



Abstract

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Grant Number: 1R43AG024733-01

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PI Title:

Project Title: Enhanced IGF-1 Production by Human Cartilage

Abstract: *DESCRIPTION (provided by applicant): Aging is associated with a decline in levels of insulin-like growth factor-1 (IGF-1). In some individuals this decline is further exaggerated by the production of Th1 cytokines e.g. IL-6 and TNF. This imbalance leads to a greater risk for mortality and morbidity. While therapeutic strategies exist to reduce cytokine responses, including redox active inhibitors of transcription (green tea catechins and cat's claw) which limit the inflammatory process that promotes cartilage degradation, to date there are no strategies available that promote the production of peripheral IGF-1 and directly activate repair mechanisms. RNI has recently discovered a vegetable extract (RNI 510) that satisfies this unmet need, by rapidly increasing the expression of IGF-1, as well as promoting anabolism. The aim of the present proposal is to extend this breakthrough to human cartilage. By enhancing chondrocyte IGF-1 production cartilage degradative processes will be limited and repair processes initiated. Given that Th1 cytokines and IGF-1 have generally opposing actions and promote a negative feedback on the respective systems, it is anticipated that cartilage repair will be further enhanced by co-administration of inhibitors of NF-kappaB, epigallocatechin gallate or cat's claw. Both of these natural products have been proven to be effective agents for treating osteoarthritis. The therapeutic potential of this natural vegetable extract, RNI 510, to reverse-aging related declines in IGF-1 production is substantial. From a successful result this concept will be further developed in an animal model of arthritis and clinical trials in the aged with compromised mobility. The advantage of an approach based on RNI 510 is that not only will joint health be improved but anabolic effects on muscle mass and tone will provide additional support and improved mobility and quality of life in the elderly.*

Thesaurus Terms:

biotherapeutic agent, cartilage, insulinlike growth factor, plant extract, technology /technique development

aging, biotransformation, chondrocyte, gene expression, nuclear factor kappa beta, osteoarthritis human tissue

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