II. Background to the Science

A. What Are Stem Cells?

Stem cells are the "body's natural reservoir."[4] They have the capacity of self-renewal or differentiation. In other words, they can copy themselves or become other specialized cell types.**(Annex II)** For instance, blood and muscle cells as such are not able to make copy of themselves, then in that case stem cells fulfill this task. As regards their capacity to differentiate into specialized cells, stem cells could be categorized as totipotent, pluripotent and multipotent. Totipotent stem cells have the ability to form any cell types that make up the extraembryonic tissues such as placenta and have the potential to develop into the whole organism. Contrary to that, pluripotent stem cells have the potency to develop into any of 220 cell types in the human body but not to the whole organism. Having the least flexibility, multipotent stem cells have the ability to develop into more than one cell type of the body.[5]

B. Source of stem cells

There are three types of human stem cells known so far with regard to their sources. These are adult stem cells, ESCs and iPSCs.[6]

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4 Euro Stem Cell, *FAQ about Stem Cells and Regenerative Medicine*, *available at* http://www.eurostemcell.org/stem-cell-faq/introduction-stem-cells#t14n43 (last visited Aug 11, 2012); California Institute for Regenerative Medicine, Stem Cell Definitions, http://www.cirm.ca.gov/StemCellBasics_Definitions#2 (last visited Aug. 11, 2012); The Nat'l. Inst. of Health, *Stem Cells Basics, Resource for stem cell research*, www.stemcells.nih.gov (last visited Aug. 11, 2012).

5 Nirupama Shevde, *Flexible Friends*, 483 NATURE, S23 (2012).

6 *Id.*.

1. Adult Stem Cells

The first isolation of blood-forming adult stem cells was accomplished by Irving Weismann of Stanford University.[7] Adult stem cells should not be confused because of the use of the term 'adult' to create a false impression that they could be found only in the body of adults. For that reason, the tissue-specific stem cell would be a more accurate choice of terminology.[8] These specialized cells can be found in tissues of adults, children and fetuses. The problem encountered by scientists in the research on adult stem cells is related to their low quantity and to the difficulty to generate it because of their location in the tissue. In addition to that, at the current state of the art, there is no full understanding about their place of derivation and the manner of differentiation.[9] For now, known locations of adult stem cells are brain, liver, intestine and skin. Because these cells go out from their niche when there is a signal from the organism for the repair of the damaged cell.[10]

Adult stem cells are multipotent, they can become a cell related to their tissue of origin. **(Annex IV)** As to their functionality, in the case of heart attack for example, one could think to refer to adult stem cells found in the heart. However, heart cells could hardly be generated because scientists do not know yet the characteristics of the necessary signal of the body to derive the stem cell able to form the heart muscle cell. Another problem is that, adult stem cells from other tissues having usually the self-renewal capacity, would only differentiate into cells similar to their origin. Shevde draws attention in her article to the latest development in 2011 related to the discovery of a protein to make the adult stem cells of different origin to become the heart muscle cell. From these findings, it seems that there is a need to get over more ground for adult stem cells.[11]

2. ESCs

With regard to the history of the research in this field, ESCs were derived for the first time in 1970 by Leroy Stevens at the Jackson Laboratory. Also

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7 California Institute for Regenerative Medicine, *supra* note 4.
8 *Id*..
9 Shevde, *supra* note 5, at S25.
10 *Id*. at S23.
11 *Id*. at S25.

human embryos could be used to generate hESC lines. The growing of hESCs was achieved for the first time by James Thomson at the University of Madison.[12] Unlike adult stem cells, ESCs are generated from the inner cell mass of the embryo at the blastocyst stage which is a period of 5-6 days after fertilisation.**(Annex III**) Embryos that have been traditionally fertilised 'in vitro', in fertilisation clinics could be one source for ESCs.[13] Another source for ESCs could be the embryos created by the transfer of a nucleus of a somatic cell (any body cells different from egg or sperm) into an egg cell without nucleus. This technology is called SCNT.[14] **(Annex V)** Resulting ESCs have the same DNA as somatic cells and they can differentiate like ESCs derived from the traditionally fertilised embryos.[15]

The uniqueness of ESCs lies in their capacity to self-renew endlessly and to differentiate into any cell type in the body; in other terms, they are pluripotent.[16] For that reason, ESCs are quite important in the field of biotechnology and medicine research.

3. iPSCs

In a fervent research environment dealing with stem cells, some exciting developments continue to occur. In 2006, Dr. Yamanaka and Takahashi showed that a regular cell being with a particular purpose which is not pluripotent anymore, could become a stem cell having similar properties to ESCs.[17] This was done for the first time by the introduction of four genes into mouse fibroblasts. **(Annex VI)** A year later, the applicability of this method to humans was also reported by the same group of scientists.[18] At the time very close to this announcement, Dr. Thomson's group have reported the generation of human iPSCs using a different method from the one

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12 Thomas F. Budinger&Miriam D. Budinger, Ethics of Emerging Technologies, 342 (John Wiley&Sons, 2006).
13 California Institute for Regenerative Medicine, *supra* note 4.
14 *Id.*.
15 Byrne J.A et al. *Producing Primate Embryonic Stem Cells by Somatic Cell Nuclear Transfer*, 450 Nature, 497, 497 (2007).
16 Budinger&Budingger, *supra* note 12, at 342.
17 Shinya Yamanaka, *Induced Pluripotent Stem Cells: Past, Present, and Future*, 10 Cell Stem Cell 678, 678 (2012).
18 *Id.*.

used by Yamanaka's group.[19] For the possible use of these cells in patient treatments, some concerns about their probability to develop tumours have been discussed. As we learn from Shevde, Dr. Yamanaka and his colleagues announced that they resolved this problem by the elimination of the tumour causing gene.[20] Although iPSCs have different origin, namely embryos are not required for their generation, they are 'remarkably similar' to ESCs according this field.[21]

19 Shevde, *supra* note 5, at S24.
20 *Id.*.
21 Yamanaka, *supra* note 17, at 681.