Dynamic Chiropractic

Apoptosis (Programmed Cell Death) and Tendinopathy

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Apoptosis is a normal bodily manifestation whereby cells literally commit suicide. Programmed cell death is essential for balancing cell division and is necessary for removing cells that are injured, tumorous or virus-infected. The term "apoptosis" is derived from the Greek word meaning "leaves falling from a tree."[1]

Genetic regulation of apoptosis, demonstrated by the discovery of cell death-specific genes and the repression or enhancement of cell death, has proven to be important in conditions such as cancer, Alzheimer's disease,[2] neurodegeneration, autoimmunity, heart disease, and other disorders.[3,4] The loss of cells in senescence may be due to this mechanism.

Science is now attempting to understand and control the mechanisms that can protect against cell loss or, in the case of malignancy, induce lysis of cells. In prostate cancer, the prostatic epithelial cells have a problem undergoing apoptosis, resulting in increased cell proliferation. In animal models, pro-apoptotic molecules capable of selectively inducing apoptosis in cancer cells are currently under study.[5]

Another form of cell death, not to be confused with apoptosis, is necrosis. Necrosis is a pathological response that occurs in cases of acute, nonphysiological injury.[1] With necrosis, there is an inflammatory response that never occurs with apoptosis. Phagocytosis of dead cells occurs in both conditions.

The term "tendinopathy" replaces tendinitis and tendinosis, since a microscopic evaluation would be nhas been determined that tendinitis is rare compared to tendinosis in tissue evaluations of the Achilles, patellar tendon, elbow flexors and extensors and rotator cuff.[6] It has recently been found that excessive apoptosis occurs in degenerating tendons (tendi-nosis), where there is an absence of inflammatory cells, as is found in apoptosis. In the rotator cuff, the apoptotic cells were identified as fibroblasts or fibroblast-like cells.[7] The increased number of apoptotic tendon cells in degenerative tendon tissue affects the rate of collagen synthesis and repair.

An important question is, how does tissue stress lead to these degenerative changes? Normal stress is important for creating increased collagen formation and content in tendon and ligaments, while a deprivation of stress weakens connective tissues. There is the theory that oxidative stress induces apoptosis, as shown in primary cultured human tendon fibroblasts *in vitro*.[8] It has been demonstrated that cyclic overload strain on tendon cells causes activation of stress-activated protein kinases (SAPKs) in cells (including the fibroblast),[9] which cause the tendon cells to undergo apoptosis, affecting the rate of collagen synthesis and repair, and resulting in a weakened collagen matrix with eventual tearing.

There are still many missing links in this cyclic, stress-activating SAPK-protein kinase causing an

apoptotic cell tendon degeneration pathway. Hopefully, science one day may be able to understand the complete chain of events and solve the problem of tendinosis.

References

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