

## TRADE-OFFS ASSOCIATED WITH THE DROSOPHILA LONGEVITY MUTANT, METHUSELAH

R. J. Mockett (P) and R. S. Sohal

Department of Molecular Pharmacology and Toxicology, University of Southern California, 1985 Zonal Avenue, Los Angeles, CA 90033

A variety of single gene mutations have been shown to extend the life span of *Drosophila melanogaster* under laboratory conditions, but it remains unknown whether the mutant flies would be sufficiently hardy to thrive in the wild. The hypothesis tested in this study was that a hypomorphic mutation at the *methuselah* (*mth*) locus, which has been reported to extend the life span by approximately 35% (Lin *et al.*, Science 282: 943-946, 1998), may have pleiotropic effects on other components of fitness. Life span studies were conducted under various conditions, and metabolic rates, locomotor activity and reproductive output were compared between homozygous *mth* mutant flies and *w*<sup>1118</sup> parental controls. The life spans of male *mth* flies were extended at 29°C and 25°C, and females exhibited increased longevity at 29°C, but the magnitude of these effects was only about half of the previously reported value. The effect of *mth* on the life span of male flies diminished with decreasing temperature, becoming neutral at 18°C and deleterious at 4°C, but *mth* had no significant effect on the life span of female flies at any temperature other than 29°C. Thus, the effects of *mth* on survivorship were temperature-dependent and sex-specific. There were no differences in rates of oxygen consumption between the two genotypes at 25°C, but both male and female *mth* mutants exhibited significantly greater locomotor activity than *w*<sup>1118</sup> controls. In contrast, the lifetime reproductive output of *mth* mutants was decreased by 23-35% at 29°C. This effect diminished or was reversed at lower temperatures. Thus, the reproductive output was diminished under warm conditions associated with increased survival times, and the resistance of *mth* mutants to cold stress was decreased. Collectively, the results suggest that the *mth* allele may not confer a competitive advantage under natural conditions.