

UCSD-Salk Team Show Protein's Gene-Silencing Role In Development of Nervous System

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Sue Pondrom

The first evidence that a group of proteins called phosphatases play a key role in the development of the nervous system, has been shown in fruit flies and mice by researchers at the University of California, San Diego (UCSD) School of Medicine, in collaboration with scientists at the Salk Institute, La Jolla, California. The phosphatases are required for maintenance of neural stem cells and for silencing expression of neuronal genes in non-nervous system tissues.

Published in the January 28, 2005 issue of the journal *Science*, the study found that the phosphatases, called small carboxyl-terminal domain phosphatases (SCPs) are expressed in almost all tissues of the body. In their "on" position, the phosphatases prevent neuronal genes from being expressed in areas of the body, such as the heart and liver, where they shouldn't be. When these phosphatases are shut off in the nervous system, neuronal stem cells can develop into specialized neurons.

The researchers determined that SCPs are a component of a previously identified master gene complex called REST/NRSF, which is known to control neuronal genes. In their investigations with mice and fruit flies, the scientists found that REST/NRSF recruits SCPs only to neuronal genes.

"These findings suggest a way to expand the pool of neuronal stem cells, which could lead to new therapeutic strategies for neurological disorders," said the study's senior author, Gordon Gill, M.D., UCSD professor of medicine.

The ability of SCPs to silence genes was first shown by Gill and his post-doctoral fellow Michele Yeo, Ph.D., in an April 28, 2003 study published in the *Journal of Biological Chemistry*. Yeo is co-first author of the new study in *Science*, along with Soo-Kyung Lee, Ph.D., a post-doctoral fellow in the lab of Samuel L. Pfaff, Ph.D., associate professor, Salk Institute. Additional authors are Bora Lee, Ph.D. and Esmeralda C. Ruiz, B.S., Salk Institute.

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Media Contact; Sue Pondrom (619) 543-6163

