Drug Testing Chemotherapies to Identify Kinase Pathways Affected by Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a common heart disease that causes sudden cardiac arrest in people of all ages. In this research, we tested 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 different molarities and then tested on fruit fly models with induced HCM. The crosses to induce HCM in the offspring of the flies were made up of dRAF males, which provided the type of mutation (HCM), and GMR females, which provided where the mutation would occur (the heart). When a homozygous dRAF male is crossed with a female GMR, the offspring (G1) have HCM that is triggered in the pupae stage, causing the flies to die as pupae. The success of various chemotherapies was measured by taking the percentage of G1 flies that survived the pupae stage without deformities (curly wings) over the total number of pupae. Results showed various stages of success with all six drugs, but the most successful drug was Sunitinib, followed by Dasatinib and Rapamycin. These three were the only drugs that resulted in G1 flies without deformities. The success with the Sunitinib, Dasatinib, and Rapamycin chemotherapies in this study indicates that there is a positive correlation between HCM and deformities in the MAP, SRC/ABL, and mTOR protein-kinase pathways, as those are the pathways affected by Sunitinib, Dasatinib, and Rapamycin respectively. This study opens new research opportunities to develop new diagnostic tests and specialized drugs targeting the MAP, SRC/ABL, and mTOR pathways to identify and treat HCM in patients.

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