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# Inflammatory response may fan the flame of dietary fats' role in obesity-related diseases

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An enhanced inflammatory response could be the key link between high saturated fat intake - a recognized risk factor for obesity-related disorders - and the development of diseases like type 2 diabetes and atherosclerosis.

A new study in the *Journal of Nutritional Biochemistry* demonstrates that ingesting fats similar to those in a Mediterranean-type diet, featuring low saturated fat and high monounsaturated fat, appears to decrease the inflammatory response, both in comparison to a high saturated fat diet, as well as in relation to a low-fat diet.

"It has been recognized that obesity - a disorder characterized by abnormally high accumulation of fats in the body - and an unhealthy diet can increase the risk of chronic metabolic diseases such as atherosclerosis, type 2 diabetes, and Alzheimer's disease, but not in everyone," says lead author C. Lawrence Kien, M.D., Ph.D., Davignon Green & Gold professor of pediatrics and medicine at the University of Vermont (UVM).

Inflammation, which involves the release of chemicals called cytokines from cells, is a normal part of the immune system's defense against infection. However, says Kien, some environmental, internal, and even dietary compounds can masquerade as inflammatory stimuli, causing side effects that also occur during infections, and this can lead to long-term health consequences.

Based on research showing that saturated fat generally has metabolic effects via indirect mechanisms, and the fact that metabolic diseases have an inflammatory component, Kien and his team had a hunch: the pro-inflammatory effect of saturated fat might be facilitating how saturated fat impacts the risk of metabolic disease.

"Scientists have strived to understand the effects of dietary fats on inflammation by studying isolated cells and animal model systems," Kien says. A 2011 study reported that palmitic acid, the most prevalent saturated fat in the diet, increased the production of the inflammatory cytokine, interleukin-1beta (IL-1beta) via a process involving activation of an innate immune system response called the NLRP3 inflammasome. However, says Kien, the question remained whether these findings were relevant to human diets.

In their latest study, Kien and colleagues, including UVM immunologist Matthew Poynter, Ph.D., demonstrate for the first time that varying the normal range of palmitic acid found in common human diets influences the production of IL-1beta. They studied healthy, lean and obese adults, enrolled in a randomized, cross-over trial comparing three-week diets, separated by one-week periods of a low fat diet. One experimental diet was similar to the subjects' habitual diet and was high in palmitic acid; the other experimental diet was very low in palmitic acid and high in oleic acid, the most prevalent monounsaturated fat in the diet. After each diet, a number of outcomes were measured, including those related to inflammation. Relative to the low palmitic acid diet, the high palmitic acid diet stimulated the production of cytokines modulated by the NLRP3 inflammasome, thus creating more inflammation and associated risk for metabolic disease.

Kien has been exploring the different metabolic effects of palmitic acid and oleic acid for about 15 years. In a 2013 study in the journal Diabetes, he and his colleagues at UVM and collaborators from Duke

University, found that, compared to an experimental low palmitic acid, high oleic acid diet, a high palmitic acid diet increased the concentration of several inflammatory biomarkers in both blood and muscle and impaired insulin action in women. In a separate study, the team also reported that this same diet was associated with a reversible decrease in daily physical activity and increased anger, suggesting that a diet high in saturated fats may interfere with normal cognitive processes.

"Ultimately, we would like to understand how these dietary fats behave - both shortly after ingestion, as well as when stored in adipose tissue as a consequence of many months of ingestion - and thus contribute to inflammation and the risk of metabolic disease," Kien says. "In other words, habitual diet and especially the type of fat ingested may determine, in part, the risks associated with obesity." However, adds Kien, "it is important to acknowledge that other factors - for example, physical activity - and other features of complex diets will determine how persistent, high intake of saturated fat will impact health."

The UVM-led research team hope to apply these recent findings to a study of obesity-associated asthma by Poynter, a UVM professor of medicine, and age-associated brain function in a project jointly led by cognitive psychologist Julie Dumas, Ph.D., UVM associate professor of psychiatry, who participated in the physical activity and anger research.

**More information:** *Journal of Nutritional Biochemistry*, www.sciencedirect.com/science/ … ii/S0955286315001783

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