. Ett embryo har förmågan att utvecklas till en människa om det implanteras i en kvinnas livmoder. Ett faktum som för somliga människor leder till slutsatsen att det har rätt till skydd från förstörelse. En annan åsikt är att ett embryo inte har rätt till detta skydd förrän det har utvecklats vidare (till exempel har implanterats i livmodern eller att det första anlaget till det centrala nervsystemet har bildats). Ett vanligt argument är att det kan vara en viktig skillnad

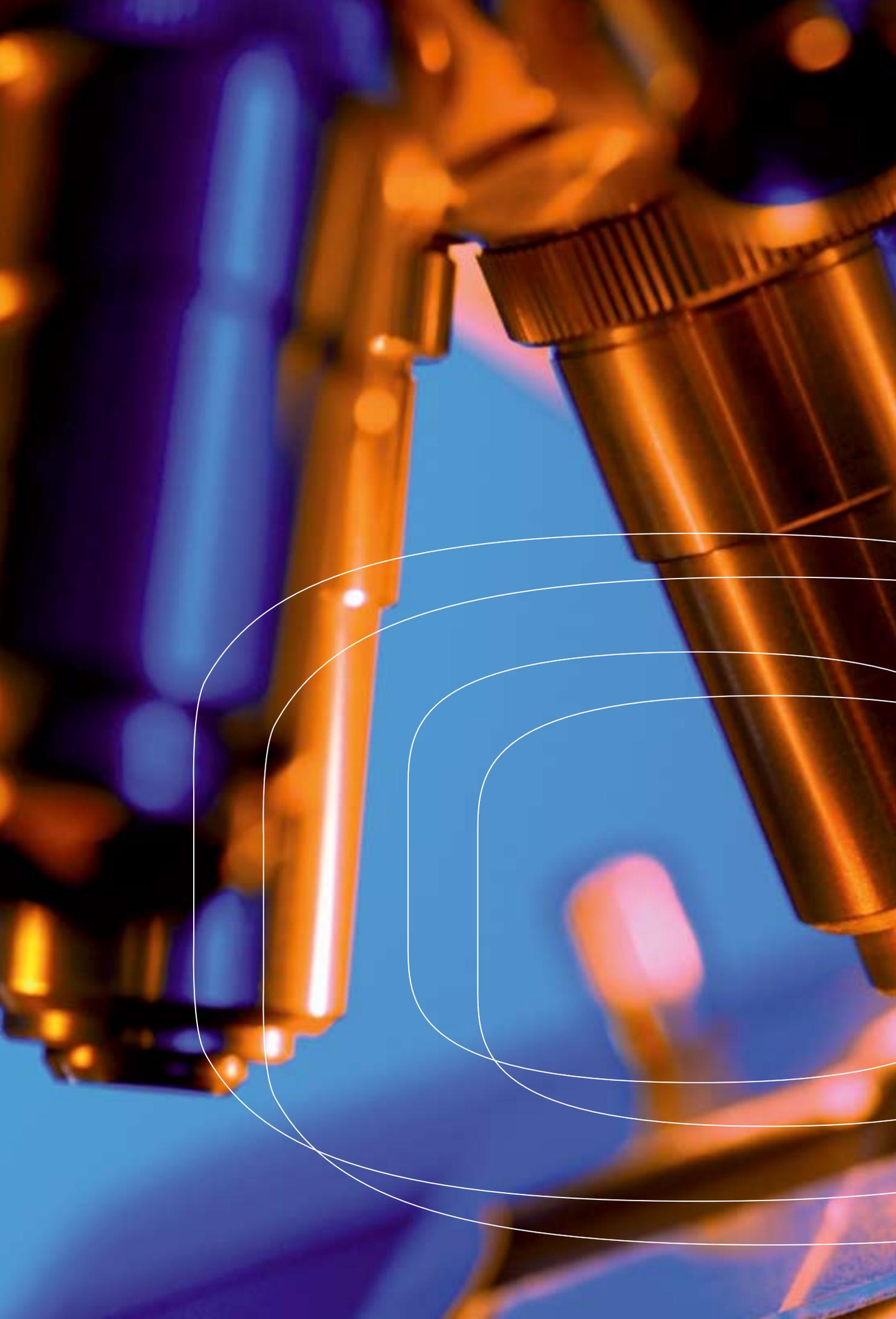
mellan användning av överblivna embryon (från konstgjord befruktning) som kommer att förstöras i alla fall, och framställning av embryon enbart i forskningssyfte, och att det förra fallet är mindre problematiskt än det senare. Man tror att genetiskt identiska stamceller kan minska risken för att en immunreaktion uppstår som leder till avstötning av vävnader, vilket är ett vanligt problem i organtransplantation. Därför används kärnöverföring för framställning av blastocyster för isolering stamceller som är genetiskt identiska med den individ som cellkärnan kommer ifrån. Kärnöverföring väcker ytterligare etiska frågor, speciellt eftersom blastocysten har en förmåga att utvecklas till ett embryo och sedan till en klonad människa om den implanteras i en livmoder. Det är viktigt att påpeka att i alla de nordiska länderna är implantation av blastocyster med överförda kärnor förbjuden. De som allmänt är emot kärnöverföring hävdar att framställning av genetiskt identiska embryon eller blastocyster är problematisk och kan leda till ett sluttande plan (slippery slope) mot kloning i reproduktivt syfte, vilket för flesta människor är etiskt oacceptabelt och är förbjudet i lag i alla de nordiska länderna och i många andra länder också. Den etiska komplexitet som berör isolering av stamceller från embryon har lett till utveckling av alternativa och kanske mindre kontroversiella metoder. Med den så kallade "ändrade kärnöverföringen" omvandlas den somatiska cellkärnan innan den överförs till äggcellen och det omvandlade ägget kan enbart användas för isolering av stamceller, men kan inte utvecklas vidare till en människa. Denna teknik kan bjuda på mindre kontroversiella källor för embryonala stamceller, eftersom argumentet mot forskning baserat på embryots potential inte längre gäller. Förutom etiska argument som är specifika för forskning på embryon och stamceller från dessa finns det också etiska frågor i samband med forskning på somatiska stamceller och etiska frågeställningar som berör biomedicinsk forskning i allmänhet.

Även om det kan finnas en bred enighet i Norden angående grundläggande etiska principer, påverkas debatten av människors moraliska värderingar, religion och kulturella bakgrund. De nordiska ländernas demokratiska samhällen är lika i många avseenden, vilket återspeglas i

debatten kring stamcellsforskningen. Men de är också en del av globaliseringen av vetenskap och teknologi, som påverkar diskussionen, lagstiftningen och beslutsfattandet.

I våra öppna demokratiska nordiska samhällen måste besluten återspegla vetenskapens metoder och kunskapen inom området och få sin legitimitet från folkets godkännande. Därför är en öppen dialog om vetenskapliga frågeställningar mellan experter och allmänheten viktig för att forskare och beslutsfattare skall känna till allmänhetens oro och för att nå samförstånd i kontroversiella frågor. Stamcellsforskning har väckt allmänhetens intresse i alla de nordiska länderna. Den offentliga debatten har varierat mellan länderna, i både karaktär och intensitet, och vad gäller deltagande av experter, patienter, patientorganisationer, beslutsfattare och media. Det finns en extra stor variation när det gäller undervisningsmaterial och skolundervisning i ämnet. Generellt har det varit större vikt på specialrapporter och rekommendationer för beslutsfattare och för lagstiftaren, än på framställning av material för allmänheten. Medborgarna borde ha tillgång till grundläggande fakta om stamcellsforskning och dens framtida möjligheter, samt möjlighet att delta i debatten om de etiska frågeställningar som uppstår. Forskare borde rapportera om vetenskapliga framgångar och svårigheter samt delta i den offentliga debatten. Prioriteringar och val som forskningsfonderna gör när de drar sina riktlinjer borde vara öppna och grunden för prioriteringarna borde vara tillgänglig för allmänheten.

De nordiska länderna har en lång tradition i biomedicinsk forskning av hög standard och nordisk stamcellsforskning är av mycket hög kvalitet. Lagstiftningen och det bioetiska klimatet är relativt gynnsamt, offentliga forskningsmedel och privata investeringar växer och det finns ett starkt stöd från allmänheten. Med en stark gemensam satsning kan de nordiska länderna fortsätta att spela en viktig roll i stamcellsforskningen och användningen av stamceller till utveckling av produkter och andra medel som bidrar till bättre hälsa i framtidens samhälle.



# 1. Introduction

Stem cell research has grown rapidly in this decade and the scientific achievements have created hopes for new treatments of severe incurable diseases. As a result of the research, the economic prospects are also growing. At the same time, ethical questions related to the sources of some stem cells, i.e. human embryos, have stimulated intense debate among scientists, ethicists, health professionals, patient organisations and the public. Funding agencies, policy makers and legislators have also responded to the rapid scientific advancement in the field.

The Nordic Committee on Bioethics (NCBio) has actively participated in the debate on stem cell and embryo research. It arranged a seminar in 2000 on “The ethical issues in human stem cell research” and published the proceedings. Stem cell research and the moral status of the embryo have also been discussed at other events organised by NCBio, a course on “Teaching bioethics”, in Hønefoss in 2002, arranged in collaboration with NorFA, a seminar on “Bioprophecy – the future of ethics and biotechnology” in Copenhagen in 2004, and an international meeting on “Preimplantation Genetic Diagnosis and Embryo Selection”, in Reykjavik in 2004. There is an overview on the legislation on embryo research, stem cell research and cloning in the booklet “Legislation on biotechnology in the Nordic countries – an overview” published by NCBio in 2003 and updated and expanded in 2005.

The present report was commissioned from the Nordic Committee on Bioethics by NordForsk in December 2006. NordForsk has funded stem cell research through the Scan-Balt stem cell research network since 2005. The network is coordinated from Norway and includes members from Sweden, Denmark, Finland, Iceland, Estonia, Lithuania, Russia, Poland and Germany. According to its strategy, NordForsk supports research collaboration where there are joint Nordic positions of strength, which certainly is true for stem cell research. One of the challenges of stem cell research is, however, to be able to handle the many ethically sensitive issues with respect and transparency. The aim of the present report is to strengthen the Nordic stem cell research community and policy makers by providing a joint Nordic knowledge base as a support to future, well-informed decision making regarding such issues. A working group was established, consisting of experts in different disciplines from all the Nordic countries. It consisted of Professor Ingileif Jónsdóttir, immunologist (Iceland/NCBio), chair, Professor Vilhjálmur Árnason, philosopher (Iceland/NCBio), Dr. Thórarinn Guðjónsson, cell biologist (Iceland), Professor Thomas G. Jensen, geneticist (Denmark/NCBio), Ellen Knutsen Rydberg, senior adviser (Norway/ NordForsk), Dr. Salla Lötjönen, lawyer (Finland/NCBio), Professor Anders Nordgren, philosopher (Sweden), Dr. Ulla Schmidt, theologian (Norway),

Dir. Thorvald Sirnes, sociologist (Norway), Heli Skottman, stem cell researcher (Finland), Katarina Uddenberg, bioengineer and business development manager (Sweden) and Professor Stellan Welin, philosopher (Sweden). Secretaries were Dr. Jakob Elster, philosopher (Norway) and Helena von Troil, microbiologist and science communicator (Finland/NCBio secretary). Several external experts (listed in the appendix) also contributed to the work.

The working group held four meetings, to frame the issues, plan the work, propose and discuss ideas, and discuss drafts of different parts of the report. The report covers an introduction to stem cell research in general and in the Nordic countries in particular, commercialisation, ethics, legislation, debate and communication of stem cell research, and a summary focusing on the Nordic dimension in stem cell research. The listed authors wrote the chapters, but all the members of the working group contributed significantly to the report as a whole with their ideas and expertise, by reviewing the work at various stages, and by actively participating in the discussions.

The working group and the Nordic Committee on Bioethics hope that this report provides basic facts on stem cell research and gives insight into stem cell research in the Nordic countries, commercial aspects and the ethical issues involved, the legislative framework in an international context and the debate and communication concerning stem cell research. We believe that there is a clear Nordic dimension in stem cell research and we hope that this report will increase the interest of politicians, policy makers and citizens in stem cell research and serve as basis for informed discussions. With a strong coordinated effort the Nordic countries can continue to play an important role in stem cell research and its translation into products and other measures that will benefit to future health and to society.

On behalf of the Nordic Committee on Bioethics and the working group on ethics and stem cell research,

*Professor Ingileif Jónsdóttir*

## 2. Stem cell research – from basic biology to therapeutic applications

### 2.1 STEM CELLS AND THEIR POTENTIAL

Stem cells are able to regenerate tissues and organs and act as building blocks for all tissues in the body. This is why there is a lot of interest in using these cells as therapeutic tools in cell replacement therapy or tissue engineering. Stem cells represent a potential therapeutic platform for many diseases such as diabetes, Parkinson's disease, spinal injury, multiple sclerosis, motor neuronal disease, certain heart diseases, cancer and other severe and incurable diseases. Furthermore, stem cells are essential for research aiming to understand processes leading to diseases and for drug development.

Stem cells can broadly be divided into two groups, 1) embryonic stem cells (ESC); and 2) somatic stem cells (also known as adult or tissue stem cells). ESCs are derived from pre-implanted early human embryos. They are multipotent cells that hold great promise for future tissue engineering. However, due to their origin in embryos the ethical and religious issues surrounding their use are being widely discussed. Somatic stem cells are long-lived tissue stem cells that are responsible for replacement of old/dying cells in body tissues and upon injury repair the tissue in which they are found. In contrast to embryonic stem cells, there is less ethical controversy regarding somatic stem cell research.

The use of stem cells in regenerative medicine requires removing the cells from their natural habitat, growing them to a large number in culture dish, and either directly grafting them into a specific tissue environment, or using them for generation of cells or tissues intended for transplantation. Differentiation of stem cells located in their own natural environment is seen as a promising path in regenerative medicine.

In the body, stem cells are located in a complex microenvironment. Called the stem cell niche, it is composed of stem cells, non-stem cell neighbour cells and the surrounding extra cellular matrix. The stem cell niche holds clues to the ability of stem cells to remain silent or to undergo controlled cell division. Local conditions (growth factors and developmental signals) are thought to play an important role in determining how these cells will develop. Understanding the cellular and molecular composition and regulation of the stem cell niches are essential in learning how to engineer novel tissue in culture. For instance, despite trying for almost two decades, researchers still have not been able to fully mimic, in artificial culture systems, the ability of blood stem cells to proliferate, and recent insights into the stem cell niches in the bone marrow suggest they are critically involved in prompting stem cell proliferation. Because stem cells behave differently in the laboratory than in real life, culture systems have to be improved. Finally, proteins

involved in determining the nature of stem cells may provide valuable drug targets for treatment of degenerative diseases and cancer. It is clear that increased research on both embryonic and somatic stem cells offers new hope of cell replacement therapy for various currently incurable diseases.

## 2.2 EMBRYONIC STEM CELLS

Embryonic stem cells (ESCs) can be multiplied in culture and induced to form all tissues of the body. This fact makes them a potential source for cell transplantation and tissue engineering. Many research groups have reported the ability of ESCs to differentiate into a variety of specific cell types, including neurons, cardio-myocytes and insulin secreting cells. Human embryonic stem cells (hESC) can be generated using left-over early stage embryos (usually at blastocyst stage around five days after fertilization) originally intended for use in in vitro fertilization (IVF). These embryos are either of poor quality or have been preserved in liquid nitrogen for a long time, and will not be used to treat childless couples. Good quality embryos are used in the infertility treatments and the left-over (surplus) embryos that would otherwise be discarded could be used to establish ESC lines. The blastocyst stage embryo contains an aggregation of unspecialized cells, the inner cell mass. The inner cell mass is a transient state and if the blastocyst is successfully implanted in the uterus of a woman it will give rise to all bodily tissues including somatic stem cells. With informed consent from donors (parents) left-over embryos can be donated to research in countries that permit the establishment of ESC lines. In certain countries, such as United Kingdom, embryos can be produced for research purposes with the informed consent of the egg and sperm donors.

Studies on hESC have resulted in increased knowledge about the complex events that occur during human development. A better understanding of how tissues in the body are generated and maintained during adulthood may unravel how diseases arise and suggest new strategies for prevention and therapy. hESC are also used to test new drugs for safety and efficacy.

The first continuous hESC line was established in 1998 by James Thomson and colleagues at the University of Wisconsin<sup>1</sup>. This breakthrough led to headlines in newspapers around the world and to political, ethical and religious debates about embryonic stem cell research. Since then, data is continuously emerging showing that ESCs can be conditioned to develop into all kinds of functional cell types. However, research on hESC is still in its infancy and much more needs to be done before human embryonic stem cells can be considered for cell replacement therapy.

## 2.3 SOMATIC STEM CELLS

A somatic stem cell is defined as an undifferentiated cell found among differentiated cells in a tissue or organ that can – when needed – proliferate and induced to differentiate to give rise to the functional cell types of the tissue or organ. The primary roles of somatic stem cells in the body are to maintain and repair the tissue in which they are found. Unlike embryonic stem cells, which are defined by their origin (the inner cell mass of the blastocyst, see above), the precise origin of somatic stem cells in most tissues is still controversial. Somatic stem cells are thought to reside in a specific area of each tissue, called the stem cell niche, where they may remain silent (non-dividing) until needed during normal cellular turnover or upon tissue injury. Research on somatic stem cells has generated a great deal of excitement. Scientists have found somatic stem cells in almost every tissue, including the brain, a fact that not even scientists believed in a few years ago. In contrast to hESC, certain types of somatic stem cells, such as skin and cornea transplants, are already used in routine therapy today, and somatic stem cells from bone marrow have been used for transplantations for over thirty years. One of the obstacles to the clinical use somatic stem cells is the lack of methods to culture them in undifferentiated state. Many scientists are trying to find ways to grow somatic stem cells in cell culture and manipulate them to generate specific cell types able to treat injury or disease.

Stem cells are also involved in cancer development. New results have shown that some

cancer types results from the accumulation of mutations in long-lived stem cells. Decades ago, studies on teratocarcinoma (tumours involving germ cells) led to the hypothesis that a small subset of proliferating cancer stem cells with differentiation potential exists in tumours. These studies showed that teratocarcinomas contain undifferentiated embryonic carcinoma cells that are able to give rise to differentiated cells. More recent studies have confirmed the existence of cancer stem cells in such diverse cancers as leukaemia, brain and breast cancer. It is, however, unclear whether cancer stem cells originate from resident stem cells or arise as a result of an acquired capacity of proliferation in tissue cells. The characterization of a cancer stem cell profile in diverse cancer types may open up new avenues for cancer treatment.

#### **2.4 SOMATIC CELL NUCLEAR TRANSFER**

Somatic cell nuclear transfer (SCNT) is a method by which a nucleus from an oocyte is replaced with a nucleus from a somatic tissue cell. This gives rise to a zygote-like cell (i.e., the very first cell after fertilization). If the zygote develops normally, within five to six days it will give rise to a blastocyst containing inner cell mass that can be removed to establish ESC lines. The aim of this method is to obtain stem cells that are genetically matched to the donor of the somatic cell nucleus. Scientists believe the method will make it possible to prevent immune rejection, a common problem in tissue transplantation. It is also anticipated that ESC lines established by SCNT could help advance research on various genetic diseases. Genetically customized stem cells could also be used to create cell lines genetically linked to a particular disease. For example, if a person with motor neuronal disease (MND) donated somatic cells, the SCNT-derived stem cells would have genes that contribute to the disease. MND stem cell lines could therefore be studied in order to better understand the initiation and disease progress. However, it is important to note that efforts to establish SCNT-derived human stem cell lines have up until now been disappointing and to our best knowledge no such cell line has yet been established.

#### **2.5 PROMISES AND PITFALLS IN STEM CELL RESEARCH AND THERAPY**

Several difficulties need to be overcome before stem cell technology can be used for the treatment of patients on a wider scale. hESC and somatic stem cells each have advantages and drawbacks for use in cell-based regenerative therapies. Somatic and embryonic stem cells differ in the number and type of differentiated cell types they can become. While hESC can differentiate into all cell types in the body because they are pluripotent, the differentiation repertoire of somatic stem cells is more restricted. Large numbers of embryonic stem cells can be relatively easily grown and multiplied in culture, while somatic stem cells are often rare in tissues and methods for increasing their numbers in cell culture need to be improved, as mentioned above.

