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Investigating the Role of Bromodomain Proteins on Histone Post-Translational Modifications in Toxoplasma gondii

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Honors Thesis

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1. Abstract

Toxoplasma gondii is a prevalent pathogenic parasite that infects approximately 25 percent of the US population. For the parasite to successfully establish and maintain infection in its host, properly controlled regulation of gene expression is critical. One way *Toxoplasma* regulates gene expression is through modification of histone proteins that bind to DNA and can control gene accessibility. Acetylation is a modification that is added to histones that changes chromatin structure to enhance gene activation. Histone acetylation can also regulate gene expression by recruitment of important regulators such as bromodomain proteins (BDP). A previous study showed that loss of the bromodomain protein TgBDP1 leads to total dysregulation of parasite gene expression, implying that TgBDP1 plays an essential role in genetic regulation of the parasite. The direct role of TgBDP1 is unknown, but based on the protein complex TgBDP1 associates with, we hypothesize TgBDP1 is recruited to specific acetylation marks on histones before depositing additional marks on those histones to influence gene expression. To determine if loss of TgBDP1 affects histone modifications, we cultured two parasite lines; one with TgBDP1 intact and one with TgBDP1 inactivated via gene knockdown. Western blotting to detect and quantify different histone marks was performed. In parallel, the samples will be submitted for global proteomic analysis to precisely quantify levels of individual histone marks. With this data, I will determine how TgBDP1 influences gene expression by altering histone modifications. This will provide insight to TgBDP1's potential as a drug target for treatment of this prevalent disease.