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Investigation of FAP (Fibroblast Activation Protein) in Thymic Epithelial Tumors

Autor: Zhihan Yao
Institut / Klinik: Pathologisches Institut
Doktorvater: Prof. Dr. A. Marx

Thymic epithelial tumors (TETs), encompassing thymomas and thymic carcinomas, are rare neoplasms with diverse clinical behaviors, posing challenges in prognosis prediction and treatment.

This study investigates the role of cancer-associated fibroblasts (CAFs) and Fibroblast Activation Protein (FAP) in TET progression. Using the EPIC algorithm to analyze The Cancer Genome Atlas (TCGA) data, we identified a higher proportion of CAFs in thymic carcinomas compared to thymomas, correlating with poorer prognosis. FAP mRNA levels were significantly elevated in thymic carcinomas across multiple cohorts. In vitro experiments demonstrated that CAFs from thymic carcinomas secreted higher FAP levels, promoting thymic carcinoma cell proliferation and migration. Immunohistochemical analysis further revealed stronger FAP expression in aggressive TET subtypes, suggesting its potential as a diagnostic marker to distinguish thymic carcinomas from thymomas and atypical type A thymomas from conventional ones. Gene expression analysis linked high FAP levels to pro-tumorigenic pathways, including inflammation and extracellular matrix remodeling.

These findings highlight CAFs and FAP as potential prognostic and diagnostic markers, as well as therapeutic targets in TETs, particularly in aggressive subtypes, warranting further exploration of FAP-targeted therapies to improve outcomes in this challenging disease.