220 STAT3 Inhibitors and Their Anti-Cancer Usage

Asset Overview

Product Type	STAT3 Inhibitor
Indication	Oncology
Current Stage	Lead Identification/optimization
Target(MoA)	STAT3 Inhibitor
Brief Description	Researchers at the Ohio State University, led by Dr. Chenglong Li, have designed novel, non-peptidomimetic molecules for use as anti-cancer inhibitors of STAT3, a protein involved in gene expression and associated with various cancers. The molecules were developed using Fragment-based Drug Design (FBDD) and tested for half maximal inhibitory concentration (IC50).
Organization	The Ohio State University

Differentiation

□ **The Unmet Need**

- The search for more potent drug delivery candidates for cancer therapy remains a challenge within the medical community. Efforts to target cancer at the genetic level have led to numerous discoveries, including the role that constitutive activation of signal transducer and activator of transcription 3 (STAT3) plays. STAT3 has been found in a wide variety of cancers, including breast cancer and sarcomas, which makes the protein an attractive therapeutic target. As STAT3 monomers have the potential to bind to another's Src Homology 2 (SH2) domain to form the STAT3 dimer, which then can bind to DNA and result in transcription
- This process can result in cell proliferation, anti-apotosis and even the formation of cancers. Ultimately cancer therapies are some of the most researched technologies in medicine, and the broad potential use of STAT3 inhibitors would create new market opportunities across a rapidly growing field

□ **The Technology**

- Researchers at the Ohio State University, led by Dr. Chenglong Li, have designed novel, nonpeptidomimetic molecules for use as anti-cancer inhibitors of STAT3, a protein involved in gene expression and associated with various cancers. The molecules were developed using Fragment-based Drug Design (FBDD) and tested for half maximal inhibitory concentration (IC50)

□ **Commercial Applications**

- Drug-based treatment of various human cancers, including many carcinomas and sarcomas, through competitive inhibition of STAT3 dimerization
- Inhibition of the transcription factor induces natural apoptosis in proliferative cancerous tissues

□ **Benefits/Features**

- High affinity for STAT3 and low effective IC50 increase clinical potential for cellular anti-cancer treatment
- Ease of small molecule synthesis and higher in vivo stability compared to peptidomimetic and phosphopeptide inhibitors compared to existing antibiotics

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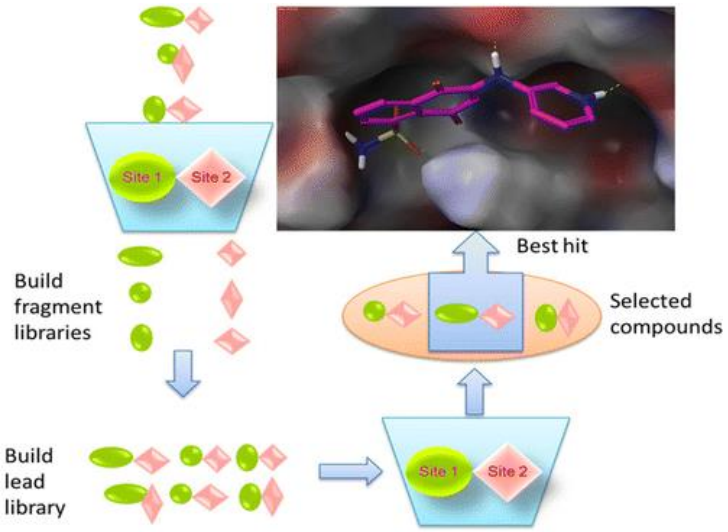
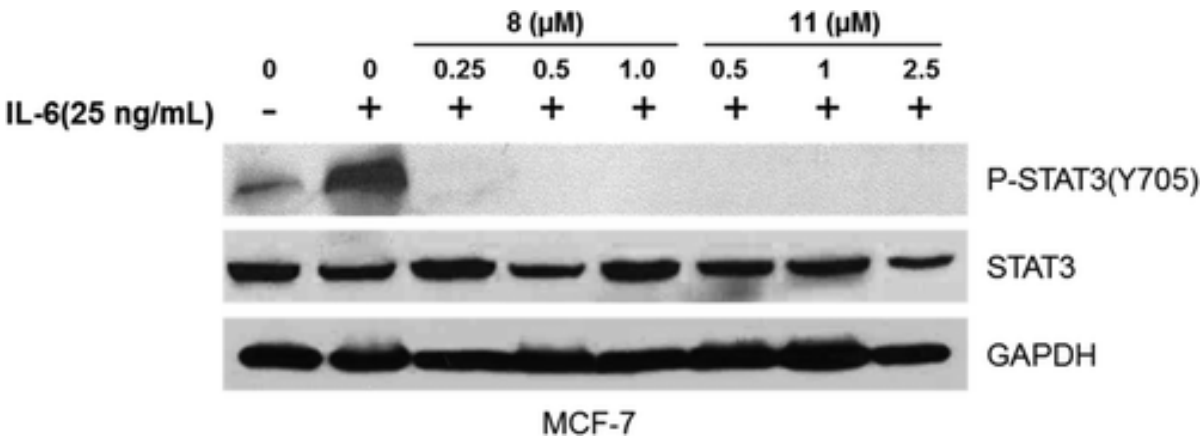
Key Data

New fragment-based drug design (FBDD) strategy



A new fragment-based drug design (FBDD) strategy, in silico site-directed FBDD, was applied in this study. A designed novel compound, 5,8-dioxo-6-(pyridin-3-ylamino)-5,8-dihydronaphthalene-1-sulfonamide (LY5), was confirmed to bind to STAT3 SH2 by fluorescence polarization assay

Candidates inhibit IL-6 induced STAT3 phosphorylation in MCF-7 breast cancer cells



The MCF-7 cells were serum-starved overnight, then left untreated or treated with 11 (0.5–2.5 μM) or 8 (0.25–1 μM) for 5 h, followed by stimulation by IL-6 (25 ng/mL). The cells were harvested at 30 min and analyzed by Western blot assays.

