GMR Genetics and Molecular Research
Online Journal
ISSN:1676-5680

WY14643 combined with all-trans retinoic acid acts via p38 MAPK to induce "browning" of white adipocytes in mice

J. Wang[1], G.J. Sun[1], J. Ding[2], J.X. Zhang[3], Y. Cui[1], H.R. Li[1] and S.J. Wang[1]

[1]Department of Endocrinology and Metabolism, the First Affiliated Hospital, Zhengzhou University, Zhengzhou, China
[2]Department of Obstetrics, the First Affiliated Hospital, Zhengzhou University, Zhengzhou, China
[3]Department of Breast Surgery, the First Affiliated Hospital, Zhengzhou University, Zhengzhou, China

Corresponding author: S.J. Wang
E-mail: shoujunwangcn@163.com

Genet. Mol. Res. 14 (2): 6978-6984 (2015)
Received August 13, 2014
Accepted March 5, 2015
Published June 26, 2015
DOI http://dx.doi.org/10.4238/2015.June.26.6

ABSTRACT. The ability of mammals to resist body fat accumulation is linked to their ability to expand the number of "brown adipocytes" within white fat depots. All-trans retinoic acid (t-RA) and peroxisome proliferator-activated receptor-α (PPARα) have been implicated in "browning-like" or "browning" programs, respectively. However, a PPARα-agonist (WY14643) failed to regulate the expression of the uncoupling protein 1(UCP1) gene unless combined with retinoic acid. This study investigated the effects of the PPARα-agonist WY14643 combined with t-RA, on the "browning" of white adipocytes in mice mediated by UCP1, and the molecular mechanisms involved in this process. We compared the effects of WY14643 alone and WY14643 combined with t-RA or the p38 MAPK-inhibitor, SB203580, on white adipocytes after 24 h using the expression of UCP1, detected with RT-

PCR and western blot. We also determined the mechanism by which p38 MAPK and phospho-p38 MAPK influence the process of "browning" using western blot. All concentrations of WY14643 failed to induce UCP1 mRNA expression, protein expression, or phosphorylation of p38 MAPK ($P < 0.05$). WY14643 combined with t-RA was observed to induce UCP1 mRNA expression, protein expression, and phosphorylation of p38 MAPK ($P < 0.05$). SB203580 combined with WY14643 and t-RA suppressed UCP1 mRNA expression, protein expression, and p38 MAPK phosphorylation ($P < 0.05$). WY14643 combined with t-RA can induce the transformation of white adipocytes to brown adipocytes through activation of the p38 MAPK signaling pathway.

Key words: Brown adipocytes; Proliferator-activated receptor-α; All-trans retinoic acid; Uncoupling protein 1; p38 MAPK pathway

