

Adult Stem Cells—2004 Update

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For the President's Council on Bioethics

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Over the last year since submission of the final addendum for the Stem Cell Report in October 2003, literally dozens of additional published articles have added to our knowledge of the substantial abilities of adult stem cells. This brief summary will not attempt to list all of these papers, but will highlight some of the more interesting and significant reports.

Several new reports highlight the pluripotent ability of adult stem cells from new sources including a new isolate from bone marrow¹ and umbilical cord blood.² These references also indicate the ability for extensive proliferation of adult stem cells, especially those derived from cord blood. One group reports efficient generation of neural stem cells from bone marrow stromal cells.³

The pancreas and potential to treat diabetes has been highlighted in several recent studies. Several published references address the possible existence of a pancreatic stem cell. One reference indicates that regeneration of beta cells in the pancreas is solely due to existing beta cells,⁴ while another reference indicates the existence of a multipotent progenitor within pancreas that can form either pancreatic or neural cell lineages.⁵ Another group has provided evidence of transdifferentiation of bone marrow-derived stem cells into pancreatic cells.⁶ A Harvard group has shown that pancreatic islet progenitors can engraft in mice,⁷ and has also shown permanent reversal of diabetes in mice⁸ (they are now preparing to move to their first clinical trial.)

Another group has shown effectiveness of endogenous adult stem cells, stimulated by growth factor treatment, in stroke recovery in animals.⁹ This again points to the potential of identification of stimuli for endogenous stem cells for use in therapy, obviating culture of stem cells for treatments and relying on the patient's own stem cells to effect tissue repair.

¹ 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 (published online 1 June 2004)

² Kögler 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

³ Hermann A *et al.*, "Efficient generation of neural stem cell-like cells from adult human bone marrow stromal cells," *J Cell Sci* 117, 4411-4422, 2004

⁴ Dor Y *et al.*, "Adult pancreatic beta-cells are formed by self-duplication rather than stem-cell differentiation," *Nature* 429, 41-46, 6 May 2004

⁵ Seaberg BM *et al.*, "Clonal identification of multipotent precursors from adult mouse pancreas that generate neural and pancreatic lineages", *Nature Biotechnology* 22, 1115-1124, Sept 2004

⁶ Oh S-H *et al.*, "Adult bone marrow-derived cells transdifferentiating into insulin-producing cells for the treatment of type I diabetes," *Laboratory Investigation* published online 22 March 2004

⁷ Abraham EJ *et al.*, "Human Pancreatic Islet-Derived Progenitor Cell Engraftment in Immunocompetent Mice", *Am J Pathol* 164, 817-830, March 2004

⁸ Kodama S *et al.*, "Islet regeneration during the reversal of autoimmune diabetes in NOD mice", *Science* 302, 1223-1227; 14 Nov 2003

⁹ Shyu W-C *et al.*, "Functional recovery of stroke rats induced by granulocyte colony-stimulating factor-stimulated stem cells", *Circulation* 110, 1847-1854, 2004

An interesting report on use of a small molecule termed “reversine” indicated the potential of transforming committed adult cells to a stem cell-like state; in the report the researchers induced committed myogenic cells to revert to a multipotent state that could form bone and fat lineages.¹⁰

Another group reported on the potential ability of olfactory ensheathing cells to promote repair of spinal cord injury, in this case by inducing axonal sprouting.¹¹

Building on previous reports of the ability of adult stem cells to repair components of the visual system, a new report shows use of bone marrow-derived stem cells to rescue retinal degeneration in animals.¹²

The potential use of adipose tissue continues to generate papers, including a report on the use of adipose-derived stem cells to heal bone defects in mice.¹³

The potential of adult stem cells for repair of kidney damage was reported by an Italian-UK team.¹⁴

Reports continue on the use of adult stem cells for repair of heart damage, in this case by another group from Germany.¹⁵

Construction of new corneas for patients using corneal limbal stem cells has continued to improve, and now a new report indicates that corneas can be constructed and used to treat patients starting with oral mucosa as the cell source.¹⁶

A very interesting case of patient reconstructive treatment was reported by a German-Australian team. The patient’s jaw was reconstructed using a titanium mold seeded with bone marrow stem cells to regrow the jaw and provide blood vessel formation.¹⁷ After transplantation the patient was able to eat solid food for the first time in years.

¹⁰ Chen S *et al.*, “Dedifferentiation of lineage-committed cells by a small molecule,” *Journal of the American Chemical Society* published online December 2003.

¹¹ Chuah MI *et al.*, “Olfactory ensheathing cells promote collateral axonal branching in the injured adult rat spinal cord,” *Experimental Neurology* 185, 15-25, 2004

¹² Otani A *et al.*, “Rescue of retinal degeneration by intravitreally injected adult bone marrow-derived lineage-negative hematopoietic stem cells,” *J. Clinical Investigation* 114, 765-774, September 2004

¹³ Cowan CM *et al.*, “Adipose-derived adult stromal cells heal critical-size mouse calvarial defects,” *Nature Biotechnology* 22, 560-567, May 2004

¹⁴ Morigi M *et al.*, “Mesenchymal stem cells are renotropic, helping to repair the kidney and improve function in acute renal failure,” *J Am Soc Nephrol* 15, 1794-1804, 2004

¹⁵ Wollert KC *et al.*, “Intracoronary autologous bone-marrow cell transfer after myocardial infarction: the BOOST randomised controlled clinical trial,” *Lancet* 364, 141-148, 10 July 2004

¹⁶ Nishida K *et al.*, “Corneal reconstruction with tissue-engineered cell sheets composed of autologous mucosal epithelium,” *New England Journal of Medicine* 351, 1187-1196, 16 September 2004

¹⁷ Warnke PH *et al.*, “Growth and transplantation of a custom vascularised bone graft in a man,” *Lancet* 364, 766-770, 28 August 2004