

中文題目：活化轉錄因子-3 及相關小分子草藥誘導劑，ST32DB，能藉由脂質轉錄因子 ChREBP 和白脂轉化來對抗肥胖和代謝功能障礙

英文題目：Activating transcriptional factor-3 and related small molecule herbal inducer, ST32DB, against obesity and metabolic dysfunction through lipogenic transcription factor ChREBP and white adipocytes trans-differentiation axis

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Background: Altering the balance between lipogenesis/lipolysis or altered white fat remodeling is a potential strategy for treating obesity and metabolic syndrome.

Methods and Results: Genetic deletion of Activating Transcriptional Factor-3 (ATF-3) decreased energy expenditure but increased body weight, insulin resistance and hepatic steatosis during high-fat diet regimens, in addition, restored ATF-3 expression by AAV-mediated in ATF-3 knockout mice were abrogate these metabolic changes. In vitro study in 3T3-L1 adipocytes also shown that ATF-3-overexpressing exhibited less lipid accumulation with diminished expression of adipogenesis, lipogenesis and inflammation-related genes but increased lipogenesis, β -oxidation and brown/beige genes as compared through ChREBP and SCD1 dependent pathway. Finally, the beneficial metabolic change, thermogenesis elicited, reduced lipogenesis and increased lipolysis by a new finding ATF-3 inducer selected by ATF-3 stable clone in 3T3-L1 adipocytes were emerged in normal mice but in ATF-3 knock out mice when feeding high fat diet. In addition, consistent results between in vitro and in mice.

Conclusions: Our finding identify ATF-3 and a new ATF-3 single compound inducer from herbal as a regulator of lipogenesis/lipolysis balance and enhance energy expenditure and mediate adipocyte differentiation from white fat to brown fat through CHREBP and SCD1 pathway represents a possible therapeutic strategy to treat obesity and obesity induced metabolism syndrome.