2016 RESEARCH AWARD UPDATE

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Molecular MR imaging of Desmoplasia after Neoadjuvannt Treatment of Pancreatic Cancer

Neoadjuvant chemoradiotherapy (CRT) can potentially downstage borderline resectable pancreatic ductal adenocarcinoma (PDAC) and improve the rate of margin clear resection. In response to CRT, PDAC undergoes a desmoplastic reaction, replacing tumor mass with dense fibrotic tissue. Standard contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are unable to distinguish residual cancer from newly fibrotic tissue, thus radiographic downstaging after neoadjuvant therapy is rarely observed even when evidence of cytotoxic activity is found during pancreatic resection. Accordingly, reliable noninvasive markers of treatment response after CRT are urgently needed in order to facilitate patient selection for an operation.

Type I collagen is a major component of the fibrotic response to chemotherapy and radiation in PDAC, and is used as a biomarker for measuring treatment response in standard pathologic scoring systems. Due to its extracellular nature, collagen is easily targetable with molecular probes, and our group has previously shown that collagen molecular MRI can be used to measure baseline fibrosis in pancreatic tumors.

Working under the mentorship of Dr. Kenneth Tanabe and Dr. Bryan Fuchs, we developed a syngeneic, immunocompetent orthotopic murine model of PDAC with phenotypic similarity to the human disease, including a dense fibrotic response to FOLFIRINOX chemotherapy. Using this model, we compared a novel Type I collagen MRI probe, CM-101, which has been optimized for clinical translation, to the standard contrast agent, Dotarem, for their abilities to identify FOLFIRINOX-induced fibrosis as a non-invasive biomarker of treatment response.

Using a specialized rodent MR scanner, we first showed that CM-101 provided superior imaging resolution of untreated PDAC tumors compared to Dotarem. PDAC tumors are inherently fibrotic, and collagen-targeted probe uptake into tumor tissue was significantly greater compared to a non-specific agent. We subsequently showed that we were able to objectively measure increases in tumor fibrosis after FOLFIRINOX chemotherapy with CM-101, which was not possible with Dotarem.

In summary, we found that collagen molecular MRI with CM-101 provides a novel imaging technique that could be used to monitor the fibrotic response to neoadjuvant therapy in order to improve patient selection for an operation.

AHPBF *Supported in part by the AHPB Foundation*