As it is still not possible to conclude which types of stem cell will best meet the therapeutic needs, more research needs to be carried out simultaneously on hESC and somatic stem cells. And as novel biological insights from research on one type of stem cells often can be used in other research areas, this effort should ideally be conducted in parallel on both embryonic and somatic stem cells. As described below, the Nordic countries have already made important contributions to stem cell research. A broad, interactive and collaborative research programme in the Nordic countries that addresses both basic and clinical questions in stem cell biology, platform technologies and safety concerns may be the crucial ingredient needed to catalyze further progress in this field.

# 3. Stem cell research in the Nordic countries

The Nordic countries are at the forefront of biomedicine. The reasons for this include a long tradition of biomedical science and research, strong public support, favourable bioethical climate, tradition for science and research, and reasonable government funding. It has resulted in opportunities for the Nordic countries to relative quickly establish an environment that facilitates stem cell research. In that regard, important discoveries in both somatic and embryonic stem cell biology have been accomplished and both basic research and applied research are being performed at the highest international level. If we count all kinds of stem cells – embryonic and somatic, human and animal – a very large number of research projects are under way in the Nordic countries. In this report it is not possible to give a comprehensive overview of all aspects of stem cell research in the Nordic countries, but we wish to highlight certain facts to, at least, give the reader some insight into the extent to which this kind of research is conducted and where the “hotspots” are.

## 3.1 DENMARK

The Danish Centre for Stem Cell Research (DASC), was established in 2002, funded by the Medical Research Council and involved parties. DASC consists of nine research groups located at the universities of Aalborg, Southern Denmark (Odense) and Copenhagen, Odense University Hospital, NsGene A/S and Hage-

dorn Research Institute. DASC concentrates its research on the study of somatic stem cells, derived from somatic tissue, developing foetal tissue and umbilical cord blood. The focus is on applied research on stem cells with the potential of becoming functional active insulin producing cells, brain, liver, muscle, cartilage and bone cells.

In addition to the centres that are partners in DASC, stem cell research is conducted also at Aarhus university and university hospital, Copenhagen university hospital and the Royal Veterinary and Agricultural University (KVL).

In Denmark the Danish Stem Cell Research Doctoral School (DASCDOC) has been funded by the National Research Agency since 2003. It is an interdisciplinary network consisting of 26 research groups from Danish universities and university hospitals, veterinary and other research institutions, and biotechnology industry.

The focal areas of the research are early embryonic development, transgene technologies, and stem cell isolation and differentiation in relation to stem cell-based therapies. Stem cell sources are tissue-derived, adult or foetal stem cells from the corresponding tissues and organs and umbilical cord blood, as well as embryonic stem cells derived from early embryos of rodents, domestic animals and also human embryonic stem cells.

Several clinical trials using somatic stem cells are being performed. Blood stem cells

are used at all the Danish University hospitals for a variety of diseases, and at the Danish National Hospital in Copenhagen, mesenchymal stem cells are evaluated for treatment of ischemic heart disease.

In addition to these public research institutions several companies, such as Exiqon, H. Lundbeck, Novo Nordisk, Novozymes and NsGene are also involved in stem cell research and development.

### 3.2 FINLAND

In Finland stem cell research is conducted at all major universities, Helsinki, Kuopio, Tampere, Turku and Oulu, at the Helsinki university hospital and at the Family Federation (Väestöliitto). These have all received funding from the Academy of Finland. The funding agency for technology and innovation, Tekes, also funds stem cell research projects.

At least six research groups are currently working on human embryonic stem cells (hESC) in basic science and for applications in developmental biology and regenerative medicine. Two groups have also derived hESC lines of their own. These two groups are at the University of Tampere, where four new hESC lines have been derived and at the University of Helsinki where six new lines have been derived. The stem cell research unit at Tampere is also working with twenty lines from Karolinska Institutet and both the Helsinki and Tampere teams are involved in several collaborative projects on cell line development. In addition to the above, existing hESC lines at the University of Turku and University of Oulu are used for research.

There are many more teams working with mouse ESC and tissue-derived stem cells from humans and animals, and it is difficult to identify all of them. For example, there are teams at the universities of Turku, Oulu and Kuopio using bone marrow-derived mesenchymal stem cells in various situations (e.g., cartilage, neural tissue, blood vessel forming) and University of Tampere using adipose tissue-derived stem cells (e.g., bone, cartilage, soft tissue).

Clinical research trials involving stem cells have been conducted at the university hospitals

of Helsinki, Tampere and Oulu. At Tampere, stem cells from the patients themselves were used to treat severe chronic frontal sinusitis with good results. Finnish cardiothoracic surgeons are running a prospective randomized study on bone marrow cells in connection of angioplasty for myocardial infarction, at the University of Oulu. At Helsinki university hospital a clinical study involving the injection of stem cells into cardiac muscle is under way.

At present two commercial ventures are active in the stem cell field. Novagenesis specializes in the development of unique regeneration products for the nervous system and Evostem develops and markets stem cell and tissue technology-based products for the treatment of tendon damages in animals.

### 3.3 ICELAND

In Iceland the stem cell research is centred around the University of Iceland and Landspítali-University Hospital. At the University, research at the Department of Biochemistry and Molecular Biology is looking into melanocyte stem cells in the bulge region of the hair follicle and their differentiation into specialised cells, neural development and differentiation of embryonic stem cells into cardiomyocytes and endothelial cells. This latter group is working with both mouse and human embryonic stem cells.

The Department of Anatomy, University of Iceland and Department of Laboratory Haematology, at the University Hospital, are jointly running a Stem Cell Research Unit (SCRU). SCRU focuses on stem cells in branching morphogenesis and cancer in epithelial tissues such as the breast and lung tissue. The SCRU also studies the mechanisms by which leukaemia stem cells contribute to chronic myelogenous leukaemia in a clinical setting. A research group at the blood bank of the Landspítali University Hospital is studying in partnership with the National Cancer Institute, USA and the University of San Diego, blood and mesenchymal stem cells and how they differentiate into specialised cells. The researchers are also running a clinical stem cell therapy programme with blood stem cells, the only clinical programme involving stem

cells in Iceland. These academic groups have received funding from the Icelandic Research Fund, Thematic Programme on Post-Genomic Biomedicine, the Research Fund of the University of Iceland and the Science Fund of Landspítali University Hospital, as well as from the European Science Foundation.

Three Iceland-based companies are involved in stem cell research and development. NimbleGen Systems of Iceland is a supplier of products and services for research. Ossur is a company not directly involved in stem cell research, though it collaborates with a number of stem cell researchers in orthopaedic research and regenerative medicine. ORF Genetics manufactures growth factors and other proteins for research and drug development. A number of these are essential for stem cell culture, making stem cell research an important market for many of the products.

### 3.4 NORWAY

Research on human adult stem cells has been a strategic policy concern of the Norwegian government since 2002 and is mentioned as an item in the national budget. The Research Council of Norway is responsible for dispensing funds under the programme. Calls for applications have been open, aiming to establish a national stem cell research network. During the first programme period (2002–06), three projects involving thirteen research groups received funding. The Norwegian Centre for Stem Cell Research (NCS) was established after receiving a strategic grant. The Centre brings together eleven research groups based at Rikshospitalet–Radiumhospitalet HF, Universities of Oslo, Bergen and Trondheim. Two groups at the University of Oslo are affiliated to the centre. The Centre is mandated to enabling a scientific network in the field of basic and applied research on stem cells. A particular focus is the use of stem cells in regenerative medicine. In addition, implications of stem cell biology on cancer development are studied. By the call for the second period (2007–09), the Research Council decided to fund seven projects, several of which are conducted by these same groups.

Stem cell research is funded under other

Research Council bodies as well. They include the Norwegian Centres of Excellence, Centre for Molecular Biology and Neuroscience, and as the recently established Centre for Stem Cell Based Tumour Therapy (SENIT), one of the Centres of Research-based Innovation.

Research on embryonic stem cells is prohibited in Norway. However, the new Biotechnology Act, which comes into force January 1, 2008, will allow research on embryonic stem cells. The new law will bring legislation in Norway into closer alignment with that of other European nations.

### 3.5 SWEDEN

Sweden is probably the Nordic country with the largest community of research groups and businesses working directly with stem cells, in particular human embryonic stem cells. All the big Swedish universities with a medical faculty have ongoing stem cell research. Around sixty human embryonic stem cell lines have been established in Sweden, about half of them at Karolinska Institutet and half at the company Cellartis.

Several groups at the Karolinska Institutet study stem cells and research is also being done on stem cells and neural differentiation connected to Parkinson's disease.

At the Lund Stem Cell Centre at Lund University, 24 groups are carrying out research on stem cells in the fields of cancer, developmental biology, haematopoiesis and neuroscience. These researchers use both human embryonic and adult stem cells. A group at Lund University studies stem cells for the development of neural transplant technology and understanding neurodegenerative mechanisms in Parkinson's and Huntington's diseases.

The Centre for Brain Repair and Rehabilitation at Gothenburg University is a leader in the field of neuronal stem cell research. At the Research Centre for Endocrinology and Metabolism at Sahlgrenska Academy, a group is studying cartilage regeneration using chondrocytes and human embryonic stem cells. Work at the Department of Medical Biochemistry at Gothenburg University is looking into the production of stem cells by nuclear reprogramming, mainly on frogs, and

at Kristineberg Marine Research Station, there is research ongoing on stem cells of starfish.

At Linköping University, stem cells are studied in connection with wound healing and biomaterials, while at Umeå University the focus is on pancreatic development.

The largest Swedish companies specializing in stem cells are Cellartis and NeuroNova. NeuroNova is leading the development of therapeutic neurogenesis through its work with somatic neuronal stem cells and has two drug candidates in preclinical development. Cellartis is focused on differentiation of specialised cells from human embryonic stem cells and as well being the world's largest single source of human embryonic stem cells developed in house. Other businesses directly involved in stem cell research are NeuroTherapeutics, 3H Biomedical, OvaCell and NovaHep. Some of them are doing stem cell research and development themselves, others supply the cells and cell lines.

### 3.6 FUNDING OF STEM CELL RESEARCH

As in any kind of research today, many funding agents are involved in funding stem cell research. Since the beginning of this decade both public and private funders have had stem cell research on their programmes. In addition to government funding channelled through the research councils, international funding is available. The European Union funds stem cell research through the framework programmes, and the European Science Foundation funds this kind of research too. Nordic funding of stem cell research is channelled through NordForsk which also funds a research network and post-doc programme.

Under its sixth framework programme 2002–06 the European Union funded a total of 104 stem cell research projects. Eighteen of these projects involved the use of human embryonic stem cells and fourteen of them had Nordic partners. Overall EU spending on these fourteen projects amounted to almost 113 million Euros. In terms of project participants, 22 came from Sweden, 13 from Denmark and six from Finland. Most were affiliated with public research institutions, though fourteen were industry based.

The European Science Foundation has a programme called Development of a stem cell tool box (EuroSTELLS). It aims at generating fundamental knowledge on stem cell biology, setting up the bases for comparative analyses of stem cells of different origins and their clinical application in the future. The programme funds the project Translational Stem Cell Research: from basic biology to regenerative medicine. This is a good example of Nordic collaboration with partners from all the Nordic countries, the Netherlands and the United Kingdom.

An agreement establishing a Nordic European Molecular Biology Laboratory (EMBL) Partnership for Molecular Medicine is due to be signed October 3, 2007, by the host institutions of each node, i.e., University of Oslo, Umeå University and University of Helsinki and EMBL. This partnership will also involve stem cell research.

NordForsk funds stem cell research through the ScanBalt stem cell research network in the years 2005–07. The network is coordinated from Norway and has members in Sweden, Denmark, Finland, Iceland, Estonia, Lithuania, Russia, Poland and Germany. In addition, NordForsk will be funding a three year post-doctoral research programme called Nordic Stem Cell Mobility Programme, 2007–10, aiming to promote Nordic collaboration and a network of leading Nordic institutes and experts in stem cell research.

Several foundations fund stem cell research in the Nordic countries. Among these are Sigrid Juselius Foundation in Finland, Lundbeck Foundation in Sweden and Denmark, Novo-Nordisk Foundation and Knut and Alice Wallenberg's Foundation in Sweden.

# 4. Commercialisation of stem cell research

## 4.1 STEM CELLS AS PRODUCTS

Commercialisation of stem cell research is necessary for the development and manufacturing of stem cell based therapies. There is wide agreement that commercialisation is the only way in today's market economy to meet the high expectations of stem cell research. The discussions around commercialisation should be focused on clarifying the extent to which this field can be commercialised and how patent law and intellectual property (IP) structures should be shaped to create the most suitable layout for the rapid development of stem cell research to benefit society. However, this is tied to an intricate debate concerning, what is by some considered ethical dilemmas regarding the source of the "raw material", the legislative aspects and the public perception of the final product. This chapter will, with commercialisation and ethics in focus, discuss the road of stem cell research to a product on the market. By product is meant a functional product that can be manufactured under quality controlled conditions, scaled up, sold and used as desired for treatment of disease, as well as for enhancement of drug discovery and toxicity testing processes.

Although the use of somatic stem cells have ignited ethical debates as well, when it comes to commercialisation most controversy surrounds the human embryonic stem cells. The widespread use of human embryonic

stem cells is due to in the wide range of their potential applications compared to somatic stem cells. Human embryonic stem cell lines can be grown in laboratory conditions without an apparent limit. Since they are likely to differentiate into derivatives of all cells of the human body they represent a potentially valuable source of cells where cells from the patient's own body cannot be used. Also for scaled up screening systems, such as high through-put screening, where human cell sources of mature specialised somatic cells today are scarce and heterogeneous, derivatives of human embryonic stem cells have great potential for development of more accurate screening systems.

The successful isolation and propagation of pluripotent human embryonic stem cells in the late 1990s started a new field of research with rising expectations that pluripotent stem cells could provide a unique source of functional human cells for future cell therapy and tissue engineering, as well as an efficient tool for drug discovery and toxicity testing. Our quest for longer and healthier lives underpins this development. Organizations of patients with incurable diseases have much hope in pluripotent stem cells as a way of reducing debilitating human suffering by treating such diseases as Alzheimer, Parkinson's and diabetes. The pharma and biotech industries, today severely restricted by the lack of functional human systems, are in urgent need of

more efficient and accurate tools for the early drug development process and toxicity testing. Novel improved laboratory models based on physiologically relevant human cells offer better precision and more cost-effective test systems, ultimately leading to lower attrition rates and safer new drugs. Heading towards a product, basic research has made progress and breakthroughs in differentiating pluripotent stem cells towards specific cell types such as neural cells, hepatocyte-like cells, pancreatic cells, cardiomyocytes and connective tissue cells – though the step to clinical trials on humans and fully developed cell therapies still have several years to go before becoming reality. Challenges such as producing human stem cell lines under good manufacture practice (GMP) as well as scale-up of the culturing protocols and separation techniques, are essential fundamentals for the field to conquer.

There are today commercial actors in the stem cell field in all Nordic countries. Sweden and Finland have focused more on human embryonic stem cell research as a cutting edge technology and a research area which might have a market potential and benefits for the national economy, whereas Denmark, Norway and Iceland today primarily have commercial actors in the field of somatic stem cells.

In general, companies and institutions working with human embryonic stem cells warrant that all research and handling of hES cells as well as somatic stem cells are based on careful ethical considerations and that they do not see any need for somatic cell nuclear transfer (therapeutic cloning) in the foreseeable future. The companies find cloning of human beings (reproductive cloning) unethical and support initiatives aimed at a global ban.

## 4.2 PATENT LAW AND NATIONAL LEGISLATION

Fulfilment of the promises of stem cell research depends to a large extent on one's ability to convert research ideas into inventions, and further to translate the invention into practice and a final product. Taking stem cell inventions all the way to clinically approved therapies is expensive. This research, with its

long developing times to a functional, fully evaluated and approved product, would benefit from a clear framework of international and national legislation of commercialisation and patent laws. Clear guiding principles and legislation would give a framework for researchers to carry out their work with good transparency and well within the limits of what is permissible. Policies and development of regulations should be designed so that they maximise the social, medical and economical benefit of stem cell research. Clear legislation could also prevent unfounded allegations and public misunderstandings which otherwise are a risk in a new and previously unknown field.

Due to different cultural approaches, there are today differences in the national legislations on research, commercialisation and intellectual property of stem cells. This is the case within the European Union, as it is among the Nordics (for further details see chapter 7 on legislation). Regardless of dissimilarities of standpoints, a fundamental criterion for commercialisation and patenting of human stem cells has to be practised with respect for the principles of human dignity and integrity.

As a product resulting from a technical invention by scientists, isolated pluripotent stem cell lines and derivatives thereof can be considered a product of research which has no counterpart in nature. Questions of the morality of profiting from such stem cell lines should be viewed in the light of the distinction between isolated results and body parts. This distinction is illustratively stated in the Swedish legislation (Lag om genetisk integritet m.m. 351:2006) where unlinked anonymised human embryonic stem cell lines are considered results of research and therefore exempted from profit ban.

Where the results of the invention carry enough novelty, inventive step and potential for industrial application, stem cells could, as a matter of principle, be patentable. It is generally accepted that results from stem cell research done with somatic stem cells can be patentable. The question, though, is to what extent this should be applied to human embryonic stem cells. The EU Directive on

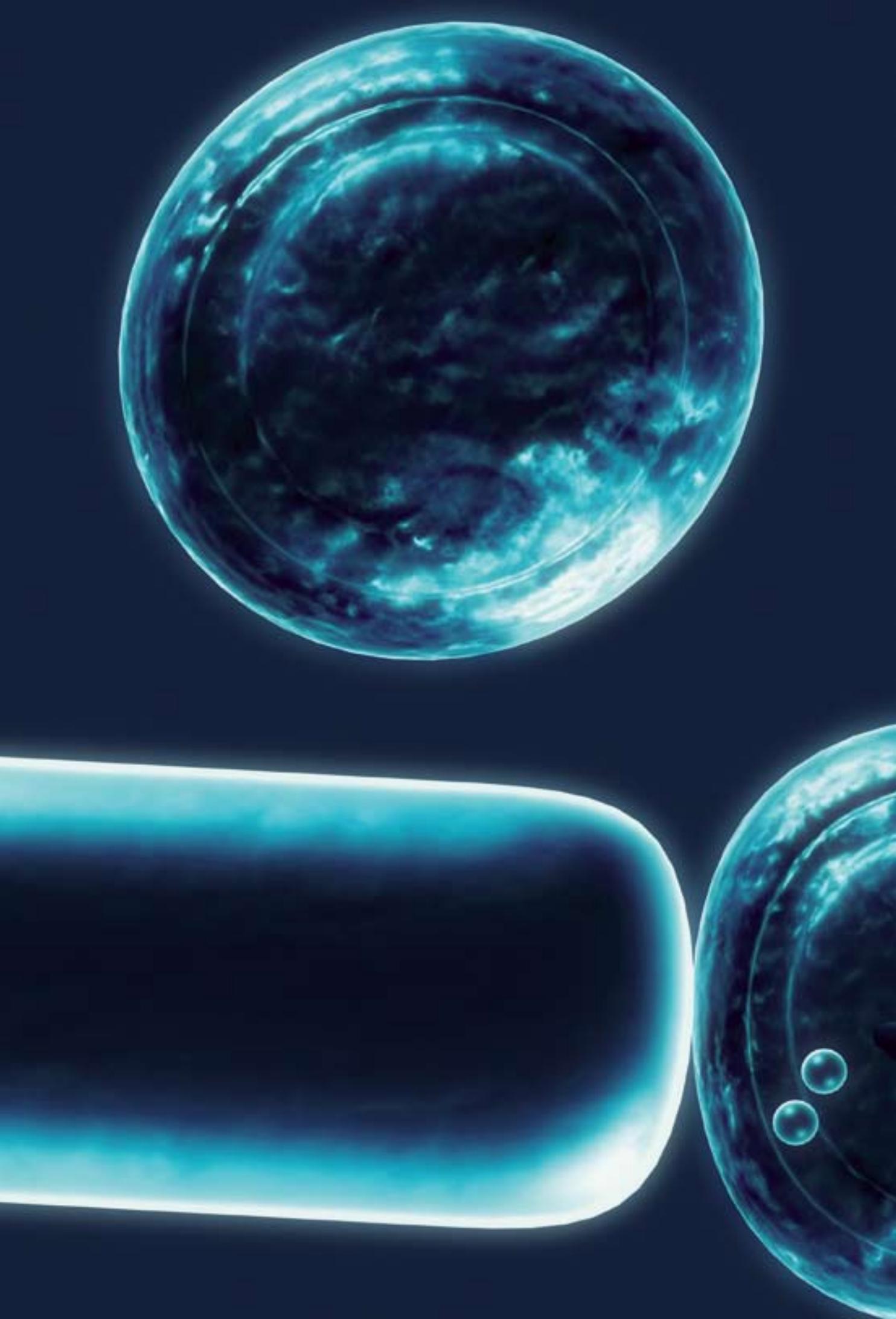
biotechnology patents (EU directive 98/44) gives some guiding, though since this directive was ratified in the late 1990s, around the time when the first human embryonic stem cell was isolated, the directive does not include sufficiently precise considerations regarding patenting of human embryonic stem cells. The question still remains whether the use of blastocysts as a source for human embryonic stem cells for industrial use should be considered as against “*ordre public*” and morality according to the EU Directive on biotechnology patents, article 53. And if so, how narrowly/broadly should this be interpreted? Can products further up the value chain be granted patents even though the source material is a blastocyst? The European Patent Office (EPO) has not yet taken a decision as to which type and on how broad human embryonic stem cell patents it can grant. In contrast to Europe, the US patent law clearly allows patenting of stem cell research and numerous patent applications on human embryonic stem cells have been granted. Also the UK patent office has granted several patents on human embryonic stem cells. The practice adopted by the EPO will most likely harmonise national practice and legislation of the Nordic countries in the future.

