Reverse Testing Chemotherapies on Drosophila Models to Determine Protein-Kinase Pathways Affected by Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a cardiovascular disease that triggers sudden cardiac arrest in people of all ages. We conducted tests with six chemotherapy drugs that reinforced separate protein-kinase pathways to determine which pathways are affected by HCM. Each chemotherapy drug was mixed into the fly food at three varying molarities and tested on Drosophila models with induced HCM. Two separate models, GMR-GAL4 and MS1096, were used to ensure higher accuracy in the results. Both crosses, listed above, had offspring (G1) with induced HCM that would die in the pupae stage. The HCM gene in G1 is also linked to observable phenotypes to ensure that the HCM gene was carried through. The success of various chemotherapies was measured by taking the percentage of G1 flies that survived the pupae stage without deformities over the total number of pupae. Results showed various stages of success with all six drugs, but the most successful drug was Sorafenib, followed by Sunitinib and Dasatinib. These three were the only drugs that resulted in G1 flies without deformities. The high level of success with the Sorafenib chemotherapy in this study indicates a positive correlation between HCM and deformities in the RAF/MEK/ERK protein-kinase pathways, and the success with Sunitinib and Dasatinib suggests HCM may also affect MAP/Tyrosine and SRC/ABL pathways, respectively. The study inspires opportunities to develop specialized drugs targeting the MAP/Tyrosine, RAF/MEK/ERK, and SRC/ABL pathways to diagnose and treat HCM in patients.

Awards Won:

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