HHS Public Access

Author manuscript

Obesity (Silver Spring). Author manuscript; available in PMC 2018 October 16.

Published in final edited form as:

Obesity (Silver Spring). 2015 July ; 23(7): 1329. doi:10.1002/oby.21141.

Dietary fatty acids: Friends or Foes?

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Uncontrolled energy intake, along with reduced energy expenditure, is considered a prime driver of the obesity and diabetes epidemics. Intake of excess saturated fatty acids is correlated with increased adiposity and insulin resistance. On the other hand, unsaturated fatty acids are considered to be less harmful, and, in some instances, even shown to impart metabolic benefits (1). Systemic inflammation is regarded as a strong promoter of metabolic dysfunction although its causative or consequential role is debated. Similarly, changes to the gut environment are known to either positively or negatively influence the metabolic state (2). Thus, the role of changes to the gut microflora, and that of the levels of gut hormones, has received widespread attention with regards to either promoting or warding off metabolic dysfunction. Changes to gut permeability are observed in metabolic disease, with “a leaky gut” considered to promote metabolic dysfunction (3). While these various mechanisms all seem to be at play during disease progression, the inter-relationships amongst them are less clear.

In this issue, using a high-fat diet mouse model, Lam and colleagues provide important insight into the interactions amongst gut epithelial permeability, gut microflora adaptations, inflammation and the metabolic state in response to variations in dietary fatty acid intake (4). Dietary fatty acids (dFAs) are implicated in the onset of metabolic syndrome (1), although the underlying benefits or risks associated with specific types of dFAs are unclear. Using a high-fat diet mouse model, Lam et al (4) demonstrate beneficial metabolic effects of supplementing n-3 dFA or its metabolite Resolvin D1. The metabolic benefits occur via improved gut integrity, reduced inflammatory state, decreased adiposity and reduced insulin resistance (Figure 1). Importantly, the authors find increased abundance of H_2S producing bacteria in mice fed with saturated fats, while the levels of those bacteria is significantly reduced upon n-3 dFA supplementation. They show that alteration to the H_2S bacterial abundance is associated with improvement in gut barrier integrity and reduced inflammation, but not with obesity or insulin resistance.

In summary, this paper addresses several disease causing/promoting mechanisms – body weight gain, insulin resistance, systemic inflammation, gut barrier permeability and gut flora changes – and suggest that they are under purview of specific dietary fatty acids. It is unclear if the different dFAs cause morphological or functional changes to the epithelial, entero-endocrine or mucosal immune cells resident within the gut. Also unclear is if levels of gut hormone change upon either acute or chronic dFA intake. Further, considering that H_2S interferes with cellular mitochondrial function (5), the effects of H_2S on other cells involved in energy metabolism warrants further study. This paper paves the way for further detailed examination of the role of specific dFAs in causation and/or progression of metabolic disease with a viewpoint to translate those findings to clinical utility.

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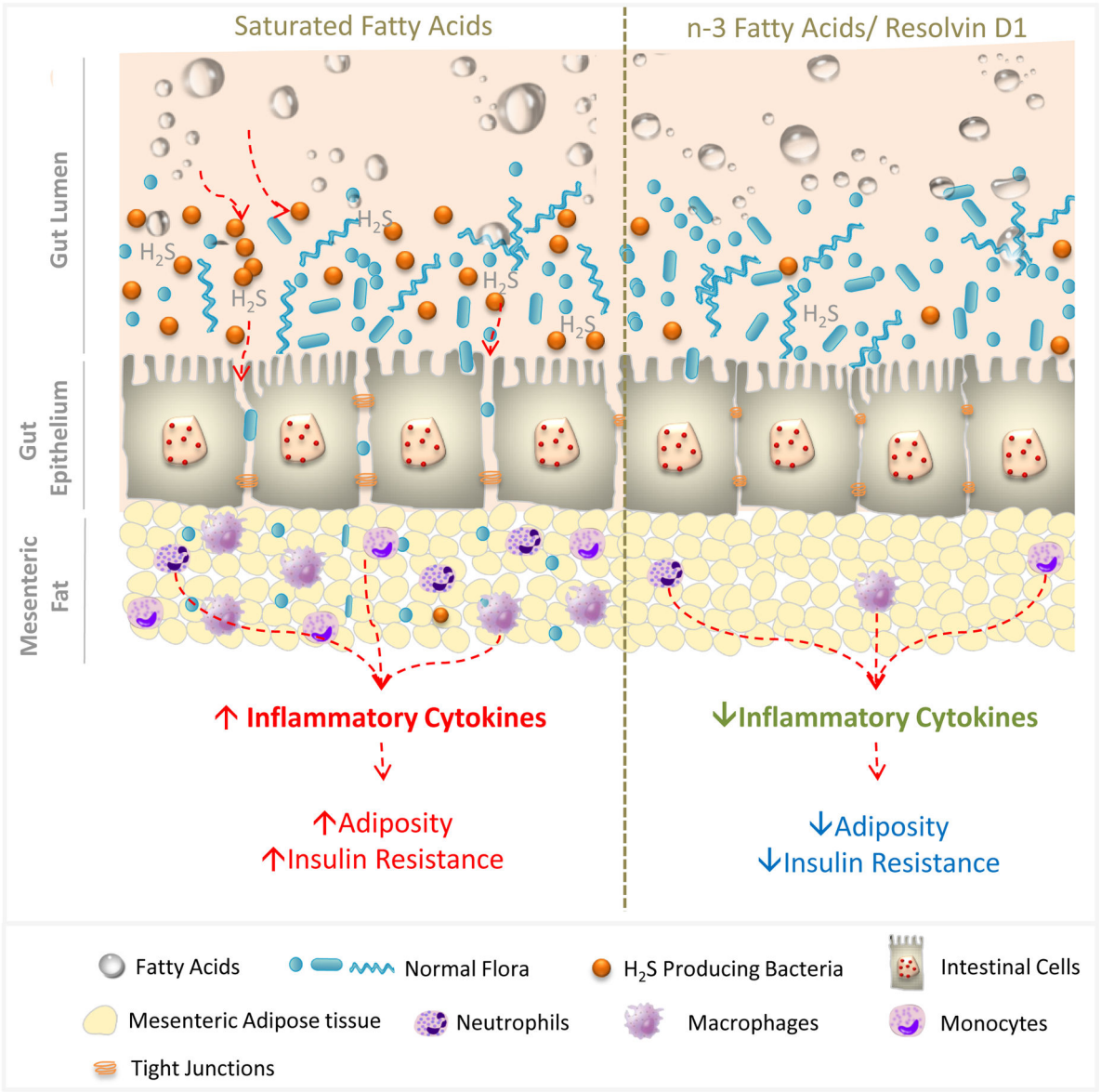

Figure 1. Effect of dietary fatty acids on gut health and metabolism.

Saturated fatty acid intake results in increased abundance of H_2S producing bacteria that is associated with reduced gut integrity (*leaky gut state*). This state allows certain bacteria to invade mesenteric fat and promote the inflammatory state that drives adiposity and insulin resistance (left panel). In contrast, n-3 fatty acids and their metabolite Resolvin D1 preserve normal gut integrity that precludes bacterial translocation, thus reducing the inflammatory response, resulting in protection from adiposity and insulin resistance (right panel).