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## Adult Stem Cells

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## Stem Cells, Growth Factors, and Brain Nutrients

by Parris M. Kidd, Ph.D.

Cells are the fundamental unit of independent life, and we humans have nearly one trillion of them. Approximately one in every 10,000 is a stem cell. Among life science researchers, stem cells are currently the hottest topic, and for good reason—they are a biologically reminiscent of the fountain of youth.

Stem cells are the cells held in reserve throughout our healthy tissues. As we lose cells to injury, aging, or for other reasons, our own stem cells are able to make new cells to replace at least some of those that are lost. Stem cells make possible tissue renewal based in our own body. Previously the human brain was thought to lack stem cells, but by 1996 stem cells were pinpointed in its cortex, hippocampus and elsewhere.

Experiments with rats, mice and monkeys have demonstrated that stem cells can become active following transfer into a new host. For example, in animal models of stroke new nerve cell formation, new circulation, and a degree of structural and functional recovery is seen in the damage zone. Similar findings in monkey brains indicate there is no insurmountable barrier to the same occurring in humans.

### Switching On Stem Cell Activity

#### Using Growth Factors

Adult brain stem cells can be very hard to convert to fully-developed brain cells. In experimental animals, stem cell conversion to nerve

cells requires mental stimulation, and physical exercise also helps. Growth factors are absolutely required.

Growth factors are small protein molecules naturally put out by our healthy cells. They are a class of messenger molecules that bathe each of our tissues and stimulate the cells of that tissue to carry out ongoing cell replacement. It seems growth factors must be present for stem cells to divide and make more cells. Our brain tissue produces a bunch of different growth factors.

The quality and quantity of stimuli reaching the brain affects growth factor status, which in turn affects stem cell activity. In animal experiments, increasing stimulation of the brain typically up-regulates growth factor production and release. Conversely, blocking brain stimulation tends to down-regulate the growth factors. And intense positive stimulation results in stem cells converting into mature brain cells. These findings give new meaning to the adage, "use it or lose it."

Nerve growth factor, or NCF, was the first growth factor to be discovered. NCF is particularly abundant



in zones of the brain endowed with chormergic circuits. These rely heavily on the transmitter acetylcholine and are usually the first circuits to begin dropping out as Alzheimer's develops. Clinical researchers at the University of California at San Diego conducted a small clinical trial ("Phase 1") that probed the importance of one key growth factor in the human brain.

### Nerve Growth Factor Grows New Circuits in Human Brains

Following the usual ethical requirements of the university and the state and federal governments, including appropriate

informed consent from the patients, this team injected eight Alzheimer's patients with each patients' own cells primed to secrete nerve growth factor. The research was reported by Tuszynsici and collaborators in Nature Medicine (2005;11:551-5).

The study procedures were very high tech. Skin cells (fibro-blasts, not stem cells) were taken from each patient, cultured using appropriate support nutrients, and "transfected" with a harmless virus carrying a gene for nerve growth factor (NGF) This made the skin cells able to produce and release NGF. Then each patient was prepped for surgery and her/his specific cells were injected into her/his own brain (the basal fore-

brain zone, often the most affected by Alzheimer's).

The experiment was a success, but unfortunately involved tragedy. Two patients moved their heads during the delicate brain surgery, sustained bleeding into the brain, and had to be removed from the study. One died after five weeks. Fine-structural examination of the forebrain from this deceased patient showed that the injected cells had indeed survived, and had released NGF. Around this zone of NGF release, new nerve circuits had formed. This confirmed that the human brain, like that of the monkey and the rat, has the capacity to make brain circuits from scratch. And this in an Alzheimer's patient!

The six patients who remained in the study were carefully followed for a total 22 months. In cognitive tests and clinical assessment they showed improvement in their rate of Alzheimer's decline. Brain imaging of four of them (using PET, positron emission tomography) found significantly improved energy generation in the cortex and cerebellum. The enhancement of tics levels in the basal forebrain of these patients, achieved by transplanting their own cells primed to make NGF seems to have partially ameliorated their progression to dementia.

### Stem Cells Already in Clinical Use in Mexico

David Steenblock, M.S., D.O., a highly respected physician, is founder and director of the Brain Therapeutics Medical Clinic in Mission Viejo, California. Dr Steenblock has written (together with Anthony Payne, Ph.D.) a highly informative book on the treatment of degenerative brain diseases with stem cells entitled *Umbilical Cord Stem Cell Therapy: The Gift of Healing from Healthy Newborns*. This book introduces stem cell therapy as an immediate clinical reality.

In this landmark book, Drs. Steenblock and Payne present much of

the useful science behind stem cell therapy. They make a compelling argument for the use of human umbilical cord stem cells (hUCSC). These stem cells are readily harvested from human umbilical cords that are usually discarded once the healthy infant is born. They can, be persuaded to form, just about any cell type in culture, using appropriate growth factors, nutrients, and other culture conditions. The book details protocols for collecting these cells, expanding their numbers, and delivering them into the patient.

Besides circumventing the ethical problems associated with embryonic stem cells, cord stem cells are safer and more cost-effective. While the embryo-derived cells can give rise to tumors, the cord cells are sufficiently developed ("differentiated") not to pose this threat. Yet they are sufficiently undeveloped to avoid triggering immune rejection in their new host. Abundant and easy to harvest, these are the stem cells of choice for clinical practitioners to provide their desperate patients.

Dr. Steenblock's nonprofit Steenblock Research Institute has accrued case histories and documentation on more than 125 patients treated with human umbilical cord stem cells (hUCSC) in Mexico. It provides technical support and data analysis to research-oriented hUCSC therapy programs there, including the pioneering practice of Fernando Ramirez, M.D.

