

Abstract

Charles University in Prague

Pharmaceutical Faculty in Hradec Králové

Department of Pharmacology and Toxicology

Student: Anastasiya Shkut

Supervisors: Mgr. Jana Mandíková, Virginia Motilva Ph.D.

Title of diploma thesis: The role of melatonin in SIRT1 and p-AMPK regulation in HT-29 cell line.

Sirtuin 1 (SIRT1) is NAD⁺ dependent deacetylase present in wide range of organisms including mammals. It was found to extend life span in yeasts during calorie restriction (CR) conditions. SIRT1 deacetylates many regulator proteins and thus control metabolic status of cell as well as AMP-activated kinase (AMPK), which is also energy regulator enzyme depending on NAD⁺ levels in cell. Both of them play roles in cancer and could influence autophagy, although the exact mechanism remains unclear. We focused our study on hormone melatonin, which has anti-inflammatory and anti-cancer effects, to study its influence on human colon cancer cell line HT-29. If it has impact on SIRT1 and AMPK and what is hierarchic relationship between SIRT1 and AMPK. Also we observed its possible influence on autophagy. We used Western blotting (WB) technique and from our results it seems that melatonin has significant effect on SIRT1, which might activate AMPK as well as autophagy. Nevertheless some of results did not have sufficient number of experiments to make clear statement. More studies using different methods would be necessary to declare if melatonin has significant influence on SIRT1 and AMPK, if this fact is useful for colon cancer therapy in any way, and what role could play autophagy in this process.