Deconstructing SMA: from RNA Processing to Motor Neuron Disease

June 6

Tuesday, 12:30 pm Billings Building—Rosedale Room and Zoom

SPEAKER:



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

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Burke Neurological Institute Academic Affiliate of Weill Cornell Medicine 785 Mamaroneck Avenue, White Plains, NY 10605 burke.weill.cornell.edu/events Research in the Pellizzoni laboratory investigates the mechanisms by which RNA binding proteins (RBPs) and molecular chaperones that mediate their assembly into RNAprotein complexes (RNPs) regulate gene expression. The laboratory also focuses on the question of how general perturbations of RNA metabolism cause synaptic dysfunction and neuronal death in neurodegenerative diseases such as

SMN major snRNPs U7 snRNP minor snRNPs U11 U12 U4atac U1 U2 U4 U7 target snRNPs U5 U6 U5 U6atac histone mRNA U12 splicing U2 splicing 3' end processing dysregulated mRNAs Stasimon Mdm2 and Mdm4 histones disease effectors P p53 Agrin p380 synaptic loss motor neuron death NMJ denervation neuronal deficits skeletal muscle motor neuron SMA

spinal muscular atrophy (SMA). In these studies, we employ cellular and animal models as well as a wide range of genomic, biochemical, molecular, and imaging approaches. High-throughput screens are also used to discover chemical and genetic modifiers of disease pathways. On one hand, these efforts are designed to advance our knowledge of how RNA regulation contributes to neural circuit function. On the other, they aim to deconstruct disease mechanisms and identify potential therapeutic targets.

Abstract

Publications

1. M. Van Alstyne, C.M. Simon, S.P. Sardi, L.S. Shihabuddin, G.Z. Mentis and L. Pellizzoni*. (2018). Dysregulation of Mdm2 and Mdm4 alternative splicing underlies motor neuron death in spinal muscular atrophy. Genes Dev. 32, 1045-1059. <u>https://pubmed.ncbi.nlm.nih.gov/30012555/</u>

2. M. Van Alstyne, I. Tattoli, N. Delestree, Y. Recinos, E. Workman, L.S. Shihabuddin, C. Zhang, G.Z. Mentis and L. Pellizzoni*. (2021). Gain of toxic function by long-term AAV9-mediated SMN overexpression in the sensorimotor circuit. Nat. Neurosci. 24, 930-940. <u>https://pubmed.ncbi.nlm.nih.gov/33795885/</u>

3. S. Tisdale, M. Van Alstyne, C.M. Simon, G.Z. Mentis and L. Pellizzoni*. (2022). SMN controls neuromuscular junction integrity through U7 snRNP. Cell Rep. 40, 111393. <u>https://pubmed.ncbi.nlm.nih.gov/36130491/</u>



