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gene expression analysis, we found 57 upregulated and 71 downregulated genes in high HER/HER3 expressing tumors. By filtering genes with the strongest correlation (r>0,48) and worst OS, we identified 4 upregulated genes related to treatment resistance, and among 10 downregulated genes associated with immune infiltration.
CONCLUSION: Our results suggest that the co-amplifications of HER family members can affect the outcome of HER2 BC patients, by affecting the regulation of other genes involved in resistance. Further studies are required to better understand how these oncogenes "work together for the family".

ST-12

APOLIPOPROTEIN-AI INDUCE p62 EXPRESSION VIA Nrf2-DEPENDENT

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Apolipoprotein A-I (apoA-I) is the major protein component of high-density lipoproteins (HDLs). The apoA-I interaction with cells produces a complex intracellular signal transduction system activation that leads cholesterol endogenous pools movilization and anti-inflammatory respons. We have performed a proteomic profile in THP-1 cells treated with apoA-I in order to study differences in the level of total protein expression compared to controls without protein treatment. The total protein extract was analyzed in an orbitrap/quadrupole and processed by two different software to obtain robust data. Several proteins with a significant level of expression ($p \leq 0.05$) in cells treated with apoA-I were identified, such as the protein Sequestosome-1 (P62). P62 is a multifunctional chaperone that transports non-functional macromolecules to autophagosomes for degradation and could be regulated by the nuclear factor-erythroid 2-related factor 2/Kelch-like ECH-associated protein 1 (Nrf2/keap1) antioxidant response system. Also, we have observed a significant increase in the heme oxygenase1 (HO1) expression levels, a key enzyme transcribed by Nrf2. When Nrf2 was inhibited by retinoic acid (ATRA), P62 expression levels decreased by 40-50% in treated cells (ATRA+ ApoA-I). We conclude that the P62 expression increase in apoA-I cells treatment would be related to the activation of the Nrf2/keap1 antioxidant system.

ST-13

ANTI-ANGIOGENIC AND APOPTOTIC ACTIONS OF THE NATURAL FLAVONOID QUERCETIN IN A CELULAR MODEL OF KAPOSI'S SARCOMA

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Quercetin (QUE) is a flavonoid that belongs to the family of phytoestrogen and exhibits anticancer properties in multiple types of solid tumors; nevertheless, its effect on virally oncogenic transformed cells is less studied. The viral G Protein-Coupled Receptor (vGPCR) is one of the molecules from the lytic phase of human herpesvirus-8 able to induce cellular modifications through a paracrine oncogenic signaling cascade in Kaposi's sarcoma. We preliminary showed that QUE exerts antiproliferative effects on endothelial cells that stably express vGPCR. In this work, we further explore the mechanism of QUE-induced cell death in vGPCR

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cells. First, the IC50 of QUE was calculated by crystal violet technique after the treatment of SVEC and vGPCR cells with different concentrations of QUE (1-100 µM) or vehicle (0.1% DMSO) for 48 h. We found that SVEC cells (IC50 = 14.09 µM) were more susceptible to QUE treatment than vGPCR cells (IC50 = 30.078 µM). Herein, 30 µM of QUE was selected to further characterize the cell death of vGPCR cells. Cell cycle analysis revealed that QUE increase sub G0 phase and reduce S phase of vGPCR cells treated with QUE for 24 h presuming an apoptotic event. Annexin V/PI stain and caspase-3 activity confirmed that apoptosis takes place in vGPCR cells after QUE treatment. The vGPCR activates and controls the HIF-1α transcription factor promoting the expression of pro-angiogenic molecules such as VEGF. Consistently, qRT-PCR studies indicated that QUE downregulates the expression of HIF-1α and VEGF mRNA in a concentration dependent manner. In conclusion, our findings from this study suggest that QUE promotes its anticancer effects triggering both, anti-angiogenic and pro-apoptotic, programs to induce the cell death of the vGPCR cells.

ST-14

EFFECTS OF AUTOCRINE EXPRESSION OF SEX PHEROMONES IN THE YEAST S. CEREVISIAE

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In Saccharomyces cerevisiae, mating between cells from the two mating types, MATa and MATα, is initiated when secreted pheromones (a- and alpha-factor) activate specific GPCR receptors in each partner, Ste2 and Ste3, respectively. GPCR activation triggers a prototypical signal transduction MAP kinase cascade that drives mating behavior, including cell cycle arrest, chemotropic growth and large changes in gene expression.
The magnitude of the response in MATa cells is proportional to the extracellular concentration of alpha factor. Thus, ectopic expression of alpha-factor by MATa cells should lead to an exacerbated response through autocrine stimulation of Ste2. However, in our lab, using various assays, including fluorescent transcriptional reporters, we found that in these conditions yeast cells shut down the pheromone response pathway. Here, we studied the mechanism behind this unexpected response. We found that desensitization takes place at the level of the receptor, but is not mediated by its endocytosis, since cells expressing Ste2 point mutations that prevent it are still desensitized when alpha factor is expressed. Rather, fluorescence microscopy revealed that Ste2 is unable to reach the plasma membrane when alpha factor is co-expressed and that it is re-routed to the vacuole. In addition, we found that the three alpha arrestins, Rog1, Rod3 and Ldb19, involved in Ste2 recycling, do not mediate this effect. Finally, we show that the signal for re-routing is present in the C-terminal tail of Ste2, since truncation mutants are resistant to alpha-factor.
Our results shed light on the mechanisms by which cells prevent activation of signaling by ectopic activation of their GPCRs. This mechanism resembles that used by the quality control of protein folding machinery to dispose of mutant membrane proteins.

ST-15

GENE EXPRESSION IS ROBUST TO VARIATION IN TRANSCRIPTION FACTOR ABUNDANCE IN THE S. CEREVISIAE PHEROMONE RESPONSE PATHWAY

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Cells sense signals from the environment and integrate their information to make cell fate decisions. In doing so, they process that information using diverse molecular systems, responding at various levels, from changes in molecular states, activating or inactivating proteins, to changing the concentrations of components in those systems via transcriptional responses. The specific architecture of the system that decodes those signals into the cell responses determines, among other things, to which extent extrinsic noise, in the form of variability in the system elements concentrations, affect them and, conversely, how robustly cells