Argonaute's distribution in protrusional structures reveals its implementation in intercellular trafficking and in cell segregation.

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Argonaute (AGO) proteins are at the hub of all the fundamental complexes in RNA bioprocesses. They play a key role in gene regulation through silencing, by guiding translational repression, in a post-transcriptional level. In the canonical RNAi pathway, AGO2 functions as the catalytic enzyme that cleaves mRNA-targets through miRNA-loading whilst AGO3 has a recently uncovered, complicated, and selective slicer activity regarding its substrates. AGO2 is compartmentalized into structures such as GW- and P-bodies, stress granules and adherens junctions as well as the midbody. Here we show using immunofluorescence, image- and bioinformatic analysis and cytogenetics that AGO2 also resides in membrane protrusions such as open- and close-ended tubes. The latter are cytokinetic bridges where AGO2 colocalizes at the midbody-arms with cytoskeletal components such as α-Tubulin and Aurora B, and various kinases. AGO2, phosphorylated on serine 387 is located together with Dicer at the midbody ring in a manner dependent on p38 MAPK activity. We further show that AGO2 is stress sensitive and important to ensure the proper chromosome segregation and cytokinetic fidelity. We suggest that AGO2 is part of a regulatory mechanism triggered by cytokinetic stress to generate the appropriate micro-environment for local transcript homeostasis.