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**EFFECTS OF SELECTED PLANT POLYPHENOLS ON SIRT GENE EXPRESSION AND ANTI-TUMOR ACTIVITY IN CULTURES OF COLORECTAL CANCER CELLS**

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Colon cancer stem cells (CSC) play critical role in the resistance of colorectal cancers to radiotherapy/chemotherapy, metastasis and relapse. Author's compared the effects of plant polyphenols, Celastrol and Resveratrol on human colon cancer cell lines: Sensitive to cytotoxic drugs (LOVO) and doxorubicin resistant (LOVO/DX). Both polyphenols caused cell-cycle arrest at S phase in LOVO and LOVO/DX cells. Resveratrol exerted a strong proapoptotic effect against LOVO cells, but it does not affect the viability of LOVO/DX cells. Celastrol caused an increase (up to 50%) in the percentage of cells in apoptosis in both LOVO and LOVO/DX cells, which correlated with decreased expression of BRCA1 and PPAR genes. Importantly, Celastrol and Resveratrol inhibited the functional activity of multidrug resistance proteins (MDRs). Resveratrol increased the expression of SIRT 1, 2 and 3 genes whereas Celastrol strongly increased the expression of SIRT 1 and decreased SIRT 3 gene expression, in both LOVO and LOVO/DX cells. Expression of the SIRT 6 gene was increased by Celastrol in LOVO/DX cells (depending on concentration), while resveratrol did not affect gene expression of this sirtuin in LOVO/DX cells. In conclusion, the effect of tested polyphenols on sirtuin gene expression may have different influence on the progression of colon cancer. According to literature data, the increase in SIRT 1 expression may potentiate and SIRT6 may inhibit the progression of colon cancer. Because celastrol and resveratrol have significant pro-apoptotic effects and they inhibit cell cycle progression and block the function of multidrug resistance proteins in both types of colon cancer cells, they concluded that the antitumor effect of these polyphenols occurs through multiple mechanisms of action and is largely unrelated to their effects on sirtuin gene expression.

## BIOGRAPHY

Helena Moreira is Assistant Professor at the Department of Basic Medical Science of the Faculty of Pharmacy at the Medical University of Wroclaw, Poland. She completed her Doctoral studies at the Institut Gilbert-Laustriat at Department Physicochimie des Interactions Cellulaires et Moléculaires in Strasbourg in France where she was working on the molecular mechanisms of TNF- $\alpha$  secretion, a key cytokine in chronic inflammation. She is deeply interested in research on cancer treatment, especially in studying the anti-cancer mechanisms of various natural plant polyphenols. Her research interest mainly focus on cancer stem cells in colorectal cancer. She has a strong laboratory experience, including in cell culture and flow cytometry.

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