Sidney Strickland, Ph.D.

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The brain is critically dependent on sufficient blood flow. Strickland's laboratory investigates how dysfunction of the circulatory system contributes to neurological conditions such as Alzheimer's disease in humans and in mice.

Neurological disorders of the central nervous system represent profound medical problems worldwide. For example, Alzheimer's disease affects millions of people and has severe physical, psychological, and financial consequences. By studying patients and mouse models with neurological diseases, Strickland is working to elucidate the molecular mechanisms by which neural function is disrupted.

In investigating neurovascular dysfunction, the Strickland lab studies the mechanisms underlying the pathogenesis of Alzheimer's disease. Cerebrovascular defects contribute to the progression of Alzheimer's pathology, and members of the lab are using transgenic mouse models of Alzheimer's to evaluate blood-brain barrier damage and the roles that blood clot formation and degradation play in this disease. Their research has determined that the β-amyloid peptide, which is considered to be a causative factor in Alzheimer's, interacts with fibrinogen to promote irregular fibrin accumulation in the brain and increase brain inflammation. This peptide also hinders blood clot degradation, which could compromise blood flow, exacerbate inflammation, and lead to neuronal death. These findings suggest that fibrin and the mechanisms involved in its accumulation and clearance may present novel therapeutic targets for slowing the progression of Alzheimer's disease.

The Strickland lab has also recently found that β-amyloid can activate coagulation Factor XII (FXII) in the plasma of both Alzheimer's patients and mouse models. The activation of FXII initiates fibrin clotting as well as inflammatory processes, both of which are recognized pathologies in Alzheimer's disease. Promotion of FXII activation by β-amyloid could help explain the association between Alzheimer's disease and vascular diseases. This knowledge may ultimately identify new pathogenic mechanisms that could disrupt neuronal function, aiding in the discovery of novel diagnostic and therapeutic approaches.

EDUCATION

B.S. in chemistry, 1968
Rhodes College

Ph.D. in biochemistry, 1972
University of Michigan

POSTDOC

The Rockefeller University, 1973–1975

POSITIONS

Assistant Professor, 1975–1980
Associate Professor, 1980–1982
The Rockefeller University

Associate Professor, 1983–1987
Professor, 1987–2000
State University of New York at Stony Brook

Research Professor, 2000–
Dean and Vice President for Educational Affairs, 2000–2022
The Rockefeller University

AWARDS

John Simon Guggenheim Memorial Foundation Fellow, 1998

Innovative Research Award, Alzheimer's Drug Discovery Foundation, 2009

SELECTED PUBLICATIONS

Chen, Z.L. et al. Anti-HK antibody inhibits the plasma contact system by blocking prekallikrein and factor XI activation in vivo. *Blood Adv* (2022).

Chen, Z.L. et al. Anti-HK antibody reveals critical roles of a 20-residue HK region for Aβ-induced plasma contact system activation. *Blood Adv* 6, 3090–3101 (2022).

Cajamarca, S.A. et al. Cerebral amyloid angiopathy-linked β-amyloid mutations promote cerebral fibrin deposits via increased binding affinity for fibrinogen. *Proc. Natl. Acad. Sci. USA* 117, 14482–14492 (2020).

Singh, P.K. et al. Increased plasma bradykinin level is associated with cognitive impairment in Alzheimer's patients. *Neurobiol. Dis.* 139, 104833 (2020).

Strickland, S. Blood will out: vascular contributions to Alzheimer's disease. *J. Clin. Invest.* 128, 556–563 (2018).