Characterization of Role of the Plant-derived Polyphenol Resveratrol in Human Articular Cartilage and Chondrosarcoma

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INTRODUCTION: The inflammatory process initiated by cytokines (e.g., fibroblast growth factor-2 or interleukin-1) plays a pivotal role during the pathogenesis of osteoarthritis (OA). Resveratrol (trans-3,4',5-trihydroxy-stilbene) is a natural phytoalexin occurring in various fruits with anti-inflammatory and anti-oxidant properties that may have both cartilage-anabolic and chondroprotective effects.

METHODS: We investigated whether resveratrol has therapeutic benefit in osteoarthritis by performing biochemical and molecular analyses using a long-term culture (three-dimensional alginate cell culture) as well as a short term culture approach (monolayer cell culture).

RESULTS: Resveratrol improves cell viability in a long-term culture and effectively antagonizes cartilage-degrading protease production that was initiated by catabolic cytokines (e.g., fibroblast growth factor-2 or IL-1β) in human articular chondrocytes. In addition, resveratrol significantly enhances BMP7-promoted proteoglycan (PG) synthesis assessed by 35S-sulfate incorporation. Results from Protein-DNA interaction array profile suggest that resveratrol potently inhibits the activations of a set of transcription factors involved in inflammation and the cartilage catabolic signaling pathways, including direct downstream regulator of MAPK (e.g., AP-1, PEA3) and NFκB. Our results suggest that resveratrol-mediated chondroprotective function may be, in part, via regulating tumor suppressor p53-induced apoptosis in chondrocytes. However, resveratrol selectively compromises survival of human chondrosarcoma cells, but not primary articular chondrocytes. These differential actions between cancerous and non-cancerous cells (e.g., chondrocytes versus chondrosarcoma) are one of the unique features exerted by resveratrol. Further studies should be undertaken to define a possible implication of resveratrol in OA therapy in vivo.

CONCLUSION: Dozens of studies were published in this past year alone. Research has uncovered a diverse range of activities that may make resveratrol one of the most useful agents ever discovered for a wide range of human health problems. Our studies suggest the multi-faceted therapeutic profile of resveratrol promises it to be a novel intervention in the treatment of OA as well as chondrosarcoma due to its unique nature of little or no toxic effects in healthy cells with selective induction of apoptosis in cancerous cells. Research directed at understanding these mechanisms would be inherently significant and may lead to novel therapeutic approaches and identification of new treatment strategies for cartilage degenerative diseases such as OA.

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