



Dennis O'Leary

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The Problem

When studying diseases ranging from cancer to dementia, researchers have found that, in some cases, a surprising number of genes are involved which originally help the brain develop in an embryo. If these genes are incorrectly regulated or turned back on in an adult, it turns out, they can boost cell division (leading to cancer) or mistakenly kill brain cells (one cause of dementia). To understand how developmental genes can relate to adult diseases, researchers need to first uncover their normal role early on. Answering this question could not only lead to treatments for cancer and dementia but for developmental disorders including autism and paraplegia.

The Approach

Dennis O'Leary tackles questions about brain development in order to better understand the genes and molecules which not only help neurons form and find their place in a developing brain, but also play key roles in neural function and health throughout life. He focuses on genes that aid neurons in a growing brain to connect from one place to another, following chemical cues to find their target. He also strives to understand how other genes are involved in pruning back neurons later in development, removing unneeded connections from the brain. This same process, scientists suspect, may also play a role in the later disappearance of certain adult neurons whose absence may be tied to dementia.

O'Leary has also integrated stem cell research into his laboratory in order to develop related therapies tied to the genes

he studies. In this arena, he's identified molecules that help determine what type of neuron stem cells develop into.

The Innovations and Discoveries

- O'Leary probed how the brain maps its sensory areas, with distinct brain sections for specific body parts. Changing this map in the brain, he's found, alters how an animal can sense its environment.
- O'Leary collaborated with Salk researchers Inder Verma and Rusty Gage to discover that a gene most commonly linked to breast and ovarian cancer, called BRCA1, also plays a crucial role in brain development. When brain stem cells in mice were missing BRCA1, the brains formed in a disorganized and incomplete fashion. The newly found role of BRCA1 in the brain helps explain why some patients with breast cancer also get seizures.
- His lab showed that for the cortex of the brain—a region associated with thought and consciousness—to develop properly, it must receive input from the brain's thalamus. Blocking the connections between these areas led to improper cortex development in mice. The finding could have implications for understanding autism, which has been correlated with unusual cortex size.

For more information, please visit:

<http://www.salk.edu/faculty/oleary.html>

Brain Cancer, Dementia, Developmental Disease, Neurological Disease, Genetics, Neurobiology, Stem Cells, Therapeutics