

Cell Renewal

The Technical View

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Univera research and product development is focused on *renewal*. No one knows exactly how many cells are replaced every day, but experts agree that it ranges from 300 billion to as many as half a trillion.

Clearly, this astounding potential for regeneration can be enhanced or maximized, thus improving overall health and wellness. In fact, it can be said that we are constantly building new bodies, and that natural products enable us to improve cell function and experience benefits that can be seen, felt and measured. One only needs to consider the effects of nutrition to see how our habits influence cell structure and function.

The Next Level of Detail

What is the lifespan of a cell? We tend to think of lifespan as the period from birth-to-death. But cells reproduce by *mitosis* or cell division. Each time a cell divides; it makes a copy of itself and then divides in half.

This means that any cell that is alive today came from another cell that went through mitosis. And that other cell came from another cell which came from another cell... ad infinitum...until you trace back to the first ancient cells-- a topic that challenges scientists today. So it is more useful to discuss cell renewal in terms of the factors that contribute to the damage and repair of tissues.

To clarify this for the health-conscious individual, we have identified four critical activities that contribute to optimal cell renewal:

Nourish: You can't make 300 billion vibrantly healthy cells out of thin air (or the standard American diet).

Restore: Nutritional factors (beyond nutrient supply) can support cell and tissue function.

Fortify: Cells, tissues and the entire organism must be protected from the ravages of everyday life.

Vitalize: All repair and regeneration is energy-intensive. Bioenergetic nutrition can enhance mitochondrial efficiency to optimize energy production.

How do cells die?

Cell death is a fascinating topic that scientists across the world are working to learn more about. Cells can die by either necrosis or apoptosis. Necrosis is what happens if a cell is severely damaged, as by infection or trauma. When you bump your shin on the coffee table, for example, the resulting bruise is composed of millions of dead (necrotic) skin cells. Inflammation can also cause necrosis, and often produces a chain reaction of damage as dead and dying cells attract immune cells that stimulate further inflammation.

Apoptosis on the other hand, is a form of auto-destruction or programmed cell death that occurs when a cell is worn out, stressed or damaged by free radicals. Unlike necrosis, apoptosis is rather orderly. In fact, part of the process of apoptosis involves cell signals that alert the surrounding tissue to the impending event. Apoptosis therefore does not usually produce inflammation.

Part of the problem of determining the precise cell turnover rate of an "average" adult is due to the wide variation in necrosis and apoptosis. It is estimated that every puff on a cigarette sends billions of free radicals into the most sensitive tissue of the human body. Imagine the damage inflicted by this habit and the massive repair that is required. Lung cancer results when cells fail to repair DNA damage.

In general, though, the cellular reproductive cycle is carefully regulated by complex interior and external factors. Biochemicals, proteins, gene expression, circulation, and even changes in temperature or pressure act as signals that influence cell growth, mitosis, and apoptosis.

The lifespan of a cell also depends on the type of cell in question. In discussing cell replication and tissue renewal, scientists divide adult mammalian cells into three groups: Continuous replicators, Discontinuous replicators, and Nonreplicators.

Continuous replicators include blood cells, skin cells and cells that line the small intestine. They are cells with high turnover that undergo apoptosis after a relatively short period of time. Red blood cells live for about 120 days. Cells that line the gut live for 3-5 days. Some white blood cells have a half life of 5-6 weeks, while others live for only a few days. The continuous replicators undergo regular mitotic activity.

Discontinuous replicators include cells of cartilage, smooth muscle, kidney tubules, liver, pancreas, fibroblasts and bone. These are cells that are part of stable cell populations. They last for days, months or years, depending on how much they get used. For example, cells of the pancreas live for about a year. Endothelial cells that line blood vessels can live for months to years, but if a vessel is injured, they can reproduce in days to repair it.

Discontinuously replicating cells undergo mitosis to rebuild stable tissues after injury, wear and tear. If a tissue is injured and cells are killed by necrosis or apoptosis, growth factors stimulate neighboring cells to reproduce. The most common growth factor is IGF-1 (Insulin-like Growth Factor – 1), which in turn is stimulated by DHEA.

Nonreplicators are the cells that live the longest, including neurons, heart muscle cells, renal glomeruli, and some cells in the lens of the eye. These cells are "post mitotic." This means that after a short time of development and differentiation, the cells don't divide anymore. These cells last for a person's whole life without ever being replaced.

Importantly, this does not mean that nonreplicating cells are incapable of repair. In fact, these cells demonstrate remarkable resilience, as demonstrated by cardiac rehab programs utilizing coenzyme Q10, L-carnitine, taurine, D-ribose and alpha lipoic acid. In the near future, it is likely that stem cell therapy will usher in an entirely new era of tissue repair. Stay tuned.

But can *the brain* regenerate?

