## Phylogeny

Based on the Manning et al. 2002 kinome analysis, STK31/SGK396 is classified within the AGC group of kinases, which includes the protein kinase A, G, and C families (anti2009nonspecificserinethreonineprotein pages 84-87, anti2009nonspecificserinethreonineprotein pages 27-29). It is placed in the RSK subfamily within the AGC group (anti2009nonspecificserinethreonineprotein pages 45-47). The kinase is categorized as a non-specific serine/threonine protein kinase with the enzyme commission number 2.7.11.1 (anti2009nonspecificserinethreonineprotein pages 119-121, anti2009nonspecificserinethreonineprotein pages 32-34).

## Reaction Catalyzed

The enzyme catalyzes the transfer of the gamma-phosphate group from ATP to a serine or threonine residue on a protein substrate (anti2009nonspecificserinethreonineprotein pages 84-87). The reaction is represented as: ATP + a protein ⇌ ADP + a phosphoprotein (anti2009nonspecificserinethreonineprotein pages 84-87, anti2009nonspecificserinethreonineprotein pages 119-121).

## Cofactor Requirements

Kinase activity requires a divalent metal ion cofactor (anti2009nonspecificserinethreonineprotein pages 32-34). Specifically, Mg2+ is necessary to coordinate ATP binding and stabilize the transfer of the phosphate group during phosphorylation (anti2009nonspecificserinethreonineprotein pages 84-87, anti2009nonspecificserinethreonineprotein pages 119-121). Mn2+ is also mentioned as a potential cofactor for this class of kinase (anti2009nonspecificserinethreonineprotein pages 27-29, anti2009nonspecificserinethreonineprotein pages 45-47, anti2009nonspecificserinethreonineprotein pages 19-22).

## Substrate Specificity

I cannot answer.

## Structure

The STK31 gene has two splice variants that encode proteins of 1,019 and 996 amino acids (kwak2019serinethreoninekinase31 pages 1-2). The protein contains an N-terminal Tudor domain and a C-terminal kinase domain (kwak2019serinethreoninekinase31 pages 1-2, zhou2014stk31tdrd8agerm pages 3-5). The provided context does not contain information on the 3D structure, key catalytic features, or unique structural features.

## Regulation

Expression of STK31 is regulated in a cell cycle-dependent manner (kuo2014stk31isa pages 1-2). This regulation is mediated by the ubiquitin-proteasome degradation pathway through a putative destruction box (D-box) located near its C-terminal region (kuo2014stk31isa pages 1-2).

## Function

STK31 is highly expressed in the testis and is involved in male germ cell development and spermatogenesis (kwak2019serinethreoninekinase31 pages 1-2, kuo2014stk31isa pages 10-11). It is also expressed in primordial follicle oocytes (zhou2014stk31tdrd8agerm pages 3-5). In mitotic cells, STK31 localizes to centrosomes throughout the cell cycle and additionally to centromeres, the central spindle, and the midbody during mitosis (kuo2014stk31isa pages 1-2).

The kinase physically interacts with the tumor suppressor protein programmed cell death 5 (PDCD5) (kwak2019serinethreoninekinase31 pages 1-2).

Its function in cancer is contradictory across studies. One study reports that STK31 overexpression promotes cell migration and invasion, while its knockdown induces microtubule assembly defects, mitotic prolongation, and apoptosis, indicating a role in promoting tumorigenicity (kuo2014stk31isa pages 1-2, kuo2014stk31isa pages 10-11). Another study reports that STK31 overexpression promotes PDCD5 stabilization, which in turn activates p53-dependent apoptosis in response to genotoxic stress, inhibits tumorigenic growth, and increases chemosensitivity, indicating a tumor suppressor function (kwak2019serinethreoninekinase31 pages 1-2).

Functionally, STK31 is implicated in spindle assembly checkpoint (SAC) signaling and centrosome function (kuo2014stk31isa pages 1-2, kuo2014stk31isa pages 10-11).

## Inhibitors

No specific small molecule inhibitors of STK31 have been identified or mentioned in the provided literature (kuo2014stk31isa pages 1-2, kwak2019serinethreoninekinase31 pages 1-2, kuo2014stk31isa pages 10-11, zhou2014stk31tdrd8agerm pages 3-5).

## Other Comments

STK31 is classified as a cancer/testis antigen (CTA) due to its high expression in testis and various human cancers, including colorectal, gastric, and esophageal cancers, while being largely restricted in other normal tissues (kuo2014stk31isa pages 1-2, zhou2014stk31tdrd8agerm pages 3-5, kuo2014stk31isa pages 10-11). Its overexpression is associated with tumorigenicity in colorectal cancer cell lines and tissues (kuo2014stk31isa pages 1-2). It is implicated as a positive regulator of the PDCD5–p53 apoptotic pathway in human colon cancer cells (kwak2019serinethreoninekinase31 pages 1-2).

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