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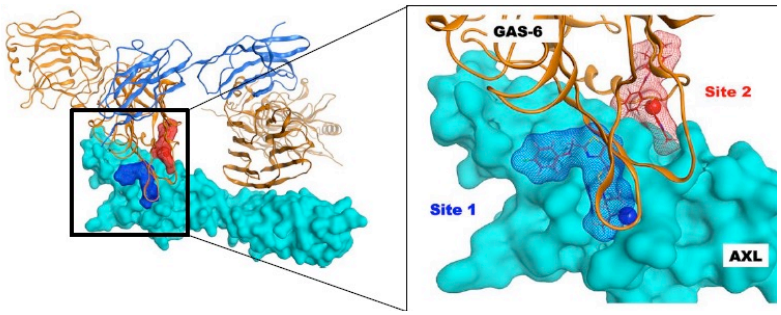
Commercializing Rutgers Technologies

First-in-Class Pan-TAM Inhibitors for Cancer Therapy

Novel small molecule compounds block Gas6-TAM receptor interactions

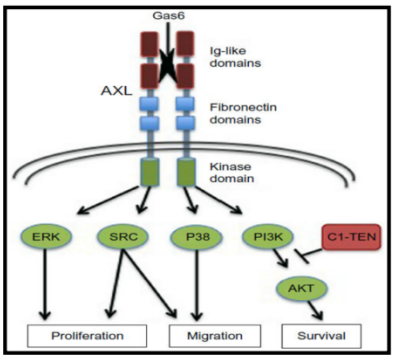


Two identified binding pockets occupied by the molecules are in red and blue.

William J. Welsh is a Professor in the Dept. of Pharmacology and Associate Director Div. of Cheminformatics, Cancer Institute of NJ at Rutgers University and is committed to the development and application of computational tools and techniques in cancer research and early-stage drug discovery and design.

Raymond Birge is a Professor of Biochemistry and member of the New Jersey Medical School Cancer Center. Dr. Birge's research focuses on apoptosis and cancer biology, emphasizing genes and signaling pathways that promote tumor progression, metastasis, and immune escape.

TAM receptors are receptor tyrosine kinases that are involved in proliferation, migration and survival of cells. Inhibition of TAM pathways has been shown to inhibit cancer tumor growth and metastasis and to activate the immune system to eliminate tumors.



Intellectual Property: PCT application filed in June, 2017

Invention Summary: Rutgers researchers have developed a novel family of druglike small molecule compounds that block Gas6-induced activation of the TAM (**T**YRO3, **A**XL, **M**ER) receptor tyrosine kinases. Overexpression of the TAMs is correlated with poor patient outcomes, aggressive staging of cancer, drug resistance, and immune escape. Unlike traditional tyrosine kinase inhibitors (TKIs) that target the intracellular ATP binding pocket, the subject molecules target the TAM-Gas6 interface located in the extracellular domain. This distinction may confer intrinsic advantages over TKIs and other conventional therapeutic modalities, such as more efficient receptor targeting, fewer and less severe side effects, and lower risk of drug-induced resistance.

Advantages:

- Extracellular domain targets potentially leading to a lower off-target effect profile and greater efficacy
- Pan-TAM: One drug that inhibits all three kinases
- Can be used as standalone or combination therapy
- Potential immune checkpoint inhibitors that activate the patient's immune system to eliminate tumors

Market Applications: The market application will be an anti-cancer therapeutic, which can also be combined with other therapies such as PD-1 immune checkpoint inhibitors. In addition to cancer, TAMs have been shown to be required for viral entry into host cells and pathogenesis. It is possible that the Rutgers compound could be used in the treatment of infectious diseases

Potential Social and Economic Impact: In recent years, immuno-oncology (IO) is dramatically changing the way cancer is being treated. Modulation of the immune system with small molecules offers several advantages that may be complementary and potentially synergistic to the use of large biologicals. Based on emerging knowledge of the central role of TAMs in the tumor microenvironment by the Birge lab and other research centers, it is now recognized that under pathophysiological conditions the TAMs function as immune checkpoints akin to CTLA-4, PD-1, and PD-L1. Consequently, combinations of targeted TAM inhibitors with these existing IO therapies may significantly raise prospects for long-term survival and possibly even cures for patients.

Next R&D Steps:

- Synthesize the computationally designed compounds (upwards of 40 compounds)
- Complete initial screening of the bioactivity/efficacy, safety/toxicity, and pharmacokinetics (PK)
- Select the top performing compounds for in vitro efficacy studies
- Select the top performing compounds for in vivo efficacy studies in mouse cancer models