



apoptosis

BY MICHAEL Q. PUGLIESE
AND PETER T. PUGLIESE, M.D.

THE SCIENCE OF SKIN

MULTI-CELLULAR ORGANISMS RELY ON A

perfectly working system that integrates the activity of all the cells in the body. At times, some of these cells may undergo significant changes for a variety of reasons that make them no longer functional in the organism. These cells cannot be allowed to exist if they are unable to function in a normal manner. In fact, some abnormal cells develop into cancer cells, which may eventually destroy the body. To protect itself against these abnormal cells, the body has developed a system to destroy them, which is controlled by a specific type of gene. This process is called apoptosis; it is defined as "programmed cell death." This is not a rare biological event. In the average adult, as many as 50 to 70 trillion

cells are destroyed every day! Apoptosis is not always bad; it is essential in the development of embryos, as well as in certain functions of the immune system, and as a protective mechanism against abnormal cells.

Apoptosis is pronounced as "ah-po-TOE-sis." There is a continuing debate concerning the pronunciation of this word. Some scientists insist on pronouncing it "A-POP-toe-sis," which is incorrect.

The process of apoptosis is controlled by cell signals, either extracellularly or intracellularly. Toxins, hormones, growth factors, nitric oxide and cytokines cross the plasma membrane to produce a response in this cell. They may have either a positive effect and trigger apoptosis, or

continues

they have a negative effect and inhibit apoptosis. The process of apoptosis is essentially the programmed dismantling of the cell, resulting in the death of the cell.

The most important enzyme to remember in apoptosis is the caspases. Caspases (or cysteine-aspartic proteases, or cysteine-dependent aspartate-directed proteases) are a family of cysteine proteases that play essential roles in apoptosis (programmed cell death), necrosis and inflammation. The end result of all the processes involved in apoptosis eventually end in the caspases taking proteins apart. Enzymes of this type are known as proteases.

Apoptotic signaling begins in a cell in response to some type of serious stress, which then triggers the mechanism for the cells to self-destruct, if the stress is serious enough to

mitochondrial membrane and cause apoptotic effectors to leak out. These effectors are very closely related to the intrinsic pathway. An example of such an effector is nitric oxide, which is able to induce apoptosis by helping to dissipate the membrane potential of mitochondria and therefore make it more permeable. Another material that acts as an effector is a mitochondrial protein known as SMAC (small mitochondria-derived activator of caspases). This is released into the cytosol following an increase in permeability. The SMACs bind to an inhibitor of apoptosis proteins (IAPs). The inhibitors of apoptosis are capable of arresting the process and stopping apoptosis from occurring. When the SMAC proteins deactivate them, the IAPs are prevented from stopping apoptosis. IAPs also normally suppress the activity of the

photo: Nicolea/Shutterstock.com



EXPOSURE TO EXCESSIVE AMOUNTS OF ULTRAVIOLET RAYS, PARTICULARLY UVB, DAMAGES THE P53 GENE IN THE CELL, WHICH IS THE CHIEF REGULATOR OF APOPTOSIS.

cause damage to the cell structure. One of the most common destructive forces on the skin is ultraviolet B irradiation, which produces a damaged cell known as a sunburn cell. These sunburn cells, if left alone, are known to produce skin cancers. Other agents that can trigger apoptosis are glucosteroids, poor nutrition, viral infections, low levels of oxygen and high levels of calcium within the cell. There are two major signaling pathways that initiate and direct apoptosis—the mitochondrial pathway and the adapter protein pathway.

Mitochondrial regulation pathway

Without mitochondria, a cell ceases to respire aerobically and quickly dies. Apoptotic proteins that target mitochondria affect them in different ways. They may cause mitochondrial swelling through the formation of membrane pores, or they may increase the permeability of the mi-

caspases, which carry out the degradation of the cell. Therefore, the actual degradation enzymes can be seen as indirectly regulated by mitochondrial permeability.

Direct signal transduction

Two theories of the direct initiation of apoptotic mechanisms in mammals currently being studied intensely are the TNF-induced (tumor necrosis factor) model and the Fas-Fas ligand-mediated model. Both of these systems involve the TNF receptor (TNFR), which is coupled with extrinsic signals. TNF is a cytokine produced by macrophages. It is the major extrinsic mediator of apoptosis. It is a major cytokine in the process of cell destruction.

The Fas receptor binds the Fas ligand (FasL), a transmembrane protein part of the TNF family. The interaction between Fas and FasL results in
continues

THE DEVELOPMENT OF EFFECTIVE NEW PRODUCTS REQUIRES MANUFACTURERS TO HAVE A SOLID SCIENTIFIC BASIS FOR THE SELECTION AND INCLUSION OF FUNCTIONAL RAW MATERIALS.

the formation of the death-inducing signaling complex (DISC), which contains the FADD, caspase-8 and caspase-10. In some cells, processed caspase-8 directly activates other members of the caspase family, and triggers the execution of apoptosis of the cell. In other cells, the Fas-DISC starts a feedback loop that spirals into increasing release of proapoptotic factors from mi-

tochondria, and the amplified activation of caspase-8. All of this is very complex and exquisitely controlled. We can only touch on the surface of the subject in this short article.

