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Key protein molecule linked to diverse human chronic inflammatory diseases

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Liwu Li, associate professor of biological sciences at Virginia Tech, has revealed a common connection between the cellular innate immunity network and human chronic inflammatory diseases, including atherosclerosis, Type 2 Diabetes, and neurodegenerative diseases. The finding presents a viable cellular and molecular target for the diagnosis and treatment of serious human inflammatory diseases, according to Li.

"Researchers and physicians have long recognized that there is an association between these conditions. For example, obesity increases the risk of heart attack or stroke, Type 2 Diabetes or insulin resistance, and Alzheimer's Disease," said Li, who is the founding director of the Inflammation Center at Virginia Tech.

"Inflammation is the common mechanism," he said. "Inflammation is a double-edged sword. Proper inflammation is necessary to fend off infection and abnormal cell growth. On the other hand, excessive inflammation contributes to diverse chronic diseases, including atherosclerosis, diabetes, and lupus." However, the complex cellular and molecular networks controlling inflammation are still poorly understood, he said. "The lack of understanding impedes our progress in treating serious chronic inflammatory diseases."

In a series of studies published throughout the last decade, Li's group has defined several critical signaling networks essential for the modulation of inflammation. In particular, a key cellular protein kinase named interlukin-1 receptor associated kinase 1 (IRAK-1) was shown to be

critical for processing diverse inflammatory signals, including microbial products, cytokines, and insulin. Li's group discovered that excessive IRAK-1 activation is linked with the risk of atherosclerosis and diabetes. Using transgenic mice without the IRAK-1 gene, Li's group demonstrated that IRAK-1 deficient mice are protected from developing atherosclerosis and insulin resistance.

At the molecular level, Li's laboratory discovered that IRAK-1 prefers to phosphorylate transcription factors harboring the Serine-Proline motif including STAT-3 and NFAT. Subsequently, STAT-3 and NFAT are involved in modulating the expression of distinct inflammatory mediators responsible for the excessive activation of specialized macrophages and T cells. These cells eventually contribute to diverse inflammatory symptoms including cardiovascular diseases, diabetes, Alzheimer's diseases, and lupus. "Chemical compounds targeting this molecule will have enormous therapeutic potential," Li said.

"There is still a long way to go for finding the actual cure for these diseases," he said. "That is why we are combining expertise from various disciplines, including experimental biology and computational simulation. The Inflammation Center integrates faculties with expertise in experimental molecular biology, cutting edge imaging of inflamed cells and tissues, computational simulation of cellular signaling networks, human and animal studies, and nano-technologies designing novel intervention."

Virginia Tech Intellectual Properties Inc. (VTIP) filed a patent application for Li's discovery and its use as a diagnostic tool and treatment strategy. "This technology will still take some time before there is a product," said Li.

Source: Virginia Tech