A search for mechanism of anticancer properties of vitamin C; possible link between epigenetic DNA modifications and vitamin C (ascorbate) oral supplementation: in vivo study

Every cell of human organism has exactly the same genetic information (genetic code-genome). However, there are hundreds of different kinds of cells/tissues with different functions and shapes. These differences depend on epigenetics – changes in gene expression (activation or inactivation of certain genes) which decide how cell read the genes. 5-mCyt, which was discovered more than half a century ago, is the central DNA epigenetic mark. Only in 2009 several different DNA epigenetic marks, which play a role in DNA demethylation, were conclusively detected in human DNA. In our laboratory highly sensitive and precise methodology was developed to analysed all DNA epigenetic modifications. Using this technique we have found that physiological concentrations of ascorbate in human serum guarantee stable level of the main product of DNA demethylation, a modification necessary for epigenetic function of the cell.
Although Vitamin C is relevant to cancer in many ways, our focus here is on its role as a necessary part of DNA demethylation enzymes,(TETs) i.e. as a modulator of the epigenetic state of cancer cells.

The **goals of this project are to characterize: 1) in tissues, the link between vitamin C concentration and markers of active DNA demethylation, before and after supplementation; 2) whether the reported antitumor effect of vitamin C in the case of solid tumor-prostate (PC) and in hematological disorder - chronic lymphocytic leukemia (CLL), depends on remodeling of epigenetic DNA modifications** in leukocytes and target organ (prostate, lymphocytes B) and whether there are inter-individual differences in this response; **3) associations between vitamin C supplementation and therapy efficacy for treating malignancies in general.**

We hypothesize that vitamin C supplementation restores levels of TET products in malignant cells and thereby impedes their rates of progression in some patients. We will characterize how the spectra of epigenetic modifications, relates to vitamin C concentrations inside cells. Improved understanding of vitamin C anticancer properties will better our understanding of inter-individual differences in treatment responses.

Vitamin C was first suggested to have anticancer properties dozens years ago and have been subject of controversy ever since. Vitamin C may be administrated by vain (IVC, pharmacological doses) or by mouth (oral supplementation).

Intravenously administered vitamin C can increase serum levels about 100-fold: up to 20-30 mM. After reaching this range of concentrations vitamin C generates the cytotoxic reactive oxygen species, including hydrogen peroxide which, can selectively kill cancer cells. In contrast physiological concentration of vitamin C in blood can reach values up to **100µM, even after oral supplementation.**
Although some literature data suggest that IVC has a good safety profile also **potential serious toxicity of intravenous ascorbate was identified.** It is possible that intravenously administrated vitamin C may not be safe particularly for elderly patients with PC and CLL who cannot tolerate high/cytotoxic doses. That is the main reason why we have chosen oral supplementation.
Overall our study should improve our understanding of still poorly recognized mechanism of anticancer properties of vitamin C