Abstract

Cancer is a disease of the genome. Tumor cells contain many genetic and epigenetic mutations affecting diverse genes involving relevant cellular processes, such as proliferation or the evasion of apoptosis. Recently, advances in genomics and transcriptomics research have achieved the discovery of biomarkers and therapeutic targets, positioning these methods as the main tools for cancer research. The complete multi-omic landscape of most cancer types is still unknown, a significant gap in understanding cancer as the past focus on genomics alone can't provide a full picture of the mechanisms inside the tumor cells. The integration of different molecular profiling technologies (multi-omics) is the central topic in the studies, presented as a tool to give a more complete molecular phenotype of the diseases.

The first study combines mass spectrometry along with genomics and transcriptomics from a cohort containing more than four hundred esophageal adenocarcinoma samples. The analysis of changes in expression between the RNA and the proteins provides the identification of tumor-specific genes involved in the disease, revealing deregulatory mechanisms in the tumor cells and creating new opportunities for the development of new therapies.

The second part of the thesis focuses on the study of undifferentiated pleomorphic sarcoma. The search of a common altered pathway is carried through the genomic characterization of twenty patient samples, the mutational landscape, and its heterogeneity. Although alterations shared between most of the patients were detected, and a possible therapy is suggested, the high variability between samples suggests that a patient-specific treatment might be the best approach. Therefore, a computational model was conceived to predict the immunological presentation of mutation-borne neoantigens. The model is based on proteogenomics integration and will aid the development of personalized therapies.

The last study presents a case report of Gorham-Stout disease, a rare syndrome characterized by the uncontrollable growth of vascular tissue and the consumption of the surrounding bone matrix. Through the integration of genomics and transcriptomics, new possible disease markers and improvements in the current therapies are revealed.