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Repetitious elements constitute a major portion of eukaryotic genomes. Silencing mechanisms are required to recognize and prevent their expression in cells. Silencing of repetitious elements can be achieved by formation of heterochromatin. To study this mechanism we utilized a transgenic construct containing 256 copies of a 36 bp *lac Operon* fragment placed upstream of an *hsp70-white* reporter, inserted into the *Drosophila melanogaster* genome. In *Drosophila*, expression of the *white* gene results in a red eye phenotype; sporadic silencing of this gene following juxtaposition with heterochromatin results in a patchy red eye phenotype referred to as Position Effect Variegation (PEV). Previous studies from the Elgin laboratory have shown that insertion of the *lacO-hsp70-white* transgene at the base of chromosome arm 2L results in strong silencing, sensitive to HP1 depletion, indicating heterochromatin packaging. A genetic screen suggested that the *lacO-hsp70-white* PEV phenotype is sensitive to mutations in genes coding for histone deacetylases (HDACs). These results led us to test several small molecule HDAC inhibitors (HDACIs), including novel HDACIs designed and synthetized by the Marshall laboratory (Biochemistry Dept, Washington University). An initial test of 12 potent human HDACIs, with diverse selectivity profiles for the ~10 HDACs present (Apicidin, Entinostat, Panobinostat, PCI-34051, SAHA, Scriptaid, Largazole, SD-L-256, Trichostatin A, Tubastatin A, T247, and Compound 4), performed on the *Drosophila* reporter line showed that the selected drugs did not cause any detrimental effects on fly development, with the exception of SAHA at its maximum concentration. We selected HDAC3 and HDAC6 inhibitors, compounds SD-L-256, Largazole, 6q, and 4l (Marshall lab, unpublished) for a second, more precise drug screen with optimized drug concentrations and fly population densities. Results from this screen suggest that selective inhibition of HDAC3 or HDAC6 differentially affects suppression of *lacO-hsp70-white* silencing. In the future, more detailed investigation is needed to fully characterize the process.