HONG KONG RNA CLUB

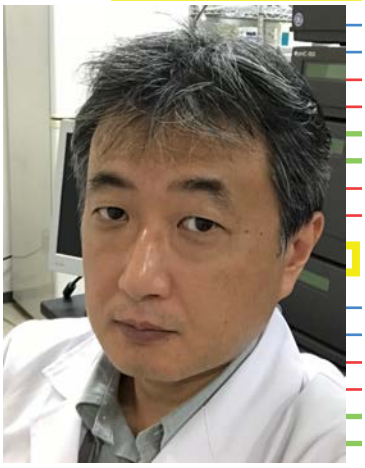
Seminar

香港城市大學
City University of Hong Kong

21 Sep 2018 (Fri) / 3:00-4:00pm
B5-208, Yeung Kin Man Acad. Building (AC1)
City University of Hong Kong

Guest Speaker:

Prof. Akira Ishiguro
Research Center for Micro-Nano Technology
University of Hosei



Molecular mechanisms of interaction between TDP-43 and RNA G-quadruplex

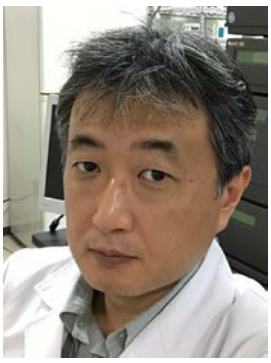
Sponsors:

RNA Society
QIAGEN
ThermoFisher SCIENTIFIC
eppendorf
IDT INTEGRATED DNA TECHNOLOGIES
GLEN RESEARCH part of Maravai LifeSciences

Refreshment provided!

Sign-up: kitkwok.com/hk-rna-club
Contact: hkrnaclub@gmail.com

Molecular mechanisms of interaction between TDP-43 and RNA G-quadruplex



Professor Akira ISHIGURO
Research Center for Micro-Nano Technology
University of Hosei

Abstract

Local protein synthesis within neurites depends on long-distance transport of a specific set of mRNAs from neuron soma to restricted area, but its mechanism remains unsolved. I have found that trans-activation response (TAR) DNA-binding protein of 43kDa in size (TDP-43) recognizes G-quadruplex (G4)-containing mRNAs and transports them up to neurites for local translation. In neurons of patients with amyotrophic lateral sclerosis (ALS), frontotemporal lobar degeneration (FTLD) or some neurodegenerative disorders, TDP-43 exists as a major component of the ubiquitin-positive inclusions, the pathological hallmarks of neuron diseases. Recently, some familial and sporadic ALS patients have been identified to carry mutations in the TDP-43 gene.

ALS-related mutations in the TARDBP gene encoding TDP-43 are clustered within the exon-6 coding for the C-terminal Gly-rich domain. I have overproduced 10 mutant proteins and examined the binding kinetics of wild-type rTDP-43 and mutant proteins to G4-containing mRNA. All these mutant proteins exhibited a low affinity for G4-containing mRNA.

ALS is considered a multifactorial disease that is, genetic, environmental, or oxidative stress in aging may lead to motor neuronal degeneration. However, it is unclear that the molecular mechanisms on the pathological process underlying neuronal degeneration in ALS patients. Here I report that guanine oxidation affects RNA G4 formation and defects the interaction to TDP-43. 8-oxoguanine (8OG) is the common product from reactive oxygen species in cells. The in vitro binding ability of rTDP-43 mutant proteins to 8OG-containing G4 RNA decreased markedly compared with wild-type rTDP-43. It may indicate the possibility of “RNA aging” on the pathological process in ALS patients.