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Inflammation: the Link between Normal Aging and Disease

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Aging is the most well recognized risk factor for many chronic diseases. Both epidemiological and clinical research revealed the inflammatory process underlies most of chronic age-related diseases as exemplified in atherosclerosis, arthritis and diabetes. Recent emerging evidence concur the activated inflammatory condition in elderly with markedly elevated proinflammatory cytokines and its biomarkers. Molecular explorations on the age-related chronic inflammatory process further revealed the activated inflammation is most likely due to the altered intracellular signaling pathways from disrupted redox balance during aging because of increased oxidative stress. Experimental data well documented that several major inflammatory redox sensitive transcription factors are chronically activated with aging. For instance, the most important, versatile nuclear transcription factors, NFkβ, is responsible for the generation of well known inflammatory mediators, such as TNF-α, IL-1, IL-6, IL-8, IL-18 and inducible nitric oxide synthase. Furthermore, the age-related systemic inflammatory process is exacerbated by the decreased activity of anti-inflammatory transcription factor, PPAR, to off set toward to the increased risk for chronic diseases.

One most interesting revelation on the age-related diseases like cardiovascular diseases, cancer, diabetes, arthritis, dementia, osteoporosis, metabolic syndrome and obesity is that they are all related with inflammatory disorders as indicated by increased inflammatory cytokines in these patients. The significance of this revelation is highlighted recently by a proposal for the molecular inflammatory hypothesis of aging based on the molecular events linking normal aging to disease. Adipose tissue mass is the only tissue showing age-related increase, unlike muscle mass and others that decline with age, making elderly metabolically obese.

To illustrate the convergence of normal aging to disease process, metabolic syndrome and obesity will be exemplified in the presentation. It is now well accepted that the increased adipose tissue that is inflamed by the infiltrated macrophages is the major problem of metabolic syndrome and obesity. The adipose tissue is the major production site of TNF-α, IL-1, and IL-6, and TNF-α in particular plays a major key role in causing insulin resistance, and hyperglycemia.

This presentation is organized by four parts: 1. aging as inflammatory state,2. age-related increase of adiposity as the causal factor for metabolic syndrome, 3. inflamed adipose tissue by macrophage invasion, and 4. endogenous anti-inflammatory lipoxins The last portion of the presentation discusses well-known anti-inflammatory lipoxins that are endogenous lipoxygensae-derived lipid mediators, and aspirin-triggered 15-epi lipoxins biosynthesized by acetylated COX-2 for the possible non-invasive long-term intervention on chronic diseases and aging.