

# Novel Mer and Axl Compounds for use in the Diagnosis and Treatment of Cancer

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## **IP Status:**

Available for partnering.

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#### Background

Mer and Axl are receptor tyrosine kinases whose aberrant expression and activation has been associated with several cancers, including: acute myeloid leukemia (AML), non-small cell lung cancer (NSCLC), glioblastoma, breast cancer, acute lymphoblastic leukemia (ALL), lymphoma, kidney cancer, prostate cancer, and melanoma. Mer and Axl activation have been shown to favor tumor growth through activation of intracellular pathways that signal proliferative, anti-apoptotic, and metastatic events. In addition, Axl and Mer activation have been tied to thrombotic disease.

### Technology

A research team headed by Doug Graham of the University of Colorado has developed two related technologies concerning diagnostic and therapeutic applications of Mer and Axl. Dr. Graham's team has developed a novel anti-human Mer monoclonal antibody (mAb) that can detect unique Mer glyocoforms expressed in tumor cells. Following a simple blood draw Mer levels can be measured by RT-PCR, microarray etc. As the scientific literature indicates, over-expression of Mer may be used as a diagnostic or prognostic marker for cancer.

Dr. Graham's alpha-Mer590 mAb demonstrates great promise in the treatment of cancer. Dr. Graham has shown, in cancerous cells, that alpha-Mer590 is able to reduce Mer expression, leading to subsequent decreased activation of the Akt and Erk1/2 pro-survival pathways, increased susceptibility of the cancer cells to apoptosis, and reduced cellular migration. In addition to the novel Mer inhibitor, Dr. Graham has also developed an Axl inhibitor with similar promise in inhibiting and treating cancer. A 2010 publication (see below) illustrates that decreasing Mer and Axl activity causes approximately a 75% reduction in cancer cell proliferation and a significant increase in chemo-sensitivity. Further, these inhibitors of Axl and Mer have shown promise in preventing thrombosis.

#### **Potential Applications**

- + Diagnostics and therapeutics for human cancers and thrombosis
- Receptor tyrosine kinases research
- Proteins in the development of human cancer research
- Translational research

## Key Publications

Inhibition of Mer and Axl receptor tyrosine kinases in astrocytoma cells leads to increased apoptosis and improved chemosensitivity. Mol Cancer Ther. 2010 May;9(5):1298-307.

<u>Mer receptor tyrosine kinase is a novel therapeutic target in pediatric B-cell acute lymphoblastic</u> <u>leukemia</u>. Blood. 2009 Sep 24;114(13):2678-87.

<u>A soluble form of the Mer receptor tyrosine kinase inhibits macrophage clearance of apoptotic cells</u> and platelet aggregation. Blood. 2007 Feb 1;109(3):1026-33.

Ectopic expression of the proto-oncogene Mer in pediatric T-cell acute lymphoblastic leukemia. Clin. Cancer Res. 2006 May 1;12(9):2662-9.

Lymphoblastic leukemia/lymphoma in mice overexpressing the Mer (MerTK) receptor tyrosine kinase. Oncogene. 2006 Oct 5;25(45):6092-100.

Patent Documents

Mer Diagnostic and Therapeutic Agents. U.S./WIPO, priority date Nov. 24, 2004.

<u>Methods and Compounds for Enhancing Anti-Cancer Therapy</u>. U.S./WIPO, priority date Jul. 29, 2008.