CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

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Interaction Between RNAi And RNA Editing Mechanisms

Date: Tuesday, 12 January 2016
Time: 11am – 12pm
Venue: LT35, Level 1 Auditorium, Centre for Translational Medicine (MD6)
(14 Medical Drive, Singapore 117599)
Host: Dr. Polly Chen

Abstract:

Adenosine deaminases acting on RNA (ADARs) are involved in RNA editing that converts adenosine residues to inosine specifically in double-stranded RNAs (dsRNA) (1). This A-to-I RNA editing pathway and the RNA interference (RNAi) pathway seem to interact antagonistically by competing for their common dsRNA substrates. For instance, A-to-I editing of certain microRNA (miRNA) precursors by ADAR1 and ADAR2 inhibits their processing to mature miRNAs (2). Recent studies unexpectedly revealed the presence of a completely different type of interaction between the RNA editing mechanism and the RNAi machinery (3). ADAR1 forms a complex via direct protein-protein interaction with Dicer, an RNase III gene family member involved in the RNAi mechanism. ADAR1 in the Dicer complex promotes pre-miRNA cleavage by Dicer and facilitates loading of miRNA onto RNA-induced silencing complexes, giving rise to an unsuspected stimulative function of ADAR1 on miRNA processing and RNAi mechanisms. ADAR1 differentiates its functions in RNA editing and RNAi by formation of either ADAR1-ADAR1 homodimer or Dicer-ADAR1 heterodimer complexes. Expression of miRNAs is globally inhibited in ADAR1 null mouse embryos, which in turn alters expression of their target genes and may contribute to their embryonic lethal phenotype. Current efforts are focused on identification of the mechanism that switches ADAR1 function from RNA editing to RNA silencing.

(1) Nishikura, K. 2010. Functions and regulation of RNA editing by ADAR deaminases. Annu. Rev. Biochem. 79: 321-349.
(2) Kawahara, Y., Zinshteyn, B., Sethupathy, P., Iizasa, H., Hatzigeorgiou, A.G., and Nishikura, K. 2007. Redirection of silencing targets by adenosine-to-inosine editing of miRNAs. Science 315: 1137-1140.
(3) Ota, H., Sakurai, M., Gupta, R., Valente, L., Wulff, B-E, Ariyoshi, K., Iizasa, H., Davuluri, R.V., and Nishikura, K. 2013. ADAR1 forms a complex with Dicer to promote microRNA processing and RNA-induced gene silencing. Cell 153: 575-589.

Biography:

Kazuko Nishikura is a Professor at The Wistar Institute in Philadelphia, Pennsylvania, where she oversees a research group focused on the molecular biology and genetics of RNA editing and RNA interference. After receiving a B. Sc. from Kanazawa University in Japan, she carried out her doctoral research primarily in the laboratory of Max Perutz at the MRC Laboratory of Molecular Biology, Cambridge, England. She received a Ph.D. in 1979 from Osaka University in Japan for her thesis work characterizing the structure and function of hemoglobin. This was followed by postdoctoral research periods working with Eddy De Robertis on tRNA processing and splicing in Xenopus oocytes at the MRC Laboratory of Molecular Biology and then with Roger Kornberg on differential polyadenylation of IgM heavy chain mRNAs at Stanford University. Her experience during this period became the basis for her major research interest in RNA processing and its role in the regulation of eukaryotic gene expression. In the last several years Professor Nishikura's research has been directed toward examining interactions between RNA editing and RNA interference pathways. She is the author of over 100 publications and has been funded continuously by the National Institutes of Health.