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Targeting the thromboxane A2 pathway suppresses Barrett's esophagus and esophageal adenocarcinoma development

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Esophageal adenocarcinoma (EAC) is a major cause of cancer-associated morbidity and mortality worldwide. Barrett's esophagus (BE), a complication of gastroesophageal reflux disease (GERD), predisposes patients to EAC. The discovery of potential drug targets is urgently needed for improved BE and EAC patient outcomes. Our previous study showed that cyclooxygenase-2 (COX2) and thromboxane A synthase (TBXAS) are highly expressed in BE and EAC patients accompanied by a pronounced elevation of circulating thromboxane A2 (TXA2) levels. Aspirin suppressed BE and EAC growth by targeting the TXA2 pathway. Additionally, biopsies from 49 patients (with similar baseline characteristics) showed that aspirin substantially decreased serum TXA2 levels, resulting in reduced inflammation. Our results showed that TXAS and TXA2 are correlated with the progression of BE and EAC. This study establishes the importance of the COX1/2-driven TXA2 pathway in BE and EAC pathophysiology and lays the groundwork for introducing a TXA2-targeting strategy for EAC prevention and early detection. Aspirin targets the TXA2 pathway and suppresses BE and EAC development. These findings drove us to study the role of TBXA2R (the receptor of TXA2) in the development of BE and EAC. We found that TBXA2R is highly expressed in BE and EAC patient biopsy samples. Knocking down the expression of TBXA2R markedly suppressed BE and EAC cell growth. Our goal is to establish

the TXA2 pathway as a novel target for preventing BE and EAC development. A novel TBXA2R inhibitor is a potential agent for the prevention and treatment of BE and EAC.

Recent Publications

1. Tianshun Zhang, et.al, (2021). Gastric tumorigenesis induced by combining *Helicobacter pylori* infection and chronic alcohol through IL-10 inhibition. *Carcinogenesis*. 43(2).
2. Tianshun Zhang, et.al, (2021). Prostaglandin Pathways: Opportunities for Cancer Prevention and Therapy. *Cancer Research*. 82. canres.2297.2021.
3. Tianshun Zhang, et.al, (2021). 229 Local and Systemic anti-inflammatory effects of Fatty acids in Barrett's esophagus patients: results from a randomized double-blind placebo-controlled trial. *Gastroenterology*. 160(6). S-48-S-49.

Biography

Tianshun Zhang received his PhD in Applied Chemistry in Bioscience from Kobe University, Japan. He currently works as a Senior Scientist at The Hormel Institute-University of Minnesota, USA. He focuses on identifying the mechanisms of cancer development or novel drug discovery for cancer prevention and treatment. He published his research in many prestigious journals including *Cancer Research*, *Theragnostic*, and *EbioMedicine*, and is serving as guest editor of reputed Journals.

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