Surfaceome profiling in Osteosarcoma: identification of the candidate immunotherapeutic target

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Osteosarcoma (OS) is the most common primary malignant bone tumor in pediatric patients still needs efficient therapeutic strategies. Current developments in targeted therapeutic strategies using CARs and other ADCs shows potential clinical implications in cancer treatments. Immune-based therapies such as antibody -drug conjugates (ADCs) or CAR-T cell therapy have not been sufficiently studied in OS because of lack of immunotherapeutic target. In this study, we developed a multi-step RNA-seq based pipeline. First, we did RNA sequencing for our 6 PDX models and 17 patient derived OS cell lines. The results are then pooled with the RNQ-seq data from 111 OS patient via the Therapeutically Applicable Research to Generate Effective Treatments project (TARGET). All these tumor data are subsequently compared with normal tissue RNA-sequencing data from NIH Genotype-Tissue Expression (GTEx) database. The significantly differentially expressed genes (log fold change tumor versus normal >1 for each tissue, $p < 0.01$) are selected. We further filtered this gene list by cell surface protein prediction based on Gene Ontology, the TransMembrane prediction using hidden Markov models (TMHMM), and glycosylphosphatidylinositol (GPI)-anchored protein annotations.

Based on the transcriptomic result, ranks of differentially expressed genes were generated. OR10H1, NMUR2, ODF4 and ZAN are the surface markers with high ranks. To validate the transcriptomic results, we prepared surface protein extraction of the PDX models and patient derived OS cell lines. We plan to profile these surface proteins by proteomic mass spectrometry. Further validation for the expression level and location of these markers are underway. Our current finding is not previously reported in OS. The results warrant further development of ADC and car-T cell therapy.