In-silico analysis of identified proteins from HER-2 positive breast cancer cell lines resistant and sensitive to Trastuzumab treatment.

Fernandes,T.F.B.[1,2], Pinheiro, R.C.F[3],Oliveira-Carvalho, A.L.[4,5], Magalhães, A.V.[4,5], Kalume, D.E.[4,6], Zingali, R. B.[4,5], Pereira, D. de A.[1,4].

[1]POCM, COPQ, INCA,[2]Instituto Biomédico, IB-UNIRIO, [3]FAMED, UFCA, CE, [4]UEMP, IBqM-UFRJ, [5]LABHEMOVEN, IBqM-UFRJ, [6]IOC, FIOCRUZ, RJ, Brazil.

INTRODUCTION

Cancer is one of the main public health problems in most countries, with breast carcinoma being one of the most affecting women in the world. Overexpression of human epidermal growth factor 2 (HER-2) is responsible for about 30% of breast cancers and is associated with an increased in tumor invasiveness. The main signaling pathways activated by HER-2 are the Ras/MAPK, PI3K/Akt and JAK/STAT pathways that lead to the activation of signals to promote cell proliferation, survival, differentiation and motility. Integrins are transmembrane glycoproteins comprising a large family of heterodimers responsible for modulating cellular adhesion, motility and polarity signals. The integrins and receptors of the EGFR family have a cooperative signaling network that are related to invasiveness and tumor formation. Trastuzumab is a humanized monoclonal antibody target-specific to the extracellular domain of the HER-2 receptor, and thus can inhibit the proliferation of HER-2 positive tumor cells, but despite of being widely used in the clinic, 70% of patients acquire resistance to treatment. Here, we investigated the differences in the proteomic profiles of BT-474 (sensitive) and HCC-1954 (resistant) cell lines untreated and treated with Trastuzumab .

METHODS

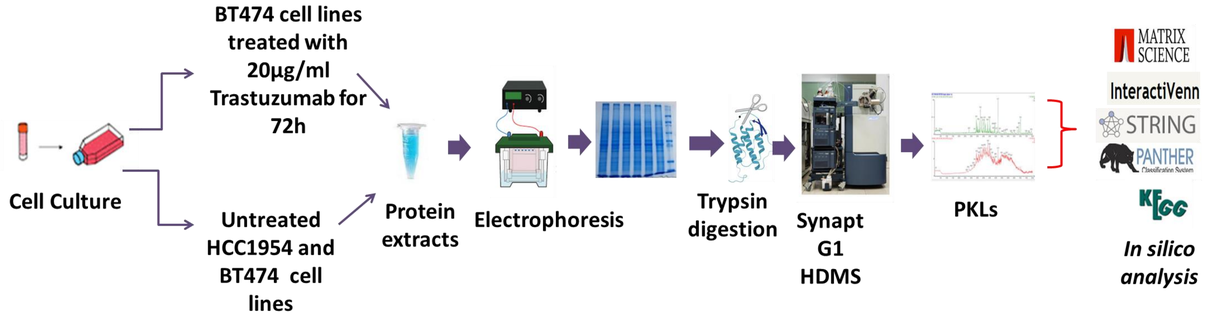

Fig 1- In gel protein hydrolysis, mass spectrometry analysis and *in-silico* studies were carried out using the online tools Mascot, String, Panther and KEGG.

RESULTS

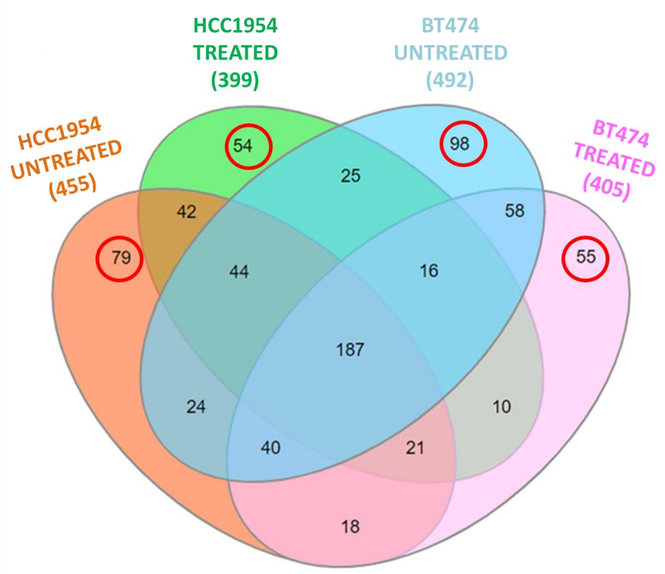

Fig 2-Venn diagram of proteins identified in HCC-1954 and BT-474 cell lines untreated and treated with Trastuzumab. The red circles shows unique proteins used in GO and KEGG analysis

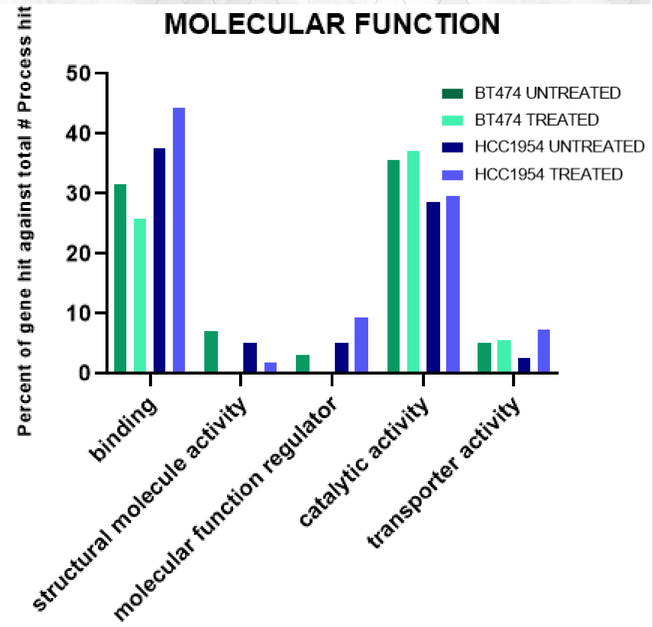

Fig 3- Gene Ontology classification using the PANTHER tool showing the Molecular Function of the unique proteins in the treated and untreated HCC-1954 and BT-474 cell lines.

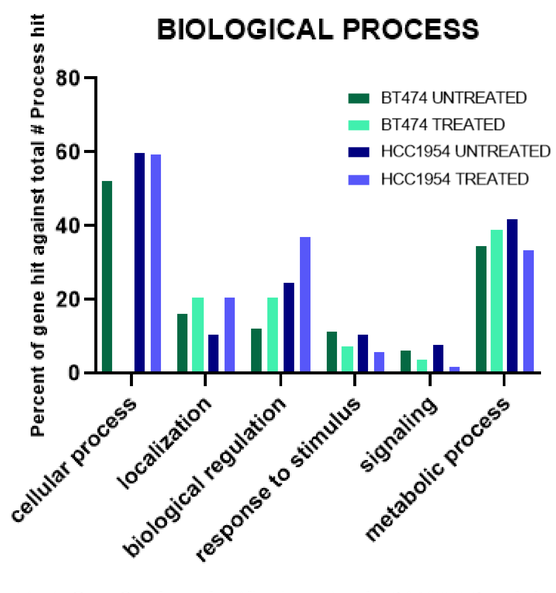

Fig 4- Gene Ontology classification using the PANTHER tool showing the Biological Processes of the unique proteins in the treated and untreated HCC-1954 and BT-474 cell lines.

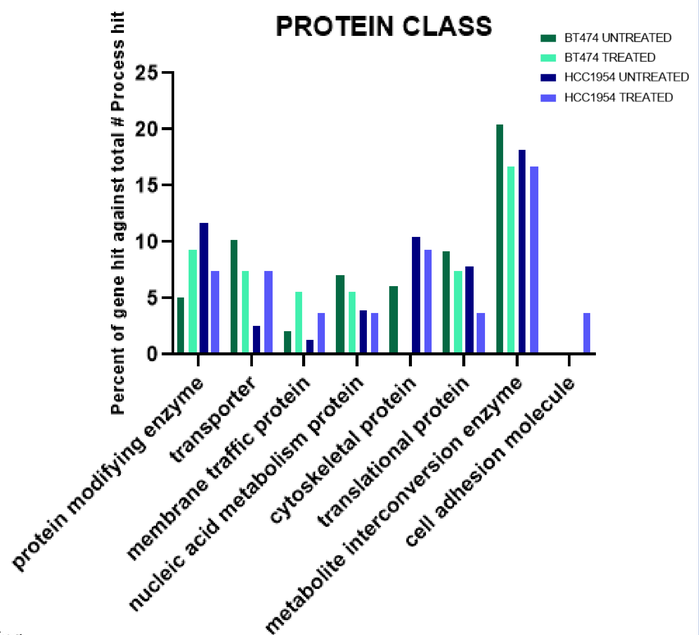

Fig 5- Gene Ontology classification using the PANTHER tool showing the Protein Class of the unique proteins in the treated and untreated HCC-1954 and BT-474 cell lines.

