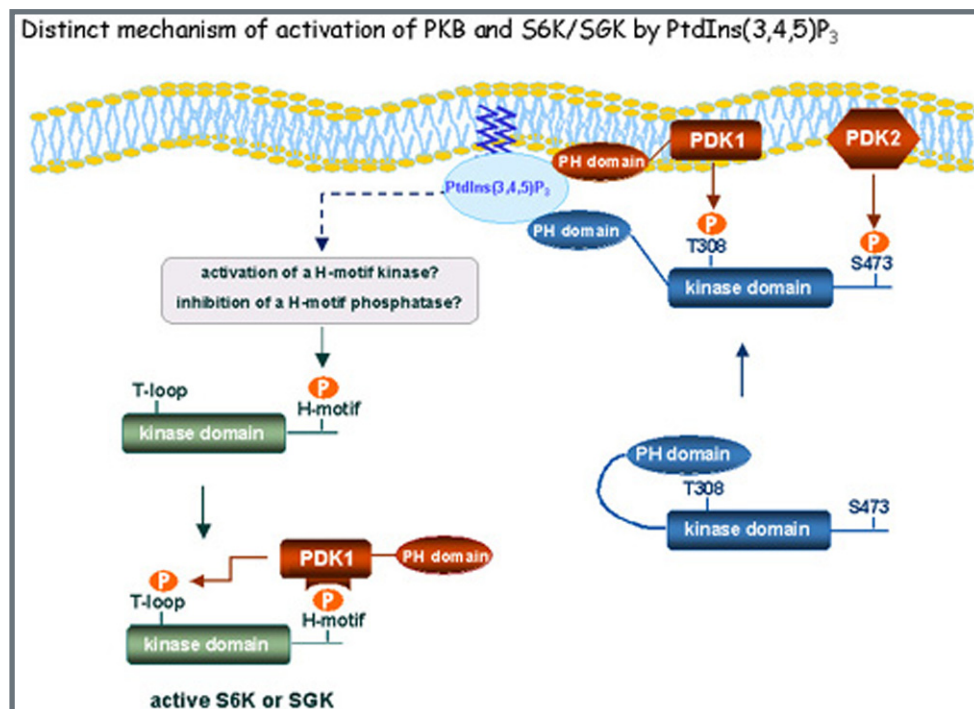


A Novel Kinase (SGK) Target for the Treatment of Diabetes, Cancer and Stroke



A team of research scientists at the Wellcome Trust Biocentre at the University of Dundee have developed specific inhibitors and activators of protein kinases in the insulin signalling pathway with the aim of identifying novel drug targets for a variety of diseases including diabetes, cancer and ischaemic injury.

Background

The binding of insulin or other growth factors to the insulin receptor leads to the activation a system of second messenger mediated signal transduction pathways, which ultimately regulate many of the physiological responses to insulin stimulation. PKB is thought to mediate many of the metabolic responses to insulin, such as the stimulation of glycogen synthesis via the inactivation of GSK3, as well as the antiapoptotic effects of survival factors such as IGF-1. Activation of PKB involves phosphorylation by 3-phosphoinositide-dependent kinase 1 (PDK1).

Serum and glucocorticoid-induced protein kinase (SGK) is activated by a similar pathway to PKB in response to

insulin stimulation and can also, in turn, stimulate glycogen and protein synthesis. Additional interest in SGK came about when tissue mRNA levels were also induced in response to follicle stimulating hormone, high extracellular osmolarity and injury of the brain.

New Methodology/Advances

Research scientists at the University of Dundee have identified novel SGK isoforms, SGK2 and SGK3, and have demonstrated expression of these isoforms in different tissues. A number of cellular responses previously ascribed to the actions of PKB may have been carried out by an SGK isoform thus creating novel drug targets specific to distinct cellular functions.

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Applications

A compound that is capable of modulating the activity of SGK can play a vital role in mediating cellular effects that are regulated by insulin as well as other agonists such as growth factors. SGK mRNA levels are increased in response to FSH, aldosterone, increased extracellular molarity and injury of the brain.

Compounds capable of activating SGK activity may be useful in treating diabetes, obesity, tissue injury and ischaemic injury including stroke.

Compounds capable of reducing SGK activity may be useful in treating cancer.

Commercial Opportunity

Researchers at the University of Dundee have developed a method of modulating SGK activity providing a screening method for new drugs or lead compounds. Licences are available to the methods

Patent Status

Technology protected in Europe, USA and Japan.

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