Haruhiko Siomi, Ph.D., is Professor in the Department of Molecular Biology at Keio University of Medicine School in Shinjuku, Tokyo. He earned his Ph.D. from Kyoto University, where he worked in the laboratory of Dr. Masakazu Hatanaka, and then was a Gakushin Postdoctoral Fellow at the Institute of Virology, Kyoto University in the laboratory of Dr. Hisatoshi Shida. From April 1990 through July 1998, he was a Research Associate in the laboratory of Gideon Dreyfuss of the Department of Biochemistry and Biophysics at the University of Pennsylvania in Philadelphia, PA. His research focus is on RNA-based gene regulation, and his laboratory has made fundamental contributions to the understanding of RNA interference/RNA silencing pathways. He is an Editorial Board member of *Nucleic Acids Research* and an Advisory Editorial Board member of *EMBO reports*, and he currently serves on the Board of Directors of the RNA Society, as well as numerous grant review panels, scientific advisory boards, and editorial boards. He is a co-founder of Tokyo RNA Club.

(*if space allowed*)
Research accomplishments:
His laboratory has focused on elucidating how RNAi mechanistically occurs. His early major findings were as follows; a physical association between a fly fragile X protein and AGO2, implicating defects in RNAi in human disease, a division of labour between the Argonautes, and unwinding of siRNA duplex through Slicer activity of AGO2. Then his group identified a new class of small RNAs, 'endogenous siRNAs' in 2008, which function in transposon silencing. Recently, he demonstrated that Argonaute itself is a sensor of small RNA asymmetry *in vivo*, precluding the previous model with Dicer and R2D2 together sensing the asymmetry.

His group has also elucidated piRNA biogenesis in the germline, a process required for transposon silencing and germline development. He identified piRNAs associated with fly PIWI proteins and found that piRNAs are produced in the primary pathway and then they are amplified in the ping-pong cycle. Using a cultured ovarian somatic cell line (OSC) we established, he have identified genes necessary for the primary piRNA production. His group also demonstrated that Zucchini is an endonuclease required for the primary piRNA processing, how antisense bias of piRNAs is enforced and how piRNA precursors are distinguished from other cellular transcripts. Recently, he found that Piwi directs specific histone modifications on transposon loci, thereby silencing transposons.

Monoclonal antibodies and cell lines developed in his laboratory are famous and widely used by many scientists, including his competitors and with whom he always share reagents. His biochemical studies are complemented with genetic studies - his recipe for high quality publications.

Transposon silencing by the Piwi-piRNA pathway

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Mobilization of transposable elements (TEs) can lead to natural insertion mutations that generally have negative effects on the host genome either by disrupting genes or by inducing non-allelic homologous recombination. Thus, our cells have evolved control mechanisms that restrict the TE activity. One such mechanism is RNA silencing, in which small RNAs of 20–30 nucleotides trigger multiple forms of sequence-specific gene silencing. In animal gonads, PIWI-interacting RNAs (piRNAs) are produced from single-stranded long non-coding RNAs that are transcribed from piRNA clusters on the genome. Mature piRNAs are loaded onto PIWI proteins to yield piRISCs and guide the complexes to target RNAs to silence them. piRNAs in the germ cells are amplified by the cytoplasmic ping-pong cycle, in which TE transcripts are consumed as both the source of piRNAs and the targets of PIWI cleavage, thereby repressing TEs in the cytoplasm. Some piRISCs get imported into the nucleus where they induce heterochromatin formation by modifying chromatin to repress target TE loci at transcriptional levels. We have been using cultured cell lines, Drosophila OSC and silk warm BmN4, to elucidate the mechanisms underlying piRNA biogenesis, the ping-pong cycle, and transcriptional repression. Results from these studies will be presented. In addition, we have recently elucidated the molecular structure of Siwi, the Bombyx mori PIWI protein, with piRNA by X-ray crystallography. The structure will also be presented and, based on the structure resolved, the molecular basis of piRISC formation and structural differences between PIWI and AGO proteins will be discussed.