

γ -Secretase Modulatory Proteins: The Guiding Hand Behind the Running Scissors

March 29

Tuesday, 12:30pm

Online Webinar

For Researchers



Speaker:

Yueming Li, Ph.D.

*Member and Professor
Chemical Biology Program
Memorial Sloan Kettering Cancer
Center
Professor of Pharmacology and
Neurosciences
Weill Graduate School of Medical
Sciences of Cornell University*

Host: Jian Zhong, Ph.D.

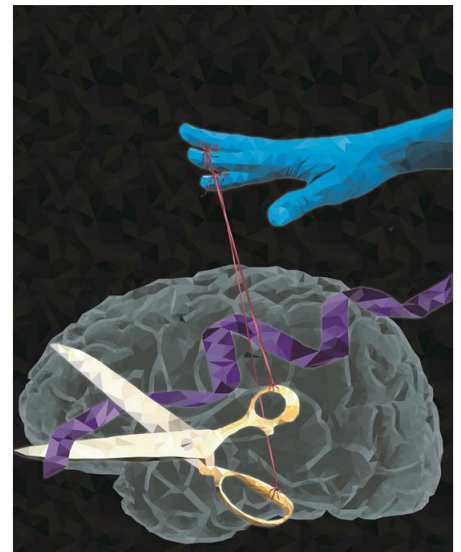
For more information contact

Darlene White

daw9085@med.cornell.edu

Abstract

γ -Secretase is a four subunit, 20-pass transmembrane enzyme that cleaves amyloid precursor protein, catalyzing the formation of amyloid beta peptides that form amyloid plaques, which contribute to Alzheimer's disease pathogenesis. γ -Secretase also cleaves Notch and other more than 100 type I transmembrane substrates. Despite its seemingly promiscuous enzymatic capacity, γ -secretase activity is tightly regulated. This regulation is a function of many cellular entities, including but not limited to the essential γ -secretase subunits, nonessential (modulatory) subunits, and γ -secretase substrates. We will discuss how γ -secretase is regulated by modulatory proteins under hypoxia and neuroinflammation. A better understanding of these mechanisms will aid in the development of effective therapeutics for γ -secretase-associated diseases like Alzheimer's disease and Notch-addicted cancer.



1. Hur, J. Y., Frost, G. R., Wu, X., Crump, C., Pan, S. J., Wong, E., Barros, M., Li, T., Nie, P., Zhai, Y., Wang, J. C., Tcw, J., Guo, L., McKenzie, A., Ming, C., Zhou, X., Wang, M., Sagi, Y., Renton, A. E., Esposito, B. T., Kim, Y., Sadleir, K. R., Trinh, I., Rissman, R. A., Vassar, R., Zhang, B., Johnson, D. S., Masliah, E., Greengard, P., Goate, A., and Li, Y. M. (2020) The innate immunity protein IFITM3 modulates gamma-secretase in Alzheimer's disease. *Nature* 586, 735-740
2. Nie, P., Kalidindi, T., Nagle, V. L., Wu, X., Li, T., Liao, G. P., Frost, G., Henry, K. E., Punzalan, B., Carter, L. M., Lewis, J. S., Pillarsetty, N. V. K., and Li, Y. M. (2021) Imaging of Cancer gamma-Secretase Activity Using an Inhibitor-Based PET Probe. *Clin Cancer Res* 27, 6145-6155
3. Villa, J. C., Chiu, D., Brandes, A. H., Escorcía, F. E., Villa, C. H., Maguire, W. F., Hu, C. J., de Stanchina, E., Simon, M. C., Sisodia, S. S., Scheinberg, D. A., and Li, Y. M. (2014) Nontranscriptional role of Hif-1 α in activation of gamma-secretase and notch signaling in breast cancer. *Cell Rep* 8, 1077-1092