Exploring Changes in Histone Post-translational Modifications Linked to the Rnq1 Prion

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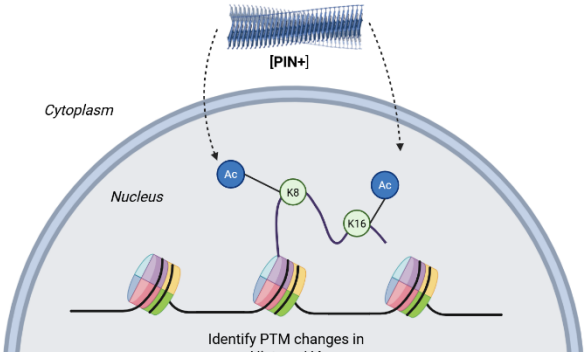
Abstract: Epigenetics is the study of heritable information not encoded by DNA. One mechanism of epigenetics involves the post-translational modification (PTMs) of histones in chromatin. Chromatin is the DNA-histone protein complex that makes up chromosomes. The N-terminal tails of the histones bear PTMs which can promote or repress transcription. [1]



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Yeast prions, which are self-replicating, amyloid protein conformations, can result in advantageous phenotypes, such as prolonged life span or a thicker cell wall. These yeast prion states transmit through the cytoplasm from mother to daughter cells, enabling heritable phenotypic changes without altering DNA sequence, akin to an epigenetic mechanism. However, it is not known how some prions lead to changes in phenotype. Unraveling the mechanisms of yeast prions as a model for non-genetic inheritance can lead to new knowledge regarding how yeast cells can adapt to their environment.[1]

Rnq1 is a yeast protein whose prion form, [PIN+], induces the formation of other prions. Puzzlingly, the function of Rnq1 in its native function is not known. Unlike most yeast prions, [PIN+] is commonly found in yeast. This suggests that [PIN+] is beneficial to yeast, but the mechanism by which it functions in yeast is not properly explored. Preliminary data linked [PIN+] to decreases in H3 PTMs such as H3K36me3 compared to the non-prion state [pin-]. In addition, there is an increase in RNA levels in [PIN+] compared to [pin-], thus linking [PIN+] to canonical epigenetic channels.[2]

Puzzlingly, H3K36me3 is enriched in transcription start sites and recruits transcription factors, and thus reduction in the levels of H3K36me3 in the presence of [PIN+] indicates that [PIN+] promotes the repression of gene transcription. However, the increase in RNA levels in [PIN+] compared to [pin-] suggests otherwise. One possibility for conflicting data is that PTMs in other histones, such as H4, are impacted by [PIN+]. We investigated whether the [PIN+] state connects to histones H4K16ac H4K8ac and H4K20me3 through immunoblotting and found no changes compared to the nonprion state [pin-]. We plan to investigate the levels of histone PTMs beyond histone H4, such as histone H2B to identify one of the unknown mechanisms of yeast prions as a model for non-genetic inheritance.

References

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