



Drug Targeting

An analysis of the properties of genes and proteins that serve as targets for nearly a thousand drugs approved by the US Food and Drug Administration identified characteristics that are common among effective and high-revenue medications. The analysis was conducted by researchers from Columbia University in New York City and the University of Chicago Medical Center (Yao L and Rzhetsky A. *Genome Res.* 2008;18[2]:206-213).

The researchers found that 62% of successful drugs have only one target. "Connectivity" of the target also appears to be important—effective targets interact with about 9 other genes or proteins. Successful drugs also tend to bridge 2 or more clusters of interacting molecules. Also, limited variation of a target is best, so that the drug works the same way in most individuals. The best targets also are primarily expressed in one specific tissue.

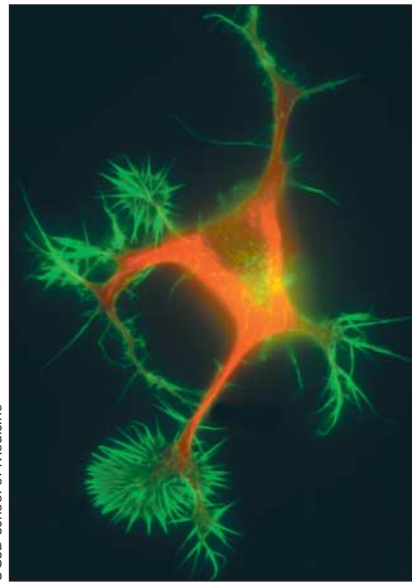
The computational techniques used in this study may help pharmaceutical companies decide which gene and protein targets to pursue among potential candidates under investigation for a particular condition, the researchers said.

Neuronal Map

A new map of mouse neuronal proteins constructed by researchers at the University of California, San Diego, School of Medicine may help investigators discover how neurites in the brain develop and function (Pertz OC et al. *Proc Natl Acad Sci USA.* 10.1073/pnas.0706545105 [published online ahead of print February 1, 2008]).

Neurons regenerate by sending out long, thin neurites that differentiate into axons or dendrites. The researchers developed a microporous filter technology that can isolate and purify these long membrane extensions, which bud from neuronal bodies, or somata. They

then used quantitative mass spectrometry, computational software, and bioinformatics to match neurite proteins to their cellular functions and to construct a blueprint of how the proteins



A mouse neuron reveals multiple neurites budding from the neuronal body. Researchers have constructed a map of neuronal proteins to study neurite development and function.

work together to facilitate neurite formation. They mapped 4855 proteins in neurites and somata, revealing distinct types of signaling proteins in each.

The scientists hope their findings will be integrated with emerging genomic and proteomic data to help decipher the role that neuritogenesis may play in the regeneration of nerve connections damaged by neurodegenerative conditions.

Avian Flu Vaccine

A vaccine against H5N1 avian influenza has been engineered and tested by researchers at the University of Pittsburgh's Center for Vaccine Research and the pharmaceutical company Novavax Inc, in Rockville, Md (Bright RA et al. *PLoS ONE.* 2008;3[1]:e1501).

The vaccine, which encodes genes for 3 influenza viral proteins, uses a virus-

like particle that lacks genetic information to reproduce, making it safer than other avian flu vaccines that are partially developed from live viruses.

When administered either intramuscularly or intranasally to mice, the vaccine produced strong immune responses and protected the animals from a lethal challenge with the H5N1 avian virus. Mice injected in muscle developed more antibodies in the blood, while mice receiving the vaccine via nasal administration had more antibodies in the lungs.

The vaccine is currently being tested in humans.

Drug-Arrhythmia Link

The cyclooxygenase 2 (COX-2) inhibitor celecoxib can induce arrhythmic beating of heart cells, according to laboratory studies conducted at the State University of New York in Buffalo (Frolov RV et al. *J Biol Chem.* 2008;283[3]:1518-1524). The drug's effect is caused by a novel pathway unrelated to its COX-2 inhibition.

The researchers discovered that celecoxib inhibited certain potassium channels from *Drosophila* fruit flies, rats, and humans and led to pronounced heart arrhythmias in *Drosophila* and arrhythmic beating of rat heart cells in culture. Specifically, the drug inhibited the passage of potassium ions into and out of heart cells through what are known as delayed rectifier potassium channels. These effects occurred despite the absence of cyclooxygenases in *Drosophila* and in the face of an inhibitor of both COX-1 and COX-2 administered to rats.

The investigators now are examining the underlying molecular mechanisms responsible for celecoxib's action and its effect on other ion channels. They do not yet know whether the drug binds directly to ion channels or whether it acts by blocking these channels or by some other mechanism. —Tracy Hampton, PhD