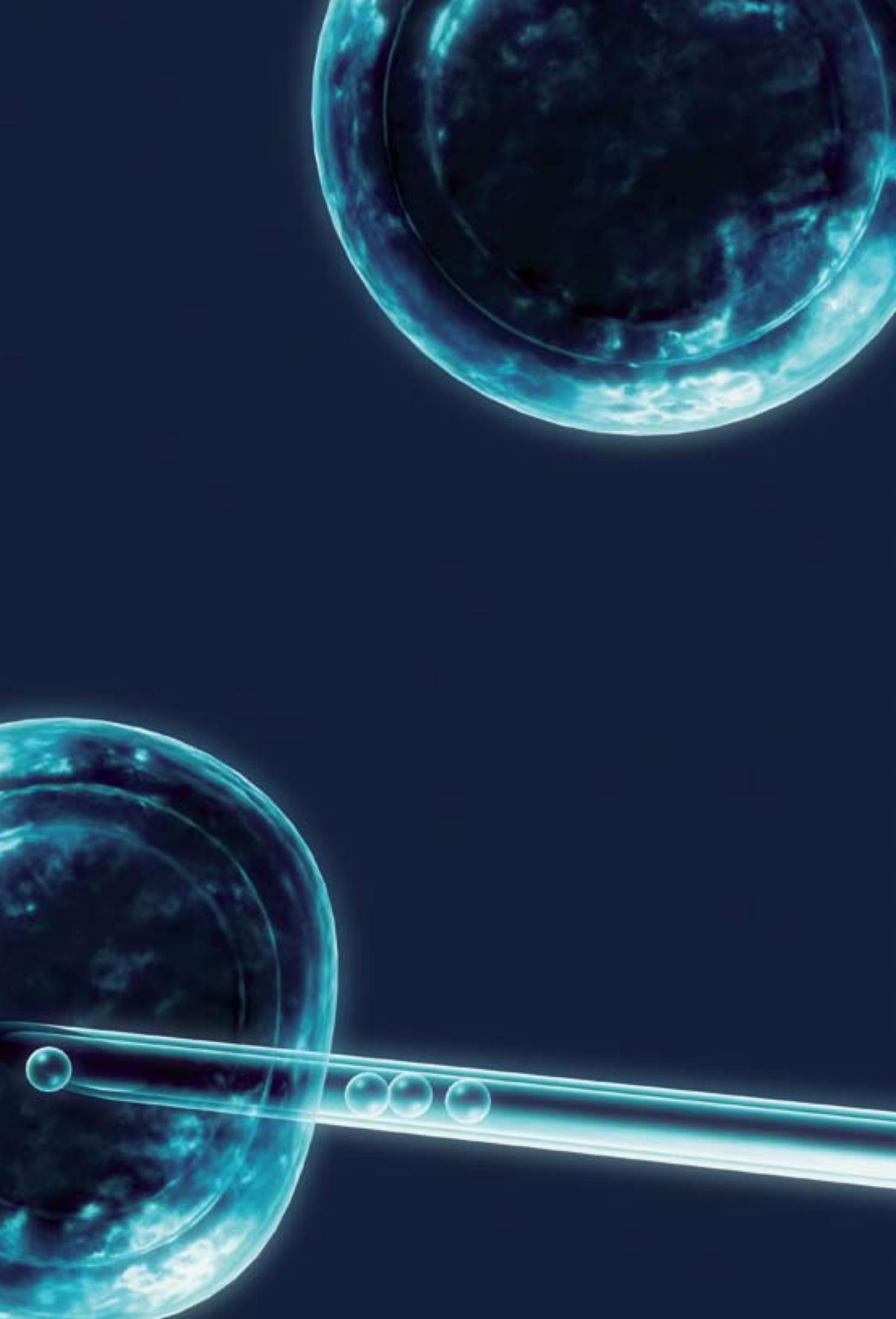
It would be a burdensome development for the stem cell field if the arena of patents becomes a minefield of overlapping patents – a patent thicket hampering companies’ and researchers’ use of developed techniques – and if too broad patents are granted, it would limit research for others. The US-granted WARF-patent (Patent number US7029913 B2, Primate embryonic stem cells, Wisconsin Alumni Research Foundation), claiming primate human embryonic stem cell lines, is often used to exemplify a broad patent giving implications on the stem cell research in the US. This patent is now being re-examined by the US patent and trademark office. A good framework for intellectual property handling would maintain access to research results and property rights rather than forcing companies to handle their results as trade secrets.

## 4.3 CONCLUSION

Patenting is essential for a company to regain the investments ventured in research and development. For an inventor, patenting works as an incitement, since research is expensive and time consuming. In particular for stem cell product development, the road towards finalised therapies is expensive and time consuming. Securing lasting financing for research and development depends to a large extent on the possibilities to protect IP rights through patenting. Exempting stem cells from patent protection might impede development in the pharma and biotech industry.

Commercialisation of stem cell research is necessary to take basic research further into products as new therapies. The field would benefit from a clear legal framework both when it comes to the moral aspects as well as the commercial aspects of stem cell research.





# 5. Ethical issues related to stem cell research

## 5.1 WHAT ARE THE ISSUES?

The primary goal of this chapter is to discuss the various ethical issues involved in stem cell research, raise awareness of the main issues involved and point to the kind of factual questions that could be relevant to their solution. The aim is not to solve these issues, in part because the ethical issues are extremely complex and any attempt is bound to be controversial, and in part because the solution to some of the ethical issues depends on complicated factual questions.

We will discuss ethical issues that are specific to stem cell research generally and, more particularly, to embryonic stem cell research. We also discuss wider ethical issues in medical research of pertinence to stem cell research.

The specific ethical issues raised by stem cell research share the fact that many of the sources of stem cells are ethically controversial. In particular, some sources of stem cells – embryos, whether surplus embryos resulting from assisted reproduction or embryos specifically made for the purposes of research by traditional in vitro fertilization, IVF or by nuclear transfer – could become human beings if they are implanted into a woman's uterus. When stem cells are derived from an embryo, the embryo is destroyed. It is a complex ethical question whether it is permissible to destroy something that has the potential to become a human person. Other sources, of course, such

as aborted fetuses, come with their own ethical issues, insofar as the research is done on material which requires respect. In this chapter we focus mainly then on the ethical issues related to research on embryos, since these issues account to a large degree for why stem cell research is so controversial. We should add two comments before we go further. First, aborted fetuses do not play a central role as sources of cells for stem cell research today. Second, in practice, most research on human stem cells today is done on somatic stem cells, which does not evoke the same ethical questions.

At the same time, stem cell research, even on somatic cells, involves the same kind of *general* ethical issues as other types of research. We can mention for instance:

- *Proper treatment of the donor.* All sources of stem cells require a human donor, either of bone marrow or of eggs and sperm, or at least involve a person whose consent is necessary, as in the case of aborted fetuses. As with other forms of medical research requiring donors, proper treatment of the donor, informed consent, etc. is necessary. Proper treatment is particularly important in cases where donation is physically (as in egg donation) or emotionally (as with consent to the use of aborted fetuses) demanding.
- *Just use of resources.* Stem cell research is

expensive, and the treatment which might eventually ensue might be expensive as well. This raises the general question of whether stem cell research represents a proper allocation of resources for medical research and treatment, and issues of patenting and access to the outcome of stem cell research.

Before discussing the ethical issues mentioned above, we will make some introductory remarks about the debate.

### **Promises and overselling**

Stem cell research would not be such an ethically difficult and complex issue if there were not good ethical reasons in its favour as well as good ethical reasons advising against it. Advances in medical science from stem cell research might save lives and increase the quality of life of patients.. Stem cell research poses ethical difficulties because there is a conflict between the possible positive consequences of stem cell research – which everyone agrees would be desirable – and the possibility that embryonic stem cell research might involve actions that are wrong in themselves. If we seek to settle this conflict with a trade-off between the reasons for and against embryo research, we need to know as far as possible what positive consequences could plausibly be expected from stem cell research. Today, however, this remains largely a question of conjecture, and it is important for a good ethical debate that we do not oversell the possible gains from stem cell research and that we have the uncertainties involved clearly in mind.

It is also important, however, to bear in mind that the expected advantages of stem cell research are not limited to concrete advances in medical treatment; the research could also lead to an important advancement of our knowledge of human biology. This kind of knowledge is necessary for scientific progress in general, even if we are unable to tell today what technologies or treatments will result from it. Furthermore, the knowledge to be gained from stem cell research has value in itself, independently of the applications which may derive from it.

### **How many embryos are needed?**

Another relevant issue is how large the need for embryos will be, both for stem cell research and for treatment. There are two possible scenarios. One is that as stem cell research progresses, and as treatment based on stem cells one day becomes available there will be a continuous and increasing demand for embryos and other stem cell sources. The second envisages a need for embryos (and other sources) for a limited period of time, while the research is done and permanent stem cell lines established. With these lines in place, new embryos may no longer be required for either research or treatment.

Which of these scenarios comes to pass is irrelevant for the principled question of the moral status of embryos. But the moral acceptability of embryo research does not necessarily rest only on the question of the moral status of the embryo. The numbers of embryos used and destroyed is also a relevant factor, in particular if we want to consider a trade-off between the respect due to embryos and the consequences of stem cell research. If the consequences are sufficiently good, some people, while condemning the destruction of embryos per se, might accept the sacrifice of a limited number. This kind of trade-off is common in consequentialist ethical reasoning. By contrast, were embryos to enjoy full moral standing on a par with human beings, most people would refuse to sacrifice even a small number.

The number of embryos necessary for research is not the only relevant consideration. We need to know *when* it is necessary to use them for research. If we know they will only be required for a limited period of time, we might accept this as an exception to a generally valid moral rule, if the consequences are good enough. But we might not accept the creation of a permanent regime of use and destruction of embryos for stem cell research. One reason for this is that we might fear that permanently institutionalizing what is seen as an inherently immoral action (the destruction of embryos with an important moral status), might encourage a certain view of the importance of moral status of the embryo, and as a result lead to more embryo research in general.

We might accept exceptions to the general moral rule where we do not accept a change in the moral rule.

### **Advantages and disadvantages of different sources of stem cells**

When assessing the ethics of stem cell research, we should look further a field than the moral status of the different sources of stem cells, and include the relative advantages and disadvantages of available stem cell sources for stem cell research and treatment. It might be the case that the sources that pose the least ethical problems are not the best sources for the purposes of research and treatment. For example, it might be less morally problematic to use embryos that are deemed not to be of good enough quality for assisted reproduction, and that, if implanted into a uterus, would probably not develop into a fully grown foetus. Yet these embryos, precisely because they fail to meet the quality criteria, might not be best suited for research either.

More generally, although the question is disputed among scientists, it is generally recognized that there are several advantages to using embryonic stem cells in addition to somatic stem cells, in particular because they are pluripotential – capable of specializing into a large number of cell types. And we might also need research on embryonic stem cells in order to know how to use somatic stem cells to best advantage as well as for basic research more generally. It is a common opinion that, although it is too early to say exactly what is to be gained from looking at embryonic stem cells, research should proceed in parallel on both embryonic and somatic stem cells. The possible advantages of embryonic stem cells must, however, be weighed against the moral problems involved their use. According to one argument, if the advantages of embryonic stem cells are still uncertain, whereas the moral cost of using such cells is certain, this is a reason for not using embryonic stem cells.

We must also consider more broadly the advantages and disadvantages of allowing various kinds of stem cell research. Banning certain forms of stem cell research might lead to the study of alternative ways of treating

the diseases, for which we seek cures based on stem cell research, and these alternative methods might or might not be ethically problematic as well; this is an open question, and should be taken into account when we evaluate embryonic stem cell research.

A ban in one country on e.g. embryonic stem cell research will mean that such research takes place in other countries, and we must ask whether it is legitimate for one country to let other countries do morally objectionable research, from which all countries in the end might profit, or if this is a case of moral hypocrisy. The argument that it is hypocritical to profit from embryo research even when one refrains, for moral reasons, from such research oneself, has been criticized on several counts, however. One is that, unless the country refraining from embryonic research has a real possibility to influence the policy of the countries permitting embryo research, it does nothing wrong in using the benefits stemming from this research, since this research would have taken place anyway. It might even be seen as a positive thing that, once the research is performed, as much good as possible comes from it. Another criticism posits a fundamental moral difference between what one does and what one merely allows to happen, and that even if it were wrong to actively engage in embryo research, it need not be wrong to allow such research to take place.

### **Ethics and language**

When discussing controversial ethical issues such as stem cell research, one must be aware that one's choice of language can influence the moral argument. (This effect is seen in other domains too: whether we speak about "genetic modification" or "genetic manipulation" will influence our reaction to these practices.) For example, reproductive cloning is widely considered to be morally wrong; and so when the technique of somatic cell nuclear transfer (SCNT) with the intention of creating embryonic stem cells for research is labelled "therapeutic cloning", the negative associations related to reproductive cloning are carried along, even if the ethical issues are not the same in the two cases. On the other hand, it

# REPRO- DUCTIVE CLONING IS WIDELY CONSI- DERED TO BE MORALLY WRONG

might be claimed that a highly technical term like “somatic cell nuclear transfer” hides the ethical issues involved.

The problem of ethical implications of the choice of language is particularly striking when talking about embryos, where a large number of terms are in circulation, and each with its particular ethical connotation. People speak of “embryos”, of “pre-embryos”, and of “fertilized eggs”, and although these expressions are not always synonymous, they tend to overlap in use, and the distinctions between them do not always correspond to clear-cut biological distinctions. The issue is complicated by the fact that different terms are used in different countries, and by the existence not only of biological, but also juridical and moral reasons for choosing this or that terminology. If, for example, the law bans research on embryos, it might be circumvented by defining the fertilized egg at a certain stage of its development not as an “embryo”, but as a “pre-embryo”.

Ideally, the ethical issues involved in stem cell research should be discussed in a morally neutral language. But it is far from sure whether we can find expressions which are completely neutral with respect to the ethical debate. One should at least strive to be aware of the effect on the ethical discussion of choosing various terms, and that choice of expression is not in itself a moral argument, even if it might be effective as a rhetorical means of influencing the moral discussion.

## 5.2 HOW TO DEAL WITH THE MORAL STATUS OF EMBRYOS

Stem cell research which uses, and destroys in the course of the research, surplus embryos or embryos created solely for the purpose of research, is seen as problematic because embryos are often seen as having a special moral status. A being’s moral status denotes what we may do to it and what we owe it. A stone does not have the same moral status as an animal, which again does not have the same moral status as a human being; hence, we can do almost anything to a stone, whereas there are limits to what we may do to animals (we may not expose them to unnecessary suffer-

ing, for example); and there are things which it is commonly thought we may do animals (breed and kill them for food), but which we may not do to human beings.

A central question for stem cell research concerns the moral status of an embryo. Some claim that it has the same moral status as a born human being, because it can develop into a human being; in that case, destroying it for research clearly is inadmissible. At the other extreme, it can be claimed that an embryo at the early stages of development has the same moral status as any cluster of cells, and that we need have no more constraints on research on embryos than on research on blood donated by adults. And intermediary positions can be found, according to which an embryo does not have the full moral status of a born human being – and so it might be acceptable to use embryos for research – and yet it does have an important moral status, which bars certain forms of use.

Determining the legitimacy of research on embryos depends to a large degree on the moral status of the embryo. However, it is extremely difficult, perhaps impossible, to reach, by reasoned argument from uncontroversial premises, a conclusion as to the moral status of the embryo. The question of the moral status of the embryo has been discussed for years by philosophers, theologians, scientists and others, and no consensus has yet emerged. This is of course not proof that a solution cannot be found, but it is an indication that we cannot reasonably hope to find an uncontroversial one soon.

Given this state of affairs – both the centrality and the difficulty of the question of the moral status of the embryo – there are two approaches one might take to the question of stem cell research on embryos. We could

- a. attempt to reach a conclusion as to the moral status of the embryo, despite the difficulties involved
- b. recognize that the question of the moral status of the embryo is one which will not be settled through rational discussion, and find a way of regulating stem cell research based on this recognition.

It might seem as if the second approach

makes the first superfluous. If we can find a way to settle the issue of regulating stem cell research without agreeing on the moral status of the embryo, why do we need to ask this question at all? One reason is that we should pursue the two approaches in parallel. Both approaches to regulating stem cell research involve very difficult problems, and instead of supposing that one will yield a solution rather than the other, it is better to attempt both solutions.

Both of these approaches assume that the goal of both ethical and political argument is not just to reach a conclusion supported by the majority, but a solution which ideally everyone can agree on, and which is justified by sound ethical reasons. Both full agreement and a sound ethical justification are ideals which we might never achieve in practice when it comes to complex issues like embryonic stem cell research; but they are nevertheless the ideals that should guide our ethical thinking on these issues.

These ideals separate the *ethical* investigation into the ethics of stem cell research from the more pragmatic question of how a political solution concerning the regulation of stem cell research can be reached. First, an ethically adequate solution should not simply reflect the opinion of the majority; the policy must also be justified, by way of ethical argument, to the minority which disagrees. Second, even if there is full agreement, the solution might not be ethically adequate if a sound justification is lacking. For example, if embryonic stem cell research turns out to succeed in delivering the cures and treatments which are sometimes promised, most or even all members of society might come to accept embryo research, not because they have made an ethical assessment to the effect that the benefits outweigh the moral costs, but simply because they appreciate the benefits so much that they do not bother to make a proper ethical assessment.

We should also note that the legitimacy of embryonic stem cell research does not depend uniquely on the moral status of the embryo. It also depends on the compromise we are willing to make between competing concerns: in

this case, the duties imposed by the status of the embryo versus the promotion of welfare ensuing from embryo research. We must also ask whether, given a certain conclusion as to the moral status of the embryo, there is a moral difference between creating new embryos for research and using surplus embryos destined for destruction anyway. A common argument is that the latter can be legitimately used for research, whereas we may not create new embryos. However, there are also arguments against embryonic stem cell research which do not rely on claims about the moral status of the embryo; rather, these arguments state that embryonic stem cell research represents an unacceptable instrumentalisation of life, turning living things into mere objects to be manipulated.

### 5.3 THE MORAL STATUS OF THE EMBRYO

Embryos as sources of cells for stem cell research can today have three different origins: they can be surplus embryos after IVF treatment; they can be created by fertilization of an egg with a sperm for the purpose of research; or they can be created through somatic cell nuclear transfer for the purpose of research, although today this is still only a theoretical possibility. In all three cases, the embryo, if it is healthy, has the potential to become a human being if it is implanted in a woman's uterus. It is this potential which normally is the reason for claims about the embryo's moral status, and in this respect, whatever its origin, the embryo enjoys the same moral status. When the purpose is reproduction, it makes a large difference whether the embryo is created by fertilization of an egg with a sperm, or through somatic cell nuclear transfer, which would give origin to a cloned child; but when the purpose is stem cell research, the ethical issues related to reproductive cloning are not directly relevant. They are, however, indirectly relevant since stem cell research based on somatic cell nuclear transfer might lead to a so-called "slippery slope" towards reproductive cloning. (See below, section 3.1.)

More important for the question of the moral status of the embryo might be the stage

of development of the embryo. The importance of this depends on the reason why we take an embryo to have moral status. We can distinguish three lines of argument concerning the moral status of the embryo: an argument based on continuity; an argument based on graduality; and an argument based on potentiality.

