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## Modulatory effect of the green alga *Ulva fasciata* sulphated polysaccharides (SPs) on metabolic biomarkers in hypercholesterolemic rats

**Maha Z Rizk**

National Research center, Egypt

Hypercholesterolemia (HC) is frequently associated with oxidative stress, and release of inflammatory cytokines. The objective of this study is to determine the hypolipidemic effects of sulphated polysaccharides from the seaweed *Ulva fasciata* algal extracts (UFP) through measuring certain biomarkers related to liver and kidney functions in hypercholesterolemic as compared to normal rat serum. Rats were fed high-fat diet with oral cholesterol administration. Total lipid profile, liver and kidney functions, inflammatory cytokines (TNF- $\alpha$ , CRP, MPO and IL-10), oxidative stress markers (GSH, MDA and NO), and cell adhesion molecules (ICAM-1 and VCAM-1), were assessed before and after treatment with UFP. Histological examination of heart, liver and kidney were performed and revealed increased cholesterol, triglycerides, LDL, oxidative stress and inflammatory markers in HC-rats. Histopathological examination of heart aorta revealed obvious fatty plaques and that of liver demonstrated severe degeneration of liver cells, necrosis and presence of fatty droplets. In addition, nephron-histological examination showed mild glomerular injury, vascular and inflammatory changes. Treatment with UFP effectively reduced the number and intensity of heart plaques, diminished formation of fatty liver, as well as improved hepatic and renal function as compared to the reference drug; fluvastatin. It could be concluded that consumption of UFP may be beneficial in amelioration of biomarkers related to hypercholesterolemia disorders; such as obesity and heart injury, hence reduce the possibility of heart strokes in hypercholesterolemic patients.

[maha\\_zaki\\_rizk@yahoo.com](mailto:maha_zaki_rizk@yahoo.com)

## Proteomics analyses to identify targets within the tumor microenvironment

**Principe Simona**

Princess Margaret Cancer Center, Canada

Cancer-associated fibroblasts (CAFs) represent the most abundant cell type within the stroma and are key components involved in the regulation of carcinogenesis. During the development of cancer, CAFs create a supporting niche by maintaining a bidirectional crosstalk with epithelial cells, mediated by extracellular matrix components, cell-cell contact, classically secreted soluble factors and extracellular vesicles, such as exosomes. To investigate stromal heterogeneity in oral cancers and identify cancer-associated proteins, we employed a shotgun proteomics approach for a comprehensive analysis of CAF-derived proteins. We isolated matched pairs of human primary fibroblasts from oral cancers (CAFs) and adjacent tissue (AFs) and characterized them according to morphology, expression of myofibroblast markers and the ability to contract collagen matrices *in vitro*. We collected total lysates, conditioned media and exosomes and analyzed each sample by Ultra-High Pressure Liquid Chromatography (UHPLC) coupled to a Q-Exactive mass spectrometer. We applied quantitative proteomics to our comprehensive dataset of 4160 proteins, to select a list of ~200 proteins that are associated with a CAF-activated state. Our proteomic analyses provide a detailed overview of signaling factors, receptors and intracellular proteins, associated with the induction of a pro-tumorigenic stroma. Our findings highlight differential expression of key signal transduction molecules previously associated with cancer and we validated a CAF-specific exosomal and intracellular signature that can represent a novel source of promising biomarkers in oral cancer.

[simonaprincipe83@gmail.com](mailto:simonaprincipe83@gmail.com)