UNIVERSITY of GUELPH

COLLEGE of BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY

Distinguished SPEAKER SERIES

2019 - 2020

OCT **WED 30** **10:30 AM**

Summerlee Science Complex
SSC 2315

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MCB HOST: DR. NINA JONES

Post-transcriptional and post-translational mechanisms shaping vertebrate social behavior

The ability to fluidly engage in social interactions is more challenging for individuals affected by autism spectrum disorders (ASD) or Cri du Chat Syndrome (CdCS). The majority of the several hundred genes associated with ASD affect three molecular pathways: translational regulation, synaptic function and Wnt signaling. Thus, we have searched for molecular hubs that direct these genetic programs and for their key target genes that might affect specific behaviors with the ultimate goal to improve diagnosis and treatment for ASD and CdCS patients.

We, together with Dr. Ben Blencowe, have shown that a neuronal-specific alternative splicing network of microexons (short 3-27 nt exons) is misregulated and expression of the vertebrate-specific neuronal microexon regulator SRRM4/nSR100 reduced in the brains of a substantial proportion of ASD individuals. Moreover, mutant mice with reduced levels of nSR100 and its target splicing program display hallmark ASD features. Recently, we have identified microexons governing key translational regulatory events, which affect select behaviors.

In concert with alternative splicing, post-translational modifications, such as ubiquitination, shape our nervous system. Linear ubiquitin (Met1Ub) chains, in which one ubiquitin is fused to the starting methionine of another, evolved alongside increasingly nuanced social interactions in vertebrates. Linear ubiquitin chains are added to proteins by the linear ubiquitin assembly complex (LUBAC) and removed by *OTULIN* (GUMBY/FAM105b), a deubiquitinase dedicated to the cleavage of Met1Ub chains. Haploinsufficiency of *OTULIN* is associated with the anti-social behaviors seen in CdCS patients. We have shown that linear ubiquitination modulates Wnt signaling and are identifying key Otulin client proteins governing neuronal function and behavior.

Taken together our findings deepen our understanding of the molecular and neurobiological mechanisms governing vertebrate behaviors and underlying these disorders and set the stage for developing further tools for modulating specific behaviors.

All welcome to attend
Light refreshments will be served

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