

**Human Fertilisation and Embryology Authority
Scientific and Clinical Advances Group**

Tabled item for SCAG(06/05)02

Further comments we have received from members of the horizon scanning panel since the papers were sent out:

“Unlikely to be of practical relevance because blastomere biopsy for PGD would not normally be done as early as the 4-cell stage. One should keep in mind however that removal of any cellular material at any stage of preimplantation embryonic development is likely to impact subsequent development to a greater or lesser extent. Whether this is likely to be physiologically significant is moot. Risk benefit analysis will always be required in every situation”. Stephen Hiller

“Zernicka-Goetz paper is fascinating and turns on end the dogma I learned from the start of my embryology career. Inevitably the fact that blastomeres are not necessarily totipotent must have potential implications for any technique that destroys some blastomeres. It is encouraging that the fate of an individual blastomere is not all or none but is influenced by its neighbours.

As well as PGD, these findings may also have relevance for the outcome of embryo freezing. Most clinics consider that an embryo has survived if 50% of the cells are intact after thawing. In the absence of better embryos clinics would transfer 4-cell embryos with only 2 intact blastomeres. The poor outcome from such transfers may indeed reflect a failure of cell potential rather than simply a paucity of cells.” Maureen Wood

“The Zernicka-Goetz research is fascinating as it (at the very least) casts some doubt on the commonly-held assumption of plasticity/regulation between mammalian blastomeres and their progeny. Work used to demonstrate such

plasticity in the past is not inconsistent with the Z-G experiments, mainly because failures on blastocyst removal tended to be ascribed to experimental shortcomings, rather than restricted developmental potential. However, even Z-G shows that even if there is not full equivalence, there is some plasticity in blastomere potential. Thus, before any implications for PGD etc can be assessed, it will be necessary to assemble evidence from at least other mammalian species and ideally from human blastocysts. Although I have not thought the details of this through, it should be possible to characterise human blastomeres at equivalent stages well enough to be able to selectively remove individual cells in order to follow their lineages that arise on subsequent tissue culture.” David Edgar