SOUTHWESTERN NEWS

Media Contact: Angela Genusa
214-648-3404
angela.genusa@utsouthwestern.edu

**EMBARGOED UNTIL 1 P.M. CDT THURSDAY, AUG. 16, 2001**

# RESEARCHERS AT UT SOUTHWESTERN DISCOVER LINK BETWEEN GENE IN RARE DISORDER AND GROWTH FACTOR

DALLAS – Aug. 17, 2001 – Researchers at UT Southwestern Medical Center at Dallas in collaboration with scientists at the University of Helsinki, Finland, have discovered a previously unknown connection between *Lkb1*, a tumor-suppressor gene associated with a rare genetic disorder called Peutz-Jeghers syndrome, and vascular endothelial growth factor (VEGF), a key regulator of blood vessels.

The discovery will help researchers better understand Peutz-Jeghers syndrome and the development of the cardiovascular system. Their findings appear in the Aug. 17 issue of *Science*.

"We found that *Lkb1* is very important for regulating the formation of the heart and blood vessels in the embryo," said Dr. Mark Henkemeyer, a professor in the Center for Developmental Biology at UT Southwestern.

Mutations of the *Lkb1* gene cause Peutz-Jeghers syndrome, which is characterized by polyps in the intestines and freckle-like spots on the lips, mouth and fingers. People with Peutz-Jeghers syndrome are also at increased risk for cancerous tumors of the colon, rectum, stomach, ovaries and pancreas.

"We wanted to know what *Lkb1* does in the mouse," Henkemeyer said. "Is this gene also going to cause Peutz-Jeghers syndrome phenotypes (physical or biochemical characteristics) if we mutate it in the mouse? In other words, can we develop an animal model to study Peutz-Jeghers syndrome?"

Henkemeyer and his colleagues generated mutant mice to breed in order to study their offspring. "Then the question is, 'What happens to the mice that have no Lkb1 protein?'" Henkemeyer said. "The bottom line is: These mice die during embryonic development."

The key reason the Lkb1-deficient mice die at mid-gestation is due to defects in cardiovascular development. Additional experimentation revealed the mice in the study that

(MORE)

lacked the *Lkb1* gene had difficulty producing VEGF.

"These findings place Lkb1 in the VEGF signaling pathway and suggest that the vascular defects accompanying Lkb1 loss are mediated at least in part by VEGF," the authors wrote.

"Lkb1 may be a protein that is important for the up-regulation of VEGF, which is crucial for normal development of the heart and blood vessels," Henkemeyer said.

"What we found is that cells that don't have Lkb1 make less VEGF. If you don't have Lkb1, you have vascular abnormalities and you don't have normal regulation of VEGF."

The study provides another important clue to how blood vessels are regulated, Henkemeyer said. "It gives a whole new view into the regulation of VEGF and the development of the cardiovascular system."

###