Myotrophin and miR-375 as pharmacological target for 9cisRetinoic Acid

1)Gallelli L. 2)Perri M. 3)Cione E. 4)Liu N. 5)Kagechika H. 6)Caroleo MC. 7)De sarro G.

University of Catanzaro

Functional studies indicate that essential cellular processes are controlled by Vitamin A derivatives. Among these the retinoic acid isoforms, all-trans- and 9-cis (9cRA), regulate the expression of various genes in both physiological and pathological conditions. Using several in vitro experimental models such as pancreatic β-cells, pre-adipocytes and breast cancer cells with different phenotypes, we demonstrated the capability of 9cRA to modulate myotrophin (Mtpn) and miR-375 expressions. The 9cRA effect in pancreatic β-cells line INS-1 832/13 point out a decreased expression of Mptn at both mRNA and protein levels associated to a concomitant increase of miR-375. We also studied the effect of this molecule on 3T3-L1 pre-adipocytes cells demonstrating a down-regulation of Mtpn and a dramatic increase of miR-375. Moreover, in the in vitro breast cancer model such as MDA-MB-231 and MCF-7 cells, 9cRA showed different effect on both Mtpn and miR-375 expression. In INS-1 832/13, 3T3-L1 pre-adipocytes and MCF-7 but not in MDA-MB-231, the effect of 9cRA on Mptn gene expression and its miR was under the control of RARs and RXRs receptors, as revealed by the exposure of these cell line to LE540 or HX603 receptor antagonists. In our findings 9cRA emerges has a hormone with a regulatory action on miR-375 that in most cases interfere with Mtpn expression.

Key words: 9-cis Retinoic Acid; Myotrophin; Pancreatic β-cells; Pre-adipocyte; miR-375