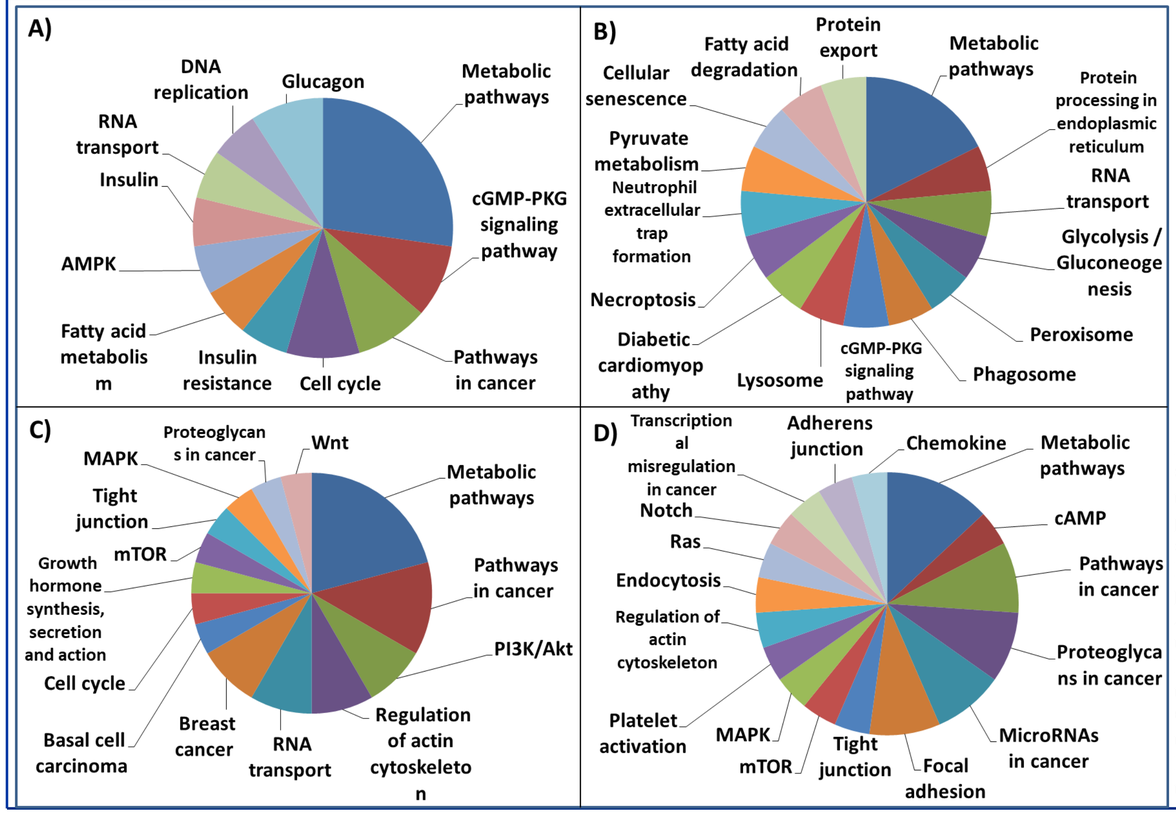

Fig 6- Graphics of the unique proteins classified on KEGG's pathways . **A**)BT-474 untreated; **B**) BT-474 treated; **C**)HCC-1954 untreated; **D**) HCC-1954 treated .

CONCLUSIONS AND PERSPECTIVES

The in-silico GO analysis of the sensitive cell line showed proteins related to endocytosis processes and a decreased in proteins classified in tumor progression pathways after treatment. In the resistant cell line, the tumor progression pathways remained even after the treatment, with the appearance of focal adhesion proteins in the treated cell, suggest these can be possible related to the mechanisms of therapy's resistance. Further experimental analyses are needed to confirm the results already obtained.

SUPPORTED BY

CNPq FAPERJ