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**Research in the Heintz laboratory aims to identify the genes, circuits, cells, macromolecular assemblies, and individual molecules that contribute to the function of the mammalian brain and to its dysfunction in disease. Understanding the distinct classes of neurons and the circuits that control specific aspects of cognition and behavior can lead to more targeted treatments for central nervous system disorders.**

Cognition and behavior emerge from hundreds of different classes of cells in the mammalian brain, arranged into specific circuits that control various functions of the nervous system. Heintz has developed a suite of tools to investigate the molecular mechanisms that address complexities of the mammalian brain, enabling the characterization of different cell types and furthering our understanding of the biochemical basis behind this diversity.

The focus of the Heintz laboratory has been to characterize the transcriptional and epigenetic mechanisms that distinguish cell types from one another and to discover how these mechanisms are altered in the context of neurological or neurodegenerative disease. The lab's initial studies of the mouse brain led to the finding that each brain cell type expresses about 12,000 genes. These studies also demonstrated that identifying the molecular events that control physiological function and dysfunction in disease requires deep and comprehensive molecular profiling data.

Further work in the Heintz laboratory led to delineation of the circuits, cell types, and molecular mechanisms that modulate social and addictive behaviors and to an improved understanding of cellular dysfunction in mouse models of neurological and neurodegenerative disease. For example, the lab demonstrated the critical role of 5-hydroxymethylcytosine (5hmC) in the nervous system, and showed how this novel epigenetic mark functions in the development and differentiation of post mitotic neurons. This work has contributed to important new directions in efforts to understand mechanisms of aging and disease.

Additionally, the lab has developed new technologies for isolating many thousands of nuclei of each specific cell type from human postmortem brain. These novel methods led to the observation that molecular mechanisms of human brain function differ significantly from those operating in mouse models. This is a particularly important consideration for investigating late onset neurodegenerative disorders like Huntington's disease (HD) and Alzheimer's disease (AD). The Heintz laboratory and the Fisher Center are now engaged in large scale efforts to understand the molecular mechanisms governing selective vulnerability of specific cell types early in disease progression and to identify age-dependent molecular events that contribute to the pathophysiology of these devastating disorders. These efforts are guided by the belief that development of effective interventions in HD and AD will be accelerated by precise and accurate characterization of the earliest molecular events that occur in the human brain during disease onset.

### EDUCATION

B.A. in biology, 1974
Williams College

Ph.D. in biological sciences, 1979
University at Albany, State University of New York

### POSTDOC

Washington University, 1979–1982

### POSITIONS

Assistant Professor, 1983–1987
Associate Professor, 1987–1992
Professor, 1992–
Director, Fisher Center for Alzheimer's Disease Research, 2022–
The Rockefeller University

Assistant Investigator, 1987–1988
Associate Investigator, 1988–1992
Investigator, 1992–2022
Howard Hughes Medical Institute

### AWARDS

Pew Biomedical Scholar, 1985

Junior Faculty Research Award, American Cancer Society, 1986

### HONORARY SOCIETIES

National Academy of Sciences

Fellow, American Association for the Advancement of Science

### SELECTED PUBLICATIONS


Pressl, C. et al. Selective vulnerability of layer 5a corticostriatal neurons in Huntington's disease. *Neuron* 20, 924–941 (2024).

Mätlik, K. et al. Cell-type-specific CAG repeat expansions and toxicity of mutant Huntingtin in human striatum and cerebellum. *Nat. Genet.* 56, 383–394 (2024).

Antolin-Fontes, B. et al. The habenular G-protein-coupled receptor 151 regulates synaptic plasticity and nicotine intake. *Proc. Natl. Acad. Sci. U.S.A.* 10, 5502–5509 (2020).

Kriaucionis, S. and Heintz, N. The nuclear DNA base 5-hydroxymethylcytosine is present in Purkinje neurons and the brain. *Science* 324, 929–930 (2009).

Heiman, M. et al. A translational profiling approach for the molecular characterization of CNS cell types. *Cell* 135, 738–748 (2008).