METABOLISM IS ALTERED IN THE PROCESS OF DRUG RESISTANCE ACQUISITION

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Introduction

One of the main features of many types of cancer cells is that they present an altered metabolism. They tend to capture glucose more efficiently and increase glycolysis. The regulation of energy metabolism is complex, there are regulatory proteins such as HIF (a prometastatic protein), which decreases oxidative metabolism, while p53 (tumor suppressor) promotes oxidative phosphorylation. These facts indicate that one of the possible primary functions of activated oncogenes and inactivated tumor suppressors is the reprogramming of cellular metabolism.

Objectives

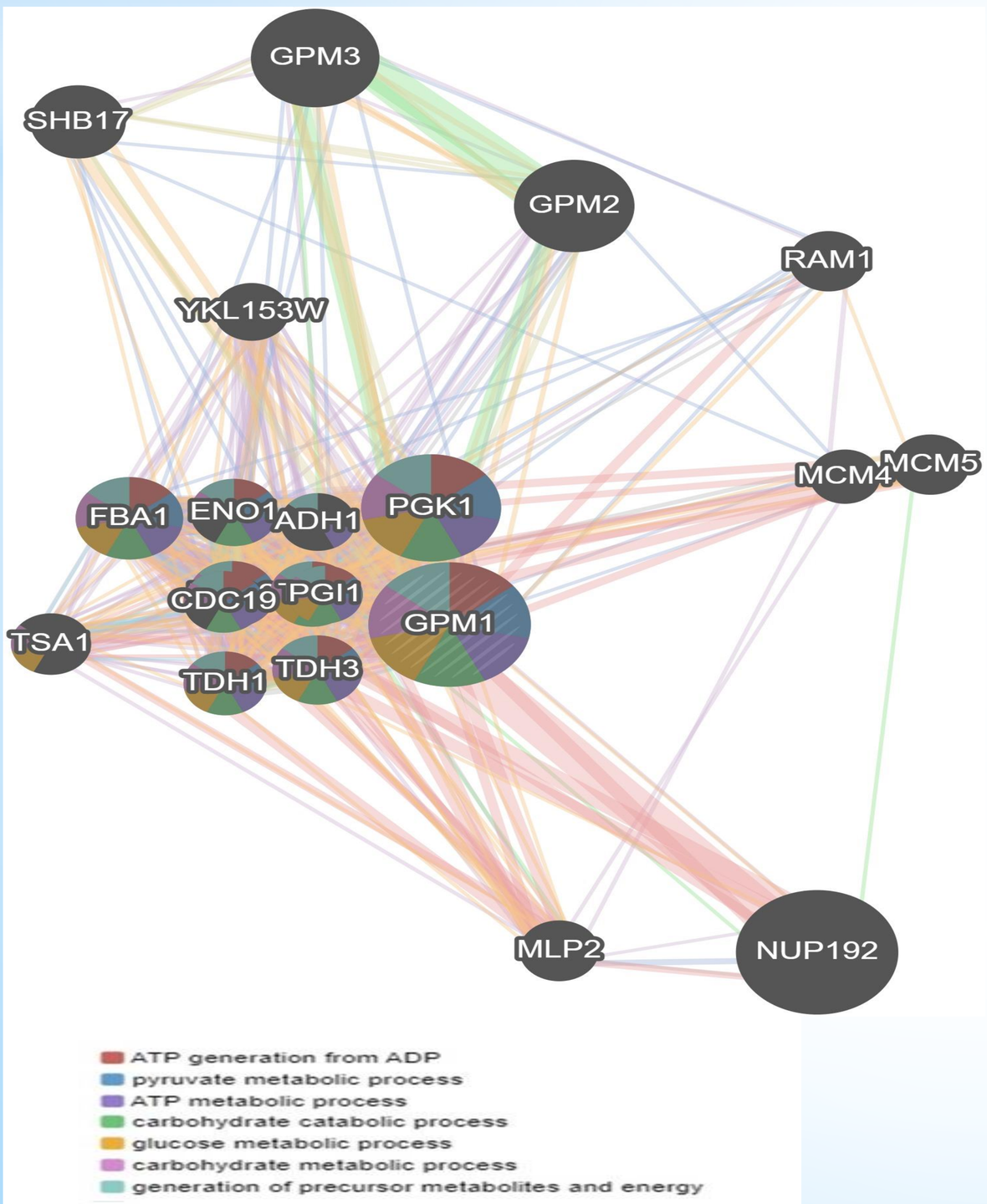
The aims of this work is the assess the metabolic pathways related to energy production in relation to the process of drug resistance acquisition.

Methods

As a biological model of drug resistance we used a parental cell line and its bleomycin resistant derivative. A proteomic study by tandem mass spectrometry using a "nano HPLC-ESI-MS / MS" ion trap system was carried out.

Results

In relation to glycolysis and gluconeogenesis, we found an overexpression of the PMG1 protein (GPM1 gene) and the ALF protein (FBA gene) with reference to the parental cell line (2,31 and 2,26 times more, respectively). PMG1 protein mediates the conversion of 3-phosphoglycerate to 2-phosphoglycerate during glycolysis and the reverse reaction during gluconeogénesis. ALF protein catalyzes the conversion of fructose 1,6 bisphosphate to glyceraldehyde-3-P and dihydroxyacetone-P. Thus, in response to stress, the cell increases the metabolic machinery in order to obtain energy and survive. The homologous genes in humans for GPM1 is PGAM4 and is unknown for FBA gene.



Functions and interactions between genes that encode proteins with ΔemPAI > 2.5 in bleomycin-resistant strain.

Conclusions

Cells need energy to survive, therefore, they increase the different pathways available to obtain it. This suggests that the cell, due to the cytotoxicity of bleomycin, increases the routes to obtain energy. For this reason, GPM1 could be a good candidate as bleomycin chemo-resistance biomarker. Knowing of the homologous gene in humans facilitates more studies of the expression of this protein in tumors.