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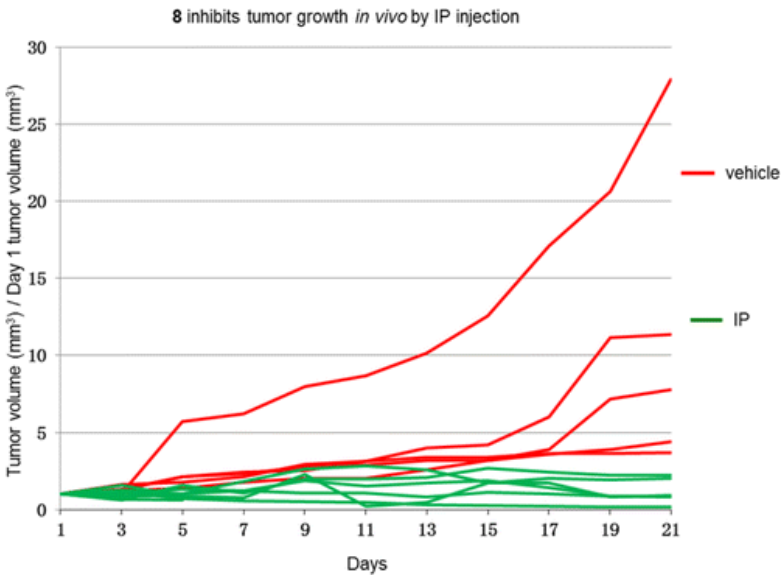
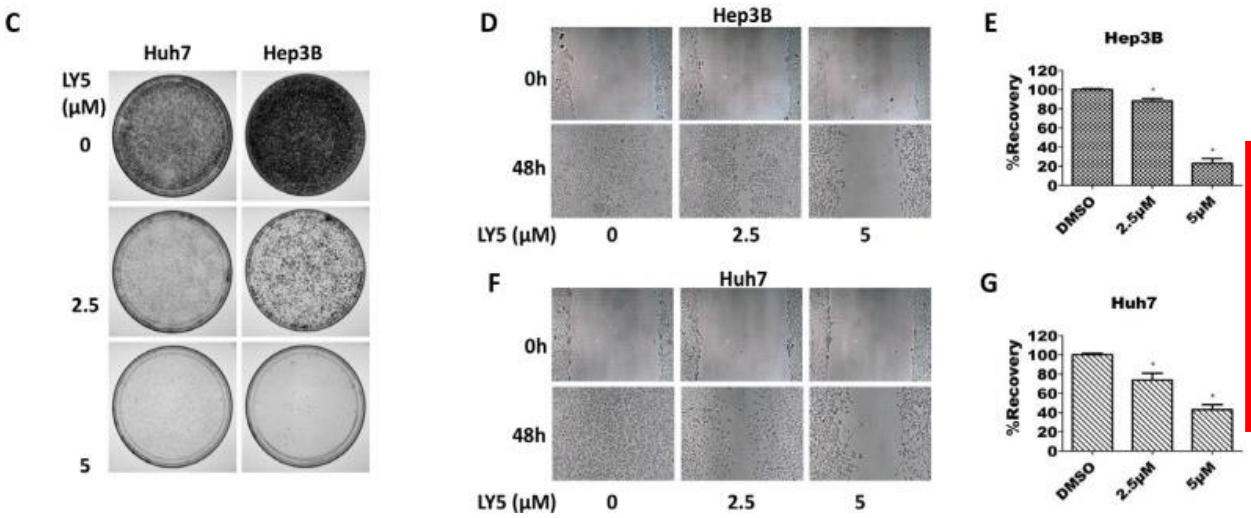
Compound 8 suppresses tumor growth of MDA-MB-231 breast cancer cells in mouse tumor model in vivo.



Tumor growth was determined by measuring length (L) and width (W) of the tumor every other day with a caliper. The tumor volume was calculated according to the formula: tumor volume = 0.5236 × L × W2. The treatment lasted for 21 days. The results showed that 8 significantly suppresses the tumor growth ($P < 0.001$).

A novel small molecule STAT3 inhibitor, LY5, inhibits cell viability, colony formation, and migration of colon and liver cancer cells



Oncotarget. 2016 Mar 15; 7(11): 12917–12926

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Intellectual Property

Patent No.	US 9783513 B2
Application Date	2013.08.16
Status	Registered
Country	US, EP, JP, CA, AU

Contact Information

Contact Person	Khountham, Soun
Email	oun.Khountham@osumc.edu
URL	https://innovate.osu.edu/available_technologies/37671/STAT3-Inhibitors-and-Their-Anti-Cancer-Usage