RNA-silencing induces target gene relocalization toward a specialized nuage domain

Yuchen Yang[1], David Grunwald[1], James R. Priess[2,3], Craig C. Mello[1,4,5]

1RNA Therapeutics Institute, University of Massachusetts Medical School, Worcester, MA 01605
2Fred Hutchinson Cancer Research Center, Seattle, Washington, United States
3Department of Biology, University of Washington, Seattle, Washington, United States
4Program in Molecular Medicine, University of Massachusetts Medical School, 368 Plantation Street, Worcester, MA, 01605 United States
5Howard Hughes Medical Institute, University of Massachusetts Medical School, Worcester, MA, USA

The authors wish to withdraw this manuscript and apologize for errors in the initial submission. All the original experiments were performed by YY. Unfortunately, JP and members of the Mello lab have not been able to replicate some aspects of the study. JP has failed to independently reproduce the specific results showing RNAi-triggered relocalization of target RNA, and P granule specific accumulation of (the P granule component GLH-1) as reported. The conditions/strains analyzed by JP were as follows: (1) *oma-1* FISH on WT worms [control, 6 hr and 12 hr *oma-1(RNAi)*]. (2) *oma-1* FISH on OMA-1:GFP worms [control, 6 hr oma-1(RNAi), or 6 hr gfp(RNAi)]. (3) *oma-1* FISH on WT worms [control, 4hr, 6hr, 8 hr, and 10 hr *oma-1(RNAi)*]. 10-23 gonads were analyzed per experiment. Fixation conditions were essentially as described, with the only known difference being that gonads were not exposed to detergent prior to fixation. Using YYs reagents and protocol the Mello lab has not observed an obvious relocalization of target RNA to P granules (marked by GFP::GLH-1) after 6 hrs *oma-1(RNAi);* n=92 gonads. CM, JP and DG consider that the published images accurately represent the image stacks provided by YY as representative, raw data, but JP and CM note configurations of FISH signals in germ nuclei and gonad anatomy that they consider unusual. CM, JP and DG have not detected any evidence of image manipulation.

YY states that none of the raw image data were manipulated beyond standard adjustments for brightness and contrast prior to processing images for publication as described. However, YY reports that the images were not representative of the majority of sample gonads, and instead were pre-selected under low magnification for rare examples with asymmetrical, expanded P granules.

Efforts to identify conditions that explain the rare gonads imaged by YY continue in the Mello lab, as do efforts to reproduce independently each of the other reported results; we plan to provide an update in the near future.