



RNAi mechanisms in gene regulation and epigenetic memory



My group has investigated the mechanisms underlying RNA interference gene silencing phenomena for 11 years. For this, we leveraged a combination of proteomics, genetics, genomics, and cell-free assays in the celebrated nematode *C. elegans* as an experimental model, but also in a diversity of physiological and cancer mammalian cell lines. Our most recent advances point to a profound impact of the developmental and environmental contexts on the RNAi mechanisms.

My presentation will first reflect on the developmental impact on microRNA-mediated silencing mechanisms. We uncovered how dynamic interactions built sequentially on target mRNAs in the early embryo, and distinct in different cell lineages, tweak the outcome and functions of microRNA-mediated silencing. Secondly, I will present recent results on the linkages of nuclear RNAi with the epigenetic machinery and their regulation. We discovered a novel family of nuclear Argonaute interacting proteins (NIP), composed of paralogs dedicated to somatic and germline tissues. NIP proteins control the availability of nuclear Argonautes by preventing their loading and nuclear translocation. Their stability is in turn regulated by exposure to dsRNA signals, which appear to converge on the Ubiquitin/proteasome machinery. We propose that the NIP proteins tune the potency of somatic and long-term epigenetic memory of RNAi in response to environmental cues.

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Date: Thursday October 26th, 2017
Time: 3PM
Place: MaRS2, Room 1522