Impact of BCL-6 downregulation in the oncogenic properties of breast cancer cells

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Breast cancer (BC) is the most frequent type of cancer and the leading cause of cancer-related deaths in women. In recent years, the improvement in diagnosis techniques led to an earlier detection of the disease and a consequent decline in the mortality from BC in developed countries. Moreover, the development of targeted therapies contributed to increased treatment efficacy, reducing the number of fatalities from this type of cancer. However, BC is still a major health issue, in which the acquisition of therapy resistance, disease recurrence, and the formation of metastasis accounts for most BC-related deaths. Therefore, the understanding of the mechanisms behind BC resistance and recurrence is crucial for developing new therapeutic strategies to reduce BC mortality and morbidity. The host lab has identified a signaling pathway through which the downregulation of the transcriptional repressor BCL-6 contributes to colorectal cancer cell survival and chemoresistance [1,2]. Meanwhile, the lab discovered that BCL-6 is also downregulated in BC and, using a transcriptomic approach, identified a cluster of candidate genes that become upregulated in BCL-6-depleted BC

cells. The proposed Master's project, envisions the validation of BCL-6 as a regulator of these candidate genes in BC cells and the evaluation of the impact of downregulating BCL-6 or its identified target genes in the viability, migration and invasive properties of BC cells.

Methodologies: Culture and transfection of breast cancer cell lines; RNA interference, isolation and purification of nucleic acids; RT-qPCR; MTT assays (cell proliferation and viability); Boyden chamber assays (chemotactic cell migration); 3D-matrix invasion assays (cell invasive behavior).

References:

1. Barros P, Lam EW, Jordan P, Matos P (2012). Rac1 signaling modulates a STAT5/BCL-6 transcriptional switch on cell-cycle-associated target gene promoters. Nucleic Acid. Res. 40, 7776-7787 (doi: 10.1093/nar/gks571).

2. Barros P, Jordan P and Matos P (2009). Rac1 signaling modulates BCL-6-mediated repression of gene transcription. Mol. Cell. Biol. 29, 4156-4166 (doi: 10.1128/MCB.01813-08).