Post-Natal Immune Activation Causes Social Deficits in a Mouse Model of Tuberous Sclerosis: Role of Microglia and Clinical Implications

November 17

Tuesday, 12:30pm

Live Webinar
via Zoom Conference

Speaker: Alcino J. Silva, Ph.D.
UCLA Distinguished Professor
Departments of Neurobiology, Psychiatry & Biobehavioral Sciences, and Psychology
Director, Integrative Center for Learning and Memory
Brain Research Institute
Los Angeles, CA

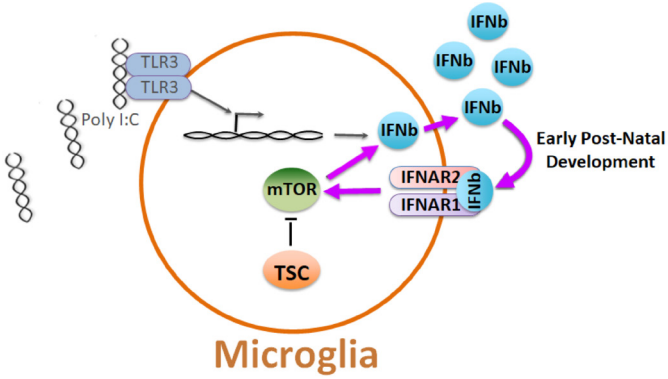
Host: Rajiv R. Ratan, M.D., Ph.D.

For more information, please contact
Darlene White
daw9085@med.cornell.edu

Burke Neurological Institute
Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue
White Plains, NY 10605
burke.weill.cornell.edu

Abstract

There is growing evidence that pre-natal immune activation contributes to neuropsychiatric disorders. We will show that early post-natal immune activation resulted in profound impairments in social behavior, including in social memory in adult male mice heterozygous for a gene responsible for tuberous sclerosis complex (Tsc2+/-), a genetic disorder with high prevalence of autism. Interestingly, early post-natal immune activation did not affect either wild type (WT) or female Tsc2+/- mice. We demonstrate that these memory deficits are caused by abnormal mammalian target of rapamycin (mTOR)-dependent interferon signaling and impairments in microglia function. By mining the medical records of over 3 million children followed from birth, we show that the prevalence of hospitalizations due to infections in males (but not in females) is associated with future development of autistic spectrum disorders (ASD). Altogether, our results suggest the importance of synergistic interactions between strong early post-natal immune activation and mutations in ASD.



1. Joy, M. T., E. Ben Assayag, D. Shabashov-Stone, S. Liraz-Zaltsman, J. Mazzitelli, M. Arenas, N. Abduljawad, E. Kliper, A.D. Korczyn, N.S. Thareja, E.L. Kesner, M. Zhou, S. Huang, T.K. Silva, N. Katz, N.M. Bornstein, A.J. Silva, E. Shohami and S.T. Carmichael (2019). "CCR5 Is a Therapeutic Target for Recovery after Stroke and Traumatic Brain Injury." Cell 176(5): 1143-1157 e1113.
2. Howe, J.R.t., M.F. Bear, P. Golshani, E. Klann, S. A. Lipton, L. Mucke, M. Sahin and A.J. Silva (2018). "The mouse as a model for neuropsychiatric drug development." Curr Biol 28(17): R909-R914.
3. Frank A.C., Huang S., Zhou M, Gdalyahu A, Kastellakis G, Silva T.K., Lu E, Wen X, Poirazi P., Trachtenberg J.T., Silva A.J. Hotspots of dendritic spine turnover facilitate clustered spine addition and learning and memory. Nat Commun. 2018 Jan 29; 9(1):422. doi: 10.1038/s41467-017-02751-2. PMID: 29379017

Burke Neurological Institute | Weill Cornell Medicine