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Interaction between RNAi and RNA editing pathways

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Adenosine deaminases acting on RNA (ADARs) are involved in RNA editing that converts adenosine residues to inosine specifically in double-stranded RNAs (dsRNA). 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. Recent studies unexpectedly revealed the presence of a completely different type of interaction between the RNA editing mechanism and the RNAi machinery. 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 andmay contribute to their embryonic lethal phenotype.

Biography

Kazuko Nishikura first joined The Wistar Institute in 1982, and became a full Professor in 1995. Raised in the Ishikawa Prefecture along the western coast of Japan, she went to Kanazawa University, where she received both a bachelor's and master's degree in biochemistry. She obtained her PhD in medical science from Osaka University, but much of her thesis work (on the properties by which oxygen binds to hemoglobin in red blood cells) was performed in the laboratory of Dr. Max F. Perutz at the Medical Research Council Laboratory of Molecular Biology (LMB) in Cambridge, England. She returned to the LMB for her first Postdoctoral fellowship working in laboratories of Dr. Eddy De Robertis and Sir John B Gurdon, before obtaining a second fellowship at Stanford University, where she explored the role of RNA processing in the immunoglobulin heavy chain gene expression in the laboratory of Dr. Roger D. Kornberg.

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