TGFBI, an ECM interacting protein, enhances glycolysis and promotes pancreatic cancer cell migration

B. Costanza, G. Rademaker, A. Turtoi, A. Bellahcène, V. Castronovo, O. Peulen*

Metastasis Research Laboratory
GIGA-Cancer & Center for Interdisciplinary Research on Medicines - ULiège

Introduction

Pancreatic ductal adenocarcinoma (PDAC) remains a deadly malignancy with no efficient therapy available up-to-date. Thanks to a patented technology for mass spectrometry-assisted identification of accessible tumor markers, developed in our laboratory, we have identified transforming growth factor-beta-induced protein (TGFBI) as a targetable protein in pancreas adenocarcinoma. We focused our attention on its biological significance in PDAC.

Results

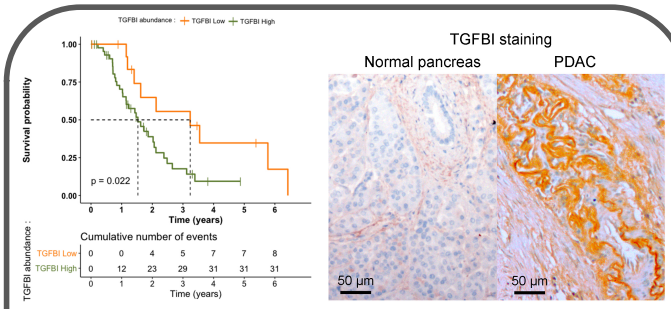

Fig 1: High TGFBI abundance is correlated to poor patient outcome. FFPE samples (n=80) were stained for TGFBI. Kaplan-Meier curve was constructed to assess disease specific survival according to TGFBI abundance.

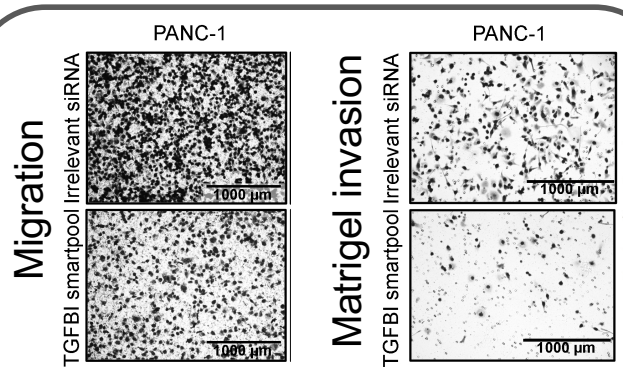

Fig 2: TGFBI depletion reduces migration and invasion of PDAC cells in Boyden chambers

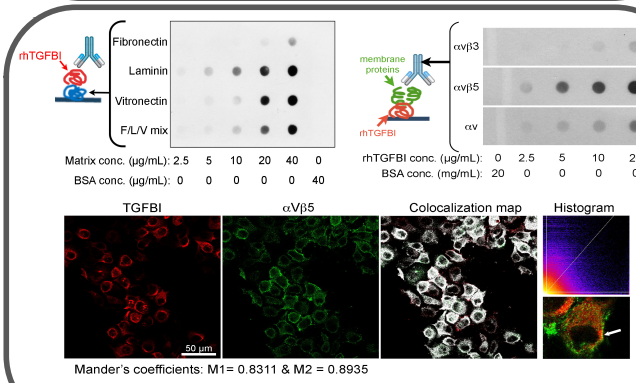

Fig 3: rhTGFBI binds to ECM and to membrane proteins.

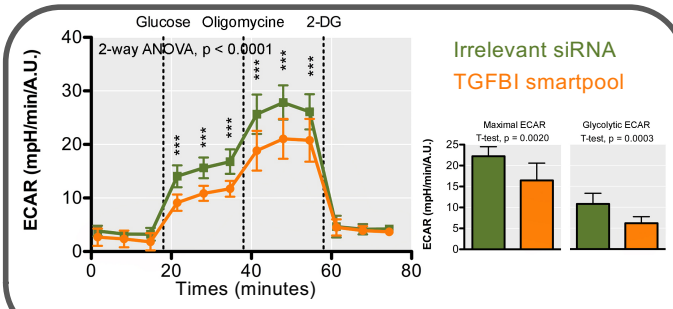

Fig 5: TGFBI enhances glycolysis in PDAC cell line.

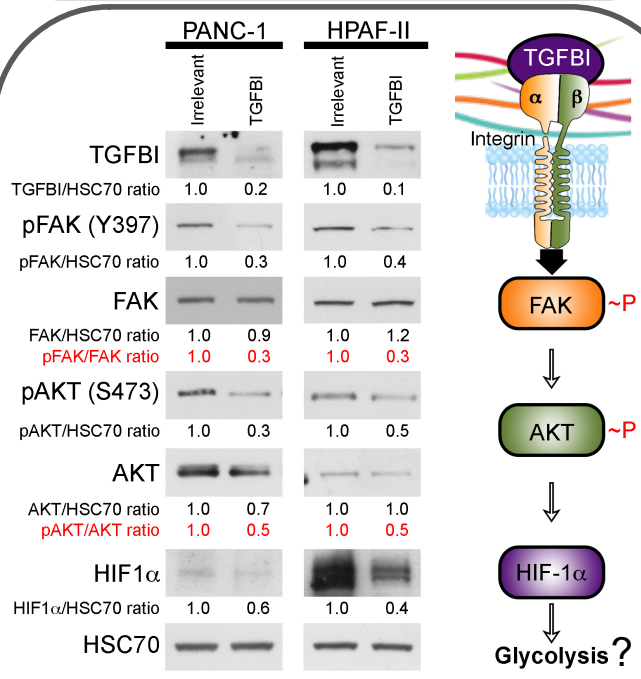

Fig 4: TGFBI activates FAK signaling cascade culminating with increased HIF-1α abundance

What's new ?

While PDAC continues to have exceedingly low 5-year survival rates, there is hope that the discovery of reliable biomarkers and therapeutic targets can improve early diagnosis and treatment outcomes. To that end, we identify the ECM TGFBI as a promising target. In PDAC patients, high TGFBI expression was associated with poor outcome. Mechanistic analyses show that TGFBI activates FAK signaling via integrin αVβ5 binding, enhancing glycolysis and invasiveness in PDAC cells.

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olivier.peulen@uliege.be