Novel asTF-specific Humanized Antibody hRabMab1 May Help Treat Metastatic PDAC

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Introduction: Bogdanov lab previously created a monoclonal antibody (hRabMab1) that binds the alternatively spliced isoform of human tissue factor (asTF), a soluble secreted isoform of tissue factor whose total protein levels correlate with the histological grade of pancreatic ductal adenocarcinoma (PDAC). This antibody could help treat metastatic PDAC, either alone or in combination with current standard of care therapies, and its efficacy was set to be evaluated in a murine model once the PDAC cell lines involved were characterized and a reliable hepatic metastasis model was established.

Methods: Human PDAC cell lines were evaluated for their expression of asTF, flTF, and total TF by means of qPCR and Western blot evaluated from three separate samples from each cell line all collected at roughly 70% confluency. Murine hepatic metastasis models were attempted by means of hemisplenectomy with cell lines PaCa44-luc, MiaPaca2-luc, Pt45-luc, and HS766T-luc. Because of time constraints, no murine models were treated with hRabMab1 alone or in combination with other therapies.

Results: The different cell lines were assessed for their expression of asTF and flTF mRNA, with PaCa44 and Pt45 showing the highest concentrations of both TFs. The hemisplenectomies resulted in the formation of mainly primary pancreatic tumors with no significant hepatic metastases.

Conclusions: Because of the characterization of the cell lines involving both asTF and flTF, new conclusions can be drawn about flTF's role in increasing the aggressiveness of the cell lines in combination with asTF, the previously assumed culprit of such aggressiveness. As the hemisplenectomies did not provide reliable results, the Bogdanov lab will be switching to orthotopic injections to establish a model for hepatic metastases and investigating the efficacy of hRabMab1 as a single agent and in combination with other therapies on primary tumors, as a reliable murine model has already been established in that case.

Acknowledgements: This study was supported in part by NIH grant T35 DK060444.