Novel Kinase Inhibitors Targeting the PH Domain of AKT for Preventing and Treating Cancer

Summary (1024-character limit)
The National Cancer Institute's Medical Oncology Branch is seeking statements of capability or interest from parties interested in licensing and co-development collaborative research to further develop, evaluate, or commercialize novel kinase inhibitors targeting the PH domain of AKT.

NIH Reference Number
E-212-2009

Product Type
- Therapeutics

Keywords
- Cancer
- Chemotherapeutics
- Therapeutics
- Leukemia
- Alzheimer's Disease
- Kinase Inhibitor
- Akt
- PH Domain
- Combination Therapy
- PI3K/Akt Signaling Pathway
- Colony Stimulating Factor-1 Receptor (CSF1R)

Collaboration Opportunity
This invention is available for licensing and co-development.

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Description of Technology

The National Cancer Institute's Medical Oncology Branch is seeking statements of capability or interest

from parties interested in collaborative research to further develop, evaluate, or commercialize novel kinase inhibitors targeting the PH domain of AKT.

Activation of the PI3K/Akt signaling pathway has been implicated in the development of cancer. Akt, a kinase that is central to this pathway, is found at elevated levels in many tumors and is associated with a poor disease prognosis. Many research studies have validated Akt as a therapeutic target for the development of anti-cancer drugs. Most efforts of drug development targeting Akt have focused on inhibitors of the ATP-binding domain which tend to interfere with other physiologically important kinases. An alternative strategy that has been proposed to improve drug specificity is the targeting of the unique pleckstrin homology (PH) domain of Akt.

Investigators at the National Institutes of Health have screened a library of small chemical compounds with drug-like characteristics that likely bound to the PH domain and have identified several candidates previously unknown to interact with Akt. These compounds were tested and found to inhibit Akt activity specifically through the PH domain. Some of these compounds demonstrated broad cytotoxicity to a wide variety of tumor cells. These novel Akt-inhibiting compositions target the PH domain and help in the prevention and treatment of cancer. Since it has been shown that reducing the activity of the PI3K-Akt pathway sensitizes malignant cells to chemotherapy or radiotherapy, these novel Akt inhibitors have potential either as single anti-cancer agents or in combination with conventional cancer therapies.

One of the candidate compounds inhibited Colony Stimulating Factor-1 Receptor (CSF1R) from binding to ATP but had no activity for other kinases. CSF1R has been implicated in development of cancers like chronic myelomonocytic leukemia, but also in Alzheimer's disease so this specific compound may have use in treating other diseases in addition to cancer.

Patent Status:
U.S. Provisional Application No. 61/226,328 filed 17 Jul 2009

Potential Commercial Applications

- Treating or preventing development of cancer or preventing progression of premalignant lesions to cancer
- Used as a single agent or in combination with other anti-cancer treatments like chemotherapy, biological therapy, or radiation
- Inhibiting the activity of CSF1R receptor to treat diseases like chronic myelomonocytic leukemia and Alzheimer''s disease or an adverse condition, such as brain injury

Competitive Advantages

Targeting the PH domain improves specificity against Akt kinase in comparison to inhibitors of the ATP domain which typically are unspecific

Inventor(s)

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Development Stage

- Basic (Target Identification)

Patent Status

- **Research Material:** NIH will not pursue patent prosecution for this technology
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Therapeutic Area

- Cancer/Neoplasm