The continuity argument begins from the claim that the development of the foetus from an embryo to born human being is a continuous process with no sudden changes. Since we grant full moral status to born human beings, and since we can point to no specific point during the development of the foetus at which the foetus undergoes a change radical enough to warrant its sudden acquisition of moral status, we are committed to acknowledging that even an embryo has full moral status. If this is our argument for claiming that the embryo has moral status, whether we can identify the stages in the foetal development at which something radically new appears becomes of prime importance. According to the graduality argument there are such stages. For example, the 14-day limit, after which the primitive streak – the beginning of the nervous system – appears, and after which an embryo can no longer separate and give rise to twins, is often considered to mark such a radically new stage. If we thus can differentiate clear-cut stages in the development of the foetus, we might argue that the moral status, and hence the rights, of the foetus change from stage to stage.

But whether the foetal development involves clearly distinct stages loses some of its importance if what we focus on is the potential to become a human person, as the potentiality argument does. The potential can be important even if the development is not gradual, and even if we recognize that the embryo as such is not a human person. We can use as an analogy a child's right to do, when it becomes adult, things it is not yet able to do; the philosopher Joel Feinberg calls this right "a right-in-trust". (Joel Feinberg. "The Child's Right to an Open Future", in *Freedom and Fulfilment*, 76–97: Princeton University Press, 1992.) Feinberg notes that a child's right-in-trust to walk freely about is infringed if we cut off the

legs of a two-months old infant, even though the infant has no right to walk freely about before it can walk. A right-in-trust is thus the right to develop according to one's potential so that one acquires rights in the future. According to this view, an embryo might have the rights-in-trust of a human person even if we consider that it lacks the essential attributes of a human person, as long as it has the capacity to develop into a human person. And so the embryo might be protected against us destroying it for research, not because it has moral status, but because it will become a being with moral status, and thus has rights-in-trust.

This potentiality-based argument has, however, been criticized. One criticism consists in asking whether the embryo's right-in-trust gives it the right not to be destroyed. According to this view, a right-in-trust to X only says that one should have the right to X if one reaches the stage at which one normally has X; not that the embryo has a right to reach the stage of a human person. Furthermore, someone could ask what it means to say that an embryo is potentially a human being. It is only potentially a human being if it is implanted into a uterus, and receives the necessary nourishment, etc. Following this logic, might we not say that even an unfertilized egg is potentially a human being, because it can become one if it is fertilized and then implanted into a uterus? That would seem like a *reductio ad absurdum* of the potentiality-based argument. Against this argument, one could reply that the potentiality of the embryo and that of the unfertilized egg are different, since while all the former needs to develop into a human being is a certain environment, the latter requires fertilization, which involves more than just a certain environment.

We have here sketched out just some arguments concerning the moral status of the embryo. As we have said, the question of the moral status of the embryo is extremely hard to resolve. And in theory, even if we have established what moral status the embryo has, we have not answered whether we may justifiably use it for research; this answer will require a trade-off between what we owe the embryo given its moral status and the benefits

to be gained from using embryos in research. For example, although we grant animals a certain moral status, so that they should not be made to suffer unnecessarily, it is commonly accepted that if the gain is great enough, it is legitimate to subject them to painful research. So in theory, we could have solutions which allowed the use of embryos in research for some purposes, but not for others; e.g. the development of life-saving treatment, but not cosmetics. If, however, we really do acknowledge the moral status of the embryo as equal to that of a born human being, it is hard to see what purpose would be important enough to accept sacrificing the embryo. We do not accept research which kills human beings, no matter how large the benefits.

#### **Somatic cell nuclear transfer and reproductive cloning**

As far as the moral status of the embryo is concerned, there is no fundamental difference between embryos created through IVF and embryos created through somatic cell nuclear transfer, as both have the potential to develop into a human person. There might, however, be other reasons to oppose the use of SCNT. One is that this technique can also be used for *reproductive* cloning, if the embryo is implanted into a uterus. By itself, the fact that a technique can be put to illegitimate use is not a reason to ban otherwise legitimate uses of the same technique. But there is a fear that allowing SCNT for stem cell research might induce movement down the *slippery slope* to reproductive cloning. The idea is that SCNT is the *first step* towards reproductive cloning, and that once we have taken this first step, there is no natural point at which we can stop before we have gone all the way and accepted reproductive cloning.

There are at least two arguments for this view. The first is that if we continue to develop the technology of SCNT for the purpose of stem cell research, we will also be developing a technology of reproductive cloning, making reproductive cloning more likely. The second argument is that accepting SCNT will have as a social and psychological consequence that people become accustomed to the idea of

# THE MOST COMPLEX ETHICAL ISSUES CONCERN THE MORAL STATUS OF THE HUMAN EMBRYO

nuclear transfer and, as a result, less dubious of reproductive cloning as well.

When assessing such slippery slope-arguments, we must ask how probable it is that the use of SCNT for research would in fact lead to an acceptance of reproductive cloning. And if it is probable, we must also ask whether we can prevent it from happening, for example by introducing and maintaining strict laws against such cloning.

SCNT can play another and more positive role in the search for ethically acceptable stem cell research. In a variant technique, called altered nuclear transfer (ANT), the nucleus is transformed before it is transferred into the egg, so that the embryo (if indeed it should still be called an embryo) can no longer develop into a human being. This technique is seen by some as promising an ethically acceptable source of embryonic stem cells, since the potentiality argument against embryo research no longer applies. Indeed, it was introduced explicitly in response to the ethical problems of “traditional” embryonic stem cell research. It should be noted, however, that it is still in its very early stages, and as little is absolutely certain in biology, we cannot exclude completely the possibility that an embryo resulting from ANT could develop into a human being.

## **Chimeras**

The creation of chimeras (combinations of two animal species or even of animals and humans) is a further form of research to be taken into consideration. This research might raise general issues of animal welfare, for example if an animal is born with traits likely to cause it to suffer. However, in the case of stem cell research, the chimeras created might never be born, but used as stem cell pools at an early level of development. Given that no animal suffers from this research, does it involve any specific ethical issues? We can point to two such issues. First, we might object that combining two animals into a chimera involves a lack of respect for natural boundaries.

Next, regarding combinations of humans and animals, one might claim that not only have natural boundaries not been respected, but human nature as such. It might be dif-

difficult to pinpoint exactly what is wrong with such chimeras, because no person is harmed in any standard sense, at least when no such chimera is actually born (for example when human stem cells are inserted into a mouse foetus and allowed to develop there). However, we often have an intuitive reaction against this type of thing – referred to as “the yuk factor”. Depending on the value we accord our moral gut reactions, we may try to explain and justify this feeling in various ways, or we might find it morally irrelevant.

### **Christian religion and the moral status of the embryo**

As indicated, the question of moral status of the embryo is unlikely to be settled beyond dispute through shared, rational principles. Positions and arguments in this question are linked with and dependent on broader belief-systems. These might not be accessible to a complete, rational integration and harmonisation, even though they are open to rational discussion.

For some, the question of the embryo’s moral status and worth is grounded in non-religious, secular worldviews or philosophies. For others these views and arguments are closely associated with religious belief-systems. However, this significance of religiously inspired arguments and views can take different forms and positions, and might also be associated with different positions on the moral status of the embryo.

Christian religious ethics has traditionally taken a restrictive standpoint regarding moral protection of unborn life, including pre-implantation embryos, either rejecting absolutely any use that threatens the embryo’s continued life and foetal development into a born human being, or accepting such use within strict limits only.

A prominent argument within Christian ethics starts from the view that human life is created, indeed, created in the image of God. As created, human life is a gift and of great value. It should be received in gratitude and sustained as an invaluable good. As created in the image of God, human life has a specific worth and dignity distinctive from all other

forms of life, endowed with an inviolable moral status that requires its protection and respect, and forbids its destruction or harm. And this quality of human life as being created in the image of God, is – especially within a Protestant tradition, prevalent in the Nordic countries – viewed as rooted in human beings’ receptive and relational position to God, and not in human life’s inherent qualities (such as rationality, conscience, a human soul).

This value of human life as created, and created in the image of god, is related to the more specific question of the moral status of embryos in different ways. Some views see this understanding of human beings’ moral status as severing the question of moral status and protection from human life’s individual qualities. The dominant view inferred from this would be that the status of inviolability comprises human life at its earliest beginning, though some might claim that it allows a distinction between, for example, pre-implantation embryos and implanted embryos with regard to moral status. Others maintain a position close to the above-mentioned view of embryonic and foetal development as a continuous process without morally significant leaps, and draw the conclusion that the inviolable status associated with the quality of being created in the image of God pertains to human life even from its very beginning.

Others, in particular from within Roman-Catholic ethics, would maintain a position closely related to the argument from potentiality, suggesting a connection between human being created in the image of God, and its potentiality for personhood.

Either way, the conclusion tends to be that even at its earliest stages human life should be treated with the utmost respect and protected against destruction and harm. Using embryos for research or medical treatment in ways that would jeopardise their continued life, would in principle violate this entitlement to respect and protection. For some this leads to an absolute rejection of any kind of research on embryos disallowing their implantation and continued life. For others it leads to a reluctant opening for research on surplus embryos, often based on the fact that these embryos will

be destroyed one way or the other, and considering the potential benefit that can be harvested from their destruction in the course of medical research rather than simply throwing them away. However, also in cases where a restricted form of embryo research is (reluctantly) accepted, it is considered a grave, moral cost as human life at its beginning is instrumentalised, although for highly beneficial purposes.

#### 5.4 HOW TO LIVE WITH DIS-AGREEMENT ON THE MORAL STATUS OF EMBRYOS

The question of the moral status of embryos is extremely difficult to settle. Not only does it have moral and biological aspects, it also involves issues of a more metaphysical nature. It might even be a question on which agreement is impossible. If this is the case, we nevertheless need to find a way to answer the practical question of how embryo research should be regulated. To do this we need to examine the relation between the moral and metaphysical question of the embryo's moral status, and the practical and political question of how embryonic stem cell research should be regulated.

The relationship between these two questions is particularly important in a democracy where there will be widespread and irreducible disagreement in the population concerning the moral status of the embryo. But even for a person who seeks to make up her mind on how embryonic stem cell research should be regulated, it matters, because many individuals do not have a settled view on the moral status of the embryo. The question is therefore not simply about how we deal with moral disagreement between individuals who are all entirely certain what the right answer is; it is just as much about how we regulate embryonic stem cell research in a situation of moral uncertainty.

One approach to the political question of legislating regulation of embryonic stem cell research is to simply abandon the goal of agreement and let the majority decide. But it is a common democratic ideal that such fundamental moral issues should not be decided

simply by majority rule. Another approach is to seek a way of framing the question of what research on embryos is acceptable which does not require us to solve the question of the moral status of the embryo. In this view, our goal should be to find an argument for a conclusion about embryonic stem cell research where no claims about the moral status of the embryo are part of the premises of the argument. We would then have a chance of finding an overlapping consensus on the question of stem cell research, where people can agree on the regulation to be adopted even though they disagree as to the moral status of the embryo.

One example of such an overlapping consensus in a related domain concerns abortion. Some people might accept the right to abortion on the grounds that before a certain age the moral status of the foetus is negligible. Others might accord the foetus full moral status, but nevertheless accept abortion, because they think the mother's right to decide trumps the foetus's right to life. These two groups can agree on a concrete policy concerning abortion, even if they disagree about the moral status of the foetus. This example also shows, however, the limits of the search for an overlapping consensus involving all citizens, since those who do not believe the mother's right to choose trumps the foetus's right to life will not agree with the proposed policy of permitting abortion.

The search for an overlapping consensus does not need to imply that the question of the moral status of the embryo is not important. On the contrary, it is important to find a justification of the choice of regulation which respects everybody's personal conviction on this issue. If the justification of public policy does not take a stand on the moral status of the embryo, the views of no citizens on this question are rejected is invalid. It is important to recognize, however, that when it comes to issues such as the moral status of the embryo, where there are very strong and conflicting moral convictions involved, finding a *policy* that is acceptable to all (and not just to a majority) can be an extremely difficult task.

One example of a kind of consensus on embryonic stem cell research which many

people have found attractive consists in saying that as long as we find assisted reproduction through IVF legitimate, we will, at least for the time being, end up with surplus embryos. We will then have the choice either of simply destroying the embryos, or using them in research. Whatever one might think about the moral status of embryos, it seems better to use them for research than simply to destroy them with no gain ensuing. Here, the view that research on embryos is only acceptable if the purpose is noble enough might have some validity. The reason need not be that we accept a trade-off between these purposes and the moral status of the embryo; it could be that, although we may allow embryonic stem cell research, we do not want to provoke the sensibilities of those who take objection to it by doing embryo research for trivial purposes.

This argument does not tell us, however, to whether we may create embryos in order to use them as sources of stem cells. However, it might make this question less urgent, since the practical need for creating embryos will be less great if we are allowed to do research on surplus embryos.

This argument for allowing research on surplus embryos is also open to criticism. First, it can be seen as question-begging, since it presupposes that using a method of assisted reproduction that creates surplus embryos which must be destroyed is acceptable. If we truly believe that embryos have the same moral status as a born human being, we will not accept this position. Next, the argument ignores other solutions to the problem of surplus embryos, such as embryo adoption by infertile couples. Finally, the use of surplus embryos for research may reduce the incentive among doctors working on assisted reproduction to fertilize as few embryos as possible, in order to avoid the problem of surplus embryos.

## 5.5 PROPER TREATMENT OF THE DONORS

A number of general ethical points relating to the donation of biological tissue – how specific the consent should be, privacy, whether the donor can object to patenting of the research

resulting from the donation, etc. – are also relevant for the donation of stem cell sources. Furthermore, since the research is ethically controversial, and the donor is often in a difficult situation, the utmost care must be taken to treat donors decently.

One aspect which is particular to stem cell research is that the donated source might be used to create stem cell lines which may, in theory, live forever. By contrast, when one donates e.g. blood for research, it ceases to exist when it has served its purpose. The donors should be told that stem cell lines resulting from their donation might persist forever. This issue also involves the possibility of revoking one's consent. Can a donor revoke consent after she has donated e.g. an embryo, and thus require that all stem cell lines produced from that embryo be destroyed? If the standard proviso that one can always revoke one's consent is taken to hold, this might create insuperable obstacles for researchers. But donors must be given clear information about the limits on their possibility to revoke consent.

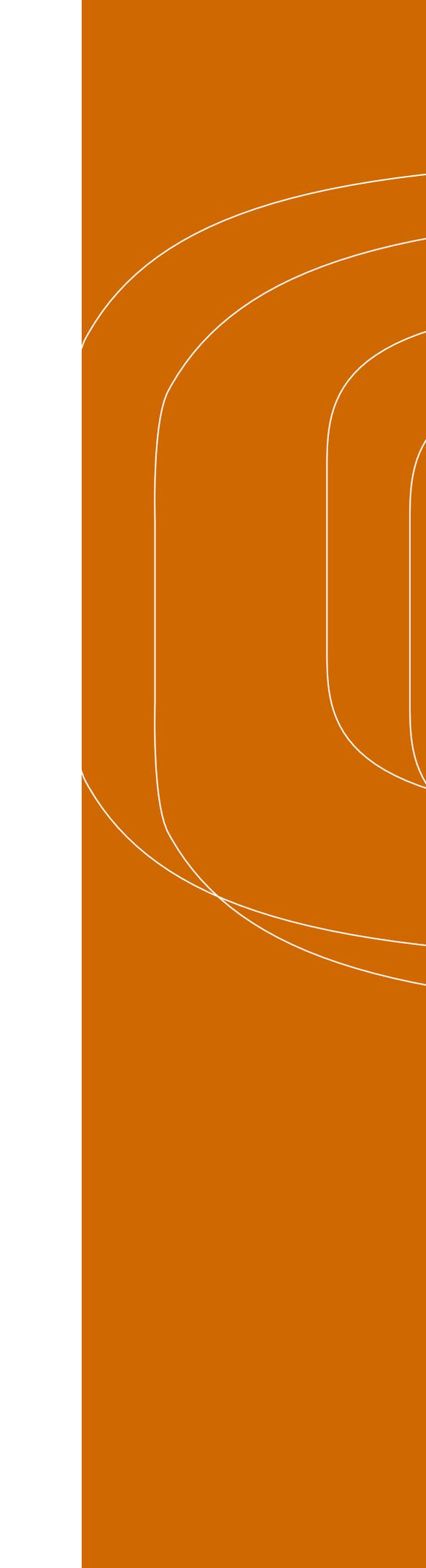
Also relevant is the question of the commercial use to which the cell lines or the research resulting from the donation may be put. Donors should be informed that profit might be made from research to which they have contributed as donors, so that if they object to such commercial use, they have the opportunity to back out.

Other factors to take into account depend on the source of the stem cells for which one seeks donor consent. We will now briefly discuss these.

### **Aborted foetuses**

The use of foetuses for research requires the consent of either the mother or both parents. A woman who has undergone an abortion will often be distraught and tired both psychologically and physically; the doctor asking for consent must be careful not to ask in such a way as to make the experience more distressing. At the same time, it might be comforting for some people to know that something good can result from the abortion.

There is also a risk that the possibility of using foetuses for stem cell research may



influence the very decision to have an abortion or not, because the abortion is seen as having at least one positive consequence. Doctors, nurses or others giving advice before the decision is taken should take care not to unduly influence the patient one way or the other by evoking possible benefits ensuing from stem cell research.

#### **Surplus embryos**

“Donation” of surplus embryos might also be psychologically problematic for the woman/couple who has had recourse to assisted reproduction. The purpose for which they had the embryos created was to have a child, and thus they might have made a psychological connection between the embryos and possible future children. Allowing the use of their surplus embryos for research might therefore be emotionally taxing.

#### **Unfertilized eggs**

To create embryos for research, donated eggs are required. This involves a hormonal treatment of women which is highly disagreeable, and which might involve risk for the donor. Recent medical developments might, however, make it possible to reduce this risk.

There are two kinds of donor of unfertilized eggs: those who undergo IVF treatment, and who in any case would need to undergo treatment, but who donate some of the eggs they produce; and those who undergo the treatment to donate eggs to others. It would be desirable to use only eggs from women who undergo IVF treatment anyway – if they have eggs to spare – so that donors do not have to undergo treatment simply in order to be donors. But we might not get a sufficient number of eggs from such donors. A further concern with egg donation is that, if women are paid for being egg donors, women, especially in Third World countries, might feel economically constrained to become donors.

#### **Bone marrow (and other sources of stem cells from adult human beings)**

The donation of bone marrow can involve a somewhat disagreeable operation, but does not by itself occasion any particular ethical problems.

## 5.6 A JUST USE OF RESOURCES

Stem cell research, as other forms of medical research, is often expensive, and the treatment resulting from stem cell research might be very expensive as well. It might thus be asked if stem cell research constitutes the best use of limited resources for medical research and treatment. This question is particularly important in view of the fact that in a global context, epidemics cause far more deaths than the diseases which stem cell research promises to cure. Some of these diseases could easily be cured or prevented if only the necessary funds were made available; for other such diseases, medical research is much needed and not prioritized today. Given this context, one might ask if expensive stem cell research from which only a relatively few and rich people in the world will profit can be defended morally.

One answer involves denying the factual premise, viz. that only the richest will profit from stem cell research. Indeed, it is possible that in the long run stem cell research will benefit everyone, because treatments might be developed for some diseases which are prevalent among poor populations as well. Even if this is the case, we must ask whether resources are best spent on developing treatments for future generations or on providing existing treatment for the benefit of today's generation.

Although these questions are certainly relevant and important, they are in no way unique to stem cell research. Global inequalities and the suffering resulting from them impinge on almost all aspects of the lives of citizens of rich countries. And although we might wish resources were more fairly distributed, it might seem inappropriate to single out stem cell research in particular as a case of the unjust use of resources. Achieving global justice requires large-scale changes in all aspects of society, and is not a task for which stem cell researchers alone can be made responsible.

The question of the best use of resources can, however, also be seen within the context of wealthy countries, where, even if we accept the idea that large sums of money be spent on medical treatment of relatively few persons, it

is not sure that stem cell research is the best way to spend this money. One reply to this objection, as well as to the previous objection, is to recall that medical treatment is not the only goal of stem cell research; the advancement of knowledge is also an important goal, and it is commonly accepted that we should spend resources on the advancement of fundamental knowledge.

A different approach to the question of stem cell research and just distribution consists in saying that stem cell research is desirable from the point of view of distributive justice, if the scarce resource we look at is not money for financing research and treatment, but organs and other body parts. The lack of kidneys and other organs, and even of blood, makes it necessary to make hard choices as to who should get these resources, which are often necessary for survival. The infinite reproductive potential of stem cell lines might be a solution to this problem, because in theory as many organs as needed can be produced.

