Abstract

Lipid metabolism has been implicated in changes of chromatin modifications resulting in altered gene expression. Such regulation is important for cellular differentiation or cancer progression, however, the mechanism of how altered metabolic flux leads to targeted changes in chromatin modifications which then regulate gene transcription or heterochromatin maintenance is still poorly understood. We describe that fission yeast cells defective in fatty acid synthesis show increased expression of a subset of stress-response genes. This altered gene expression depends on the SAGA and NuA4 histone acetyltransferases and is associated with increased acetylation of histone H3 at lysine 9 in the corresponding gene promoters. Moreover, diminished fatty acid synthesis results in increased cellular resistance to oxidative stress. Additionally, the lipid metabolism mutants display chromatin alterations in centromeres and subtelomeres, regions of constitutive heterochromatin. We propose that changes in lipid metabolism can regulate histone acetylation and transcription of specific stress-response genes, but also lead to more global changes in heterochromatin. And while we clearly see the consequences of increased stress-response genes which result in promoting redox homeostasis, the implications of altered heterochromatin upon fatty acid synthesis perturbation are less evident. We also show that the nitrogen signaling affects mitotic fidelity and lipid metabolism in the fission yeast, but further experiments are required to determine whether increased fatty acid synthesis is actually the cause of mitotic defects rescue as observed in *cbf11Δ* cells and other cell-untimely-torn mutants in nitrogen-rich conditions. Overall, we have elucidated how fatty acid synthesis contributes to the regulation of chromatin modifications, maintenance of genome integrity, and oxidative stress resistance.

Key words: lipid metabolism, histone acetylation, stress resistance, subtelomeric heterochromatin