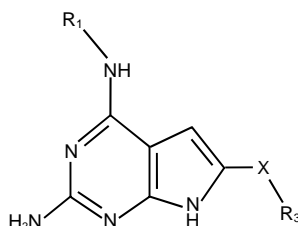


## Multiple acting anti-angiogenic and cytotoxic compounds

A significant number of promising compounds are currently in clinical trials which target cellular pathways implicated in the growth and proliferation of tumors. A number of these compounds such as SU6668<sup>1</sup>, ZD6474<sup>2</sup>, and PTK787/ZK222584<sup>3</sup> specifically target receptor tyrosine kinases and show marked anti-angiogenic activity. Angiogenesis, the process by which tumors recruit or develop new micro vasculature is an important process in tumor growth and the development of metastatic activity. Compounds which inhibit angiogenesis have the property to limit tumor growth, inhibit metastasis and provide therapies which can improve patient prognosis.<sup>4</sup>

Dr. Aleem Gangjee a Professor of Medicinal Chemistry in the Graduate School of Pharmaceutical Sciences at Duquesne University is an authority in the development of pyrimidine derivatives and their application as powerful anti-tumor agents. Dr. Gangjee has invented a series of compounds and their pharmaceutically acceptable salts described in US patent 6,770,652. These compounds target multiple tumor growth pathways, such as the inhibition of receptor tyrosine kinases (RTK), and act to inhibit angiogenesis typically associated with tumor growth and metastatic potential. They have the general formula below:



The activity characteristics of these compounds would suggest that they can be used to both limit tumor growth and metastasis by inhibiting angiogenesis through the inhibition of multiple kinases.

Representative compounds covered under this invention have been tested for angiogenic activity using the chorioallantoic membrane assay (CAM), and for RTK inhibition (EGFR, Flk-1, Flt-1). Many of the compounds tested show multiple modes of action as measured by IC<sub>50</sub>.

These novel patent protected compounds are available for license from the Office of Research at Duquesne University.

Additional information regarding the compounds, test data, or license terms can be obtained by contacting:

**The Office of Research**  
**Duquesne University**  
**Telephone: (412) 396-6326**  
**Email: [volk@duq.edu](mailto:volk@duq.edu)**

<sup>1</sup> Laird, A. D., et al. (2002) FASEB Journal 16:681-690.

<sup>2</sup> Carlomagno, F., et al. (2002) Cancer Res. 62:7284-7290

<sup>3</sup> Steward, W. P., et al. (2004) J. Clin. Oncology 22(14S):3556

<sup>4</sup> Ingber, D. E., (1997) in Cancer Therapeutics: Experimental and Clinical Agents. B. Teicher ed. Pp 283-298