Histone deacetylases (HDACs) are proteins involved in the regulation of gene expression through the modulation of chromatin accessibility. Dysregulation of normal histone deacetylation within a cell results in aberrant transcriptional programs, which can contribute to cancer initiation and progression. The contribution of HDAC activity in cancer has become increasingly appreciated over the past decade, and the development of HDAC inhibitors (HDACi) like vorinostat has shown promise in the clinic against a variety of blood cancers. Although HDACi has been found to induce cancer cell differentiation, cell cycle arrest and apoptosis through the re-wiring of transcriptional programs, the non-transcriptional effects of HDACi remain poorly understood. Recent evidence has suggested that HDACi induces genome instability in cancer cells, although the detailed mechanisms remain unclear. The current project aims to investigate the effects of HDACi on genome integrity by using standard molecular biology techniques to monitor DNA damage accumulation and DNA damage response (DDR) pathway activation in cancer cells, and a genome-wide CRISPR screen to identify genes that sensitize cancer cells to HDACi treatment. Ultimately, this research will provide new knowledge on the mechanisms leading to HDAC inhibition toxicity and should uncover new therapeutic avenues that could improve current treatments and prognosis.

Themes:

Check (highlight) the most applicable theme according to the abstract.

| Innovation and Technology | Health and Wellness | Culture and Society | Sustainability and Conservation |

Comments: Well-written primer with good explanations on complex gene regulation processes. Consider elaborating on the more technical aspects for those outside the field. All the best at MURC!