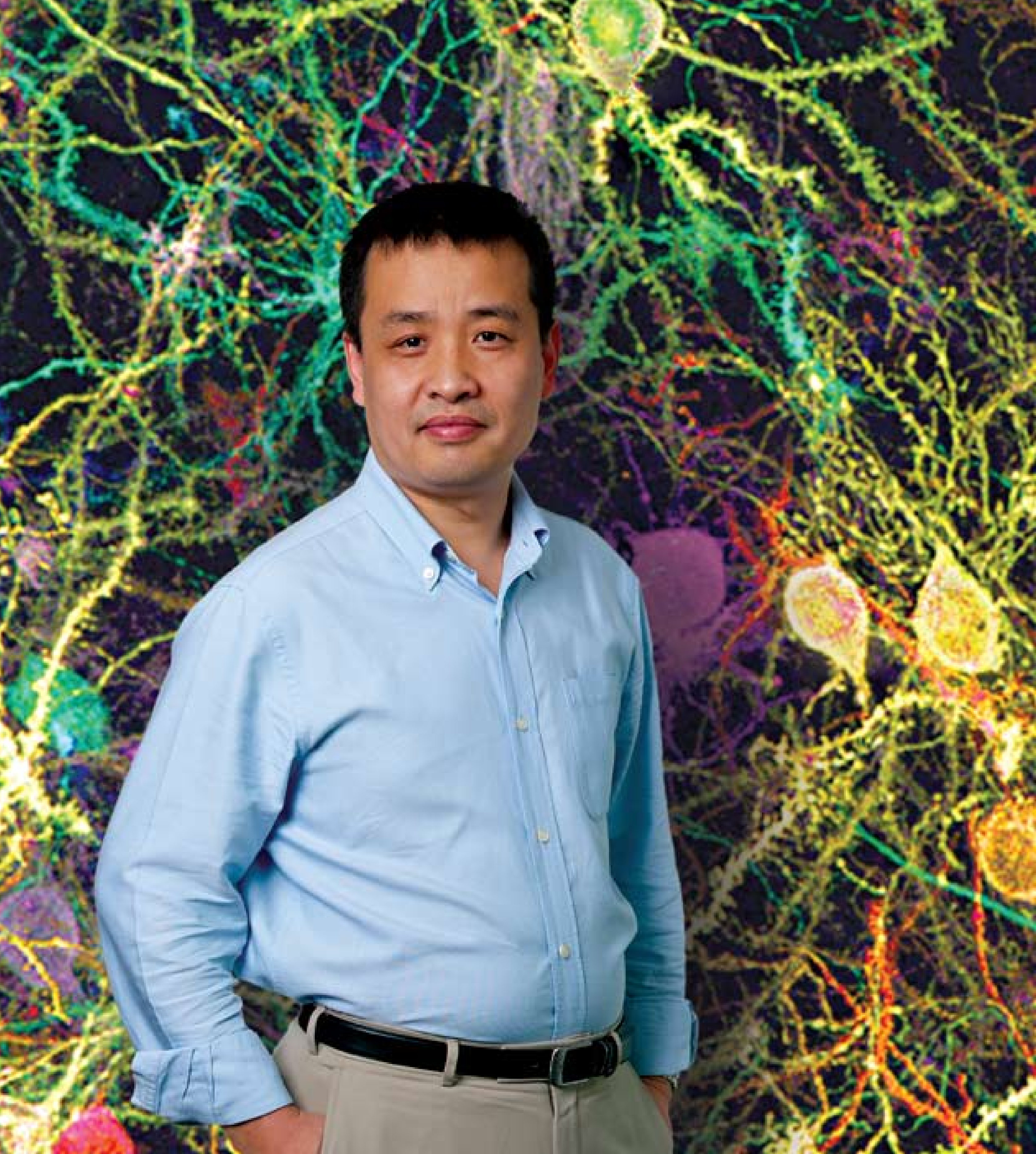

This neuroscientist's early training in laser physics was useful in developing a novel methodology that has enabled him to look at living brain neurons in mice. The unprecedented window he discovered is expanding not only our understanding of neuronal development, but also of diseases ranging from Alzheimer's to multiple sclerosis, autism to schizophrenia.

A Window on the Living Brain

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Dendrites—long fingerlike extensions of nerve cells—can be seen in this two-photon fluorescent micrograph of a living mouse brain, as captured by Dr. Gan. The thorny nubs on the dendrites are spines, which are continuously formed and eliminated. This is where synapses—neuronal connections—are made. After birth, the number of synapses increases and then decreases sharply. From early childhood to adolescence, the synaptic loss could be as much as 50 percent. Dr. Gan believes that in order for learning to occur, the brain's neurons have to be pruned. "First there is a raw material, and then it is sculpted," he says. In other words, learning isn't only about making new connections between neurons, it also involves pruning neuronal connections. Dr. Gan is now also examining neurons that have been damaged by brain disease. Early experiments in mice show that amyloid, the protein implicated in Alzheimer's disease, has a deleterious effect on dendrites, altering them in ways that lead to the atrophy.

"I attended a lecture that awakened a new curiosity about the brain and its mysteries… How do we learn? Why do we sleep?" said Dr. Wen-Biao Gan, describing the time when he decided to pursue brain research. "And unlike the stars in the sky, which also interested me, I could do more than just observe from far away—I could look closely, test, and understand."

At NYU Langone Medical Center, Dr. Gan's view of the brain has been anything but remote. Using a sophisticated optical imaging technique called two-photon microscopy and a novel method of painstakingly shaving the skulls of mice to create an ultra-thin window into the brain, Dr. Gan and his team have observed the neuron's dendritic spines (information receptors) up close and in vivo. The researchers tag neurons with a green fluorescent protein that makes it easy to identify the same cells and spines with a microscope and observe them even as they change shape over a period of time and under varying conditions. In one study, they demonstrated that sensory deprivation prevented the normal process of synaptic "pruning" that typically occurs in growing animals, revealing the important role of early experience in shaping neuronal development.

Currently, Dr. Gan is collaborating with colleagues to elucidate how the brain's only immune cells, called microglia, remodel synapses in the brain in response to disease or injury. "I would never have studied immunology," he said, "but connecting with Drs. Dan Littman and Michael Dustin on the microglia is a bridge to understanding another dimension of brain function." Clearly, advantageous connections at Skirball are not limited to the neuronal kind.