Mechanisms of action of a novel anti-obesity drug

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Obesity, a principle risk factor associated with metabolic syndrome, is an epidemic that affects 30% of adults in the United States. The main cause of obesity is an imbalance between energy intake and energy expenditure. When energy intake exceeds expenditure, the excess is stored mainly in the form of fat in adipose tissue. Pharmacological intervention might reduce the incidence of the comorbid factors of obesity including diabetes and cardiovascular disease. However, there are only two FDA-approved drugs in the market currently for the long-term treatment of obesity and neither is very effective. We have shown that the limonoid prieurianin is an effective anti-obesity drug in four mouse models of obesity, and it has multifocal anti-lipogenic effects in cultured preadipocytes in vitro. In addition, gene expression profiling study by DNA microarray showed that prieurianin upregulates the expression of TNF receptor type 2 (TNFR2) and TNF receptor-associated factor 5 (TRAF5). We further showed that prieurianin transactivates the nuclear factor kappa B (NFkB) response elements reporter. These results led us to raise the hypothesis that the anti-obesity effect of prieurianin is mediated through the TNFR-NFkB signaling pathway. Here, we investigated the molecular mechanisms of this novel anti-obesity compound.