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Study pinpoints key genetic factor behind autoimmune diseases, cancer

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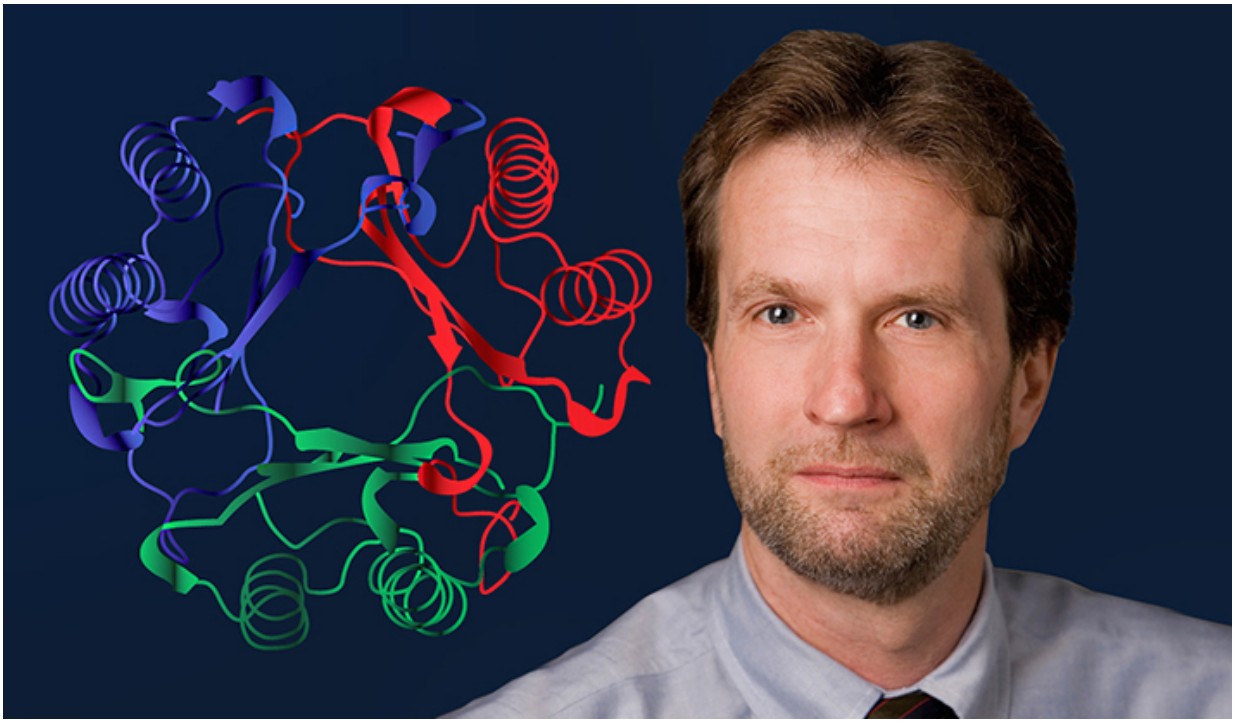

Dr. Richard Bucala studied the role of MIF (left), or macrophage migration inhibitory factor, an immune susceptibility gene product. Credit: Elias Lolis Laboratory, Yale Pharmacology

Scientists have long known that variations in specific human genes are associated with distinct patterns of disease, but an understanding of the molecular mechanisms has remained elusive until now. A team of Yale

researchers has untangled that mystery for a key immune response gene, a discovery which could lead to more personalized treatment for conditions such as lupus and cancer.

Led by professor of medicine Dr. Richard Bucala, the researchers focused on the immune response gene known as MIF. Variants of MIF that cause over-expression of the gene contribute to a range of diseases, such as rheumatoid arthritis, lupus, infectious diseases, and cancer. By reproducing the variants in the lab and studying their function in cells, they identified the specific "transcription factor," or protein, that regulates the gene.

"Now that we know the exact transcription factor, we can begin to design drugs that will interfere specifically with the disease pathway," said Bucala. "It opens the way for the most precise form of drug development that is possible."

Bucala's lab is already studying drugs that target MIF in clinical trials of cancer and autoimmunity. This deeper understanding of the gene's variants and expression will lead to precision drug targeting based on an individual's genetic profile, he said. "Knowing what the transcription factor is presents the possibility of a real personalized medicine approach."

The study was published online, Jan. 11, in the *Journal of Clinical Investigation*.

More information: Jie Yao et al. Transcription factor ICBP90 regulates the MIF promoter and immune susceptibility locus, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI81937