



SMART Teams 2013-2014

Research and Design Phase

Grafton High School SMART Team

Shabi Haider, Brendon Konon, Andrew Mosin,
Danny Potter, Yotaro Sueoka and Hannah Weber

Teachers: Dan Goetz, Fran Grant and Lisa Neeb

Mentor: Stephanie Cossette, Ph.D., Medical College of Wisconsin Department of
Developmental Vascular Biology

Liver Kinase B1 (LKB1) in Cancerous Growth

PDB: 2WTK

Primary Citation: Zeqiraj, E., Filippi, B.M., Deak, M., Alessi, D.R., Van Aalten, D.M.F. (2009). Structure of the LKB1-STRAD-MO25 complex reveals an allosteric mechanism of kinase activation. *Science* 326: 1707.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

The National Cancer Institute alone spends \$4.9 billion every year on cancer research. Liver Kinase B1 (LKB1) stands out as one important protein that regulates cell metabolism, cell division, and therefore, cancerous growth. LKB1 is a key regulator of cell metabolism and cell division acting as a tumor suppressor by turning on other proteins that suppress tumor growth. Human mutations in LKB1 cause the disease Peutz-Jeghers syndrome, resulting in benign tumor-like growth called polyps in the intestine and a 50% chance of developing cancer by the age of 50. When cell energy, ATP, is low LKB1 will be activated. Active LKB1 regulates the activity of adenosine monophosphate-activated protein kinase (AMPK). LKB1 directly activates AMPK by adding a phosphate group to Thr-172. AMPK activity increases the production of ATP by activating glycolysis and fatty acid oxidation. AMPK can also decrease the amount of energy needed by the cell by inhibiting protein synthesis and cell growth. Both of these processes play a role in cancer development. Drugs like metformin, a successful diabetic drug, are thought to activate LKB1 by phosphorylating Thr-336, which in turn causes LKB1 to activate AMPK to cease cancerous growth by shutting down anabolic pathways. The Grafton SMART (Students Modeling a Research Topic) Team modeled LKB1 using 3D printing technology.



Specific Model Information:

- The LKB1 alpha carbon backbone is colored red.
- The MO25 alpha carbon backbone is colored blue.
- STRAD is highlighted in yellow.
- The amino acid Thr 336, displayed in ball and stick and colored pink, is where metformin attaches to LKB1.
- Disulfide bonds are highlighted in yellow.
- Hydrogen bonds are colored white.
- Structural supports are colored grey.

<http://cbm.msoe.edu/smartTeams/>

The SMART Team Program is supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Number 8UL1TR000055. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.