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Transcriptome analysis of *Trl* mutants reveals the role of mitochondria in the mass death of germ cells

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Drosophila protein GAGA encoded by the *Trithorax-like (Trl)* gene is a factor of epigenetic transcription regulation of a large group of genes with a wide variety of cellular functions. In our previous works, we showed that this protein is necessary for the development of the reproductive system of *Drosophila* males. Decreased expression of the *Trl* gene in mutants induces autophagic death of spermatocytes. Previously we performed a detailed cytological analysis of *Trl* mutant's testes and revealed, in addition to autophagosomes and lysosomes, many abnormal mitochondria. We hypothesized that cell death in spermatogenesis may be associated with the mitochondrial pathologies. To test this hypothesis, we analyzed the RNA-seq data of testes from flies carrying a combination of the null allele $Trl^{R85}$and the hypomorphic mutation Trl^{362}. We revealed that *Trl* knockdown affects the expression of a large number of genes in the testes. The expression of about 2.5 thousand genes changes more than twofold. However, we did not identify anyone particular pathway whose activation could lead to germ cells death in the Trl^{R85} / Trl^{362} mutants. Whereas many genes related to mitochondrial structure and function change expression in GAGA deficient testes, 19 of them also affect cell death. Of the 778 genes belonging to the Flybase GO "mitochondrion" term (GO:0005739), 267 genes changed expression significantly: 123 increased expression, with 35 being upregulated twofold or more, and 144 downregulated, 13 of them downregulated 2 or more times. Of these, Buffy, Mdh2, Rab32, park, CG14118, and Hsp60C genes changed expression the most.

Thus, as a result of RNA-Seq data analysis, we concluded that the mass germ cells death is a consequence of mitochondrial abnormalities that may arise due to misregulation of GAGA target genes responsible for the structure and function of these organelles.

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