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FAP in a FAP+ cell line is activated by TGFβ, as in CAFs of pancreatic cancer

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Pancreatic ductal adenocarcinoma is an extremely aggressive form of cancer with poor prognosis. It is presumably due to a high content of the tumor microenvironment that promotes tumor progression. Cancer-associated fibroblasts (CAFs) are one of the main components of the tumor microenvironment. Fibroblast activation protein (FAP) is a serine protease, specifically expressed in CAFs and considered to be a potential selective target for tumor therapy. Expression of FAP was confirmed by immunofluorescence staining of FAP in primary cultures of pancreatic CAFs. Simultaneous staining of FAP and the cell membrane revealed their co-localization. Apparently, this allows FAP to perform its enzymatic function and to modify the extracellular matrix most efficiently. Previous screening of cell lines identified a FAP-positive non-fibroblast cell line OSA (SJSA-1) which was similar, in terms of FAP expression, to pancreatic CAFs derived from surgical pancreatic tumor samples. Like in primary cultures of pancreatic CAFs, the FAP protein was co-localized with the cell membrane also in the OSA cell line. It is known that TGFβ is the main regulator of FAP expression in CAFs. We attempted to investigate the effect of TGFβ on the expression of FAP in the OSA cell line. To this end, the OSA cell line was cultured in depleted medium in the presence of TGFb. In contrast to control cells incubated without TGFβ, we observed an increase in the FAP expression. Thus, TGFβ upregulated the expression of FAP in a FAP-positive cell line. We assume that the FAP-positive non-fibroblast OSA (SJSA-1) cell line can be efficiently used to study FAP targeting and regulation. This study was supported by the Russian Science Foundation (project no. 14-50-00131).

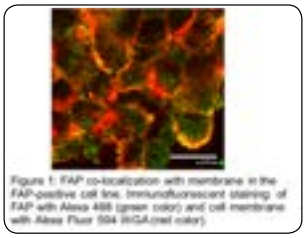

Figure 1: FAP co-localization with membrane in the FAP-positive cell line. Immunofluorescent staining of FAP with Alexa 488 (green color) and cell membrane with Alexa Fluor 594 WGA (red color).

Recent Publications:

1. Tyulkina (Antonova) D V, Pleshkan V V, Alekseenko I V, Kopantseva M R and Sverdlov E D (2016) Expression of the FAP gene in non-fibroblast human cell lines. Development of cancer-associated fibroblast models. Dokl Biochem Biophys. 470(1):319–321.
2. Pleshkan V V, Alekseenko I V, Tyulkina (Antonova) D V, Kyzmich A I, Zinovyeva M V, et al. (2016) Fibroblast activation protein FAP as a possible target of the antitumor strategy. Molecular Genetics, Microbiology and Virology 34(3):4–11.
3. Alekseenko I V, Kuzmich A I, Pleshkan V V, Tyulkina (Antonova) D V, Zinovyeva M V, et al. (2016) The cause of cancer mutations: Improvable bad life or inevitable stochastic replication errors? Mol. Biol. 50(6):906–921.
4. Didych D A, Tyulkina (Antonova) D V, Pleshkan V V, Alekseenko I V and Sverdlov E D (2015) Super-enhancers. Are they regulators of regulatory genes of development and cancer? Mol. Biol. 49(6):915–22.
5. Kuzmich A I, Tyulkina (Antonova) D V, Vinogradova T V and Sverdlov E D (2015) Pioneer transcription factors in normal development and in carcinogenesis. Bioorg. Khim. 41(6):636–43.

Biography

Dina Antonova is a PhD student of Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry. Since the beginning of her scientific work, she was able to significantly expand her knowledge in the field of interest. Her graduate work was focused on searching promoters of genes with high expression in tumor stroma for gene therapy strategies. Currently, she is involved in detailed research of genes expressed in stroma and potential role of FAP and CTGF in anti-cancer therapies. She possesses ability to process information quickly, learning to work independently and designing her experimental work. In her daily work, she uses a large number of various methods of molecular biology and cellular practice. Her labor-intensive practical work resulted in six articles indexed by PubMed and participation in various international and all-Russian conferences. Looking forward, she believes that her work is significant both for fundamental science and practical approaches in cancer therapy.

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