Biomolecular Sciences Institute

School of Integrated Science and Humanity

Seminar Announcement

Mechanisms of R-loop Dependent CAG Repeat Fragility and Instability

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Abstract

Expansion of CAG trinucleotide repeats beyond a threshold of ~35 repeats is the cause of many human diseases including Huntington's disease and myotonic dystrophy. Expanded CAG repeats form DNA structures, are prone to breakage, and repair of the breaks can cause repeat contractions and expansions. Previous *in vitro* studies showed that expanded CAG repeat tracts form stable RNA:DNA hybrids (R-loops), and in human cells, dramatic R-loop dependent CAG repeat contractions were observed (Lin et al., PNAS 2010). Recent results from Dr. Catherine Freudenreich's lab using a yeast model system show that R-loops form at expanded CAG repeats *in vivo*, and CAG contractions and fragility (DNA breaks) are caused by R-loop formation at the expanded CAG repeat (Su and Freudenreich, unpublished). But how do these R-loop dependent breaks and contractions occur? Dr. Freudenreich will describe her investigations into the mechanisms of R-loop induced genome instability, and the role of known DNA repair pathways, including base excision repair (BER). Since disease-causing CAG repeat instability occurs in transcribed regions shown to harbor R-loops, Dr. Freudenreich's findings indicate that R-loop-mediated fragility is a mechanism that could cause DNA damage and repeat-length changes in human cells. A therapeutic intervention to reduce the size of expanded repeats would be applicable to all of these and other repeat expansion diseases.

Friday, March 24th, 2017

11:00 a.m. - 12:00 p.m.

Venue: Room PG5-153

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Biomolecular Sciences Institute

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