Resveratrol as a probing molecule to interfere with signaling pathways controlling *Aedes aegypti* lifespan.

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Knowledge of central metabolic and signaling pathways may reveal new targets for *Aedes aegypti* longevity regulation, the major vector of Dengue. As polyphenols are known to enhance longevity in all animals studied, similar to calorie restriction effects, and mosquitoes also uptake resveratrol when fed on sugar we are currently identifying the mecanism of action of these substances on mosquito diet in order to block these mecanisms and make *A. aegypti* live less. The survival of two resveratrol-fed strains of *A. Aegypti* (Liverpool and Red Eye) increased up to 50% in males and 35% in females. The survival of *Anopheles aquas*alis was also improved but with a different profile. The most important bacterial population isolated from *A. Aegypti* midgut wasn't affected by resveratrol *in vitro*. Other important pathogenic microorganism didn't have their population size changed, excluding an effect based on microorganism control. The insulin signaling pathway was affected as we observed an increase on the activity of an acid tyrosine phosphatase homologous to mammalian PTP1B. The effect in this activity was more pronounced when reveratrol was offered by only 24h, and this effect was age-dependent. It suggests the possibility that resveratrol act in this pathway through a new intermediate molecule. Phosphotyrosine blotting has shown significant differences between control and resveratrol fed mosquitoes in agreement with the phosphatase activity results. This effect is organ-specific and suggests a hormonal-mediated signaling. Corroborating the xenormesis hypothesis, the PFK activity increased when resveratrol was previously fed on mosquitoes which were next exposed to a calorie restriction diet, suggesting another way of action. Total protein kinase activity assayed as AMPK was increased in male heads, although weight differences weren't detected. The phosphorylation profile assayed as AMPK of heads from old males was reverted to a profile close to that found in younger insects. It's in agreement with the repressed development hypothesis.

Supported by FAPERJ/CNPq/WHO/IFS.

Keywords: Resveratrol/Longevity/*Aedes*/Metabolism