BIO.06 - Identification of breast cancer neoantigens using *in silico* methodologies

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Introduction: Cancer is a group of diseases that involve abnormal cell growth, with potential to invade and spread to other parts of the body forming secondary tumors, called metastasis. Neoplasms are the main cause of death in the world, mainly due to the metastasis. In Brazil, there are more than 600.000 new cases in 2018, and breast cancer is the most frequent among Brazilian women. The most promising therapies, at the time, to combat this disease are immunotherapies, which deal with the manipulation of the immune system to better respond against the tumor and eliminate it. Some metastatic cancers, such as breast cancer, are poorly immunogenic and therefore difficult to eradicate. However, specific mutations in tumor proteins can be considered as targets for cancer immunotherapy, since it could be recognized as neoantigens by host T cells, allowing the development of therapeutic vaccines.

Objective: The aim of this work is to develop an *in silico* strategy to identify tumor neoantigens in invasive and noninvasive models of mouse breast tumors, in order to obtain a proof of principle for the use of this methodology in the identification of human epitopes.

Methodology: Metastatic (4T1) and non-metastatic (67NR and 168 FARN) mouse lineages were used as models for this study. First, data of RNA seq of these three lineages were selected in one study through the GEO database (NCBI). Using these data, we have selected all genes overexpressed in 4T1 lineage in comparison to the non-metastatic lineages. In order to have data from mutated proteins in 4T1 tumor, we have used the study "Mutated tumor alleles are expressed according to their DNA frequency", which identified mutated genes in these cells. So, we combined the data of overexpression with mutations and, based on the proteins selected, we have performed *in silico* prediction of T cells epitopes using NetPanMHC and IEDB softwares.

Results: For prediction at IEDB site, we obtained 14 possible epitopes generated from 11 over expressed genes when 4T1 is compared to 67NR lineage and 9 epitopes generated from 8 genes in the comparison between 4T1 and 168FARN. From the NetPanMHC site, only MHC class 1 predictions were made due to the restriction of the site, resulting in 7 epitopes from 5 genes comparing 4T1 and 67NR lineages. As a final result, we have identified 22 possible epitopes in total, generated from 18 genes, 13 of which were MHC Class 2 and 9 of MHC Class 1.

Conclusion: In this work, it was possible to develop a usefull *in silico* tool to identify neoantigens from tumors. To identify these neoantigens is important to make them a possible target of the immune system through a much more efficient treatment, once they could be tested in formulations of therapeutic vaccines.

Keywords: neoantigens; breast cancer; bioinformatics