Identification and Characterization of Novel Diagnostic and Therapeutic Targets in Pancreatic Ductal Adenocarcinoma Using an Antibody-Based Approach

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Pancreatic Ductal Adenocarcinoma (PDAC) is the fourth-leading cause of cancer related death in the U.S. with a median survival period of less than six months. Better means of detection and more effective therapeutics are needed to improve PDAC survival. In other types of cancer, antibody-based diagnostics and therapeutics such as Herceptin have been successful in the clinic. This project employed an antibody-based approach to the recently developed 3D pancreatic organoid culture system to identify and characterize novel PDAC biomarkers to be used in the detection and treatment of malignancy. Tumor-specific monoclonal antibodies (mAbs) and Antigen-binding Fragments (Fabs) were developed using the hybridoma and phage display technologies, respectively. Antibodies were then validated for tumor organoid binding and cell surface localization using cell-based ELISA, immunofluorescence, immunoprecipitation-western blot, and flow cytometry. Hybridoma mAb 31 was identified and validated as tumor-specific and was shown to bind a tumor-associated cell surface antigen. Fabs A3 and B2 were identified and validated as tumor-specific Fabs that localize to the cell surface as determined by flow cytometry. In conclusion, this study identified three novel antibody-based molecules targeting PDAC-associated antigens and validated the potential of a pancreatic organoid-based antibody approach in antigen discovery.