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Functional characterization of the conservative protein CG17337 in *Drosophila melanogaster*

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Motivation and Aim: Eukaryotic peptidases play an important role in protein and peptide metabolism. Currently, close attention is being paid to the human *CNDP2* gene encoding a protein of metallopeptidase M20 family. The CNDP2 is a tumor suppressor protein; changes of its expression level stimulate cell proliferation and are used as a biomarker of cancer. Our aim was to clarify the function of drosophila *CG17337* gene, which is the ortholog of *CNDP2,* at the level of cells and whole organism.
Methods and Algorithms: First, we have raised polyclonal antibodies specific to CG17337, which allowed us to visualize this protein in drosophila tissues and cultured cells by confocal microscopy. Second, using CRISPR/Cas9-mediated homologous recombination, we generated null mutant of the *CG17337* gene. The *CG17337* null-mutation was checked by genotyping PCR, DNA sequencing and Western Blot analysis. Also, we generated transgenic flies carrying genomic copy of the *CG17337* gene for rescue experiments. We estimated influence of the *CG17337* null-mutation on cell cycle in different tissues as well as on the lifespan of drosophila.
Results: We provide first insights on the role of the CG17337 protein in drosophila. First, we found that CG17337 is not only extracellular protein as was reported earlier [1], but also plays a role both in the cytoplasm and nucleus (chromatin). Particularly, we found CG17337 in a co-immunoprecipitation assay as a putative interactor partner of the SUUR (Suppressor of Underreplication) protein in embryonic nuclear extracts. The nuclear localization and chromatin association of CG17337 was observed in cell cycle-dependent manner. We determined by Fly-FUCCI approach that the CG17337 protein is enriched in G2 cells. Second, we have shown that depletion/lack of CG17337 in cultured S2 cells or in drosophila tissues leads to changes in mitotic cell cycle, whereas endocycle is not affected. Finally, the *CG17337* is a dominant and haploinsufficient gene. The obtained null-mutation appeared to be homozygous viable and is characterized by an elongated female lifespan. Unexpectedly we found that females null mutant for the *CG17337* gene display a prolonged period of fertility probably due to suppression of cell death in middle oogenesis during senescence.
Conclusion: Altogether, our results indicate that the drosophila CG17337 protein is necessary for proper mitotic cell cycle progression and cell death control.
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References

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