The apoptosis process

There is only one mechanism that actually causes the death of a cell. It undergoes organized degradation of cellular organelles by proteolytic caspases. This is how it happens. First the cell shrinks and rounds up, changing from its elongated form due the breakdown of the proteinaceous cytoskeleton by caspases.

1. The cytoplasm appears dense, and the organelles appear tightly packed.
2. Chromatin compacts against the nuclear envelope, a process known as pyknosis, a hallmark of apoptosis. The DNA inside is fragmented in a process referred to as karyorrhexis. The nucleus now breaks into chromatin bodies due to the degradation of the DNA.
3. The cell membrane shows irregular buds known as blebs.
4. The cell finally breaks apart into vesicles called apoptotic bodies, which are then phagocytosed.

Apoptosis is a very fast process, and the components of self-destruction are removed quite rapidly; thus it is difficult to visualize. During karyorrhexis, endonuclease activation leaves short DNA fragments, regularly spaced in size. These give a characteristic "laddered" appearance on agar gel after electrophoresis. Tests for DNA laddering differentiate apoptosis from ischemic or toxic cell death.

In summary, apoptosis is a critical biological process. It is essential to the development of the embryo as well as protecting the body from cancer by destroying abnormal cells. Exposure to excessive amounts of ultraviolet rays, particularly UVB, damages the p53 gene in the cell, which is the chief regulator of apoptosis. This is the major reason that excessive exposure of the skin can cause skin cancer.

continues



THE BEST SPA LIABILITY INSURANCE AVAILABLE!

CALL FOR AN INSTANT QUOTE

1.800.444.7546 | alliedhealth.net

Allied Health ASSOCIATION

Say you saw it in LNE & Spa and circle #209 on reader service card

A COMMITMENT TO
UNDERSTANDING
THE SCIENCE OF
SKIN IS REQUIRED
OF EVERY
PRACTITIONER
WHOSE GOAL IS
TO ELEVATE THE
STANDARDS OF
OUR INDUSTRY.

Grasping the complexity of biological processes like apoptosis may, understandably, be challenging for some estheticians. It is not necessary to become a biochemist to have a successful skin care practice; however, the development of effective new products requires manufacturers to have a solid scientific basis for the selection and inclusion of functional raw materials. A commitment to understanding the science of skin is required of every practitioner whose goal is to elevate the standards of our industry, and to create a positive change in the skin conditions of the clients we serve. ■

References

1. Reed JC. Mechanisms of apoptosis, *Am J Pathol.* 2000 Nov;157(5):1415-30.
2. Nuñez G, Benedict MA, Hu Y, Inohara N., Caspases: the proteases of the apoptotic pathway. *Oncogene.* 1998 Dec 24;17(25):3237-45.
3. Soehnle H, Ouhit A, Ananthaswamy, ON, Mechanisms of induction of skin cancer by UV radiation *Front Biosci.* 1997 Nov 1;2:d538-51.
4. Pustisek N, Situm M. UV-radiation, apoptosis and skin. *Coll Antropol.* 2011 Sep;35 Suppl 2:339-41.

Peter T. Pugliese, M.D., is a family physician. Through his intensive research into skin structure and function over the last three decades, he has become the most published skin physiologist in the world. Dr. Pugliese is the author of *Advanced Professional Skin Care, Medical Edition*, the global educational standard for students, educators, practitioners and manufacturers in the esthetics field. For more information, contact Michael Pugliese at Michael@circadia.com.



Michael Q. Pugliese is the CEO of Circadia by Dr. Pugliese and the Circadia Institute of Advanced Esthetics. Pugliese and his grandfather, Peter T. Pugliese, M.D., hold in-depth classes on a variety of subjects, including cosmetic chemistry and histology of the skin. Pugliese is a licensed esthetician in the state of Pennsylvania, and holds a degree in business management and marketing from Kutztown University.



TARGET HYPERPIGMENTATION | INFUSE HYDRATION | BRIGHTEN OVERALL SKINTONE | CALM AND REDUCE REDNESS

SESHA
SKIN THERAPY

EVANESCENT MASK

with P.E.T.[®] delivery technology

Instant skin lightening after only one treatment

The only skin care line that contains patented permeation enhancer technology. Infused with Australian Sea Water, Green Tea extract, and Octadecanediolic Acid.



Kit includes 4 applications: clarifying serum, activator, and seaweed mask.

CALL TODAY
for free samples
888.977.3742

Visit seshaskin.com to
learn about our entire Sesha
Skin Therapy Clinical Line

EVANESCENT MASK

Consists of seaweed polysaccharide gel which has passed through a solidification process to form a tissue paper thin mask. When combined with the Mask Activator, the Evanescent Mask liquefies into a gel for increased absorption.



Actual unretouched images showing result after a series of 4 treatments and home care products.