ADULT STEM CELL PLURIPOTENCY

MYTH: Adult stem cells are not as versatile as embryonic stem cells.

FACT: Numerous studies demonstrate that some adult stem cells are as flexible as embryonic stem cells.

1. **German scientists have shown that stem cells from adult mouse testis show embryonic stem cell-like properties, expressing genes for pluripotency (Oct-4, nanog) and forming tissues from the 3 representative tissue types of the body**. An American company has announced that they can isolate such cells from mouse and adult humans. Guan K *et al.*, Pluripotency of spermatogonial stem cells from adult mouse testis, *Nature* 440, 1199-1203, 27 April 2006; Kanatsu-Shinohara M & Shinohara T, The germ of pluripotency, *Nature Biotechnology* 24, 663-664, June 2006; Cyranoski D, Stem cells from testes: could it work?, *Nature* 440, 586-587, March 30, 2006.

2. Researchers in Kansas demonstrated that stem cells from the **umbilical cord express pluripotency genes Oct-4, Sox-2, and nanog and show properties of "primitive pluripotent stem cells."** Carlin R *et al.*, Expression of early transcription factors Oct-4, Sox-2 and Nanog by procine umbilical cord (PUC) matrix cells, *Reproductive Biology and Endocrinology* 4:8, doi:10.1186/1477-7827-4-8, 6 February 2006.

3. Scientists at the University of Minnesota Medical School have **verified that umbilical cord blood stem cells express pluripotency genes Oct-4, Sox-2, and can repair neurological damage**. Xiao J et al., Transplantation of a novel cell line population of umbilical cord blood stem cells ameliorates neurological deficits associated with ischemic brain injury, *Stem Cells and Development* 14, 722-733, December 2005.

4. Researchers at the University of Pittsburgh demonstrated that **placental stem cells express pluripotency genes Oct-4, nanog; and can potentially can form any tissue, with no signs of tumor formation**. Miki T et al., "Stem cell characteristics of amniotic epithelial cells," Stem Cells 23, 1549-1559, November 2005 (online 4 August 2005).

5. Researchers from U.K. and Texas reported another example of cord blood stem cell plasticity. According to the abstract, **"we report the world's first reproducible production of cells expressing embryonic stem cell markers,--cord-blood-derived embryonic-like stem cells (CBEs)."** McGuckin CP et al., "Production of stem cells with embryonic characteristics from human umbilical cord blood," Cell Proliferation 38, 245-255, August 2005.

6. Professor Mackay-Sim of Griffith University, Australia demonstrated that **nasal stem cells from patients age 2-80 could develop into cells of heart, liver, kidney, muscle, brain and nerve**. The team has now produced "patient-specific stem cells" from over 40 human patients for study. Murrell W *et al.*, "Multipotent stem cells from adult olfactory mucosa," *Developmental Dynamics* 233, 496-515 June 2005.

7. Researchers replicated an earlier study by showing that **bone marrow stem cells could be turned into nerve cells, without cell fusion**. "Transplanted human bone marrow cells generate new brain cells," Crain BJ, Tran SD, Mezey E, *J Neurol Sci.* 2005 Jun 15;233(1-2):121-3.

8. Cardiologist Douglas Losordo at Tufts University showed that a type of **bone marrow stem cell can turn**

into most tissue types, and can regenerate damaged heart. According to Losordo, bone marrow "is like a repair kit. Nature provided us with these tools to repair organ damage." "Based on our findings we believe these newly discovered stem-cells may have the capacity to generate into most tissue types in the human body. This is a very unique property that until this time has only been found in embryonic stem cells." Yoon Y-s et al., "Clonally expanded novel multipotent stem cells from human bone marrow regenerate myocardium after myocardial infarction," *Journal of Clinical Investigation* 115, 326-338, February 2005.

9. In 2005, researchers in France and Switzerland changed **pluripotent bone marrow stem cells into insulin-secreting cells**. The ability to change these cells into insulin-secreting cells is an important step towards curing diabetes. Moriscot C et al., "Human bone marrow mesenchymal stem cells can express insulin and key transcription factors of the endocrine pancreas developmental pathway upon genetic and/or microenvironmental manipulation in vitro," *Stem Cells* 23, 594-604, 2005.

10. In November 2004, a study found that **stem cells taken from the pancreas can differentiate into other cells such as: muscle cells, neurons, insulin producing cells**. These cells are self-renewing, meaning that they can divide continuously while still producing other cell types. Kruse C et al., "Pluripotency of adult stem cells derived from human and rat pancreas," *Applied Physics* A 79, 1617-1624, November 2004.

11. In July 2004, German researchers led by Dr. Peter Wernet, discovered a type of **umbilical cord blood stem cell, termed unrestricted somatic stem cells (USSC's), that are pluripotent**. They showed these stem cells could form various cell types, including brain, bone, cartilage, liver, heart, and blood cells. This means that the cells can turn into all three germ layers (all major body tissue types). Kogler G et al., "A new human somatic stem cell from placental cord blood with intrinsic pluripotent differentiation potential," *J. Experimental Medicine* 200, 123-135, 19 July 2004.

12. In June 2004 researchers in Miami **demonstrated once again that human bone marrow stem cells have pluripotent potential**, meaning that these adult stem cells can form most or all cell types of the body. D'Ippolito G *et al.*, "Marrow-isolated adult multilineage inducible (MIAMI) cells, a unique population of postnatal young and old human cells with extensive expansion and differentiation potential," *J. Cell Science* 117, 2971-2981, 15 July 2004.

13. Scientists at Argonne National Labratory showed in 2003 that **blood stem cells can form cells from all 3 major tissue branches of the body, including blood vessel cells, neuronal cells, and liver cells**. Zhao Y *et al.*; "A human peripheral blood monocyte-derived subset acts as pluripotent stem cells," *Proceedings of the National Academy of Sciences USA* 100, 2426-2431; 4 March 2003.

14. In 2003, led by Andrea-Romana Prusa of the University of Vienna, researchers found that human **amniotic fluid contains stem cells that express Oct-4, a protein that is a marker for pluripotent cells**. Researchers hope these adult Oct-4-postive cells will eliminate the need for embryonic stem cell research. Prusa A-R et al., "Oct-4-expressing cells in human amniotic fluid: a new source for stem cell research?," *Human Reproduction* 18, 1489-1493, 2003.

15. Researchers at the National Institutes of Health found that **women who received bone marrow stem cell transplants from male donors had brain cells with the Y chromosome, showing that bone marrow stem cells generated neurons**. Mezey E *et al.*; "Transplanted bone marrow generates new neurons in human brains," *Proceedings of the National Academy of Sciences USA* 100, 1364-1369; 4 Feb. 2003.

16. In 2002, a Minnesota team led by Catherine Verfaille showed that bone marrow stem cells, that they called multipotent adult progenitor cells (MAPCs), can form all of the different body tissues. **They turned these bone marrow stem cells into skin, brain, lungs, heart, retina, muscle, intestines, kidney and spleen**. Jiang Y *et al.*; "Pluripotency of mesenchymal stem cells derived from adult marrow," *Nature* 418, 41-49; 4 July 2002.