

Effects of cellular short-term starvation on conventional chemotherapy response in human cancer: understanding of molecular mechanisms and microRNA involvement.

BACKGROUND

Chemotherapy is the most adopted therapeutic approach for the treatment of tumors. However, it presents a low therapeutic index and is able to cause serious side effects.

Recent studies (in vivo and in vitro) have shown that Short Term Starvation increases the chemotherapy selectivity against cancer cells and protects healthy cells from chemotherapeutic agent cytotoxicity.

Another interesting factor that affects the "sensitivity/resistance" to chemotherapeutic agent, is represented by microRNA (miRNA), small segments of non-coding RNA involved in the regulation of gene expression.

OBJECTIVES

One of the objectives of this project is to reproduce, in vitro, Short Term Starvation on various human tumor cell lines (such as MDA and Caco2) and to assess their effects on cell vitality and proliferation after treatment with different chemotherapeutic agents.

The study also aims to analyze the expression profiles of miRNAs in these cells before and after treatment and to identify, through bioinformatic approaches, the targets of deregulated miRNAs in order to understand the role that these may have in beneficial effects of cellular starvation. Finally, we will try to confirm in vivo, in mouse models, the involvement of miRNAs.

METHODS

To evaluate the effects of short-term fasting will be used angiogenesis, proliferation and cell viability assays. MiRNA and gene expression profiles will be evaluated through Real Time PCR while the identification of their targets will be performed using online databases such as miRBase and Miranda.

The altered expression of targets will be assessed both at protein (by Western blot and ELISA assays) and mRNA (by Real Time PCR) levels.

In vivo experiments will be performed through xenograft mice with transfected cancer cells (with pre-miR or anti- miR or not transfected), undergoing to Short Term Starvation .