

Journal club



RNA SILENCING SORTED

When facing the challenge of introducing the basics of RNA silencing to a new student, I often resort to what I call the ‘Hannon trilogy’ — a set of 3 papers, among my all-time favourites, which contain essentially all you need to know to understand how double-stranded (ds) RNA directs the sequence-specific inhibition of gene expression in most eukaryotic cells. The first paper, by Bernstein *et al.*, establishes that dsRNA is processed into small (~ 20 nucleotide) RNAs by an RNase III enzyme called Dicer. The second two papers, both by Hammond *et al.*, show that the small RNAs, following their incorporation into the Argonaute (AGO) nuclease, then guide an RNA-induced silencing complex (RISC) to destroy the complementary mRNA. I sometimes re-read these articles with nostalgia,

“ the ‘Hannon trilogy’ — ...all you need to know to understand how dsRNA directs the sequence-specific inhibition of gene expression ”

as the formidable mechanistic insight they provided at the time signalled the twilight of the ‘romantic phase’ of RNA silencing — the not-so-distant time of my Ph.D. studies, when the many manifestations of RNA silencing that had just been described in various organisms were still mechanistically mysterious, and not necessarily appreciated as being related.

In fact, the transition to the ‘modern phase’ of RNA silencing started with the discovery in plants, by Hamilton and Baulcombe, of what would later be renamed small interfering RNAs (siRNAs). The development of powerful *in vitro* assays and access to genomic information in model organisms, notably in flies, then expedited the identification of the molecular machines that generate siRNAs and execute their functions, an endeavour to which the Hannon group contributed substantially. This, ultimately, greatly facilitated the identification of endogenous

siRNA-like molecules known as microRNAs, which regulate many key aspects of eukaryotic biology.

So, when my students come back to me with sparkling eyes and all sorts of questions, I know that, yet again, the Hannon trilogy has done a great job.

Olivier Voinnet
 Institut de Biologie Moléculaire des
 Plantes du Centre National de la
 Recherche Scientifique,
 Université de Strasbourg,
 12 rue du Général Zimmer,
 67084 Strasbourg cedex,
 France.
 e-mail:
olivier.voinnet@ibmp-ulp.u-strasbg.fr

ORIGINAL RESEARCH PAPERS Bernstein, E. *et al.* Role for a bidentate ribonuclease in the initiation step of RNA interference. *Nature* **409**, 363–366 (2001) | Hammond, S. M. *et al.* An RNA-directed nuclease mediates post-transcriptional gene silencing in *Drosophila* cells. *Nature* **404**, 293–296 (2000) | Hammond, S. M. *et al.* Argonaute 2, a link between genetic and biochemical analyses of RNAi. *Science* **293**, 1146–1150 (2001) | Hamilton, A. J. & Baulcombe, D. C. A species of small antisense RNA in posttranscriptional gene silencing in plants. *Science* **286**, 950–952 (1999)