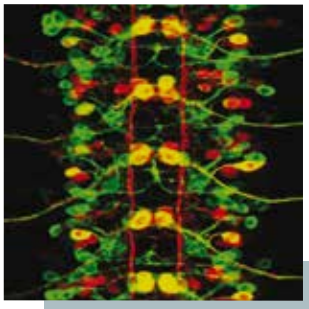
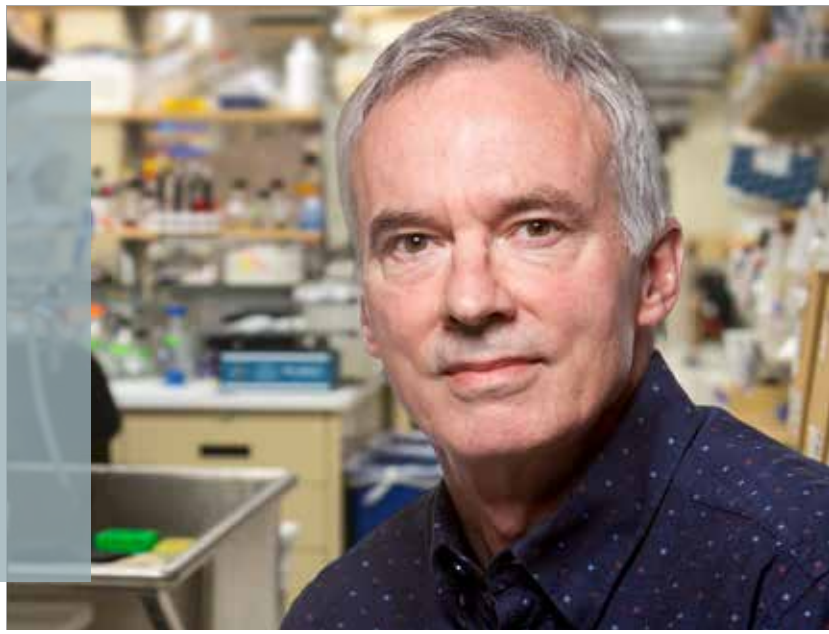


salk
Where cures begin.

John Thomas

Professor
Molecular Neurobiology Laboratory



The Problem

Glioblastomas, one of the most common types of brain tumors, are aggressive and incurable. Not only are the tumors hidden inside the skull, but they also contain many aberrant pathways acting as cohorts to drive the cancer's growth. Turning off just one of these pathways with a drug might not stop the cancer. With a better understanding of how all these pathways activate each other—like falling dominoes—researchers may be able to figure out how to reverse the cancer once and for all.

The Approach

John Thomas studies the molecules that help the brain grow in a developing embryo and which are later reactivated in many aggressive cancers of the nervous system. In both an embryo and a cancer, these molecules act in pathways that encourage the growth of brain cells; in the case of the embryo, that's a good thing, while in cancer, it's not. By studying both brain development and the molecular details of brain tumors, Thomas can determine where the two overlap—and where the pathways have weaknesses that will allow them to be turned off with drugs, stopping cancer growth.

Thomas developed a *Drosophila* (vinegar fly) model of brain tumors—using flies with particular genetic mutations allows him to probe the domino effect of these pathways as well as test potential treatments.

The Innovations and Discoveries

- Thomas showed how mutations in two genes, EGFR and PI3K, set off a cascade of events that caused the growth of glioblastomas in flies. He demonstrated how one step in this cascade—the activation of a set of proteins—could be blocked with drugs to weaken the cancer. Further research will be needed to determine whether targeting the same pathway in human patients shrinks glioblastomas.
- He discovered some of the chemical road signs that guide growing neurons on their paths through the brain in a developing embryo. The tracks that these neurons take ultimately shape organisms' thoughts and behaviors for the rest of their lives.
- Thomas has also turned his attention to how vinegar flies regulate their metabolism. Thomas is employing many of the same genetic approaches he previously used in order to study how molecular pathways in the brain are involved in metabolism, with the aim of better understanding diabetes and obesity.

For more information, please visit:
http://www.salk.edu/faculty/thomas.html

Cellular Biology, Developmental Biology, Developmental Disease, Genetics, Metabolism, Neurobiology, Neurological Disease