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YOU ARE INVITED TO ATTEND THE

DEFENSE OF THE DOCTORAL

DISSERTATION

"Oxoglutarate dehydrogenase and acetyl-CoA acyltransferase 2 occupy H2A.Z-bound transcriptional start sites and are required for histone modifications"

by

Sujung Choi

Infection, Immunity and Inflammation Track

B.S., 2010, Stony Brook University, Stony Brook, NY
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Tuesday, June 25th, 2019
1:00 P.M.
MSB G-609

ABSTRACT

Histone H2A.Z plays an essential role in regulating transcriptional rates and memory. Interestingly, H2A.Z-bound nucleosomes are located in both transcriptionally active and inactive promotors, with no clear understanding of the mechanisms via which it differentially regulates transcription. We hypothesized that its functions are mediated through recruitment of regulatory proteins to promoters. Using rapid chromatin immunoprecipitation-mass spectrometry, we uncovered the association of H2A.Z-bound chromatin with the metabolic enzymes, oxoglutarate dehydrogenase (OGDH) and acetyl-CoA acyltransferase 2 (ACAA2). Recombinant green florescence fusion proteins, combined with mutations of predicted nuclear localization signals, confirmed their nuclear localization and chromatin binding. Conclusively, chromatin immunoprecipitation-deep sequencing, confirmed the predominant association of OGDH and ACAA2 with H2A.Z-occupied transcription start sites, the former of which we confirmed is conserved in both mouse and human tissue. Furthermore, H2A.Z-deficient human HAP1 cells exhibited reduced chromatin-bound metabolic enzymes, accompanied with reduced posttranslational histone modifications, including acetylation and succinylation. Specifically, knockdown of OGDH diminished H4 succinylation. Thus, the data reveal that select metabolic enzymes are assembled at active, H2A.Z-bound, promoters, for potential site-directed production of metabolic intermediates that are required for histone modifications.