NEW MARKERS OF BLEOMYCIN RESISTANCE

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Introduction

Resistance to chemotherapy is one of the main problems of this type of therapy. Studies carried out determine the usefulness of predictive biomarkers to improve this treatment.

Preclinical studies suggest that subexpression of ERCC1 sensitizes tumor cells versus platinum agents, while overexpression induces resistance. Also, the subexpression of TYMS predicts benefit in the response to 5-fluorouracil (5-FU), while overexpression does not predict benefit. Other preclinical studies show that the subexpression of TUBB3 predicts sensitivity to Taxanos, while overexpression predicts resistance in breast cancer, in gastric cancer and in non-small-cell lung cancer. In addition, studies carried out in gastrointestinal cancer suggest that overexpression of TOP1 predicts the performance of therapies with Camptothecin.

Thus, this shows the great importance and the need to investigate biomarkers of resistance, with the aim of administering more effective and personalized therapies.

Objectives

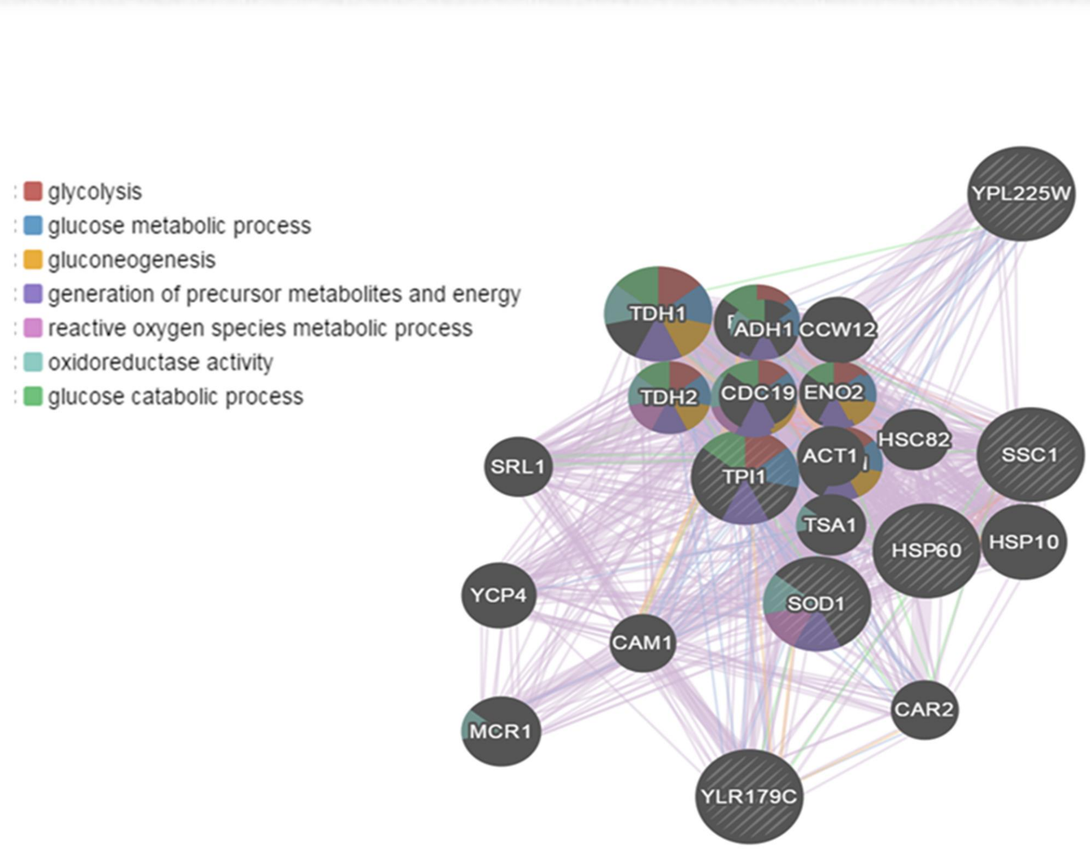
The aim of this work is to carry out a proteomic analysis in the wild type strain and bleomycin resistant strain of *Saccharomyces cerevisiae* in order to look for possible markers of resistance, as well as the mechanisms involved.

Methodology

Protein extraction, purification and identification were carried out in both the wild type strain and bleomycin resistant strain. The method was an analysis by tandem mass spectrometry using a "nano HPLC-ESI-MS / MS" ion trap system.

The exponentially modified protein abundance index (emPAI) offers a relative quantification of proteins in a mixture.

The increase in emPAI of the resistant strain against the wild strain was calculated by dividing the value of emPAI of the resistant strain between that of the wild strain.



Functions and interactions between genes that encode proteins with ΔemPAI > 2.5 in bleomycin-resistant strain WS8105-1C-R300cisPt.

Results and Conclusions

174 proteins were expressed in both strains. An analysis was carried out in order to evaluate which proteins had a higher overexpression. Proteins with an emPai increase higher than 2.5 were selected. The YL179 (YLR179C gene), TPIS (TPI1 gene), YP225 (YPL225W gene), SODC (SOD1 gene), HSP77 (SSC1 gene) and HSP60 (HSP60 gene) were analyzed. The YLR179C gene presented co-expression with the SSC1, TPI1 and SOD1 genes. The TPI1 gene presented co-expression with the SSC1 and YPL225W genes.

The YPL225W gene presented co-expression with the TPI1 and SOD1 genes.

The SOD1 gene presented co-expression with the TPI1, YPL225W and SSC1 genes.

The SSC1 gene presented co-expression with the YLR179C, TPI1, SOD1 and HSP60 genes.

The HSP60 gene presented co-expression with the SSC1, SOD1, TPI1 and YLR179C genes.

These proteins are implicated in glucose metabolic process, generation of precursor metabolites and energy, reactive oxygen species metabolic process and oxidoreductase activity.

The increase of these proteins is logical because the cells have to increase their cellular and molecular mechanisms and produce more proteins to resist to the drug and be able to survive.

In conclusion, the increased of expression of these proteins in the bleomycin-resistant strain suggests that they could be involved in the resistance process. Therefore, they could be good candidates for biomarkers of bleomycin chemoresistance.