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Obesity and colon cancer: What is the link?

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Obesity is a key risk factor for the development of colon cancer; however, the endocrine/paracrine/metabolic networks mediating this connection are poorly understood. Our goal was to explore the metabolic networks and molecular signaling pathways linking obesity, adipose tissue and colon cancer. Using in-vivo experiments, we found that mice fed a high-fat diet (HFD) and injected with MC38 colon cancer cells develop significantly larger tumors than their counterparts fed a normal diet. In in vitro assays, human colon cancer cells were exposed to conditioned media (CM) from cultured human adipose tissue fragments of obese vs. non-obese subjects. Oxygen consumption rate (OCR, =mitochondrial respiration) and extracellular acidification rate (ECAR, =glycolytic respiration) were examined vis-à-vis cell viability and expression of related genes and proteins. CM from obese (vs. non-obese) subjects decreased OCR and gene expression of mitochondrial proteins without affecting cell viability or expression of glycolytic enzymes. Similar changes could be recapitulated by incubating cells with leptin, whereas, leptin-receptor specific antagonist inhibited the reduced OCR induced by conditioned media from obese subjects.

Additional in vitro experiments, murine colon cancer cells exposed to CM from the adipose tissue of HFD-fed mice demonstrated significantly lower OCR. In addition, these colon cancer cells exposed to CM prepared from the visceral fat of HFD-fed mice or to leptin showed downregulated expression of mitochondrial genes. Additionally, we found a close link between the fat adipose tissue and cancer development and demonstrated that this effect is mediated by the JNK/STAT3-signaling pathway. We conclude that obese adipose tissue alters the metabolic networks of colon cancer cells, impinging directly on their metabolism and malignant stage. These results highlight a putative novel mechanism for obesity-associated risk of gastrointestinal malignancies, and suggest potential new therapeutic avenues.

Biography:

Betty Schwartz is a full professor in the School of Nutritional Sciences Institute of Biochemistry, Food Science and Nutrition, The Robert H. Smith Faculty of Agriculture, Food and Environment at The Hebrew University of Jerusalem, Israel. Cancer is one of the leading causes of death in the Western world including Israel. The role of diet in modulating cancer risk is a well-accepted concept, and natural compounds which have been proven safe over time and easily accessible through the diet represent ideal candidates as chemopreventive agents for the effective reduction of cancer-related morbidity and mortality. Her laboratory has searched for numerous agents present in foods that can act as chemopreventive agents and exert their activity on multiple signal transduction, transcriptional regulation and activation of several apoptotic cascades in various tumor cells and animal models of colorectal cancer or associated colon cancer (induced by inflammation of the bowel). Natural agents such as lycopene, isoflavones, allicin, omega-3 fatty acids, glucans, specific proteins etc. have been shown by us to possess chemopreventive potential. Her personal and collaborative research utilizes molecular and chemical biology approaches, including in vivo animal and even human studies to ask well as hypothesis-driven strategies, to interrogate cancer biology, identify and validate new cancer targets, discover and develop chemical, molecular tools to identify nutrients acting on these targets, identify predictive and mechanism of action.