TEMS

Temasek External Monthly Seminar

TEMASEK LIFESCIENCES LABORATORY

ALL ARE WELCOME

23 November 2018 (Friday), 3.00pm
The Auditorium (Level 1)

Hosted by: Ms Lim Yu Theng Mandy

Assembly and function of the RNA silencing complex

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siRNAs and microRNAs mediate posttranscriptional gene silencing of their target mRNAs via formation of the RNA-induced silencing complex (RISC). These small RNAs are born double-stranded and loaded into Argonaute proteins (Ago), the core component of RISC. Subsequently, the two strands of a small RNA duplex are separated and one of them is then discarded from Ago. Intriguingly, the Hsp70/Hsp90 chaperone machinery and their ATP hydrolysis are required for duplex loading—apparently simple binding between the RNA duplex and Ago—but not for strand separation—a process that disrupts ~20 base pairs between the two strands. Accordingly, we envision that the chaperone machinery mediates dynamic conformational changes of Ago so that they can accommodate bulky small RNA duplexes. I would like to discuss such actions of the chaperone machinery as the driving force for RNA silencing, in light of our recent progress in single-molecule imaging of RISC assembly and function.

Recent Publications:

1. Conformational activation of Argonaute by distinct yet coordinated actions of the Hsp70 and Hsp90 chaperone systems.
   Tsuboyama K, *Tadakuma H, *Tomari Y.
   Mol Cell. 2018 May 17;70(4):722-729.e4.
2. The poly(A) tail blocks RDR6 from converting self mRNAs into substrates for gene silencing.
   Baeg K, *Iwakawa HO, *Tomari Y.
   Nat Plants. 2017 Mar 20;3:17036.
3. Identification and functional analysis of the pre-piRNA 3′ Trimmer in silkworms.
   Izumi N, Shoji K, Sakaguchi Y, Honda S, Kirino Y, Suzuki T, Katsuma S, *Tomari Y.
   Cell. 2016 Feb 25;164(5):962-73.

Yukihide Tomari is a Professor and Vice Director at Institute for Quantitative Biosciences, The University of Tokyo. His laboratory is focused on dissecting the molecular mechanism and function of non-coding RNAs by combining biochemistry, biophysics, and cellular and developmental biology.