Antibody display libraries for pancreatic cancer diagnosis and therapeutics

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Pancreatic cancer is known as one of the silent killer among all cancer types. Early diagnosis with high sensitivity and accuracy is greatly desired for the opportunity to treat patients at treatable stages. Here, we report studies using antibody display technologies to develop 1) monoclonal antibodies (mAbs) from immunized mouse V gene repertoires for detection of putative pancreatic cancer biomarkers in serum, and 2) mAbs from a large non-immune phage display human Ab library to pancreatic cancer cell surface receptors for potential targeted therapies.

1) We have employed Ab yeast display libraries to identify a pair of mAbs with non-overlapping epitopes for each biomarker. Using these mAbs, sandwich ELISA assays with sensitivity of pg/mL were developed for 7 of 10 putative biomarkers. The assay for A1BG showed comparable ability as CA19-9 to discriminate pancreatic cancer patient serum from the control.

2) A number of mAbs developed from direct selection of a large non-immune phage display human Ab library on cancer cells were able to detect a panel of pancreatic cancer cells in vitro. These mAbs could be used to develop targeted immunotherapies, such as the Ab-targeted nanoparticles and the naked IgG with enhanced ADCC activity to treat pancreatic cancers.

The potential advantages of Ab display compared to the standard hybridoma technology would include: 1) cell surface receptors are in their native conformation on intact cells while this might not be so for recombinant proteins; 2) antibodies can be selected for both cell binding and internalization properties; 3) the antibodies can be used to identify their tumor associated antigens; and 4) such antibodies can be used for human treatment directly since they are human in sequence.