Cancers are clonal disorders of multicellular organisms that arise by accumulation of genetic mutations and step-wise induction of epigenetic events that silence transcription of tumor suppressing genes and facilitate expression of tumor promoting genes. This allows cancer cells in combination with altered response of host organism to overcome the regulatory cascades that orchestrate proper cooperation of cells within the multicellular organism.

Epigenetic regulation is executed on the level of DNA by methylation of CpG islands and on the level of post-translational modification of chromatin proteins, histones in the first place. Post-translational modifications of histones include histone phosphorylation, acetylation, methylation, biotinylation, poly(ADP ribosylation), ubiquitination and sumoylation. Histone acetylation is connected with transcription activation or "openness" of chromatin to regulation by transcriptional factors. Histones are acetylated by histone acetyltranferases (HATs). Histone acetylation is a dynamic process that is reversed by histone deacetylases (HDACs), enzymes that are able to remove the acetyl residue from the acetylated histones.

A decrease in gene expression brought about by low acetylation of histones is part of the cancer specific transcription profile that is characterized by low expression or complete elimination of expression of tumor suppressor genes. It seems possible to use inhibitors of HDACs (HDACIs) as tools for the induction of expression of silenced genes. Valproic acid is a drug widely used for the treatment of epilepsy and mania in bipolar disorder. Recently it was discovered that valproic acid acts as a potent HDAC inhibitor (HDACi).

Here, we examined the effect of valproic acid on the near-complete proteome of urothelial carcinoma cell line 5637 using two-dimensional comparative chromatography. This approach revealed a large number of differentially expressed proteins in a wide range of pI spectrum. Our results show that short-term treatment with valproic acid induces complex proteomic changes that are likely to be related with alterations of multiple regulatory proteins.