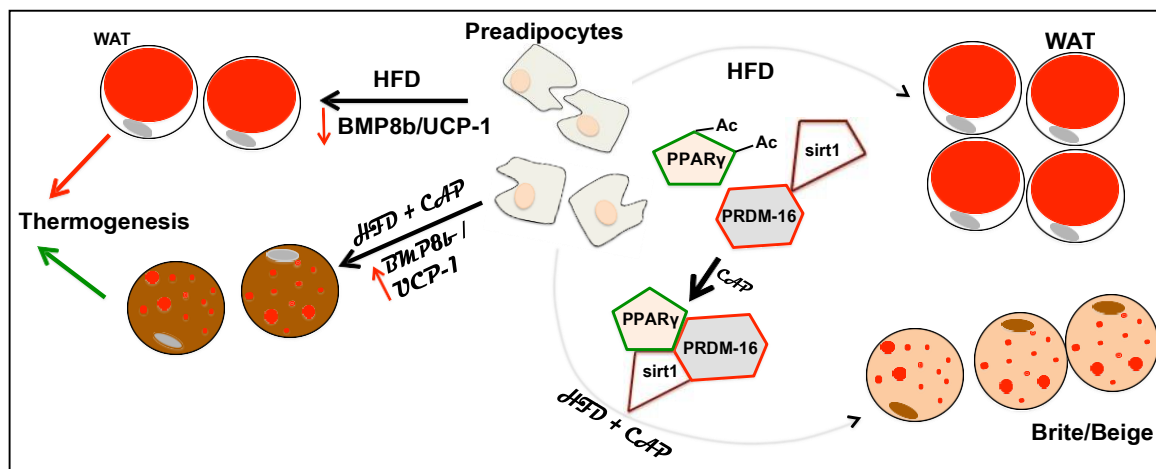


## Capsaicin triggers brown remodeling of white adipocytes to antagonize diet-induced obesity

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Recent research provides evidence for browning of white (BRITE) adipocytes is a novel mechanism to counteract obesity. The molecular mechanism of brown remodeling of white adipose tissue (WAT) is tightly regulated by the protein machinery, which consists of sirtuin-1 (SiRT-1), PR domain zinc finger protein 16 (PRDM-16) and peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ). SiRT-1 deacetylates PPAR $\gamma$  and stabilizes the interaction between PPAR $\gamma$  and PRDM-16 to cause browning of WAT. Here we evaluated the hypothesis that capsaicin, an agonist of transient receptor potential vanilloid 1 (TRPV1), inhibited high fat diet induced obesity by inducing browning of WAT. Capsaicin increased the expression of brown fat specific thermogenes, PGC-1 $\alpha$ , uncoupling protein-1 (UCP-1) and bone morphogenetic protein b8 (BMP8b) in the subcutaneous and brown fat pads of wild type mice. Capsaicin increased the expression of SiRT-1 and PRDM-16 in these fat pads and triggered SiRT-1-dependent deacetylation of PPAR $\gamma$  to facilitate PPAR $\gamma$ -PRDM-16 interaction, which we determined by coimmunoprecipitation technique. Capsaicin also increased the respiratory coefficient, heat production and locomotor activity of wild type mice. These effects of capsaicin are associated with a decrease in body weight gain. Capsaicin feeding did not modify the amount of food or water consumed by either wild type or TRPV1 $^{-/-}$  mice. Further, capsaicin prevented lipid accumulation in the adipocytes and prevented hepatic steatosis in wild type mice. The anti-obesity action of capsaicin was only observed in the wild type mice but not in TRPV1 $^{-/-}$  mice suggesting that capsaicin exerts its effects by activating TRPV1. In conclusion, our data unambiguously demonstrate that capsaicin ablates high fat diet-induced obesity by stimulating metabolism through browning of WAT.



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