NYC RNA Salon and the NYU Langone Institute for Systems Genetics

Minisymposium: RNA dynamics and phase transitions

April 30, 2019

1:30 - 5:00 pm

Seminar Series:

'Genes, Systems, and Computation'

NYU Langone Health
Science Building, Rm. 103
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Organizers

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NCDIR
National Center for Dynamic Interactome Research

LEXOGEN

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Schedule

1:30 - 1:40 pm
Welcome & brief introduction

1:40 - 2:40 pm
Brenton Graveley, UConn School of Medicine
A large-scale binding and functional map of human RNA binding proteins.

2:40 - 3:00 pm
Coffee break

3:00 - 3:50 pm
Liam Holt, Institute for Systems Genetics, NYU School of Medicine
Phase separation of the Human Retrotransposon LINE-1 enables DNA target search.

3:50 - 4:40 pm
Joshua Dubnau, Stony Brook University
Retrotransposons and ERVs drive inter-cellular toxicity in a fly neurodegeneration model.

A large-scale binding and functional map of human RNA binding proteins.

Brenton Graveley, Ph.D.

Professor and Chair of Genetics and Genome Sciences

UConn School of Medicine

Genomes encompass all the information necessary to specify the development and function of an organism. In addition to genes, genomes also contain a myriad of functional elements that control various steps in gene expression. A major class of these elements function only when transcribed into RNA as they serve as the binding sites for RNA binding proteins (RBPs), which act to control post-transcriptional processes including splicing, cleavage and polyadenylation, and the editing, localization, stability, and translation of mRNAs. Despite their importance, these functional RNA elements encoded in the genome have been much less studied than genes or DNA elements. Here, we describe the mapping and characterization of RNA elements recognized by a large collection of human RBPs in K562 and HepG2 cells. These data expand the catalog of functional elements encoded in the human genome by addition of a large set of elements that function at the RNA level through interaction with RBPs.

Periodic Table of Human RNA Binding Proteins

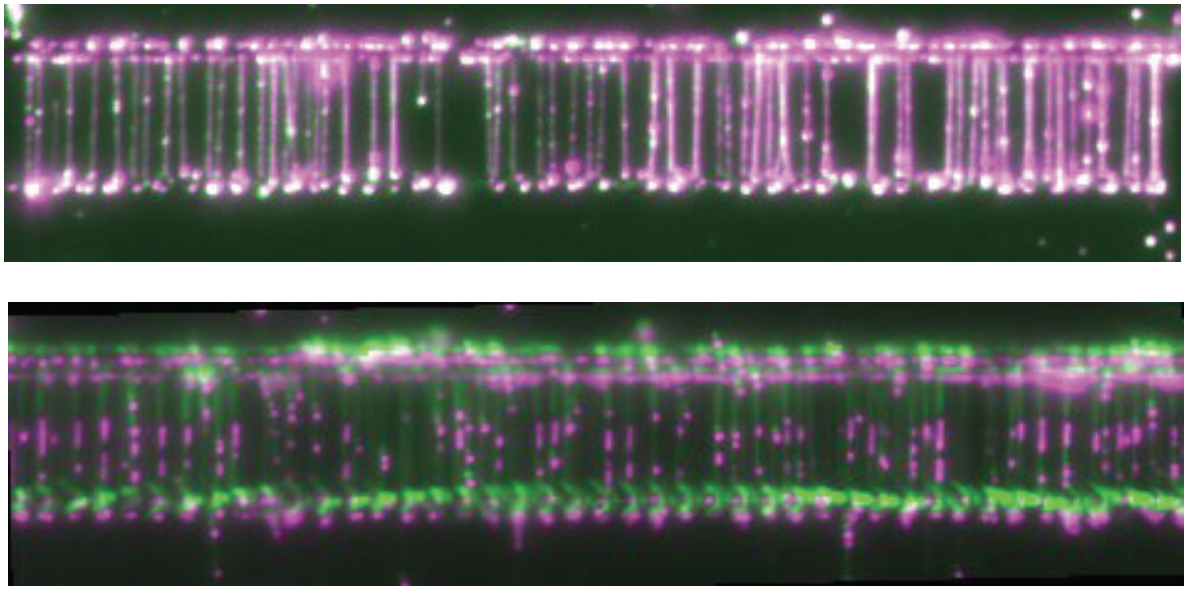
Phase separation of the Human Retrotransposon LINE-1 enables DNA target search.

Liam Holt, Ph.D.