Working at the Spinal Cord Regeneration Center in Tijuana, Mexico. Dr Ramirez has used hUCSC to treat more than do children and young adults with cerebral palsy, via subcutaneous injection near the belly button. This condition seems to respond well to the therapy, as does traumatic brain injury and acute stroke of recent occurrence (up to three days). Multiple sclerosis and early-stage amyotrophic lateral sclerosis (ALS) cases appear to be marginal responders—often improvements occur, but some are lost to disease progression. Chronic

stroke (beginning past 3 days) and later-stage ALS are so far poor responders. The book covers many fascinating case histories. I strongly recommend it.

### Total Health Management for Brain Longevity

The coming technologies of stem cell transplantation and growth factor development will undoubtedly advance progress toward ameliorating brain disorders and extending productive lifespan. However, while very exciting, they are unlikely by themselves to halt or reverse progressive brain decline.

Predictably, certain mainstream commercial interests are pursuing individual growth factors or growth factor regulators as potential monotherapies, following the same old "magic bullet" health strategy that has failed so many times. Maybe they'll get lucky. But the first requirement for reversing brain decline is total health management (Toed of the brain. In summary, THM means living actively by:

- ◆ Exercising body, mind and spirit
- ◆ Avoiding chemical and physical toxic stressors, as well as emotional stress
- ◆ Using nutrients to optimize the life functions, especially those nutrients proven very safe to use (orthomolecules)
- ◆ Making the necessary (sometimes challenging) lifestyle changes to support this personal commitment
- ◆ Working with an integrative health practitioner trained to assess total health, when professional help becomes necessary
- ◆ Turning to pharmaceuticals and other potentially toxic, life-threatening interventions only as a last resort.

The Top Ten Practices of Total Health Management are detailed in

my new book PS (Phosphatidyl Serine), Nature's Brain Booster, available through this magazine. Practice Number 1 is Avoid Toxic Agents. We need to take decisive action to eliminate (not merely restrict, per toothless regulation) such toxins as mercury, lead, other heavy metals, PCBs, dioxins, and the plethora of petroleum derivatives that currently pollute our environment.

### **Dietary Supplements Are Essential to Brain Rebuilding**

Total Health Management Practice Number 9 is Develop Your Personal Dietary Supplement Program. To begin, everyone—yes, everyone—needs to have a basic supplement program, one that involves (at the minimum) a potent multi-vitamin-mineral supplement that will require at least four capsules for an adequate daily intake. Long-chain omega-3 fatty acids and extra antioxidants are also highly indicated for a basic supplement program.

Next, for those among us who are having brain problems come the top three brain nutrients proven to support growth factor action in the brain. These are PS (Phosphatidyl Serine), GPC (Glycero-Phospho-Choline), and ALCAR (Acetyl Carnitine). All three can up-regulate cell surface receptors for NGF; numerous double blind clinical trials prove they support functional restoration in the damaged brain. All three are said to be brain trophic, that is, growth-nourishing for the brain.

Last but not least, come two other nutrients thoroughly documented as not mere antioxidants but also as essential energy enzyme cofactors. Coenzyme Q10 (CoQ) and alpha lipoic acid, R-form (ALAR) both protect the brain and help energize it. These are excellent synergists with the above mentioned PS, GPC, and ALCAR that have growth-promoting activity. Therefore, we have the Big Five brain nutrients, all clinically effective, very well-tolerated, and safe to take even for long periods:

The Big Five brain nutrients build on the basic supplement program. To ensure the most optimal metabolic processing of these nutrients, it is essential to follow your basic program with discipline. For the person who is relatively brain healthy and may just need enhanced maintenance, the lower intake ranges of the Big Five may prove useful, especially when all five are supplemented. But for someone with a serious condition, the higher intakes are more likely to produce noticeable benefits.

### **Century of the Brain:**

#### **Making Our Own Contributions**

This relatively young 21st century has already witnessed a paradigm change concerning the human brain. Just within the past decade, it has been proven that the human brain is far more adaptable and regenerative than previously thought. The automation of gene analysis (genomics) has accelerated the identification of genes

linked to brain diseases. Transplantation of cells and infusion of growth factors into the brain and spinal column have shown promise against major nervous system diseases. This could well be the "Century of the Brain."

The dogma or scientific consensus behind the earlier brain paradigm was that our brains carried only terminally developed cells, unable to multiply and make new cells. Now that it has been proven that humans have brain stem cells, and that human brain growth factors can be used to generate new brain circuits, the new dogma is that the human brain can repair itself. We just have to help it along.

But high-tech brain rebuilding (call it brain engineering) is still experimental, risky and expensive. The San Diego Alzheimer's trial was just the beginning. The clinical work with stem cells being pioneered in Mexico deserves mainstream support and taxpayer funds for larger-scale investigations. For those of us who are already having

trouble and need benefit very soon, routine brain engineering may come too late. But for the short term, there may be an easier way.

By nourishing our brain cells with the Big Five and the basic supplemental nutrients, by doing intensive mental and physical exercise, and by practicing Total Health Management, we have great prospects to reenergize our brains, activate our inherent stem cells and growth factors, and achieve new levels of mental competence. For professional guidance we can get valuable help from an integrative physician. These are safe and affordable steps to self-engineer our own brain renewal, one cell at a time.

- ◆ PS (Phosphatidyl Serine) 100-300 mg/day with meals
- ◆ CPC (Glycero-Phospho-Choline) 600-1200 mg/day between meals
- ◆ ALCAR (Acetyl-Carnitine) 750-1000 mg/day between meals
- ◆ CoQ (Coenzyme Q10) 360-1200 mg/day with meals
- ◆ ALA (Alpha-Lipoic Acid) (R-form) 300-1200 mg/day with meals