Identifying Breast Cancer Cell Surfaceome Mutations as Potential B-Cell Targets

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Despite the immense promise of cancer immunotherapies, there are significant challenges to overcoming treatment resistance and improving efficacy. Strategies such as the combination immunotherapies of existing agents have so far yielded more failures than successes in this effort, highlighting the importance of developing novel next generation immunotherapy agents. Neoantigens are peptides derived from patient-specific and tumor-specific mutations, which can be recognized by the immune system and mediate tumor recognition that leads to immune destruction of the cancer. Neoantigens are emerging as one of the next generation immuno-oncology targets with tremendous potential. We developed an analytic pipeline to identify the neoantigens from the tumor extracellular domains of transmembrane proteins that can be targeted by B-cells and antibodies. First, we downloaded the somatic mutations data from 1,098 breast cancer patients profiled by The Cancer Genome Atlas (TCGA); second, we generated a catalog of 3,702 transmembrane proteins located at the surface of human cells (surfaceome) and defined the extracellular domains of the surface proteins from literature; third, we identified breast cancer somatic mutations that resulted in altered surfaceome protein sequences and neoantigens; finally, the binding prediction was performed between B-cell receptors and mutated surfaceome neoantigens. In summary, we have established a bioinformatics workflow to identify B-cell neoantigens from surfaceome mutations. Our long-term goal is to develop personalized neoantigen vaccines that can be recognized by B-cells which will lead to immune destruction of the tumor. B-cell neoantigens have the potential to significantly improve the efficacy of the existing immunotherapy agents.

Awards Won: