Human Fertilisation and Embryology Authority
Scientific and Clinical Advances Group

Committee:	Scientific and Clinical Advances Group
Meeting Date:	30th November 2006
Agenda Item:	7
Paper Number:	SCAG (11/06)03
Paper Title:	**Derivation of embryonic stem cell lines from a single blastomere**
Author:	Hannah Darby
For Information or Decision?	Decision
Resource Implications:	No immediate resource implications. Any work required will be considered for the 2007/2008 business plan.
Communication	If the view of SCAG varies greatly from the view SCAG came to on this technique in April 2006 then this will be communicated to ELC.
Recommendation to the Committee:	Members are asked to: • Discuss the findings of the paper (Annex A). Consider in particular whether blastomere derived hESC lines will differ from conventional hESC lines in their ability to form functional differentiated cell types. • Consider the implications for assisted conception. • Consider that, in the light of the new findings of the paper at Annex A, members wish to review the opinion they came to about this technique in April 2006.

1. Background

1.1 This issue was identified through the horizon scanning process. The derivation of stem cells from blastomeres was initially postulated as an alternative source of embryonic stem cells abrogating the need to destroy an embryo in the process of deriving the stem cell line[1].

[1] The President's council on Bioethics report.

In order to derive a stem cell line from an individual blastomere, a cell would be removed at the 8-cell stage (as it would be if PGD were being performed) and this cell would then be cultured *in vitro.* If cultured in the correct conditions, a human embryonic stem cell (hESC) line could develop from the individual blastomere. The embryo from which the cell was removed would continue to develop and then be transferred back to the woman in the hope of establishing a pregnancy.

1.2 This technique was previously considered by SCAG in April 2006. At this meeting members came to the view that the use of this technique in humans is not realistic, the success rate and the number of people that will benefit from it will be low. Also, if it is possible to produce therapeutic lines embryos will be created specifically for this purpose. At this meeting SCAG considered a paper (Chung et al, 2005) in which a single mouse blastomere was cultured to form an embryonic stem cell line. In this paper the individual mouse blastomere was cultured in the presence of other mouse embryonic stem cells to promote stem cell line growth. Stem cell lines derived from individual mouse blastomeres expressed *Oct-4* (a stem cell marker) and formed embryoid bodies containing cells of all three germ layers. The embryonic stem cells were contributed to every cell type when injected into an 8-cell mouse embryo.

1.3 At the April 2006 SCAG meeting members decided that the use of this technique should next be considered in April 2007. However, since this meeting a paper has been published reporting that a group in the USA (Klimanskaya et al, 2006 – Annex A) have derived human embryonic stem cells lines from individual blastomeres. At the last SCAG meeting, members felt that it would be valuable to review the situation, and possibly the view reached at the previous discussion, in light of the new data.

2. Deriving human embryonic stem cell lines from an individual blastomere

2.1 Klimanskaya et al (2006) derived human embryonic stem cells from single blastomeres. Sixteen embryos were thawed and cultured to the 8-10 cell stage. The zona pellucida was disrupted and individual blastomeres mechanically separated. The separated blastomeres were cultured together in the same medium but arranged so as to avoid contact with each other. Nineteen embryonic stem-cell like outgrowths and two stable hESC lines were obtained.

2.2 When the hESC cultures were allowed to overgrow or form embryoid bodies, they readily differentiated into cells of all three germ layers (pluripotency demonstrated by the formation of teratomas in NOD-SCID mice). The hES cells could also be differentiated *in vitro* into cells of specific therapeutic interest. Two stable hESC lines were obtained.

2.3 The group believe that the success rate can be further increased by optimising conditions at the earliest stages of blastomere outgrowth. Additional studies will also be necessary to determine whether blastomere derived hESC lines differ from conventional hESC lines in their ability to form functional differentiated cell types.

2.4 There is a possibility that 8 cell stage blastomeres are totipotent and have the potential to implant and develop into a human. However, studies to date indicate that blastomeres at this stage or earlier have different developmental properties.

3. Potential use of hESC lines derived from individual blastomeres

3.1 This technique is not necessary for the purpose of deriving stem cell lines in the UK because the use of embryos to derive these lines is legal. However, as embryos are not destroyed using this technique it would address ethical concerns. There are also other purposes for which people may wish to use this technique:

- Patient matched hESC in case the child/adult from which the cell line was derived develops an illness in the future (potential future personal use)
- hESC to be banked for use of any HLA-matched patient that may require (potential future altruistic use)
- Stem cell line for the treatment of a HLA-matched sick older sibling

The above uses are dependent on the development of techniques that would allow the embryonic stem cell lines to be differentiated into cells that can be used in the treatment of specific illnesses.

3.2 The procedure used by Klimanskaya et al to extract the blastomeres from embryos is similar to that used for PGD. Therefore blastomeres extracted in the process of PGD could be used for stem cell generation as well as genetic testing and blastocysts could be transferred, without affecting clinical outcome, at 5 days. However, this has not been tested as Klimanskaya et al did not carry out PGD and did not transfer any embryos following blastomere extraction.

4. Ethics and Law Committee

4.1 This issue was considered by Ethics and Law Committee in July 2006. ELC members were of the opinion that parallels can be drawn between this technique and cord blood banking. In both situations there is the possibility of patients feeling pressure to bank the cells or cell lines for the future health of their child. They considered it important that, if the technique was introduced, patients should be made aware that currently there are very few conditions that may be treated using stem cells. Before this technique could be used it would be

important to ensure that patients understand exactly what the technique involves and they give informed consent.

5. Conclusions

5.1 Members are asked to:

- Discuss the findings of the paper (Annex A). Consider in particular whether blastomere derived hESC lines will differ from conventional hESC lines in their ability to form functional differentiated cell types.

- Consider the implications for assisted conception.

- Consider whether, in the light of the new findings of the paper at Annex A, members wish to review their previous opinion and whether they feel this issue should be considered further in the next business year.