Potent Inhibitors of Glycogen Synthase Kinase 3 (GSK3), Novel Template for Anti-Cancer Drugs

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Technology description

Description

Since the mid-1990s there has been a near exponential rise in the level of protein kinase and glycogen synthase kinase-3 (GSK-3) directed research. Consequently the therapeutic potential of protein kinase inhibitors in general and GSK-3 inhibitors in particular has become a rapidly growing area of interest to the pharmaceutical industry. There is particularly strong evidence to support the development of GSK-3 inhibitors as: 1) inhibitors of neuronal apoptosis and neurological decline in stroke patients; 2) therapeutics targeted to bipolar disorder and depression; 3) blockers of the accumulation and toxicity of Aï¬, /tau in Alzheimer's disease; 4) antihyperglycemic, insulin sensitizing and insulinotropin agents for use in diabetics. Researchers at Penn have developed a class of organometallic GSK3 inhibitors which are extremely potent against GSK3 in the pM range, 100x more effective than classic inhibitors such as kenpaullone. The inhibtors have been demonstrated to enter mammalian cells, inhibit GSK3 in the cell models, display good solubility, and good stability in air, water, and against reactive thiol groups. The inhibition of GSK3 is an extremely active field, with a tremendous number of issued patents in play - to our knowledge, no organometallic GSK3 inhibitors have been developed outside of Penn, making this technology very attractive from an IP perspective. Our researchers are currently looking at the effects of these inhibitors in behavioral mouse models. The central scaffold can be selectively modified to act upon other protein kinases, and the researchers have shown through kinase panel screening that other kinases are potently and specifically inhibited by the family of inhibitors developed around the scaffold.This portfolio of technologies includes methods of rational design for protein kinase inhibitors, economical methods of synthesis, and compositions to two kinases in particular. The rational deisgn method has been shown to be capable of producing organometallic compounds which are highly specific for and highly potent towards various kinases.

Institution

University of Pennsylvania

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com