In the classical central dogma of molecular biology, RNA was supposed merely to convey the genetic information encoded in DNA into proteins. However, since the discovery of RNA interference (RNAi)—an ancient defense mechanism against genetic invaders—by Nobel laureates Andrew Fire and Craig Mello in 1998, it has rapidly become apparent that ~20–30 nucleotide long, small non-protein-coding RNAs act against the dogma to silence their target genes and play critical roles in biological processes as diverse as development, cell proliferation, apoptosis, metabolism, and differentiation. Small RNAs are now extensively used in laboratory research, and are also promising therapeutic agents to specifically shut down disease-causing genes. Importantly, small RNAs by themselves do not catalyze any reactions; they form the effector ribonucleoprotein complex, termed RNA-induced silencing complex (RISC), and guide RISC to the target mRNAs to be silenced in a sequence specific manner.

Among small RNAs, microRNAs (miRNAs) are the best-characterized class of small RNAs encoded in the genome of many eukaryotes. More than 2,000 miRNAs have been identified so far in the human genome, and the number still continues to increase. Inhibition of the miRNA pathway incurs lethality in many organisms, and malfunction of miRNAs leads to severe defects and diseases including cancer. Not only animals and plants but also their viruses encode miRNAs, which likely utilize the host cells’ miRNA machinery and regulate cellular mechanisms to the viruses' own advantage.

miRNAs recognize their target mRNAs mainly via the complementarity of as few as ~7 nucleotides. Accordingly, each miRNA is thought to regulate dozens or hundreds of target mRNAs. Moreover, biogenesis, RISC assembly and functions of miRNAs are also tightly regulated by many cellular factors. Thus, the miRNA pathway forms an enormously complex gene regulatory network, and unraveling of the complete picture is extremely challenging and yet crucial. In this session, we would like discuss some clues toward this ultimate goal by focusing on the host cell-virus crosstalk via the miRNA pathway and dysfunction of miRNA biogenesis in neurodegenerative diseases.