Title of the project: Studies into effects of zinc on cell proliferation and cell death in colon cancer cells *in vitro*.

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Principal Investigator: S. John

Co-investigators: E. Rudolf

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Total funds allocated for project - Kč (thousands): 240

Summary of 2009 results

Title of the presentation: Effects of zinc pyrithinone on intracellular signaling of colon cancer cells *in vitro*

Authors: S. John, M. Červinka. E. Rudolf

Normal as well as cancer cells regulate intracellular zinc content by expressing various zinc transporters or zinc-buffering mechanisms. Increased external zinc concentrations thus often influence membrane-dependent signaling of exposed cells while any major entry of zinc ions into the cellular cytosol remains limited. To address this problem, we used zinc ionophore zinc pyrithinone which transports zinc directly into cytoplasm of cells and monitored its effects on behavior of colon cancer cell lines HCT-116, HT-29 and SW-620 representing various stages of colon cancer during 24 hours. Addition of zinc pyrithinone produced time-dependent influx of zinc ions into the cytoplasm of treated cells demonstrable by zinc-specific fluorophores. This influx was accompanied by changed expression of zinc transporters, enhanced oxidative stress, changes in mitochondrial topography and inhibition of ATP production with resulting cell death. The prevailing type of cell demise was apoptosis and autophagic cell death as visible by extensive vacuolization and expression of autophagy-specific markers. In this model, most sensitive to zinc pyrithinone treatment appeared to be SW620 cells while HCT-116 and HT-29 cells showed great resistance thus for the first time showing varying sensitivity of individual stages of colon carcinogenesis to zinc.

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