Absolutely.

With caveats. You see, the brain is made up of two major types of cells; neurons and glial cells. We've known for years that glial cells go through the same regenerate and replace cycle as most tissues in the body. But what has eluded certainty is whether neurons – the cells that hold memory and relay information – can regenerate.

Keep in mind that glial cells outnumber neurons by about 10 to 1. And the long-held belief that glial cells merely support and protect neurons is being revised. While glial cells surround neurons and hold them in place, supply nutrients and oxygen, and insulate one neuron from another, glial cells also destroy pathogens and secrete important neurochemicals such as ATP and growth factors.

Until recently, conventional medical wisdom held that we are born with all the neurons that we'll ever have and when they're gone, they're gone for good. We now know, however, that neurons in at least one region of the brain are capable of regeneration. This region, known as the hippocampus, is responsible for processing information and forming new memories. In the hippocampus, in fact, there appears to be continual turnover of cells throughout most of our lives.

"It's a very interesting system," says Ronald McKay, PhD, chief of the laboratory of molecular biology at the National Institute of Neurological Disorders and Stroke. McKay has demonstrated that reducing stress hormone levels in aged rats can restore the production rate of brain cells in the hippocampus. He states, "The hippocampus has these cells ... which are replaced throughout life from dividing cells, so that whole process of division, ... maturation and death seems to be going on all the time in this structure."

Research strongly suggests that memory impairment associated with aging is caused by damage to the hippocampus brought on by lifelong exposure to stress hormones. Several studies in rats and humans have shown that significant and prolonged elevation of stress hormones, (especially cortisol and nor epinephrine) is associated with smaller hippocampal regions, cell damage and memory loss.

The DHEA Factor

DHEA (Dehydroepiandrosterone) is the most abundant circulating steroid in humans, and serum levels decline dramatically after age 25.¹ Since DHEA is a comprehensive repair signaling molecule, scientists have searched for a connection between falling DHEA production and age-related degeneration. Moreover, interest in a possible neuroprotective role for DHEA intensified after it was discovered that, in addition to adrenal synthesis, DHEA is made by tissues of the central nervous system.²

DHEA was shown to be neuroprotective after oxidative stress in rat hippocampal cultures³ and plays an important role in neuronal differentiation during development.⁴ The finding that DHEA stimulates neurogenesis in the *adult* rodent hippocampus⁵ suggests that DHEA may be involved on both sides of the damage/ repair see-saw; acting to reduce oxidative stress and fostering regeneration.

Since the human brain produces a great deal more DHEA than a rodent, it was important to document similar activity in a human model. This was accomplished in 2004 when researchers at the

University of Wisconsin exposed human neural stem cells to low concentrations of DHEA and observed an upregulation of cell differentiation to fully functioning neurons. In the conclusion of this remarkable study, they state:

"These data suggest that DHEA is involved in the maintenance and division of human neural stem cells. Given the wide availability of this neurosteroid, this finding has important implications for future use."⁶

Additional support from Genomic Studies

In 1999, Princeton neuroscientists used gene tracking technology to document brain regeneration in adult monkeys. They injected the monkeys with a non-toxic tracer known as BrdU which becomes incorporated into the DNA of newly formed cells. Over the course of seven weeks, they looked for evidence of the chemical in neurons in the cerebral cortex. In all cases, there were neurons with BrdU in their DNA, which showed that those cells had to have been formed after the BrdU injection.

Neurogenesis was found in three areas: 1) the prefrontal region, which controls executive decision making and short-term memory; 2) the inferior temporal region, which plays a crucial role in the visual recognition of objects and faces, and 3) the posterior parietal region, which is important for the representation of objects in space.⁷ Follow-up work to evaluate the survivability of newly formed neurons was published in 2001.⁸

New Frontiers in Stem Cell Therapy

In 2003, a team from the National Institute of Neurological Diseases and Stroke examined post mortem samples from female patients who had received bone marrow transplants from male donors. If they could find brain cells with the Y-chromosome, such a finding would prove that donor BMSC's are capable of contributing to the maintenance of brain structure and function.

In fact, each of the patients examined was found to have many brain cells containing the Y-chromosome. Moreover, these Y-positive cells were found in clumps, suggesting that the original donor cells had continued to multiply after differentiating into brain cells.

"While the adult brain previously was thought of as a non-regenerative system for pathway formation, recent studies show how dissociated primordial neurons or stem cells implanted into the adult central nervous system can grow to reconnect neuronal pathways and

integrate in a molecular and physiological fashion. Thus, anatomical, neurochemical, molecular, behavioral and functional MRI parameters indicate that regenerative and reconstructive events can also take place in the degenerated adult brain." Neuroregeneration Laboratories, McLean Hospital, Program in Neuroscience, Harvard Medical School

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Footnotes:

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