Successful treatment of obesity requires a continuous reduction in adiposity and maintenance of a healthy body weight. The conventional approaches used to achieve weight loss involve exercise and diet. However, as body fat is reduced through these approaches, energy-sparing mechanisms are activated and impose a major obstacle to long-term weight loss. Therefore, identifying strategies to overcome these energy-sparing mechanisms is crucial to improve the outcome of weight loss programs. One potential approach would be to remodel white adipose tissue (WAT) to shift its metabolism toward fat oxidation instead of storage. In this study we show that by using a pharmacological approach that activates an enzyme (AMPK) that works as a cellular energy sensor, it is indeed possible to increase fat oxidation within the WAT and reduce fat mass in vivo. The important novel observations were that the pharmacological treatment reduced adiposity without triggering energy-sparing mechanisms that oppose weight loss. In fact, animals receiving the treatment increased spontaneous physical activity, energy expenditure, and were more responsive to the anorexic hormone leptin. These findings open up the possibility of using AMPK agonists, in conjunction with exercise and diet, to promote prolonged weight loss in obese individuals and successfully maintain a healthy body weight in the long-term.

Reference: Gaidhu MP, Frontini A, Hung S, Pistor K, Cinti S, **Ceddia RB**. Chronic AMP-kinase activation with AICAR reduces adiposity by remodeling adipocyte metabolism and increasing leptin sensitivity. J Lipid Res. 2011 Sep;52(9):1702-11.

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