

A case study of biomarker-guided drug discovery of kinase inhibitors for cancer targeted therapy

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Cancer is currently second only to heart disease as a cause of death and will become the primary cause in the next 10 to 20 years. Traditional cancer therapies make use of chemotherapy at the maximum tolerated dose, generally resulting in significant toxicities and often with limited success. The so called “targeted therapies”, such as Gefitinib or Imatinib, are considered less toxic and provide further ammunition in the fight against cancer but often produce responses in only a limited number of cancer patients. New, more universal, more effective, and less toxic therapeutic modalities are therefore desirable.

Angiogenesis plays an important role in the growth of most solid tumors and progression to metastasis. Recently, it has been reported that the specific inhibition of tumor-induced angiogenesis suppresses the growth of many types of solid tumors. For this reason, it is conjectured that the inhibition of angiogenesis represents a novel therapeutic approach against tumors.

In this case study, we will present that a series of kinase inhibitors related to angiogenesis has demonstrated antitumor efficacy and represents novel antitumor agents. Traditional medicinal chemistry techniques were used to quickly delineate the SAR of compounds. The surrogate metabolism SAR was implemented to predict/select compounds with better metabolism properties in vitro and helped to rapidly identify appropriate compounds for testing in in vivo PK/PD IVTI assays. A hallmark of this effort was also the successful use of the PK/PD data of biomarker to design long-term tumor xenograft efficacy studies for cancer targeted therapy.

Biography

Dr. Li is an associate professor of Medicinal and Organic Chemistry in College of Pharmacy, University of Arizona. He received his Ph.D. degree from the University of Tokyo. He did the postdoctoral training in Chemistry at Columbia University and Harvard University. Dr. Li has extensive experience in drug discovery and development, with a particular focus on Oncology. His broad expertise in the study of kinases and cancer will allow him to discover the next generation kinase inhibitors for use in cancer and Alzheimer's disease.

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