Partners in inflammation

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Credit: AI-generated image (disclaimer)

Individuals with increased levels of C-reactive protein (CRP) in the blood are at increased risk for various diseases linked to inflammation, such as colorectal cancer and cardiovascular diseases. Now, a research team in Japan including Yukinori Okada and colleagues at the RIKEN Center for Genomic Medicine in Yokohama, reports that single-nucleotide changes in three genes can affect the blood levels of CRP in Japanese individuals. Two of these genes, CRP and HNF1A, had already

been found to affect Caucasians, but it was unclear if those same genes would also play a role in Japanese people.

Doctors often measure blood CRP levels in the clinic to determine a patient's risk for inflammation-associated diseases. CRP is synthesized in the liver in response to inflammation in the body so elevated levels signal a problem, such as infectious and autoimmune diseases.

Okada and his colleagues found the three genes that were correlated with changes in blood CRP levels in a genome-wide association study (GWAS) of some 13,000 Japanese individuals (Fig. 1). Their discovery of a single-nucleotide change in the interleukin-6 (IL-6) gene in the Japanese population, however, was not detected in the GWAS of Caucasians.

The IL-6 gene encodes a pro-inflammatory cytokine, IL-6, which has been linked to a variety of immune reactions, and plays a key role in inducing fever in response to infection. Blockers of IL-6 receptor are used successfully in the clinic to reduce the severity of rheumatoid arthritis, a disease long linked to joint inflammation. "The identified variation in IL-6 could therefore be a promising target in the pharmacogenomics [matching drugs to an individual's specific genetic variants] of IL-6 blocking therapy," explains Okada.

The researchers also examined the blood of over 30,000 Japanese patients to determine whether or not the single-nucleotide change in IL-6 that leads to increases in blood CRP levels could affect any other hematological or biochemical markers used in medical practice. They found an increase in: white blood cells, which are involved in inflammation; platelets, which are involved in blood clotting; and serum protein levels, all of which are associated with the IL-6 gene variant that increases CRP levels. They also found a decrease in anemia-related markers.

The link between IL-6, CRP, and these blood parameters could explain why patients with elevated CRP have an increased risk for inflammation-related diseases, and, according to Okada, could provide a clue for how to move forward with personalized medicine. Okada next plans on extending the study to Africans and Caucasians.

More information: Okada, Y., et al. Genome-wide association study for C-reactive protein levels identified pleiotropic associations in the IL6 locus. *Human Molecular Genetics* advance online publication, 31 December 2010 (doi: 10.1093/hmg/ddq551)

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