Expression and relevance of the IMPACT protein in pancreatic cancer

Vitória Bianchi Alves (International Research Center, A.C. Camargo Cancer Center, Brazil), Maria Dirlei Begnami (Pathology Department, A.C. Camargo Cancer Center, Brazil), Helano Carioca Freitas (Clinical Oncology Department, A.C. Camargo Cancer Center, Brazil), Vilma Regina Martins (International Research Center, A.C. Camargo Cancer Center, Brazil), Martin Roffé (International Research Center, A.C. Camargo Cancer Center, Brazil), Glaucia Noeli Maroso Hajj (International Research Center, A.C. Camargo Cancer Center, Brazil)

New protein synthesis is a highly controlled process whose deregulation may affect cellular processes such as proliferation or apoptosis. One of the main points of mRNA translation control occurs through the phosphorylation of the alpha subunit of the eukaryotic translation initiation factor 2 (eIF2α), which leads to inhibition of general protein synthesis. GCN2 is an eIF2α kinases activated upon of amino acid starvation and its activity is dependent upon binding to GCN1. IMPACT is a protein that binds to GCN1 thus competing with the GCN1-GCN2 interaction. Therefore, IMPACT inhibits GCN2 activity, eIF2α phosphorylation and stimulates translation. Consequently, the deregulation in the expression or activity of IMPACT, GCN1 or GCN2 could lead to an imbalance in the translational process. Research in databases using the cBioPortal demonstrated genetical alterations in the genes encoding IMPACT, GCN1 and GCN2 in a significant number of pancreatic adenocarcinomas. In the UT Southwestern Medical Center database, 23% of cases show deep deletions, amplifications or mutations in one of these genes. The primary findings are deletions (8.3% of cases) or amplifications (6.4% of cases) in the IMPACT gene. In the Cancer Genome Atlas (TCGA) database a gene amplification of the IMPACT gene was observed in 8.3% of cases. The pancreatic adenocarcinoma originates from the glandular tissue. In Brazil, this tumor it is responsible for 2% of all cancers diagnosed and 4% of deaths from this disease. Due to the aggressive nature of the disease and late diagnosis, most patients present locally advanced or metastatic cancer, having a high mortality and 5-year survival of less than 5%. Therefore, to unravel the molecular mechanisms associated with this tumor is of utmost importance for the development of new therapeutic approaches. In this project, we intend to observe the expression and function of IMPACT in pancreatic tumor cells lines and human tumors. Supported by FAPESP.