Natural compound in broccoli could treat devastating genetic skin disorder

December 2 2007

The compound sulforaphane whose natural precursors are found at high levels in broccoli and other cruciferous vegetables has been hailed for its chemopreventive powers against cancer. Now sulforaphane has demonstrated new skills in treating a genetic skin blistering disorder called epidermolysis bullosa simplex (EBS), Pierre Coulombe and colleagues at the Johns Hopkins University School of Medicine in Baltimore report at the American Society for Cell Biology 47th Annual Meeting.

EBS is a rare but devastating inherited condition in which fluid-filled lesions called bullae appear at sites of frictional trauma to the skin. Unfortunately, treatment options for EBS are limited and palliative in nature. Much work remains to be done before sulforaphane can be tested clinically with EBS patients, but Coulombe notes that extracts from broccoli sprouts rich in sulforaphane have already been shown to be safe for use in human skin.

In EBS patients, the bottom layer of the epidermis, which is made of cells called keratinocytes, is unusually fragile and ruptures readily. Molecularly, most cases of EBS result from mutations in genes that produce the proteins keratin 5 (K5) and keratin 14 (K14). These proteins co-polymerize to form the intermediate filament cytoskeleton in basal keratinocytes. Since the discovery in 1991 that EBS is a keratin-based disease, more than 40 additional disorders affecting a broad range of tissues have been traced to defects in genes that encode intermediate filament proteins.

Coulombe and colleagues turned to sulforaphane in their search for a chemical activator that would induce the production of missing keratins in basal epidermis. There are 54 “conserved” keratin proteins in mammals -- meaning that evolution favored their survival. Many of these keratins are closely related in their genetic sequences and their properties and by their distribution within epithelial tissues. Coulombe reasoned that such a situation breeds “functional redundancy,” meaning that the genetic loss of one keratin could be partially rescued by the overlapping functions of a keratin cousin.

Could this partial redundancy serve as the basis for therapy in EBS and related conditions? Coulombe was guided by prior evidence that partial redundancy was at work. In EBS patients, skin blisters heal without scarring, correlating with an induction in the expression of the protein K6, to which K5 is related, and of K17 and K16, to which K14 is related. In transgenic mouse models, these keratins are indeed partially redundant in their ability to provide structural support in skin keratinocytes.

Sulforaphane was originally identified by Johns Hopkins colleague, Paul Talalay, as the chemical entity in cruciferous vegetables responsible for its anti-cancer properties. As originally reported in the August 2007 issue of PNAS, the researchers found that exposing keratinocytes to sulforaphane caused the selective induction of keratins 16 and 17. Moving to an EBS mouse model with a K14 deficiency, they found that treatment with sulforaphane significantly reduced epidermal blistering while it was ineffective for a K5 deficient mouse.

Source: American Society for Cell Biology

December 2) retrieved 18 April 2024 from https://phys.org/news/2007-12-natural-compound-broccoli-devastating-genetic.html