## 5.7 ACCESS AND PATENTING

Another aspect of just distribution and stem cell research is who gets to enjoy the results of stem cell research, i.e. not only the knowledge and technology, but the cell lines produced as well. There are several reasons in favour of allowing wide access to the results of stem cell research. First, if the results include efficacious medical treatment, it is desirable that this treatment be available to as many people as possible. Next, it might be argued that results from research done on human biological material and products derived from human biological material in an important way are the common property of all humankind.

Finally, the research is based on the free and willing donation of egg cells, bone marrow, etc. by donors who receive no payment in return. Commercialization of the results of this research might therefore seem unfair to the donors. When donors donate body parts (and when people participate in research more generally) it is often under an implicit contract between the donor, the people doing the research and society: the donor participates freely on the understanding that this will be to

the advantage of society at large. One response to this is to pay the donors for their donations; however, it is a common ethical principle, generally accepted at least in Europe, that body parts, including cells, are not something that can be sold for profit. They are typically seen as belonging to a “gift economy”, and not to a market economy, and introducing payment for donations might undermine the motivation of other donors to donate freely, in addition to establishing undesirable incentives for the economically deprived to donate eggs, or other body parts. As a counterpart of the ideal of donors giving for free, it is often seen as undesirable that the researchers should make profit from the research; in return for the free and willing donation and participation in medical experiments, scientists should, it is often claimed, offer their discoveries to society without making profit.

#### **Patenting**

Related to the issue of access to the outcome of stem cell research is the question of patenting. A patent gives a right, limited in time, to stop others from commercial exploitation of an invention. Patents are usually seen as an important and necessary incentive to encourage research which is often very expensive and which might have a limited chance of success, as is often the case with stem cell research. Without the guarantee that profit can be made from an invention in case of success, companies would have little incentive to fund such research. There are therefore good reasons in favour of allowing patenting in the field of stem cell research.

These reasons must be balanced against three reasons against patenting. First, patenting might make the cost of the treatment so expensive that it is inaccessible to those who need it. Next, as already mentioned, the results of stem cell research might be seen as the common property of mankind, and something which should not be patentable. Finally, European patent law has a so-called “ordre public and morality” clause, stating that a patent might not be given if the commercial use of the invention goes against public morality. This is certainly the case for reproductive cloning, and

might be the case for other results of stem cell research as well. For example, if the creation of embryos through SCNT with the purpose of deriving stem cell lines is seen as immoral because of the moral status of the embryo, a patent on a technique for SCNT might not be acceptable.

## **5.8 CONCLUDING REMARKS**

The most complex and difficult ethical issues involved in stem cell research concern the moral status of the human embryo, and whether we may allow embryonic stem cell research even if the embryo has an important moral status, or if we do not know or cannot agree on the moral status of the embryo. But other sources of stem cells than embryos are also important for stem cell research, and these too raise ethical issues – common to many forms of medical research – which, although they may not be as complex as the question of the moral status of the embryo, are important to consider carefully.

# 6. Debate and communication

## 6.1 POLICY-MAKING AND DEMOCRACY

When it comes to policy making about complex scientific issues, there is an interesting interaction in democratic society between expert knowledge and public will. On the one hand, the policy needs to reflect the scientific practices and status of knowledge in the field while respecting the ethical principles of scientific practice and research. On the other hand, policy in a democratic society receives its legitimacy from the fact that it is accepted by the general public or at least not contrary to the will of the majority.

In order to meet this challenge, it is important to look for ways to facilitate public dialogue with the aim of informing the public and providing opportunities for discussions and exchange of viewpoints and arguments on relevant policies. If this is to feed into the law-making process, public consultation should precede parliamentary deliberations. Experience has shown that law making in this field is much more likely to meet with public approval if the public is consulted and had an opportunity to voice its concerns.

Public debate will thus serve to inform the public about the scientific issues, inform scientists and policy makers about public concerns and facilitate consensus on controversial matters. The importance of this has grown with increasingly pluralistic societies where different cultural backgrounds and religious views are governed by the same laws.

## 6.2 COMMUNICATION

Public approval and respect of public opinion are particularly important when new technology evokes ethically sensitive issues. Openness and transparency are essential to promote public trust in new technologies. The public should feel well informed and able to put forward its views on important aspects of the research and the ethical issues. Stem cell research and its application are a perfect example of such an ethically sensitive technologies. It is presented as promising cures for a multitude of devastating, today incurable, diseases, and in some research projects human embryos are used as raw material.

Scientists, ethicists and other experts should not underestimate the public's interest in scientific issues. Although most lay persons do not have the requisite knowledge to understand all of the scientific facts, their views are often to the point, and even informed by expert knowledge about the ethical issues involved.

Stem cell research, and in particular the use of human embryos for research, has provoked a heated public debate. This debate emphasizes the need for communication and dialogue about those issues that concern the public. There is also a need for continuing education and dialogue to promote public involvement in policy making. The media also play a major role in this task.

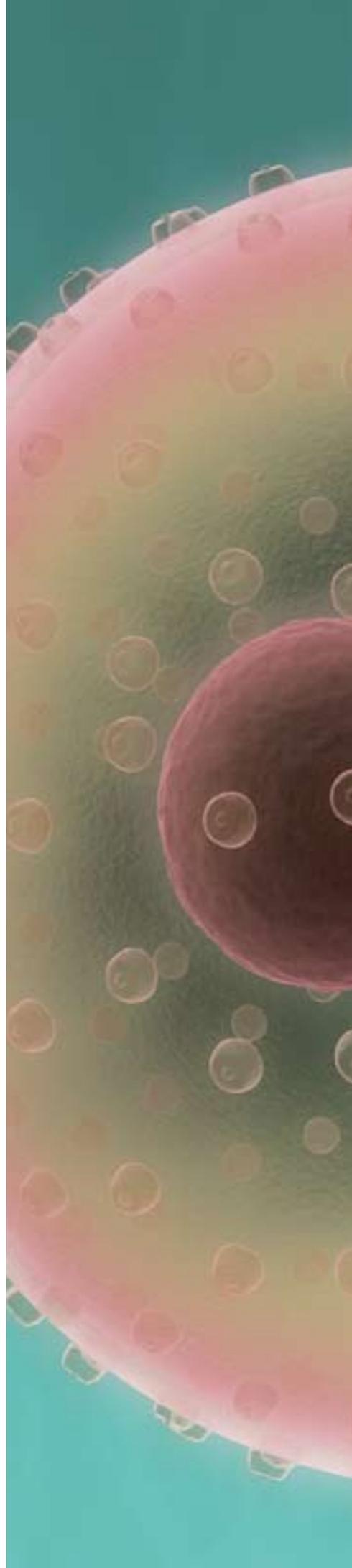
Information and communication are needed in several areas. Scientific facts and

issues involved have to be explained in readily understandable terms for non-experts. A special effort is needed to make the potential of stem cell research and embryo development more widely known and appreciated. Such knowledge will clearly inform opinions on the use of the new technology. The public should also be reminded that learning about fundamental processes is one of the key benefits of stem cell research.

The ethical issues have to be formulated and explained. Experts have discussed many important ethical issues to do with stem cell research. Often, non-experts lack the wherewithal to discuss complicated ethical questions, which makes it even more important for experts to engage in dialogue with the public in comprehensible terms.

The science funding agencies have an important task in explaining their funding policy to the public. Again, openness and transparency are essential. With increased publicity surrounding scientific breakthroughs and the promise of coming applications of use in the treatment of serious diseases, the funding bodies should take the trouble to inform the public about priority setting and how research proposals are evaluated.

As for many new technologies, stem cell research evokes expectations and hopes of rapid, spectacular discoveries. The creation of these, often unrealistic, hopes is the result of a complex process driven by diverse agents. Many patients with an incurable disease and their families have high expectations regarding the potential of the research. In view of this it becomes even more important to explain the research and its therapeutic potential realistically and in a balanced way, avoiding exaggeration. Science can fail, and positive results may not come as fast as either scientists or the public would like. Once again, the lay person may not lack the knowledge to appreciate how science works and how long it takes for a scientific discovery to become a readily available cure.



## 6.3 THE DEBATE IN THE NORDIC COUNTRIES

### Denmark

Research using human embryonic stem cells has been debated by Danes since the beginning of this century, when public awareness of this new field of research started to grow. When the Danish Council of Ethics and the Danish Ethical Council Concerning Animals released a joint report on cloning in 2001, in which they set out recommendations about therapeutic and reproductive cloning, it received extensive media coverage and fed into the public debate that was just starting on the issue of stem cell research.

The debate levelled off slightly, but was revived in 2003 by proposals to amend the Danish Act on Assisted Reproduction – which also regulates research on human embryos. The only change involved adding stem cell research to the list of purposes for which research on human embryos may be carried out. The justification was to increase knowledge of serious illnesses and facilitate the development of effective therapies. Once again the media coverage was extensive.

Public interest in stem cell research is also evident in the many locally initiated debates on cloning and stem cell research. In some of these debates, arranged by organisations all over the country, the Danish Council on Ethics has brought its opinions to bear. Different stakeholders such as universities and professional societies arrange open meetings and even “Science Theatres” to engage with the public on stem cell concerns.

It is worth noting that stem cell research is taught in most primary and secondary schools in Denmark. The Danish Council of Ethics has produced teaching materials on stem cell research for primary schools, as have private businesses and public sector bodies and institutions. The schools have responded well and taught the subject to pupils aged 14 and upwards.

### Finland

The Finnish debate on stem cell research has been limited. The media have reported some of the scientific aspects of stem cell research and there have been presentations by researchers. A new stem cell research centre opened in Finland in 2004. But there has not really been any debate on the ethical issues relating to the creation and use of human embryos for research. This may be due to the absence of legislation, though it is in the pipeline.

But if the public has been silent, experts have discussed the ethics of stem cell research since the beginning of this decade. Many articles have been published in the specialist journals and magazines. Often, these ethical concerns are raised in connection with the presentation of scientific findings.

Finnish embryo and stem cell researchers published a declaration on stem cell research in Finland in 2001. Here they made plain their views on which principles should govern human embryo and stem cell research, and how to draw the boundaries for research that is not covered by legislation. A third aim was to stimulate public debate.

In 2003 the national ethics committees arranged a meeting on stem cell research and its potential and published a press release. Later a brochure dealing with the scientific, legal and moral issues was published (*Human stem cells, cloning and research*, 2005, ISBN 952-00-1817-4).

The Finnish parliament’s standing committee for the future has also explored stem cell research and published in 2003 a technology assessment report with research-related recommendations.

### Iceland

The public debate on stem cell research in Iceland has been initiated and sponsored by independent professional organisations and research centres. The Icelandic Association of Health Care Professionals arranged the first meeting on ethical issues in stem cell research in 2002 and two years later a similar meeting was arranged by the Centre for Ethics at the University of Iceland in co-operation with the National Director of Health.

The Icelandic Research Foundation facilitated a dialogue between a geneticist and a moral philosopher as part of its popular series “Science Café” in 2005. This was very well advertised with interviews on popular TV shows and was followed by a long article in the cultural section of the main newspaper. The National Bioethics Committee and the Icelandic Society of Biologists held a joint seminar on the moral issues relating to the use of human embryos in research in 2006.

The general public has shown interest in the meetings and attendance has been good, though the issues have not sparked much controversy or discussion in the Icelandic media.

A few scientific articles were published in the Icelandic Journal of Medicine. In 2003, a paper reporting a survey of medical doctors, Lutheran ministers and lawyers found a relatively liberal attitude in these professions, something which seems also to be the case among the general public.

### **Norway**

There has been much public debate on stem cell research in Norway since 2000 when the Norwegian Biotechnology Advisory Board (NBAB) began organizing public meetings. In 2000, NBAB arranged a meeting on “Cloning and human stem cells” and one on “Therapeutic Cloning” later. Reports from both of these meetings were later published. The public debate really took off, however, one year later, when the NBAB and the Norwegian Board of Technology organized a public conference on stem cell research. A report detailing the conference was also published. The conference received enormous coverage in Norwegian print and ether media. (More than 150 articles/programmes were printed/broadcast related to the conference.) In light of the success of the conference, NBAB and the Norwegian Board of Technology published a brochure on stem cell research for use in schools. It was printed and distributed in more than 29,000 copies.

Since that time, the public debate on stem cell research has proceeded apace. This debate is largely centred on the question of embryo research, as the regulation of this research under the Norwegian Biotechnology

Act is currently under revision. A second focus of the public debate has been the use of preimplantation genetic diagnosis to select sibling who can donate stem cells (from the umbilical cord or the bone marrow) to an older sibling. A case where a couple wanted this treatment for their son caught the public eye in 2003 and sparked an intense debate. The involvement of certain newspapers and television stations are arguably swayed the government to look again at the policy. In response to the debate, the government amended the Biotechnology Act in 2004, allowing for the creation of “donor siblings” in certain circumstances. Although this debate was more about the clinical use of stem cells than stem cell research, it buoyed up public interest in the general issues involved in stem cell research. During this period, NBAB organized several public meetings on stem cell research and preimplantation diagnostics, the reports of which were also published.

### **Sweden**

The debate on stem cell research in Sweden heated up at the end of 2001. A decision on guidelines regulating stem cell research by the Swedish Research Council (Vetenskapsrådet), 3 December 2001, triggered the debate, which coincided with the international debate on stem cell research. The debate took place mainly in the morning and evening papers, and parliament. Embryonic stem cell research and therapeutic cloning were debated, more specifically questions about when life starts; if an embryo has human dignity; and if one life – an embryo – can be destroyed to bring about a cure for others. Human dignity was balanced against utility and risks against possibilities. Politicians, journalists and ethicists were active debaters. The former minister of education Thomas Östros of the Social Democratic Party, started the debate by referring to guidelines due to be issued by the Swedish Research Council in parliamentary debate with the former leader of the Christian Democratic Party, Alf Svensson. The editor-in-chief at *Dagens Nyheter* Hans Bergström was himself very active in the ensuing debate and invited the political parties to debate stem-cell research in the leading morning paper. By doing so he

helped keep the issue on the political agenda. Advocates emphasized the great potential of the stem cell technology to cure serious disease, while opponents assailed the technology for violating human dignity and pointed to the unknown risks with the technique.

When the law regulating stem cell research came into force in Sweden, 1 April 2005, allowing somatic cell nuclear transfer, creation of embryos for research by fertilisation and donation of ova directly to research, the debate started again. The same arguments were brought to bear, but this time the debate was short-lived and voices few in number. The first unusually lively debate in 2001 seems to have paved the way for the passing of a new liberal legislation on stem cell research in Sweden.

#### 6.4 CONCLUDING REMARKS

The welfare state is something the Nordic countries share as part of their histories. Their health care systems are built on the principles of and equality of access, consultation with the public and civic organisations in the creation of laws and regulations, and institution building. Unregulated market forces provoke scepticism, though the level of public trust in institutions and expert systems is relatively high. All this is often seen as constitutive of the Nordic Model, a socio-historical fact, and a welfare model for developing countries. Two other aspects of Nordic life may be of equal importance to the stem cell debate: the historical role of Protestant, Lutheran religiosity – which may also influence secular ethics – and the relative strength of women’s liberation movement, which gained force in the 1970s.

In other respects of course, the Nordic countries are different, sometimes fundamentally so. In the field of human biotechnology and stem cell research the Nordic countries could be said to embody both ends of the scale in terms of public and political discourses and regulations in Europe. Stem cell research has been debated politically and publicly more intensively in Norway than in the other Nordic countries. This is connected to Norway’s particular history of, for instance, eugenics in the 1930s and 40s, represented by the phrase “the sorting society”, and modern fears that

the liberal abortion law of the late 1970s may be under threat. These two historical forces have worked in opposite directions, creating intense political controversy. Although Sweden has witnessed even sharper public debates about the role of eugenics in “Folkhemmet” – especially the practice of involuntary sterilization, which continued into the 1950s – it has had less effect on public opinion on modern human biotechnology. This is why human biotechnology and stem cell research are conceived of in terms of “normal medicine” in Sweden, while it is conceived, and debated, as something extraordinary in Norway. The public’s trust in science and medicine extended to human biotechnology in Sweden; in Norway this was much more problematic.

Both internationally and in the Nordic countries, the use of the human embryo for research has been very central to the public and political debates about human biotechnology and reproductive technologies. However, the framing of this theme shows important Nordic differences. In Denmark, as in the UK, the main issue is the status of the embryo – whether it holds the same value as a born human or should be regarded as a cluster of cells with no specific value, – or something in between depending on the stage of differentiation and development. The justification of destroying embryos for research purposes was naturally another debated issue. In Norway this was only partly the case. Not only the destruction, but the multiple forms of manipulating the embryo for experimental purposes were highly controversial. In many ways, political and public scruples were directed at the new creative abilities of science and the threat of its constructive – in opposition to purely destructive – potentialities. This may explain why misgivings about research are not as marginalized in Norway as in the other Nordic countries. The instrumentalisation of the human body and beginning of life were irreducible to a religious/secular dichotomy terms of beliefs and worldviews, and misgivings have not only been expressed by Christian minorities. In many ways, the debate in Norway was framed in a more Germanic, Central-European cast than in the other Nordic countries.

For more than twenty years, human biotechnology and reproduction technologies have been invested with party-political interests in Norway, forming the basis of important political cleavages. This has not been the case in the other Nordic countries. In Denmark, politicians have tended to couch the central questions largely as matters of conscience or personal opinion. Although values are obviously at stake, it has not been vital for the formation of party identities. Having said that, in the last years there have been signs of increasing politicization, to which initiatives to develop and define party-standpoints are testimony.

The Nordic countries differ on the conduct of the debate. In Denmark and Norway, for instance, bioethics committees have largely led the stem cell debate. In Sweden, on the other hand, politicians and the press are mainly responsible for fuelling the debate.

THE NORDIC COUNTRIES DIFFER ON THE CONDUCT OF THE DEBATE. IN DENMARK AND NORWAY, FOR INSTANCE, BIOETHICS COMMITTEES HAVE LARGELY LED THE STEM CELL DEBATE. IN SWEDEN, ON THE OTHER HAND, POLITICIANS AND THE PRESS ARE MAINLY RESPONSIBLE FOR FUELLING THE DEBATE.

# 7. Legislation on stem cell research in the Nordic countries

## 7.1 INTRODUCTION

From a legal point of view, stem cell research can be divided into three categories according to the source material: research on human embryos or embryonic stem cells; research on foetal tissue; and research on stem cells derived from born human beings. The last category can be further divided into two subcategories: research on samples derived directly from the living donor (clinical research) and research on samples derived from archived biological materials (biobanks collected for diagnostic, therapeutic or research purposes).

Stem cell research is a very specific subject matter to legislate, and very few countries have adopted legislation devoted to stem cell research *per se*<sup>3</sup>. Much of stem cell research, namely research on stem cells taken from born humans, is covered by statutes concerning clinical medical research in general. However, some areas of stem cell research attract specific attention of the legislator and general public as they touch upon certain basic values and concern such fundamental issues as the beginning of life and respect for human dignity. Research on stem cells from human embryos (and to a lesser extent, from human foetuses) has therefore been the major motivation of many recent amendments of the relevant laws, in the Nordic countries as well as elsewhere in the world.

This chapter gives initially an account of the international and the European supranational

framework for stem cell research regulation, reviewing the measures taken by the Council of Europe and the European Union in the past 20 years. We then draw a relatively detailed picture of the legislative history of stem cell research regulation in the Nordic countries, and summarise the current regulative situation in each country. Succinctly, the perspective is widened to a global one, depicting the current situation in elsewhere in Europe with examples from the United Kingdom and Germany (Europe), USA (North America) and Singapore (Asia). We chose these countries because they play an important role in stem cell research while representing different approaches to the regulation of stem cell research. They serve therefore as a useful context for the regulation of the Nordic countries.

If not specifically mentioned, the chapter concerns the regulation of research on human embryonic stem cells, the most controversial area from an ethical and legislative point of view and where the most striking differences are seen. However, we include a few short paragraphs on legislation on clinical research and biobanks in the Nordic countries where we address some of the general legal questions on research on somatic stem cells.

## 7.2 THE INTERNATIONAL CONTEXT OF LEGISLATION ON STEM CELL RESEARCH

From a global viewpoint two observations concerning stem cell research legislation can be made. Firstly, since the turn of millennium most countries have been actively taking a stand on the matter, either by enacting specific laws or deliberately restraining themselves from such measures. Secondly, the national regulation of stem cell research appears to be divided into three categories. There are states that are very permissive and allow all embryo research and even creation of embryos for research at least by means of somatic cell nuclear transfer (SCNT) (Australia, Belgium, China, Japan, Singapore, Spain, Sweden and the UK). The next group allows research on surplus embryos from *in vitro* fertilization (IVF) (e.g. Canada, Denmark, Iceland, Finland, France, the Netherlands and Norway<sup>4</sup>). The third group bans research on human embryos (e.g. Germany, Ireland, and Italy). In addition, some countries, most markedly the US, have no (federal) legislation on research on human embryos and stem cells. This manifest divergence of legislative regimes may have profound impact on the general climate in which stem cell research takes place the overall governance of stem cell research and research may as a result move to countries and sectors with a more permissive regulatory framework and less control. The question of justice also follows: citizens of less permissive countries could reap the benefits of advances in stem cell therapies despite lack of investment by their own country. International institutions have tried to establish some common guidelines for research on embryonic stem cells<sup>5</sup>, although it is obvious that complete harmonisation even at the European level seems impossible at the moment.

