Distinct amino acids of histone H3 control secondary metabolism in *Aspergillus nidulans*.

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Abstract

Chromatin remodelling events play an important role in the secondary metabolism of filamentous fungi. Previously, we showed that a bacterium, Streptomyces rapamycinicus, is able to reprogram the histone-modifying Spt-Ada-Gcn5-acetyltransferase/ADA (SAGA/ADA) complex of the model fungus Aspergillus nidulans. Consequently, the histone H3 amino acids lysine 9 and lysine 14 at distinct secondary metabolism genes were specifically acetylated during the bacterial fungal interaction, which, furthermore, was associated with the activation of the otherwise silent orsellinic acid gene cluster. To investigate the importance of the histone modifications for distinct gene expression profiles in fungal secondary metabolism, we exchanged several amino acids of histone H3 of A. nidulans. These amino acids included lysine residues 9, 14, 18, and 23 as well as serine 10 and threonine 11. Lysine residues were replaced by arginine or glutamine residues, and serine/threonine residues were replaced by alanine. All generated mutant strains were viable, allowing direct analysis of the consequences of missing posttranslational histone modifications. In the mutant strains, major changes in the expression patterns at both the transcriptional and

metabolite levels of the penicillin, sterigmatocystin, and orsellinic acid biosynthesis gene clusters were detected. These effects were due mainly to the substitution of the acetylatable lysine 14 of histone H3 and were enhanced in a lysine 14/lysine 9 double mutant of histone H3. Taken together, our findings show a causal linkage between the acetylation of lysine residue 14 of histone H3 and the transcription and product formation of secondary metabolite gene clusters.

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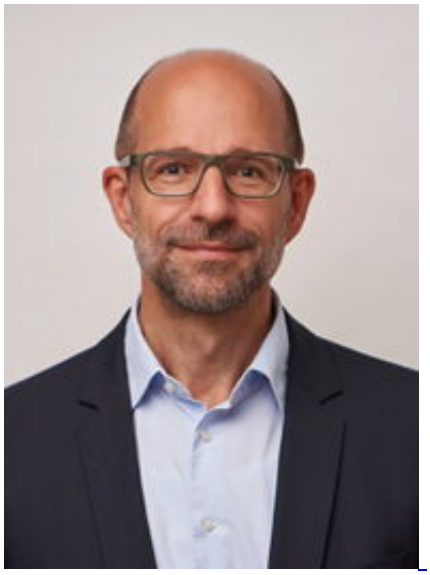
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