

ABSTRACT

Obesity is a inflammatory state associated with an elevated risk of type 2 diabetes, dyslipidemia (e.g. cardiovascular disease) and hypertension. These pathophysiological complications of obesity have been mechanistically linked to changes in key adipokines secreted from adipocytes and resident adipose macrophages. Such secreted factors circulate to central and peripheral sites regulating basic aspects of energy expenditure, satiety and immune function. The expression of adipokines is regulated in the adipocyte and macrophage largely, but not exclusively, by two transcription factors: nuclear factor- κ B (NF- κ B) and peroxisome proliferator-activated receptor- γ (PPAR- γ). NF- κ B is a pro-inflammatory transcription factor that activates the expression of a large set of genes linked to immunoactivation and inflammation. The importance of inflammation is highlighted by the fact that classical anti-inflammatory drugs such as aspirin, which have historically been considered only in the context of immunoactivation, are now in clinical trials as an anti-diabetic, anti-obesity treatment. In contrast, activation of PPAR- γ by lipophilic drugs results in an anti-inflammatory, anti-diabetic phenotype but is also obesogenic. The identification of small pharmacologic molecules capable of regulating adipose tissue NF- κ B and PPAR- γ suggests that bioactive food components may be identified that have similar beneficial properties. To that end, we propose the following hypothesis: **Utilizing a novel adipocyte cell line containing dual fluorescent reporters for NF- κ B and PPAR- γ , food component libraries will be screened using high-throughput technologies to identify and, subsequently, characterize compounds that alter the activity of NF- κ B and PPAR- γ or triacylglycerol (TAG) accumulation to promote insulin sensitivity while decreasing inflammatory signaling.** Combining reporter gene analysis with evaluation of cellular TAG levels will allow for the identification of lead bioactive food components that decrease inflammation yet do not lead to increased adiposity. Once identified and characterized in cell and animal models, lead bioactive food components can then be used individually or in combination as novel nutritional therapeutics against metabolic diseases.