### United Nations

As a reaction to the global concern over reproductive cloning, the United Nations tried for nearly two years to devise an international treaty that would ban it. The negotiating states could not, however, agree on whether to ban all forms of human cloning, including clo-

ning for research purposes (so-called therapeutic cloning), or just reproductive cloning. In the end, no treaty was adopted but the General Assembly issued a declaration banning all forms of human cloning<sup>6</sup>. The declaration was adopted by a split vote (84 for, 34 against and 37 abstentions) reflecting the divided attitudes of Member States to therapeutic cloning. All of the Nordic countries voted against the adoption of the declaration. As a declaration, the document is not a legally binding instrument.

### The Council of Europe

The Council of Europe was the first supranational European institution to react to the vulnerable position of the *in vitro* embryo in the late 1980s by giving two recommendations on the subject. Many of the principles stated in those documents dating from 1986<sup>7</sup> and 1989<sup>8</sup> are still relevant today. They include recognition of the need to protect the human embryo from the moment of fertilisation, acknowledgement of value pluralism, call for supranational regulation, and identification of human dignity as the basis for the protection of human embryos. Some of the more specific stipulations, such as the requirement of informed consent of the genetic parents of the embryo, ban on commercial use of human embryos and allowing embryo research only during the first fourteen days from fertilization are still relevant today. Optimistically, the 1989 recommendation concludes with the hope of a pan-European legal document concerning the protection of human embryos and fetuses.

The Convention on Human Rights and Biomedicine of the Council of Europe (hereafter the Biomedicine Convention)<sup>9</sup> was an important step in the regulation of modern biotechnology and medicine. The Biomedicine Convention particularised the stipulations of the European Human Rights Convention<sup>10</sup> in the field of biomedicine. Furthermore, as a convention, its legal status is stronger than that of recommendations. To date 34 countries have signed and 20 countries have ratified the Convention.

The Biomedicine Convention needs to be interpreted in the light of its out-written princi-

ples, namely i) protection of dignity and integrity of all human beings; ii) priority of individual over society; iii) right to health care; and iv) proper conduct according to professional obligations and standards<sup>11</sup>. During the preparation of the Convention there were serious doubts until the very end about whether any compromise on the wording on articles concerning embryo protection could be achieved between all the negotiating states. The discussions resulted in incorporating one article concerning research on embryos *in vitro* into the Convention. Article 18 of the Convention states that if the national law allows research on embryos *in vitro*, it shall ensure adequate protection of the embryo, and that the creation of human embryos for research purposes is prohibited. Reflecting the compromise during the preparation of the Convention, the wording of Article 18 gives a wide margin of appreciation to the states, and anything from a total ban on embryo research to the use of SCNT and creation of fertilised ova for research may be conducted without breaching the Convention<sup>12</sup>.

The protection of *in vitro* embryos was strengthened in 1998 by including an Additional Protocol on Cloning to the Biomedicine Convention<sup>13</sup>. However, this document, while banning reproductive cloning of human beings, leaves the definition of 'human being' open. The obvious reason for this seems to be to allow therapeutic cloning, if states so wish. To date, this possibility has been used by the Netherlands, which has given a written explanation stating 'that it interprets the term "human being" as referring exclusively to a human individual, i.e. a human being who has been born'<sup>14</sup>.

The Additional Protocol on Cloning is so far the most visible achievement of the Working Party on the Protection of the Human Embryo and Foetus, set up by the Council of Europe in December 1993. One of its purposes was to draft an Additional Protocol on Embryo Research, but this goal was not accomplished by the end of 2006 when the mandate of the Working Party ended.

### The European Union

The mandate of the European Union does not directly include regulation of such ethical matters as research on human embryos. However, on several occasions the Union has touched upon the issue, for example when giving directives on the legal protection of biotechnological inventions<sup>15</sup> or on the quality and safety standards of tissues<sup>16</sup>. The funding of human embryonic stem cell research through the framework programmes of research and development has also been under continuous evaluation. Furthermore, the European Group of Ethics in Science and New Technologies (EGE) established by the European Commission has actively given opinions on embryonic and stem cell research<sup>17</sup>.

The Biopatent Directive excludes the human body at the various stages of its formation and development (Art. 5) as well as uses of human embryos for industrial or commercial purposes (Art. 6) from patentability<sup>18</sup>. It is unclear whether the latter article also excludes embryonic stem cell lines from patentability. This issue is under consideration by the enlarged Board of Appeal of the European Patent Office<sup>19</sup>.

The rationale of the Tissue Safety Directive is to guarantee patient safety and ensure free movement of tissues in Europe. Accordingly, Recital 12 of the Directive states that it should not interfere with decisions made by Member States concerning the use or non-use of any specific type of human cell, including germ cells and embryonic stem cells. Otherwise, as declared in Recital 7 of the Directive, the imposed safety requirements do extend as well to adult as embryonic stem cells if they are to be used in clinical applications. The Tissue Safety Directive also requests that the Member States ensure that import of human tissues for use in humans, from countries outside of the EU Member States, come from institutions that have accreditation and permission from appropriate authorities or bodies, and fulfil standards on quality and safety that equal European standards.

The European Group on Ethics (EGE)<sup>20</sup> has been, according to its mandate, very active in issues related to research on embryos and

OF THE MORE SPECIFIC STIPULATIONS, SUCH AS THE REQUIREMENT OF INFORMED CONSENT OF THE GENETIC PARENTS OF THE EMBRYO, BAN ON COMMERCIAL USE OF HUMAN EMBRYOS AND ALLOWING EMBRYO RESEARCH ONLY DURING THE FIRST FOURTEEN DAYS FROM FERTILIZATION ARE STILL RELEVANT TODAY.

stem cells and their commercialisation. In its opinion on ethical aspects of research and use of human stem cells<sup>21</sup> it emphasised that in stem cell research the following ethical and principal values are relevant:

- i. The principle of respect for human dignity
- ii. The principle of autonomy of individuals (including informed consent, respect for privacy and confidentiality of personal data)
- iii. The principle of justice and beneficence (in relation to improvement and protection of health)
- iv. The principle of freedom of research (which shall be balanced against the other principles)
- v. The principle of proportionality (including the requirement that research methods are necessary to reach proposed goals and that no alternative more acceptable methods are available).

In addition, the EGE found it necessary to consider, based on the principle of precaution, possible long-term consequences of stem cell research and its use for individuals and societies. The EGE found that

*creation of embryos for the sole purpose of research raises serious concerns since it represents a further step in the instrumentalisation of human life” and deemed “creation of embryos with gametes donated for the purpose of stem cell procurement ethically unacceptable, when spare embryos represent a ready alternative source.*

*The EGE also stated that the creation of embryos by somatic cell nuclear transfer for research on stem cell therapy would be premature, since there is a wide field of research to be carried out with alternative sources of human stem cells (from spare embryos, foetal tissues and adult stem cells).*

In addition, EGE issued a separate opinion on the patentability of stem cell inventions<sup>22</sup> where it states that to categorically ban all stem cell patents would clearly be against both public and private interests as well as against goals set by the EU in the Biopatent Directive.

According to EGE, isolated stem cells, or even established unmodified stem cell lines, do not fulfil the established patentability criteria. In contrast, all modified stem cell lines can in principle be patentable even though their source was a human embryo, and methods for culturing stem cells are also patentable. EGE would, however, exclude methods of therapeutic cloning from patentability, since they imply instrumentalisation and commercialisation of the human embryo.

The latest opinion of the EGE concerns the ethical review of human embryonic stem cells (hESC) in research projects under the Seventh Framework Program for Research and Technological Development (FP7)<sup>23</sup>. In this opinion, EGE continues to stress the divergence of views within the Group on the moral legitimacy of research on human embryos and human embryonic stem cells. The opinion does not revisit the ethical argumentation on human embryonic stem cell research as such but concentrates on recommendations for the ethical review of FP7 human embryonic stem cell projects. In addition to the already adopted ethics rules, EGE indicates the following considerations should apply to hESC funded by the EU<sup>24</sup>:

- i. hESC lines have to result from non-implanted IVF embryos
- ii. if alternatives to hESCs with the same scientific potential as embryo-derived stem cells will be found in the future, their use should be maximised.
- iii. donors' rights (in terms of health, informed consent, data protection and free donation) have to be protected and safeguarded.

The EGE also stressed the following needs:

- i. to maximise the use of hESC banked in the European Registry on hESC Research
- ii. to take concrete actions to stimulate public debate on this research sector.

## 7.3 EVOLUTION OF LEGISLATION ON STEM CELL RESEARCH IN THE NORDIC COUNTRIES

### Denmark

The first statute to mention research on embryos in Denmark was the Act on the Establishment of an Ethical Council and the Regulation of Certain Forms of Biomedical Experiments, which was adopted by the Danish Parliament in June 1987<sup>25</sup>. The Act banned research on embryos for any purposes until the Danish Council of Ethics had developed a framework for the protection of the embryo. In addition to that, the Act banned research that aimed to create genetically identical humans beings (reproductive cloning), fusion and implantation of two genetically different embryos and the creation of hybrids from two different species. The complete ban on research on embryos was not lifted until 1992, when an Act on a Scientific Ethical Committee System and the Handling of Biomedical Research Projects was passed<sup>26</sup>. This legislation included, e.g., provisions on compulsory ethics committee review of the research project, informed consent of the research subject, and weighing and balancing of the risks and benefits to the research subjects. Although the 1992 Act concerned research on humans in general, it also included provisions on research on embryos. According to the Act, it was allowed to conduct research on fertilised eggs for the purpose of improving the results of techniques for assisted fertilisation and quality control of IVF treatment. However, the fertilised eggs could not be subjected to research more than 14 days after fertilisation, and no fertilised eggs that had been subjected to research could be implanted into a woman's uterus, unless there was no risk of hereditary illness, defects or the like. The 1992 Act also restricted research to surplus embryos only. Furthermore, the Act included the provision of informed consent of the donating couple before research could be conducted.

Denmark passed the Act on Artificial Fertilization in 1997<sup>27</sup>. With the enactment of this legislation, the provisions on research on

embryos were transferred from the 1992 Act to the new Act on Artificial Fertilization. The 1997 Act on Artificial Fertilization is the Act that governs embryo research today in Denmark, although it has been amended several times. Research on embryos is still allowed up to 14 days from fertilization, as stipulated already in the 1992 Act. However, the maximum storage time of embryos was increased to five years in 2006<sup>28</sup>, from the two years provided in the 1997 Act. The list of acceptable aims of research grew longer as well. Research for improving the results of techniques for assisted fertilisation remains as the original accepted purpose for research, but the 1997 Act added an additional purpose: research on the methods of preimplantation genetic diagnosis. The 2003 amendment added a third aim: achievement of knowledge aimed at developing cures for human diseases<sup>29</sup>. This was also the first time a specific mention of embryonic stem cell lines was added to the legislation.

It is still only permitted to use surplus embryos generated during *in vitro* fertilisation services, i.e., creation of embryos for research purposes is not allowed. Also, it is prohibited to conduct research the purpose of which is to enable the creation of i) genetically identical human beings (i.e. research on reproductive cloning); ii) human individuals created by fusing genetically different embryos or part of embryos before implantation; or iii) human individuals that are hybrids, with genetic material that includes constituents of other species. The 1997 Act added one more item to the list of prohibited research. It is prohibited to conduct research the purpose of which is to make possible the development of a human individual in a non-human (*artsfremmed*) womb.

All biomedical research in Denmark, including research on human stem cells from any source, is subject to the Act on a Scientific Ethical Committee System and the Handling of Biomedical Research Projects 2003<sup>30</sup>. Research projects must be notified to a regional committee, whose affirmative statement on ethical issues is a prerequisite for the research project to commence. However, the research use of cell lines or similar biological material

that is derived from a sample, the derivation and research use of which have already been approved by the ethics committee, need not be declared to the ethics committee, but ministerial regulations may apply<sup>31</sup>. This exception does not, however, apply to fertilised eggs, stem cells or stem cell lines derived from fertilised eggs. Written informed consent of the research subjects must have been obtained in order to use tissue from humans for biomedical research. The research subjects must be informed of the manner, significance, scope and risks of the research. However, if the sample is derived from a collection of biological samples taken in the connection of *treatment or diagnostic purposes*, only the absence of objection in the National Tissue Register is required, although the ethics committee may request a specific informed consent<sup>32</sup>. The sample may be collected and used directly for *research purposes* only with informed consent, as specified by the 2003 Act<sup>33</sup>. If the tissue can be linked to personal data, the requirements of the Personal Data Act<sup>34</sup> must be satisfied as well.

There is no specific legislation on research on foetuses. However, research on foetuses is covered by the 2003 Act on a Scientific Ethical Committee System, so an ethics committee review is required. As there are no specific provisions on who provides the consent, the ethics committee has to decide whether the informed consent of the woman who carried the foetus is sufficient.

Denmark implemented the Tissue Safety Directive through the Tissue Act of 2006<sup>35</sup>. The Act concerns mainly the collection and use of human cells for therapeutic applications or clinical experiments, and is hence not directly relevant for stem cell research as such. However, the safety standards set by the Directive and the Act must be met if the researched cells are to be used in humans.

## **Finland**

In Finland, legislating research on human embryos dates back to the enactment of the Medical Research Act in 1998<sup>36</sup>. It applies to research on born human beings, human foetuses and embryos. Research on surplus

embryos is allowed for up to 14 days from fertilization and storage of embryos is allowed for up to 15 years. The law permits isolation of stem cells from human embryos for research purposes<sup>37</sup>, but it is unclear whether it allows creation of embryos for research by way of somatic cell nuclear transfer (SCNT). The creation of embryos for research by way of fertilisation is prohibited. In the same Act, research to enable reproductive cloning is prohibited. It is also prohibited to conduct research with the purpose of creating a human being by fusion of human embryos or by combining human gametes and genes from animals.

The Medical Research Act has not been amended in relation to human embryo research since its enactment<sup>38</sup>. The Finnish community of stem cell and embryo researchers took an unusual step in 2001 when it issued a declaration on regulation in this area<sup>39</sup>. Whereas the research community unanimously condemned reproductive cloning it wanted the seemingly liberal legislative situation in Finland to continue.

In addition to the Medical Research Act, the Act of the Medical Use of Human Organs, Tissues and Cells (Tissue Act)<sup>40</sup> also stipulates on the use of human embryos, stating that embryos can only be used for fertility treatment or medical research. This restriction is grounded in the preparatory works by stating that the use of human embryos involves significant ethical questions and there are no medical reasons for other types of uses at the moment<sup>41</sup>.

The Medical Research Act covers research on living foetuses inside a uterus<sup>42</sup> whereas the Tissue Act applies to research on dead human foetuses and stem cells derived from them<sup>43</sup>. Slightly different stipulations are applied depending on the developmental state of the foetus. If the pregnancy has lasted less than 22 weeks or the foetus weighs less than 500 grams, it is considered to be dead tissue removed from the patient. The written informed consent of the woman who carried the foetus is needed, and the intended use of the foetal tissue must be explained carefully and comprehensibly. If the foetus is older or heavier, it is considered a stillborn, and con-

sent of both the woman and the father of the child are required<sup>44</sup>. As the Tissue Act stipulates that tissue from a deceased donor may be retrieved only if “there is no reason to believe that close relatives or other close persons would object”, the definition of ‘father’ should be given a broad meaning<sup>45</sup>. In both situations, it must be shown that the intended research is highly relevant and no other means to obtain the expected results exist. The Tissue Act also covers the collection and use of umbilical cord blood to which the informed consent of the woman is required. Unlike the collection of any foetal tissue, this procedure can be done without obtaining permission from the National Authority of Medicolegal Affairs.

The research on stem cells of any born person requires informed consent, either of the person herself or her legal guardian in the case of minors and incapacitated adults. Depending on the nature of the biological material, either the stipulations of the Medical Research Act (if the biological material is collected directly from the donors) or the Tissue Act (if archived samples are used) are applied. Both Acts rely on written informed consent as the general precondition for research use of the tissues and cells, but the Tissue Act allows certain exceptions if consent is not obtainable because of 1) the number or age of samples or other similar reasons (the exception applies to treatment or diagnostic samples only); or 2) the donor of the sample has died (the exception applies to both diagnostic samples and research samples). If, however, new informed consent is needed for research, the provisions of the Medical Research Act are applied<sup>46</sup>. All research on biological samples must also seek the approval of either a regional or national ethics committee according to the Medical Research Act.

As the present legislation does not cover all aspects of research on biological samples, the Ministry of Social Affairs and Health set up a Working Group in June 2006 to prepare recommendations on the utilisation of the Finnish collections of biological samples and the required statutory amendments. The Working Group is due to publish its final report in October 2007.

## Iceland

Use of human embryos for research was prohibited in Iceland by Article 11 of the Artificial Fertilization Act<sup>47</sup> (55/1996). However, according to Article 11, research on embryos is permitted if it is part of *in vitro* fertilization treatment; if the intention is to diagnose hereditary diseases in the embryos themselves; if the purpose is to advance the treatment of infertility; or if the purpose is to increase understanding of the causes of innate diseases and miscarriages. According to Article 22 of a regulation issued a year later<sup>48</sup>, it is prohibited to carry out research pursuant to the two latter purposes unless it meets the conditions of Article 1 (8) of the Regulation on Scientific Research<sup>49</sup> and the approval of the Scientific Ethics Committee or an ethics committee approval has been obtained pursuant to Article 29 of Act on the Rights of Patients<sup>50</sup>. According to Article 9 of the Artificial Fertilization Act, embryos can be stored for up to five years for the purpose of implantation into the uterus of the woman who provided the oocyte or the spouse of the man who provided the sperm. Storage of embryos for other purposes is not permitted. Article 12 in the Artificial Fertilization Act set the following limits on embryo research: it is forbidden to cultivate or produce embryos solely for research purposes; to cultivate embryos for more than fourteen days outside the body or once the primitive streak has appeared; to transplant human embryos into animals; and to perform cloning.

In spring 2007, a Government Bill (no 799/2007) amending the Artificial Fertilization Act was presented to the Parliament. It was proposed (Article 3) that when the maximum period of storage (5 years) is expired, or when destruction of embryos is mandatory, surplus embryos can be used for stem cell research by those to whom licence has been granted for such use. This would, however, only be allowed with the informed consent of the gamete donors.

When embryos are donated for research, information about their origin shall be encoded and the key to the code kept by the person responsible for the licence. The Bill proposes to widen the scope of research relative to exist-

ing legislation. According to Article 5, it would be allowed to create stem cell lines that can be used to generate knowledge in biology and medicine or to improve health and cure diseases. Before approving proposed studies, the National Bioethics Committee shall evaluate whether the proposed research fulfils these criteria. According to Article 6, creation of embryos for research purposes will be forbidden. It is, however, proposed that somatic cell nuclear transfer (SCNT) may be permitted by the National Bioethics Committee for the purpose of creating stem cell lines for treatment or to gain knowledge in biomedicine provided that both the oocyte donor and the donor of the transferred genetic material (donor of the somatic cell) have given their informed consent, and that it is not considered possible to reach the same results using stem cell lines from surplus embryos or by other research methods.

According to Article 6 of the Bill, it would be prohibited to cultivate embryos and ova that have undergone SCNT for more than 14 days, and at any stage it will be prohibited to implant a SCNT-ovum into a woman's womb. Donors shall be informed of the possibility that the created stem cell lines may be used for therapeutic purposes. According to the proposed Act, SCNT, as well as any other technique for reproductive purposes, would be prohibited. It would also be prohibited to implant human embryos into other species. In Article 8 it is proposed that the violation of the ban on reproductive cloning or violation of the legally binding conditions for the use of surplus embryos or creation and use of SCNT-ova for research, the maximum time of storage, for providing information to and obtaining informed consent from the donors, for coding and protection of the relevant information, can result in fine or imprisonment for up to one year.

It is further proposed (Article 11) to alter the name of the Artificial Fertilization Act to the Act on Artificial Fertilization and the Use of Human Gametes and Embryos for Stem Cell Research.

