

Fibroblast Activation Protein (FAP)-Targeted Antifibrotic Therapy

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Categories:

- Pharmaceuticals

Keywords:

- Cancer
- Cancer-associated fibroblasts (CAFs)
- Collagen I
- Fibroblast activation protein-alpha
- Pharmaceuticals

Researchers at Purdue University have developed new drugs to image and therapeutically target fibroblast activation protein (FAP) in solid tumors. The drugs are composed of a FAP-alpha-targeting moiety, a linker, and an inhibitory agent. The inhibitory agent inhibits a pathway associated with the formation of cancer-associated fibroblasts (CAFs), cells that regulate tumor growth. CAFs express FAP-alpha, a protein that affects the tumor microenvironment. Along with reducing CAF formation, the inhibitory agent also reduces collagen I formation, a protein that is associated with tumor growth. The researchers' drugs quickly clear from tissues not expressing FAP-alpha. The Purdue-developed targeted therapy may be used to target over 50 types of cancer. It also has the potential to treat fibrotic diseases or disorders such as pulmonary fibrosis.

Related Publications: Roy J, Hettiarachchi SU, Kaake M, Mukkamala R, Low PS. Design and validation of fibroblast activation protein alpha targeted imaging and therapeutic agents. *Theranostics*. doi: 10.7150/thno.41409.

Hettiarachchi SU, Li Y, Roy J, Zhang F, Puchulu-Campanella E, Lindeman SD, Srinivasarao M, Tsoyi K, Liang X, Ayaub EA, Nickerson-Nutter C, Rosas IO, Low PS. Targeted inhibition of PI3 kinase/mTOR specifically in fibrotic lung fibroblasts suppresses pulmonary fibrosis in experimental models. *Science Translational Medicine*. doi: 10.1126/scitranslmed.aay3724.

Technology Validation: FAP-targeted optical or radio imaging was performed to determine the specificity and selectivity of the FAP-targeting drugs for FAP in vitro and in vivo. The Purdue-developed FAP-targeting drugs showed high binding specificity and affinity in the low nanomolar range. Injection of the FAP-targeting drugs into tumor-bearing mice enabled detection of tumor xenografts with little off-target uptake. Systemic administration of the drug also promoted eradication of solid tumors with no evidence of gross toxicity to the animals.

Advantages:

- Targets CAFs and FAP-alpha
- May treat over 50 types of solid cancers
- Can be formulated as liquid suspension or solid granules

Applications:

- Targeted therapy for cancer in humans or animals
- Treatment of fibrotic diseases

People:

- Low, Philip Stewart (Project leader)
- Lindeman, Spencer D
- Mukkamala, Ramesh

Intellectual Property:

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