

SIRTINOL DECREASES ADRENOCORTICAL CANCER CELL GROWTH AND PROGRESSION INTERFERING WITH SIRT1 AND MODULATING E2/ERA/IGF1R PATHWAY

Chimento A. (1), De Luca A. (1), Nocito M.C. (1), Sculco S. (1), Avena P. (1), Casaburi I. (1), Sirianni R. (1) and Pezzi V. (1)

(1) Department of Pharmacy and Health and Nutritional Sciences University of Calabria, Arcavacata di Rende, Cosenza (Italy)

ACC is a rare tumor with unfavorable prognosis, lacking of early diagnosis and effective treatment. This tumor is characterized by IGF-II overproduction, estrogen receptor (ER)- α up-regulation and aromatase increase. Previous reports suggest that ER α expression can be regulated by sirtuin 1 (SIRT1), a nicotinamide adenine dinucleotide (NAD⁺)-dependent class III histone deacetylases that modulate activity of several substrates involved in the regulation of cellular stress, metabolism, proliferation, senescence, protein degradation and apoptosis. Nevertheless, SIRT1 can acts as a tumor suppressor or oncogenic protein. In this study we found that SIRT1 expression is inhibited in adrenocortical cancer cell line H295R by sirtinol (2-[(2-Hydroxynaphthalen-1-ylmethylene)amino]-N-(1-phenethyl) benzamide), a potent inhibitor of SIRT1 activity. In addition, sirtinol is able to decrease cell proliferation, colony and spheroids formation, cell invasion and migration. Defining the molecular mechanisms, we revealed that sirtinol interferes with E2/ER α /IGF1R pathway inhibiting ER α , IGFR, SF1 and aromatase expression. Silencing of SIRT1 by a specific siRNA reproduced the same effects of sirtinol-mediated cell growth inhibition and protein expression confirming the oncogenic role of SIRT1 in ACC. All these results suggest that SIRT1 may contribute to tumorigenesis of H295R cells and that it may be a useful therapeutic target against ACC.

XIX Congresso Nazionale
AIBG

Milano | 4 - 5 Ottobre 2019