Furthermore, implementation of the EU Tissue Safety Directive is being prepared and

its implementation in the form of Regulation on human tissues and cells based on the Act on Medicinal Products<sup>51</sup> and the Health Service Act<sup>52</sup> is expected in the autumn 2007.

In principle, tissue stem cells could be derived from biological samples (e.g. cord blood/blood cells or other tissue) stored in biobanks. The collection, storage (more than 5 years), handling, and use of biological samples are subject to the Act<sup>53</sup> and Regulation<sup>54</sup> on Biobanks.

All biomedical research involving humans in Iceland, including research on human embryonic and tissue stem cells from any source, is subject to the Regulation on Scientific Research in the Health Sector<sup>55</sup>. It is the researcher's responsibility that the research is in agreement with the Act on the Protection of Privacy as regards the Processing of Personal Data<sup>56</sup> and the researchers shall report the research to the Data Protection Authority before it is initiated.

### Norway

The use of human embryos has been regulated in Norway since the Act on Artificial Fertilisation<sup>57</sup>, which set the legal framework for assisted reproduction in 1987. The Act banned freezing of unfertilized eggs, egg and embryo donation, and embryo research. The Norwegian Ethics Committee, which published its report 'On Humans and Biotechnology' in 1991<sup>58</sup> was equally categorical in its recommendations: one of its absolute requirements was that human embryo research should be prohibited. When the 1994 Act Relating to the Application of Biotechnology in Human Medicine<sup>59</sup> was being drafted, the Government in its bill and Standing Committee on Social Affairs<sup>60</sup> both proposed a limited use of embryos for research. Despite this, Parliament decided to maintain the total ban on embryo research.

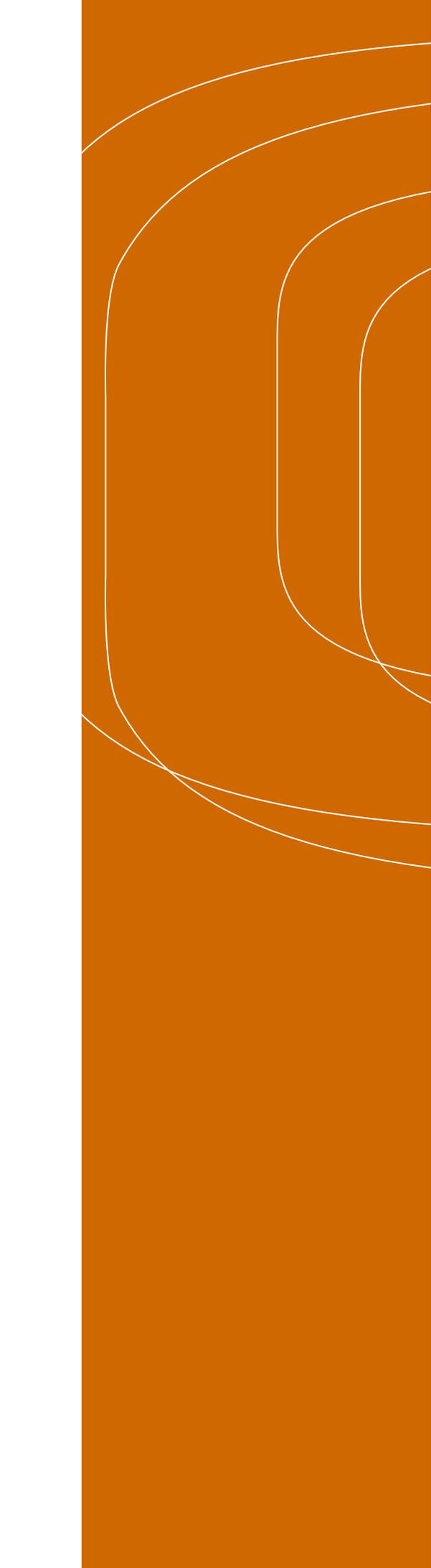
When the Labour Party came into power in 2000, a period of legislative liberalisation was expected. Instead, the government proposed in 2002 an amendment to the 1994 Act<sup>61</sup>, specifying that the ban on research on fertilised eggs also covered research on more developed embryos<sup>62</sup> and stem cell lines derived from

them. The 1998 ban on reproductive cloning<sup>63</sup> was also extended to therapeutic cloning. The Act Relating to the Application of Biotechnology in Human Medicine (Biotechnology Act)<sup>64</sup> was rewritten in 2003, and the ban on research on fertilised eggs and embryos upheld. While none of the research provisions were changed, those concerning assisted reproduction, foetal diagnostics and genetic testing were.

In January 2007, the Norwegian government proposed lifting the ban on the use of human embryos in research; such research, it said, might help the discovery of cures for a wide range of diseases. The amendment was adopted by Parliament 31 May 2007, and will come into force 1 January 2008<sup>65</sup>. According to the new law, research is permitted on surplus human embryos, i.e. embryos that have been created for the use of *in vitro* fertilisation but are not needed for that purpose anymore, and on embryonic stem cells derived from surplus embryos. The research must aim either at enhancing the *in vitro* fertilisation procedures, developing techniques and methods of preimplantation genetic diagnosis, or promote knowledge to combat serious diseases.

According to the new law, the normal limits are set for embryo research: it will not be allowed to produce embryos solely for research; to study embryos older than 14 days; to implant a research embryo into a woman; or to study methods of germ line gene therapy. The research project must be approved by the regional ethics committee. As an additional requirement, the couple receiving assisted reproduction treatment must give their informed consent to donating embryos for research. If the couple use donated sperm, also the sperm donor's consent is also required. The cloning of human beings, research on cloned embryos (i.e. embryos derived via SCNT) or cell lines derived from such embryos and production of embryos by inserting a human nucleus into an enucleated animal ovum are still banned<sup>66</sup>.

In Norway, research on biological samples from born humans is regulated by the Biobank Act<sup>67</sup>, which is applied to diagnostic, treatment and research collections of human biological samples and personal data connected to them.



A specific provision concerns the requirements of consent for research biobanks: as a general rule, the donor must be informed of the aims, methods, risks, inconveniences and expected consequences of the research project. Such factors as the risks, sensitivity of the material, and vulnerability of the donor must be conveyed to the donor. Tissue from deceased persons may be taken with presumed consent under the provisions of the Transplantation Act<sup>68</sup>, but used for research only with the permission of Department of Health, after it has received an evaluation from a regional ethics committee. The presumed wish of the deceased, sensitivity of the material, and the wishes of the family of deceased shall be taken into account by the Department. In practice, consent of the family is almost always asked for. There are certain constraints on the use of aborted fetuses in the Transplantation Act. According to the Act<sup>69</sup>, tissue from aborted fetuses can only be used for research in the absence of equally powerful methods, the use of which has been approved by the Department of Health, the woman has given her written consent to the use after the abortion, and the collection, storage and delivery of foetal material is handled by the biobank approved for this purpose.

If the collected biological material in a biobank is to be used for another purpose, informed consent must be sought again. This requirement, however, can be waived if the Department of Health, on the advice of the regional ethics committee<sup>70</sup>, approves the research. Permission to carry out research on the tissue can be withdrawn at any time. The donor can then demand that the tissue sample and any personal data linked to it be destroyed. However, if the material is already anonymised; incorporated into a biological product; data are included in a scientific work; or the law requires that the material be preserved, the donor may not ask for her sample to be destroyed.

### **Sweden**

The first Nordic country to have a specific act on research on human embryos was Sweden, which in 1991 decided to allow research on human fertilised ova<sup>71</sup>. The precondition for

such research was the informed consent of the gamete donors. The research was allowed until 14 days from fertilisation, but it was prohibited to implant research embryos into the uterus of a woman. The aims of the research were not identified as such, but research into developing methods of producing potentially hereditary genetic effects was banned. The storage of fertilised eggs was allowed for up to one year from fertilisation or longer if authorized by the National Board of Health and Welfare. The storage period was extended to five years in 1998. From 2003 onwards, the ethical evaluation of the research proposal became mandatory by law with the introduction of the Ethics Review of Research Involving Humans Act<sup>72</sup>.

The law was quite dramatically amended in 2005 when Sweden as the first Nordic country allowed the use of the somatic cell nuclear transfer technique with human embryos<sup>73</sup>. At the same time, a clarification was made in the preparatory works that allowed the creation of embryos for research by fertilisation<sup>74</sup> and donation of ova directly to research. The reform was preceded by several ethical evaluations and the Government heard experts in the field of medicine, medical law and ethics<sup>75</sup>. Although the Government recognised that the liberalisation of embryo research regulation did involve some serious ethical concerns, it nevertheless concluded that they were outweighed by the expected outcomes of such research. The preparatory works also reiterated the point made already at the preparatory stage of the 1991 Act that fertilised eggs *in vitro* were not considered embryos, as the implantation into the uterus was seen as the decisive moment for that definition<sup>76</sup>. This is also the position today in Sweden<sup>77</sup>. At the same time, the informed consent provisions were amended. If the research was conducted on fertilised eggs, which were initially created for the purposes of IVF treatment, it was considered necessary to involve not only the gamete providers, but also the man or the woman of the treated couple who was not a gamete donor. Furthermore, according to Swedish law, informed consent is required from the identifiable donor of the somatic cell for the SCNT.

In the latest revision, Sweden gathered together the regulation of gene therapy, genetic testing, preimplantation diagnostics, *in vitro* fertilisation and research on fertilised eggs under the Act on Genetic Integrity<sup>78</sup>. No substantial amendments to the law with regard to research on fertilised eggs or 'eggs that have been subject to somatic cell nuclear transfer' were, however, made in that connection. However, the more general provisions on restrictions on developing methods for producing potentially hereditary genetic effects were modified. The mere development of certain methods is no longer prohibited, only measures aimed at actually achieving such hereditary changes or research that will cause them.

According to the Act on Transplantation<sup>79</sup>, medical interventions on aborted fetuses may only be conducted with the consent of the woman who has carried the foetus. Before consent can be obtained, the woman shall be informed of the procedure and the purpose to which the biological material will be put. Additionally, the National Board of Health and Welfare must give its approval. This can only be granted on exceptional grounds. A physician who has been involved in decision-making on the abortion, or carried out the intervention, cannot take part in decisions regarding use of tissue from the foetus.

Sweden does not have a specific law on patients' rights as such; patients' rights are rather described as obligations of health care personnel by the Act on Professional Activities in Health and Medical Services<sup>80</sup>. However, any research on identifiable biological material from humans can only be conducted if the research plan has been approved by an ethics committee as depicted in the Ethics Review of Research Involving Humans Act. Furthermore, as long as the (stem) cell lines can be traced back to their original donor and the human materials originate from a biobank set up in the professional activities of a health care provider (as opposed to a research institution), the studies of foetal embryonic stem cells as well as those of born humans fall under the provisions of the Biobank Act<sup>81</sup>. According to the Biobank Act, the sample donor or

woman who carried the aborted foetus must be informed of the purpose and goals of the intended research. After receiving the information, the person may give or withhold her consent of the use of her tissue in research. Should the research purpose change, consent will need to be obtained from that same person, to the extent considered necessary by an ethics committee<sup>82</sup>. If the person has died, his or her nearest relatives shall be contacted and given reasonable time to object to the new research purpose. This requirement can also be waived by an ethics committee.

Consent may be withdrawn at any time, at which point the tissue samples must be immediately either destroyed or made irreversibly

anonymous. The coded or anonymised samples of a biobank can be forwarded to another institution for the same research if the sample donors have consented to this. When the samples are no longer needed for the original purpose, they shall be either returned or destroyed.

The creation of chimeras and hybrids has not been explicitly addressed in Swedish law and falls thus under more general provisions of the Ethics Review of Research Involving Humans Act and the prohibition against genetic modifications that could be inherited by humans set out in the Act of Genetic Integrity.

Relevant law(s)	<b>Denmark</b> Act on Artificial Fertilisation (1997:460)	<b>Finland</b> Act on Medical Research (1999:488)	<b>Iceland</b> Assisted Reproduction Act (1996:55)	<b>Norway</b> Biotechnology Act (2003:100)	<b>Sweden</b> Act on Genetic Integrity (2006:351)
Research on surplus embryos	+	+	+	- <sup>83</sup>	+
Storage of embryos solely for research	5 years	15 years	-	-	5 years
Creation of embryos for research via fertilisation	-	-	-	-	+
SCNT for creation of blastocysts and derivation of stem cell lines	-	?	-	-	+
Reproductive cloning	-	-	-	-	-
Ongoing legislative measures			Bill nr. 799/2007	Ot. prop. 26 (2006–2007)	

Table 1. Summary of the current legislative situation in the Nordic countries with regard to research on embryonic stem cells, fertilised eggs or pre-embryos created by SCNT

## SS7.4 REGULATION OF STEM CELL RESEARCH FROM A GLOBAL VIEWPOINT

### Europe

The legislation on human embryonic and stem cell research varies widely in Europe, from a total ban on all embryo research to permissive regimes allowing even the creation of embryos solely for research purposes. The area is subject to continuous legislative measures, a fact which must be borne in mind when assessing any compiled information. The following summary is based on the information provided by the National Ethics Councils of the 27 Member States of the European Union (May 2007) published by the European Group of Ethics in July 2007<sup>84</sup>. The data have been amended in light of information compiled from the two non-EU Nordic countries, Iceland and Norway. For the states for which more detailed information is given, the legislation has been individually studied for the purposes of this report.

The EGE categorises the EU Member States into four distinct groups according to how they regulate research on human embryonic stem cells<sup>85</sup>:

1. *Permissive position* (embryo creation is allowed for research purposes): Belgium, Spain<sup>86</sup>, Sweden and the United Kingdom.
2. *Permissive position with restrictions* (human embryonic stem cell derivation is allowed from embryos created as a result of assisted reproduction technology and in vitro fertilisation): e.g. Czech Republic, Denmark, Finland, France, Greece, Iceland, the Netherlands, Norway<sup>87</sup> and Portugal.
3. *Restrictive position* (derivation of new human embryonic stem cell lines is restricted, but importation (under certain conditions) is allowed: Germany and Italy
4. *No specific legislation*: e.g. Bulgaria, Cyprus, Estonia, Ireland, Luxembourg, Latvia, and Romania. However, some countries have indicated in the EU process that they are against human embryonic stem cell research although they do not currently have specific legislation covering it (e.g. Austria, Lithuania, Malta, Poland and Slovakia).

Other types of categorisations can be used. The EGE approach focuses on whether there is any specific legislation on the derivation of human embryonic stem cell lines. Earlier compilations of data from the EU Member States have, for example, focused on whether research on human embryos is prohibited or allowed in general<sup>88</sup>. Therefore, some countries in the EGE report appear to have no legislation in the area, although provisions may exist in legislation that governs e.g. assisted reproduction. Such countries include, for example, Austria and Ireland.

The Member States are unanimous on reproductive cloning, which is forbidden in all 27 EU countries as well as Iceland and Norway. Furthermore, according to a survey compiled in 2004, seven out of 20 European countries included in the survey were known to regulate on the creation, development or implantation of human-animal chimeras or human-human hybrids. Where these had been taken up in specific provisions, they are also invariably banned<sup>89</sup>.

### Germany

In Germany, the original Embryo Protection Act from 1990<sup>90</sup> was based on the principle of full protection of the *in vitro* embryo, and allowed only such actions on embryos that were of direct benefit to them. The creation of embryos was possible only for the purpose of giving rise to pregnancy. In other words, embryo research even on surplus embryos was forbidden, as was the creation of embryos for research purposes, the only acceptable form of embryo research being one benefiting the embryo in question with the intent to implant it into a uterus. Also all forms of cloning, whether for therapeutic or reproductive purposes, were forbidden by the Embryo Protection Act already in 1990. Due to the definition of embryo, research on single totipotent cells was also prohibited, but the Act did not ban research on pluripotent stem cells. However, as the derivation of pluripotent stem cells from an embryo inevitably means destruction of that embryo, it was not possible to produce embryonic stem cell lines in Germany.

As the Embryo Protection Act did not prohibit importation, distribution or acquisition of pluripotent (embryonic) stem cells, the German legislator needed to take stance on these issues when the cultivation of human embryonic stem cell lines became possible in the late 1990s. Balancing the need to protect human life, preserving human dignity and basic right of freedom of science, the Stem Cell Act was passed in 2002<sup>91</sup>. The Act prohibits in principle all importation and utilization of embryonic stem cells, in order to prevent any German contribution to the destruction of embryos worldwide.

However, embryonic stem cells can be imported into Germany for scientific research if 1) the cell lines were created before 1 January 2002; 2) the cell lines were created from surplus embryos; and 3) no economic compensation was offered for the donation of the embryos. Scientific research on embryonic stem cells must further aim either at generating basic knowledge or increasing medical knowledge for the development of diagnostic, preventive or therapeutic techniques for humans. In addition, the research question must have been studied as far as possible with animal models, and the expected results, according to state-of-the art evaluation, cannot be obtained by any other means than by studying embryonic stem cells. Each research project on embryonic stem cells is evaluated by the Central Ethics Commission on Stem Cell Research, a nine-member committee consisting of experts in biology, ethics, medicine and theology. A public registry of imported stem cell lines and research conducted on them is held.

### **United Kingdom**

The United Kingdom has been regulating research on human embryos since the Human Fertilisation and Embryology Act (HFE Act) came into force in 1990<sup>92</sup>. This Act established the Human Fertilisation and Embryology Authority (HFEA), an independent governmental agency, which licenses and monitors the conduct of all *in vitro* fertilisation procedures and embryo research in the UK. It is a criminal offence to conduct research on

human embryos without an HFEA license, and the research on *in vitro* human embryos is allowed only for the fourteen days from their formation. Originally, the Act stipulated that the aim of the research should be one of the following: to promote advances in the treatment of infertility; to increase knowledge about the causes of congenital diseases; to increase knowledge about the causes of miscarriage; to enhance knowledge in the development of more effective contraception; or the detection of genetic or chromosomal abnormalities before implantation.

As the HFE Act defines the human embryo as being a result of fertilisation, the authority of HFEA to control research on entities resulting from therapeutic cloning was challenged in early 2000s. At first, the High Court ruled that entities resulting from SCNT were not covered by the definition of embryo, but this decision was reversed by the Court of Appeal<sup>93</sup>. In order to ensure the ban on reproductive cloning, the UK Parliament passed the Human Reproductive Cloning Act in 2001. It aims to prohibit all reproductive cloning by stating that it is a criminal offence to place "in a woman a human embryo which has been created otherwise than by fertilisation"<sup>94</sup>.

In response to the scientific advancements in stem cell biology, the HFE Act was supplemented with the Human Fertilisation and Embryology (Research Purposes) Regulations in 2001. In these Regulations, the purposes for which the HFEA may grant license is extended to research that increases knowledge about the development of embryos, increases knowledge about serious diseases, or enables application of such knowledge in the development of treatments for such serious diseases. In February 2002, the HFEA approved the first two studies on human embryos for the production of stem cell lines for research purposes according to the new rules. Two and a half years later, in August 2004, the HFEA approved for the first time a study that involved production of embryos via SCNT for research use only. Scientists were permitted to transfer nuclei from skin cells or stem cells into an egg cell, with the purpose of increasing the understanding of embryo development that could be used

to develop treatments for serious diseases. In September 2007, 33 research projects are licensed by the HFEA, of which fifteen relate to derivation of embryonic stem cell lines and one involves cell nuclear replacement.

5 September 2007, the UK Human Fertilisation and Embryology Authority announced that it would be making decisions on the licence applications for human-animal hybrid embryos in November 2007 in the light of the cautiously positive response from its Hybrids and Chimeras Consultation conducted in April–July 2007<sup>95</sup>.

### USA

The USA has no federal legislation on embryo and stem cell research, although many states have legislation on these issues. In contrast with most European countries, the public debate has been less about what kinds of research should be illegal than what kinds of research should be funded with public money<sup>96</sup>. The most recent federal action concerning regulation of embryo and stem cell research dates from 2001, when President George W. Bush ruled that federal funds can only be used for research on embryonic stem cell lines that were created before August 9, 2001<sup>97</sup>. Since then there have been two legislative attempts to lift the ban on using federal funds for research on embryos and other embryonic stem cell lines. Both Bills passed through the House of Representatives and the Senate but were vetoed by the President<sup>98</sup>. In early 2007, the Senate proposed a Bill to intensify the research to derive human pluripotent stem cell lines, which would not demand creation or destruction of human embryos<sup>99</sup>. In September 2007, the Bill is under review by the House Committee on Energy and Commerce and the Subcommittee on Health of the House of Representatives.

