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Research in Shaham's lab focuses on two areas: the control of programmed cell death during animal development and the roles of glial cells in nervous system development and function. The lab uses the roundworm *C. elegans* for both areas of research, and has demonstrated that their underlying cellular programs were maintained through evolution from *C. elegans* to humans.

Nervous systems consist of two major cell types: neurons and glia. The basic properties of neurons and the mechanisms governing neuronal development and function are well studied. In contrast, the functions of glia, the most abundant cell type in vertebrate nervous systems, remain mostly unexplored, and few mediators of glial function are known. Glia are important in disease: 95 percent of brain malignancies are of glial character, and glial defects are associated with neurodegenerative diseases including amyotrophic lateral sclerosis and Alzheimer's disease, suggesting that understanding glial functions, and how these functions go awry, is indispensable for comprehending brain functions and dysfunctions.

One explanation for the gap in understanding glia may lie in their neurotrophic properties. Glial manipulation often results in neuronal loss, precluding investigations of other effects glia might have on neuronal morphogenesis or activity. The Shaham lab discovered that glia of the nematode *C. elegans* bear striking morphological, anatomical, and molecular similarities to vertebrate glia. Importantly, because of their unique development, *C. elegans* glia are not required for neuron survival, making *C. elegans* an excellent model for deciphering glial roles in the nervous system and allowing, for the first time, manipulation of these cells in vivo without the complication of neuronal loss.

The researchers have shown that glia are essential for neural development, promoting axon outgrowth and dendrite extension, and that glia are required for morphological plasticity of neuronal receptive endings; in fact, some sensory receptive structures fail to form in their absence. The lab has also uncovered morphology-independent roles for glia in sensory neuron function, showing that animals lacking glia exhibit profound sensory deficits. To understand the bases of these functional interactions, Shaham and his colleagues have identified glia-enriched proteins and studied their roles in neuronal development and function.

Although *C. elegans* glia do not control neuronal survival, the Shaham lab has explored the death of other *C. elegans* cells to understand the principles by which cell viability is controlled. In addition to discovering novel transcriptional and protein degradation-mediated controls of apoptotic cell death, the lab has identified a novel cell death program independent of known apoptotic regulators. The unique morphology accompanying this cell death program is conserved during the development of the vertebrate nervous system. The Shaham lab identified genes promoting this new cell death form, all of which are conserved among vertebrates, raising the possibility that the mechanism of this novel cell death program is also conserved.

EDUCATION

A.B. in biochemistry and mathematics, 1989
Columbia University

Ph.D. in biology, 1995
Massachusetts Institute of Technology

POSTDOC

University of California, San Francisco, 1996–2001

POSITIONS

Assistant Professor, 2001–2007
Associate Professor, 2007–2012
Professor, 2012–
The Rockefeller University

AWARDS

Sidney Kimmel Foundation for Cancer Research Scholar, 2002

Rita Allen Foundation Scholar, 2003

Irma T. Hirschl/Monique Weill-Caulier Trust Research Award, 2004

Masin Young Investigator Award, Breast Cancer Alliance, 2005

Klingenstein Fellowship, 2005

The Rockefeller University Distinguished Teaching Award, 2005

Blavatnik Award, 2009

NINDS Outstanding Investigator Award, 2018

SELECTED PUBLICATIONS

Katz, M. et al. Glutamate spillover in *C. elegans* triggers repetitive behavior through presynaptic activation of MGL-2/mGluR5. *Nat Commun* 10, 1882 (2019).

Singhvi, A. et al. A glial K/Cl transporter controls neuronal receptive ending shape by chloride inhibition of an rGC. *Cell* 165, 936–948 (2016).

Blum, E.S. et al. Control of nonapoptotic developmental cell death in *Caenorhabditis elegans* by a polyglutamine-repeat protein. *Science* 335, 970–973 (2012).

Heiman, M.G. and Shaham, S. DEX-1 and DYF-7 establish sensory dendrite length by anchoring dendritic tips during cell migration. *Cell* 137, 344–355 (2009).

Bacaj, T. et al. Glia are essential for sensory organ function in *C. elegans*. *Science* 322, 744–747 (2008).