beneficial. This beneficial effect can be explained by the extensive size of the surviving sub-population in the high heterogeneous population. Evolutionary experiments were carried out in the presence of the antifungal agent, fluconazole. The ancestral strains were cultivated in parallel cultures in 96 well plates. 10^5 cells were serial transferred into fresh medium in the adaptation experiment using constant level of fluconazole. In contrary, 10^7 cells were serial transferred in the adaptation experiment using gradually increasing level of fluconazole.

After 100 generations, there was no difference in the evolutionary adaptation rate of the different heterogeneous strains, which suggests a heterogeneity-independent adaptation. The high heterogeneity provides advantage when the population faces a higher selective pressure: the survival subpopulation is greater which provides increased chance of accumulation of beneficial mutations. The bistable system remained the same after the evolutionary experiment; therefore, the acquired resistance of HH strain is presumably caused by adaptive beneficial mutations.

We suggest that these beneficial mutations interact with the synthetic construct. The mean expression did not change, but the coefficient of variation increased after 100 generations. For the first time, our results provide experimental evidence that phenotypic heterogeneity of an isogenic population can contribute to adaptive advantage under high level of stress. In sharp contrast, under low level of stress this enormous advantage vanished.

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The role of ATAC histone acetyltransferase complex on steroidogenic gene expression

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The *Sf-1* (steroidogenic factor 1) plays an important role in steroidogenic gene expression and also in the adrenogonadal development. *Sf-1* and similarly its *Drosophila* orthologue the *ftz-f1* transcription factor belongs to the nuclear hormone receptor family. The transcriptional activity of *Sf-1/ftz-f1* is controlled by posttranslational modifications. Phosphorylation at Ser203 and acetylation by GCN5 and p300 enhance *Sf-1* function.

The *Sf-1* shows tissue specific expression (adrenal cortex, testis, ovary, hypophysis, ventromedial hipothalamus, skin and spleen) and its mutation, absence or in some cases, overexpression can lead to tumor formation.

Recently we have reported that the lack-of-function mutations of the GCN5 histone acetyltransferase (HAT)-containing ATAC complex influence steroid biosynthesis. In contrast, the lack of the other GCN5-containing HAT complex, SAGA has only mild effect on steroid biosynthesis. The mechanism by which ATAC affects steroid synthesis, however, remains to be discerned. The two most probable scenarios could be that ATAC influences the transcription of genes involved in steroid hormone biosynthesis directly by histone acetylation at their promoters, or that it acetylates FTZ-F1/SF1 and by this regulates the transcription of steroid converting gene indirectly.

We demonstrated that *Halloween* gene expression is detectable and modified by protein acetylation in S2 insect cells. We found that the stability of FTZ-F1 was increased after treatment of TSA (histone deacetylase inhibitor). Furthermore, we established that the overexpression of *ftz-f1* significantly increases the expression of *Halloween* genes in the *Drosophila* S2 embryonic cell line.

We performed chromatin immunoprecipitation experiments to answer whether histone acetylation has a role in steroid hormone biosynthesis. We found that H4K5 acetylation can be observed at the regulatory regions of *disembodied (dib)* and *shade (shd) Halloween* genes, while we did not detect H3K9 acetylation at any regions of these genes. In contrast to that, H3K9 acetylation can be observed at the initiator region of the mammalian *Cyp11a1* gene, while H4K5 acetylation can be detected at its promoter and initiator regions.

Based on our findings we conclude that the ATAC HAT complex plays a role in *Drosophila* steroid hormone biosynthesis through histone acetylation. To provide further proofs to this conclusion we continue our studies with the aim to detect the presence of the ATAC complex at the regulatory regions of the *Cyp11a1* gene.

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