Potential Treatment on SCA3/MJD Drosophila Models and patients

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We used several SCA3/MJD *Drosophila* models through which we determined that heat shock protein 22 (Hsp22), lithium chloride, and valproic acid (VPA) are potential therapeutic agents for the treatment of SCA3/MJD. Hsp22, a member of the small heat shock protein (sHsp) family, plays a significant role as chaperone. In the SCA3 *Drosophila* model, expression of the MJDtr-Q78 transgene—containing an expanded polyglutamine tract—showed a greater loss of cell integrity, and the pigmentation of adult flies was faded and showed black, point-like necrosis. Findings showed that Hsp22 expression impacted eye depigmentation, growth restriction, ability for eclosion, and average lifespan. We examined the effect of VPA and Li chloride (LiCl) in a *Drosophila* SCA3 model. We expressed the MJDtr-Q78 transgene both in the developing eyes and in neurons. Expression of the MJDtr-Q78 protein produced deleterious phenotypes including faded eye pigmentation, impaired climbing ability, and decreased mean lifespan, similar to the characteristics of human SCA3. To test the therapeutic potential of VPA and LiCl in vivo, a series of daily doses of VPA as well as LiCl were administered to SCA3 flies before cross-breeding. Results showed that long-term use of VPA and LiCl at an optimal dose partly prevented eye depigmentation, alleviated climbing disability, and extended the average lifespan of SCA3/MJD transgenic flies. Additionally, we performed a randomized, double-blind, placebo-controlled, dose-controlled study evaluated the safety and efficacy of multi-dose VPA in 36 SCA3/MJD patients and found VPA is a potentially beneficial agent for the treatment of SCA3/MJD.