In contrast, several states have been active in passing their own legislation on embryo and stem cell research; they exhibit widely varying attitudes towards embryo research. New Jersey and California are among the most permissive ones, allowing virtually any kind of research on *in vitro* human embryos, including therapeutic cloning. Both

of these states also actively promote such research via research funding. Some other states have adopted a completely opposite legislative strategy. In, e.g., Arizona, Louisiana, Michigan, North Dakota and Pennsylvania, it is currently forbidden to conduct research on living human embryos or on entities resulting from therapeutic cloning. As the terminology and legislative techniques vary from state to state, it is difficult to obtain a completely clear picture of US legislation on embryo and stem cell research. The situation is further complicated by the fact that significant review processes are continuously ongoing both at the federal and at the state level<sup>100</sup>.

### Singapore

Singapore is one of the liberal legal regimes concerning human embryonic research, and hence also a domicile of many companies and research institutes pursuing stem cell technologies. The legislative procedure on human embryonic research in Singapore began in the late 2000s<sup>101</sup>, when a Bioethics Advisory Committee was appointed to examine the ethical, legal and social issues related to embryonic stem cell research. The Committee was to balance protection of human life by curing serious diseases versus protection of human life in the form of embryos. When doing so, it concluded that the expected benefits of embryonic stem cell research for mankind are so enormous that no type of research, including production of embryos via SCNT or fertilisation for research purposes only, can be categorically forbidden<sup>102</sup>.

The Bioethics Advisory Report led to a comprehensive Bill on Regulation of Biomedical Research. However, the state decided to adopt a step-by-step model towards regulation of embryo research, and enact firstly on human reproductive cloning only. Hence, research on human embryos is at the moment governed by the Human Cloning and Other Prohibited Practices Act<sup>103</sup> only. The primary purpose of the Act is to prohibit reproductive cloning and human-animal experiments. To achieve this, it bans the placing of any human embryo clones in the body of a human; placing of any kind of human embryo (whether clones or not) into

an animal; and placing animal embryos into humans. The Human Cloning and Other Prohibited Practices Act operates via specific prohibitions, and the limits of the allowed actions must be deduced from the stipulations which explicitly ban other practices. As the Act states that “[n]o person shall develop any human embryo, that is created by a process other than the fertilisation of a human egg by human sperm, for a period of more than 14 days” and that “[n]o person shall develop any human embryo outside the body of a woman for a period of more than 14 days”, it is clear that the use of surplus embryos and the creation of embryos via SCNT for research purposes is allowed. The Act does not take an overt stance on whether it is allowed or prohibited to create embryos solely for research by means of fertilisation, but this seems permissible at the moment, until the legislator clarifies its stance on the issue<sup>104</sup>.

The ordinary time-limit for human embryo research, 14 days from embryo formation, is applied, and it is prohibited to develop embryos beyond this point outside the uterus. It is also forbidden to place human embryos anywhere else in a human than a woman’s reproductive tract. In addition, the Act contains a comprehensive section banning commercial trading of human sperm, human ova and human embryos. It is forbidden to offer or accept any inducement, discount or priority in the provision of service for the supply of any human egg, human sperm or human embryo. However, reasonable expenses incurred by the person when donating germ cells or embryos can be reimbursed.

## 7.5 CONCLUSIONS

All of the Nordic countries have responded to scientific developments in biomedical research and have passed legislation regulating research on human embryos and tissues derived from foetal material and live persons. As long as there is no international consensus on the legitimacy of embryonic stem cell research, the regulation of embryonic stem cell research will for the time being rest with the national states. Accordingly, there is some variation in the Nordic responses to research on human embryos. Sweden has one of the most liberal attitudes towards human embryo research in the world and Norway has only recently lifted its blanket ban on research of any kind on human embryos. Iceland allows research on human embryos for limited IVF-related purposes (although this may soon change), whereas Denmark and Finland allow scientifically justified research on surplus human embryos. In all the Nordic countries reproductive cloning is prohibited. The regulation of research on born humans rests on the long-established principle of informed consent in all of the Nordic countries.

## 8. Stem cell research – the Nordic dimension

There is active stem cell research of high scientific standard in all the Nordic countries, with strong intra-Nordic and international collaboration. This includes basic and applied research on human and animal embryonic and somatic stem cells. All the larger universities in the Nordic countries have stem cell research programmes or projects and there are several research centres devoted to stem cell research. All the Nordic countries have private companies focusing to a different degree on stem cell research and utilization of stem cells in research and development of products and technologies. Clinical trials involving stem cells are conducted at least in Finland, Denmark and Sweden.

The focus of the different research groups within academia and industry in the Nordic countries covers wide areas of research and development involving embryonic stem cells as well as somatic stem cells originating from a broad range of tissues. The research is addressing basic scientific questions in developmental biology, haematopoiesis, cancer and neuroscience, and covers the span from stem cell differentiation into different types of specialized cells, to highly applied research in regenerative medicine and cell replacement therapy, various types of cell based therapies and transplantations, tissue engineering and screening of drugs and other bioactive compounds. Scientists agree that the knowledge generated from embryonic stem cell research

contributes to the success of somatic stem cell research and vice versa, and there is a cross-fertilization between research on human and animal stem cells. Human embryonic stem cell lines are being created in research centres in Finland, Denmark and Sweden and several Nordic research groups are generating embryonic stem cell lines from other species. Generation of cell lines from various somatic stem cells is common and these cell lines are widely used for basic research. There is also an emphasis on development of technologies related to stem cell isolation, culture and differentiation. In this highly competitive field there is also well established and fruitful collaboration between different groups in the Nordic countries. This, together with the scientific excellence, should allow the Nordic research community to continue to play a major role in future stem cell research and development.

For the Nordic countries to further benefit from stem cell research, several factors are of importance. In addition to scientific excellence, these include access to funding, investment in research and development, good education systems, international collaboration and student exchange, a supportive legislative framework, strong democratic tradition, favourable bioethical climate and the public perception and support.

The research councils in all the Nordic countries fund stem cell research, and so does NordForsk. In addition to public fund-

ing, there are many private foundations funding Nordic stem cell research, and scientists from all the Nordic countries have been successful in receiving funds from highly competitive international programmes, such as the European Science Foundation and the Framework Programmes of the European Union. The growing number of private companies involved in stem cell research indicates that investors believe in the potential application of stem cell research for product development and financial gain.

The use of fertilised eggs for research on embryonic stem cells is regulated in all the Nordic countries, albeit in different contexts (i.e., assisted reproduction, biotechnology, medical research or genetic integrity). The recent or ongoing changes in the legislative framework regulating stem cell research in all the Nordic countries reflect a response to the rapid scientific advancement in the field. The use of somatic stem cells for research purposes is regulated by legislation on biomedical research involving humans or clinical research and by legislation on archived biological material or biobanks. All the Nordic countries, except Norway, have a fairly new legislation on clinical research (since 1999 or more recent). Iceland, Norway and Sweden have specific laws on biobanks (since 2000 or more recent)<sup>105</sup>. However, research on human embryos and embryonic stem cells touches upon basic values and concerns such fundamental issues as the beginning of life and respect for human dignity. It has therefore particularly attracted the attention of the legislators and the general public. Thus, research on stem cells from human embryos has been the major motivation for many of the recent amendments of the relevant laws in the Nordic countries, as elsewhere in the world.

There is some variation in the legal framework for research on human embryos and embryonic stem cells in the Nordic countries. Sweden has one of the world's most permissive legislation for research on human embryos and embryonic stem cells, allowing creation of embryos for research via fertilization under very specific circumstances and following strict ethical review. Norway has

only recently lifted its total ban on research on human embryos. Iceland allows research on human embryos for limited IVF-related purposes. A Bill amending the Artificial Fertilization Act, presented to the Parliament in 2007, proposes scientifically justified research on surplus human embryos, something which is already allowed by the recent legislation in Denmark and Finland. Sweden allows somatic cell nuclear transfer in order to create blastocysts for the derivation of embryonic stem cells. This is also proposed by the amending Bill in Iceland. In all the Nordic countries reproductive cloning is prohibited.

In today's market economy, commercialisation of stem cell research is inevitable for the translation of basic knowledge into products, such as new diagnostics, therapies and treatments. A clear legal framework for stem cell research, including for the patenting of the results of this research, is of major importance when it comes to application and commercial aspects.

In the Nordic countries, as elsewhere, the revision of the legislative framework to allow embryonic stem cell research is related to the hope that the research will increase the understanding of biological processes and disease pathogenesis and thus contribute to the development of novel diagnostic methods and treatment options for serious incurable diseases. However, the question of stem cell research, in particular human embryonic stem cell research, is not only a legislative question, but also a complex ethical issue, raising several important concerns. The hope for a prospective potential of increasing understanding of biological processes, as well as developing treatment for serious and currently incurable diseases is certainly an important ethical and moral concern. Another one is the question of what it is acceptable to do to a human embryo, and for which purposes. The surplus embryos are destroyed through the process of deriving the stem cells, which raises the question whether it can be accepted to destroy an embryo. This question is addressed in different ways in the ethical debate surrounding embryonic stem cell research. An embryo does have the potential to become a human

being, if implanted into a uterus, which for some leads to the conclusion that it is entitled to protection from destruction. Another view is that the embryo is not entitled to this protection until it has developed further (for example has been implanted in a uterus, or the primitive streak has developed). An argument, frequently put forward, is that there might be an important difference between the use of surplus embryos (from IVF) that will be destroyed anyway, and the creation of embryos solely for research purposes, and that the former is less problematic than the latter. Genetically matched stem cells are believed to reduce the risk of immune rejection, a common problem in tissue transplantation. Therefore, creation of blastocysts for stem cell derivation through somatic cell nuclear transfer (SCNT) is performed in order to obtain stem cells that are genetically matched to the donor of the somatic cell nucleus. SCNT, however, seems to raise additional ethical concerns, in particular as the blastocyst has the potential to develop into an embryo and then into a cloned human being, if implanted into a uterus. Importantly, implantation of SCNT-egg cells is prohibited by law in all the Nordic countries. Those who resist SCNT technology generally claim that creation of genetically identical embryos (or blastocysts) is problematic, and might start a "slippery slope" towards reproductive cloning, which is ethically unacceptable to most people and banned by law in all the Nordic countries, as generally worldwide. The ethical complexity which tends to surround derivation of stem cells from embryos has led to a search for alternative and perhaps less ethically controversial sources. When applying the so-called "altered nuclear transfer" the nucleus is transformed before it is transferred into the egg and the modified egg can only be used for derivation of stem cell lines, but can not develop into a human being. This technique may provide a less controversial source of embryonic stem cells, since the potentiality argument against embryo research no longer applies. In addition to ethical arguments specific for research on embryos and embryonic stem cells, research on somatic stem cells also raises ethical questions and more general ethical issues related

to biomedical research in general also apply.

Although there might be a wide agreement in the Nordic countries on certain fundamental ethical principles, the debate is also embedded in to people's moral values, religion and cultural background. The democratic societies in the Nordic countries are similar in many ways, as reflected in the debate on stem cell research in the different countries. But they are also part of the globalization in science and technology, as in other areas, which influence the discussions, legislation and policy making.

In our open democratic Nordic societies policy must reflect the scientific practices and knowledge in the field, while receiving its legitimacy from its acceptance by the majority of the people. Thus, open dialogue between experts and the public is important for discussions among the citizens about the scientific issues, to make the scientists and policy makers aware of public concerns and to reach consensus on controversial topics. Stem cell research has caught the interest of the public in all the Nordic countries. The intensity and character of the public debate and the degree of involvement of experts, patient organization and policy makers and the participation of the media varies between the countries. In particular, there is a large variation concerning the degree in which teaching material is produced and the subject is taught in schools. Generally, there has been more emphasis on expert reports and recommendations aimed for the policy makers and legislators than on producing material for the general public. Citizens should have access to basic facts about stem cell research and its prospects and the right to participate in the debate on the ethical issues involved. Scientists should communicate the scientific advances and obstacles encountered in the course of their research, and engage in the public debate. The choices made by funding bodies concerning policy and prioritization should be transparent and the reasons for the choices should be accessible to the citizens.

The Nordic countries have a long and highly esteemed tradition in biomedical research, and the Nordic stem cell research is in general of very high quality. The legal

framework and bioethical climate are relatively favourable, public funding and private investments are increasing, and there is strong public support. Thus, with a coordinated strong effort, the Nordic countries can play a major role in stem cell research and translation into products and other measures that will be of benefit to future health and to society.

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32 Sundhedsloven (Lov nr. 546 af 24. juni 2005), 32 §.

33 Section 16.5 §.

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43 With the amendment 547/2007, a new paragraph 2 was added to Section 1 of the Act clarifying the scope of the Act.

44 Section 5 of the Decree by the Ministry of Social Affairs and Health on the declaration of death (9.1.2004/27) states the defining measures for differentiating dead tissue from stillbirth.

45 Section 9 of the Tissue Act.

46 This issue has not been very clearly regulated, and has led to uncertainty in the field.

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50 Act on the Rights of Patients No. 74/1997.

51 No. 93/1994.

52 No. 40/2007.

53 Act on Biobanks No. 110/2000.

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57 Lov 12. juni 1987 nr. 68 om kunstig befrugtning.

58 NOU 1991:6.

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- 61 Ot.prp. nr. 108 (2001-2002).
- 62 A conceptually interesting division is made in Norwegian legislation between fertilised eggs and embryos, where embryos are more developed versions of fertilised eggs, where the division of cells has already taken place for an undefined time, albeit still in vitro. The division has not been given legal significance, however. Ot.prp. nr. 108 (2001-2002) p. 23.
- 63 Ot.prp. nr. 21 (1997-1998).
- 64 Lov 2003-12-05 nr. 100: Lov om humanmedisinsk bruk av bioteknologi m.m. (bioteknologiloven), sist endret ved lov nr.45 av 25. juni 2004.
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- 68 Lov 1973-02-09 nr 06: Lov om transplantasjon, sykehusobduksjon og avgivelse av lik m.m.
- 69 Sections 8a-8h§.
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- 75 Regerings proposition 2003/04:148.
- 76 Regerings proposition 1990/91:52 p. 33, Regerings proposition 2003/04:148 p. 28-29.
- 77 The view was taken, however, in the Governmental Bill that when Sweden ratifies the Convention on Human Rights and Biomedicine, a reservation needs to be made with regard to Article 18, which prohibits the creation of embryos for research purposes. Regerings proposition 2003/04:148 p. 43.
- 78 Lag om genetisk integritet m.m. 351:2006.
- 79 Lag (1995:831) om transplantation m.m.
- 80 Lag (1998:531) om yrkesverksamhet på hälso- och sjukvårdens område.
- 81 Lag om biobanker i hälso- och sjukvården m.m. 297:2002.
- 82 Chapter 3, section 5 and Regerings proposition 2002/03:50, p. 126-127.
- 83 Norway will allow research on surplus embryos starting from January 2008.
- 84 Copies of the response sheets are annexed in the EGE opinion no. 22 "Recommendations on the ethical review of hESC FP7 research projects", [http://ec.europa.eu/european\\_group\\_ethics/activities/docs/opinion\\_22\\_final\\_follow\\_up\\_en.pdf](http://ec.europa.eu/european_group_ethics/activities/docs/opinion_22_final_follow_up_en.pdf).
- 85 Iceland and Norway added by the authors.
- 86 The new Act on Biomedical Research passed by Spain in 2007 distinguishes between fertilisation and SCNT. Although the new law explicitly prohibits the creation of pre-embryos and embryos for the exclusive use of research, using the SCNT technique is allowed in order to obtain stem cells for research or therapy, as both 'pre-embryo' and 'embryo' are defined as the results of fertilisation.
- 87 This categorisation is based on the already accepted amendment to the Biotechnology Act that enters into force in January 2008.
- 88 Survey on Opinions of National Ethics Committees or similar bodies, public debate and national legislations in relation to embryonic stem cell research and use. Volume I EU member States, [http://ec.europa.eu/research/biosociety/pdf/mb\\_states\\_230804.pdf](http://ec.europa.eu/research/biosociety/pdf/mb_states_230804.pdf), Volume II, Countries Associated with FP6 and Third Countries, [http://ec.europa.eu/research/biosociety/pdf/non\\_eu\\_countries\\_230804.pdf](http://ec.europa.eu/research/biosociety/pdf/non_eu_countries_230804.pdf).
- 89 Survey on Opinions of National Ethics Committees or similar bodies, public debate and national legislations in relation to embryonic stem cell research and use. Volume I EU Member States, [http://ec.europa.eu/research/biosociety/pdf/mb\\_states\\_230804.pdf](http://ec.europa.eu/research/biosociety/pdf/mb_states_230804.pdf), Volume II, Countries Associated with FP6 and Third Countries, [http://ec.europa.eu/research/biosociety/pdf/non\\_eu\\_countries\\_230804.pdf](http://ec.europa.eu/research/biosociety/pdf/non_eu_countries_230804.pdf).
- 90 Embryo Protection Act 1990: [http://www.bundestag.de/parlament/gremien/kommissionen/archiv15/ethik\\_med/archiv/embryonenschutzgesetz\\_engl.pdf](http://www.bundestag.de/parlament/gremien/kommissionen/archiv15/ethik_med/archiv/embryonenschutzgesetz_engl.pdf)

- 91 Stem Cell Act 2002: [http://www.bundestag.de/parlament/gremien/kommissionen/archiv15/ethik\\_med/archiv/stammzellgesetz\\_engl.pdf](http://www.bundestag.de/parlament/gremien/kommissionen/archiv15/ethik_med/archiv/stammzellgesetz_engl.pdf).
- 92 See Plomer, Amanda: Beyond the HFE Act 1990: The Regulation of Stem Cell Research in the UK. *Medical Law Review* 10: 132-164 (2002) and Halliday, Samantha: A Comparative Approach to the regulation of Human Embryonic Stem Cell Research in Europe. *Medical Law Review* 12:40-69 for a more detailed review of the legislative process in the UK.
- 93 See *R (Bruno Quintavalle on behalf of Pro-Life Alliance) v. Secretary of State for Health*, [2001] EWHC 918 (High Court), [2002] EWCA Civ 29 (Court of Appeal) and [2003] UKHL 13 (House of Lords).
- 94 Human Reproductive Cloning Act (2001), s. 1(1).
- 95 <http://www.hfea.gov.uk/en/1517.html#consultation>.
- 96 See Taylor, Patrick L.: The Gap between Law and Ethics in Human Embryonic and Stem Cell Research: Overcoming the Effect of U.S. Federal Policy on Research Advances and Public Benefit. *Science and Engineering Ethics* 11:586-616 (2005), p. 609-610 for a critique of the current federal policy.
- 97 [www.whitehouse.gov/news/releases/2001/08/print/20010809-1.html](http://www.whitehouse.gov/news/releases/2001/08/print/20010809-1.html).
- 98 H.R. 810, "the Stem Cell Research Enhancement Act of 2005", vetoed by President Bush on July 19, 2006; S.5, "The Stem Cell Research Enhancement Act of 2007", vetoed by President Bush on June 20, 2007.
- 99 S.30 Hope Offered through Principled and Ethical Stem Cell Research Act.
- 100 Taylor, Patrick L.: The Gap between Law and Ethics in Human Embryonic and Stem Cell research: Overcoming the Effect of U.S. Federal Policy on Research Advances and Public Benefit. *Science and Engineering Ethics* 11:586-616 (2005), pp. 596-597.
- 101 Until then, research on human embryos was governed by guidelines concerning assisted reproduction practices.
- 102 See Kian, Catherine Tay Swee & Tien Sim Leng: The Singapore approach to human stem cell research, therapeutic and reproductive cloning. *Bioethics* 19(3):290-303 (2005).
- 103 Bill No. 34/2004, Act No. 35/2004, which came into force October 1, 2004.; <http://statutes.agc.gov.sg/> (search page in English).
- 104 It is expected that Singapore will issue separate laws on human embryonic stem cell research and human tissue research. Kian & Leng 2005, p. 296.
- 105 Legislation on Biotechnology in the Nordic Countries – An overview. TemaNord 2006:506 © Nordic Council of Ministers, Copenhagen 2006, ISBN 92-893-1273-4.



Stem cell research has grown rapidly in this decade and the scientific achievements have created hopes for new treatments of severe incurable diseases. As a result of the research, the economic prospects are also growing. At the same time, ethical questions related to the sources of some stem cells, i.e. human embryos, have stimulated intense debate among scientists, ethicists, health professionals, patient organisations and the public. Funding agencies, policy makers and legislators have also responded to the rapid scientific advancement in the field.

The present report was commissioned from the Nordic Committee on Bioethics by NordForsk in December 2006. The aim of the report is to strengthen the Nordic stem cell research community and policy makers by providing a joint Nordic knowledge base as a support to future, well-informed decision making regarding such issues.

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