Institute for Systems Genetics, NYU School of Medicine

Assistant Professor

LINE-1 (L1), the major autonomous human retrotransposon, encodes two proteins: ORF1p, a structural protein, and ORF2p, a catalytic protein. The role of ORF1p in the life cycle of L1 is poorly understood. We observed that ORF1p phase separates into droplets at nanomolar concentrations in vitro. Phase separation is essential for transposition in vivo. Using a single-molecule DNA curtain approach, we found that ORF1p droplets recruit LINE-1 RNA to DNA, move along the DNA, and preferentially recruit LINE-1 to R-loops. Thus, ORF1p has unique physico-chemical properties that provide a mechanism for one dimensional DNA target search.



Single Molecule DNA Curtain

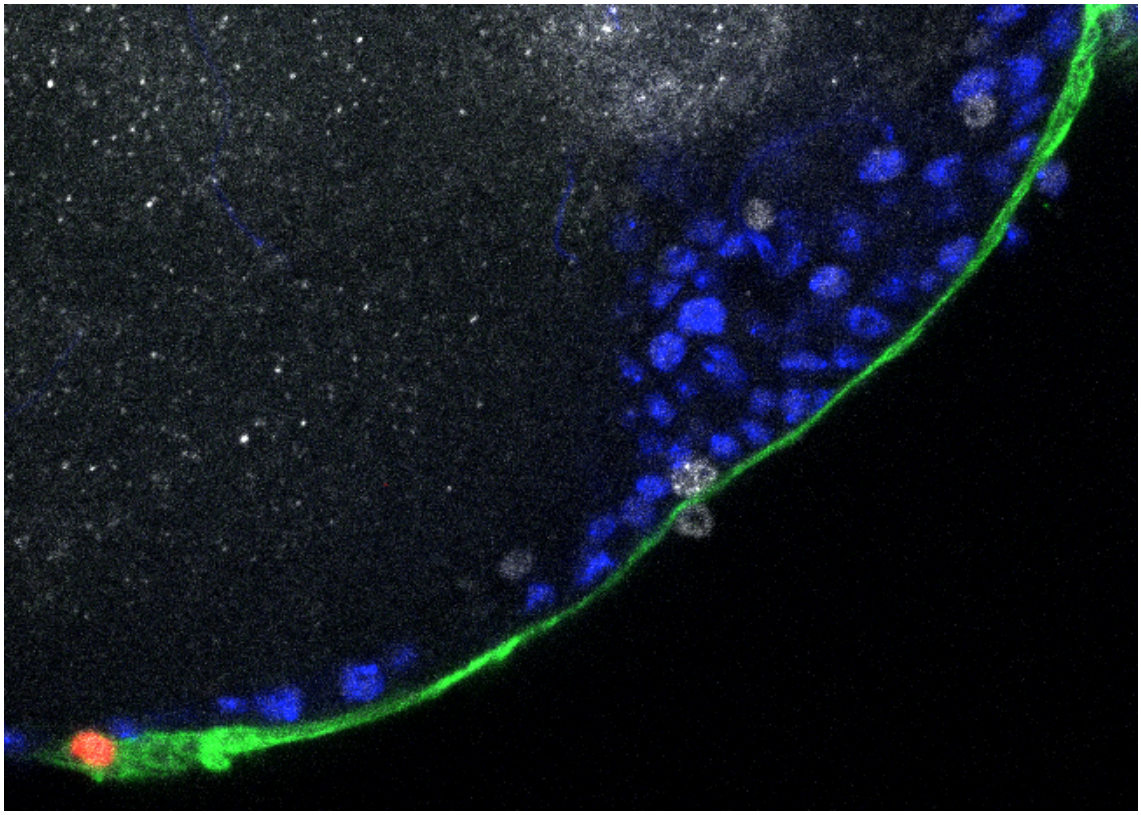
Retrotransposons and ERVs drive inter-cellular toxicity in a fly neurodegeneration model

Joshua Dubnau, Ph.D.

Stony Brook University

Professor

A hallmark of neurodegenerative disease is focal onset of pathological protein aggregation of low complexity domain proteins, followed by progressive spread of pathology to connected brain regions. In amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), pathology is often associated with aggregation of TAR DNA Binding protein 43 (TDP-43). Although aggregated TDP-43 protein moves between cells, it is not clear whether and how this movement propagates the neurodegeneration. Here we have established a Drosophila model of human TDP-43 toxicity to investigate mechanisms by which focal pathology spreads. We initiated toxic expression of human TDP-43 focally within small groups of glial cells. We found that this focal onset kills adjacent neurons. Surprisingly, we show that this spreading death is caused by an endogenous retrovirus within the glia, which leads to DNA damage and death in adjacent neurons. These findings suggest a possible mechanism by which human retroviruses such as HERV-K might contribute to TDP-43 mediated propagation of neurodegeneration.



Retrotransposon Mediated Spread of Neurodegeneration