Colon Cancer in Obesity: Prevention with Wine Polyphenolics

Background
Colorectal cancer, associated with obesity, is the third most prevalent type of cancer in men and women after lung and breast and prostate cancers. Colorectal cancer is directly related to the consumption of a diet high in fat and/or red meat, a diet low in fiber, calcium and folate, as well as a diet low in fruit and vegetables.

Polyphenols are the most abundant antioxidants compounds in the human diet. They can be found in fruits and vegetables, cereals, tea, chocolate and wine. Red wine polyphenolics have been identified as potential chemopreventive agents against a wide variety of cancers through possible mechanisms such as induction of apoptosis, modulation of signal transduction pathways, etc. Therefore the objective of this work was to study the potential anti-cancer mechanisms of a Texas red wine from Black Spanish grapes (Vitis labrusca) in colorectal adenocarcinoma cells (HT-29).

The anticancer effects of polyphenolics from red wine have previously been demonstrated, however several details regarding the underlying mechanisms are not well investigated. Apoptosis is a programmed cell death which damaged or mutated cells can undergo. However, in the presence of an activated oncogene, disorderly survival and proliferation of mutated cells can be observed. More recently, it has been found that so called micro-RNA are involved in the regulation of oncogenes. Micro-RNAs are small RNA units which do not encode proteins, but instead seem to be involved in the regulation of genes, at times one microRNA can regulate several hundreds of mRNAs. In a previous study we had discovered that the specific microRNA-27a seems to be involved in the up-regulation of an oncogene specificity protein Sp1, which is involved in the pathogenesis of many kinds of tumors. One of the objectives of this study was to determine, whether microRNA-27a was involved in the anti-cancer effects of red wine polyphenolics.

MicroRNA-27a regulates Sp1 by inhibiting a transcription factor ZBTB10, which is a known suppressor of Sp1 protein; Sp1 is over-expressed in many types of cancers. Sp proteins regulate angiogenesis, proliferation and survival of cancer cells, therefore Sp proteins play an important role in cancer development. The previously investigated mechanisms involving microRNA-27a-ZBTB10-Sp protein interaction and our findings that red wine polyphenolics decreased Sp proteins, support the hypothesis that red wine polyphenolics also involve microRNA-27a (miR-27a) in their anti-cancer effects.
What did we learn?
The prepared wine extract contained many polyphenolics, including gallic acid, p-coumaric acid, quercetin, resveratrol, as well as anthocyanins. The extract was investigated within the range from 20-300mg/L in cancer cells. The apoptotic enzyme caspase-3 was increased up to 1.8-fold within this concentration-range, indicating potential pro-apoptotic activity of the wine extract. The oncogenic Sp1 protein was significantly decreased, where the zinc-finger protein ZBTB10 a transcription factor which has been found to inhibit Sp1 was increased up to 1.3-fold with the wine extract. Additionally, the pro-oncogenic miR-27a was significantly decreased within an extract concentration range of 19-150 mg/L. Moreover, several Sp-regulated oncogenes were also decreased.

Summary & Conclusions
In conclusion, red wine polyphenolics from a Black Spanish red port wine reduced cell proliferation and induced apoptosis. Wine extract down-regulated Sp1 and dependent genes. Furthermore, ZBTB10 a known target for miR-27a was increased, therefore the reduction of miR-27a seems to be involved in a ZBTB10-mediated reduction of the oncogenic Sp1 transcription factors.