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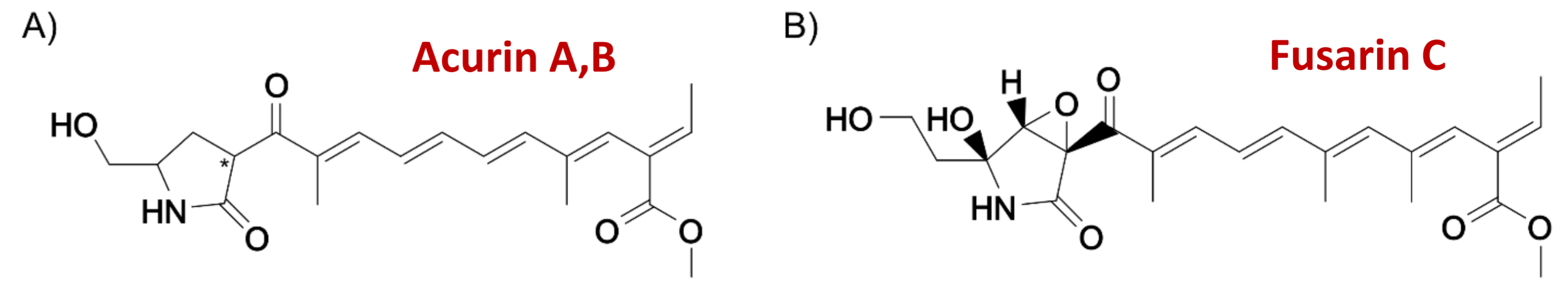
# Biosynthesis of acurin A and B in *Aspergillus aculeatus*



Maria L. Nielsen†, Peter P. Wolff†, Lene M. Petersen, Lasse N. Andersen, Thomas Isbrandt, Dorte K. Holm, Uffe H. Mortensen, Christina S. Nødvig, Thomas O. Larsen, Jakob B. Hoof\*

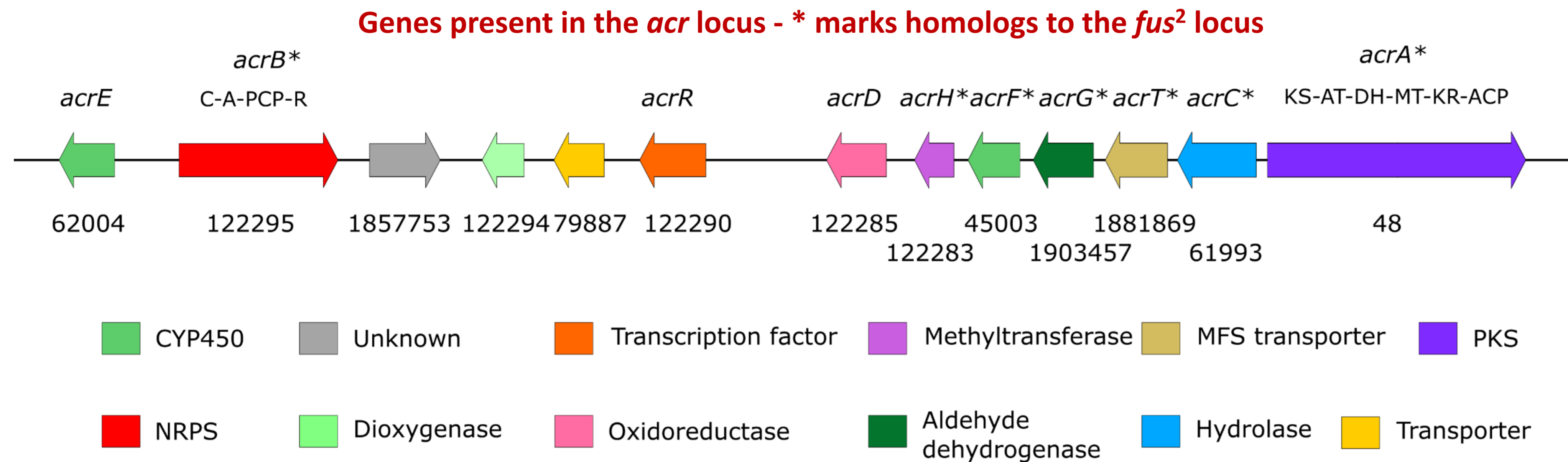
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*Aspergillus aculeatus* is known for the commercial utilization in production of several enzymes. We have identified two stereoisomeric compounds of mixed polyketide-nonribosomal peptide (PK-NRP) origin in the extracts of *A. aculeatus* that we named acurin A and acurin B. Acurin resembles fusarin C, although without the epoxide. CRISPR-Cas9<sup>1</sup> was used to generate an *akuAD* strain (Ku70<sup>-</sup>) facilitating strain construction.

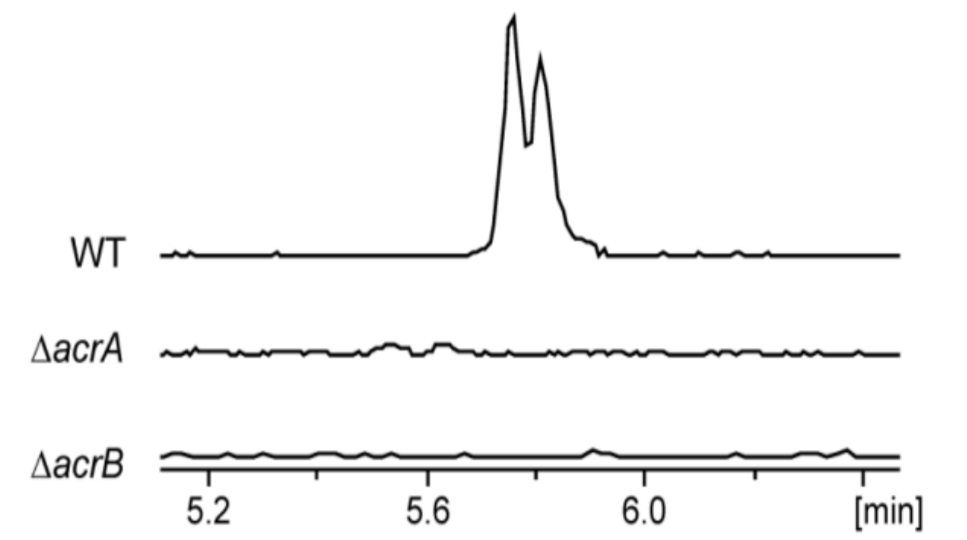


INTRODUCTION

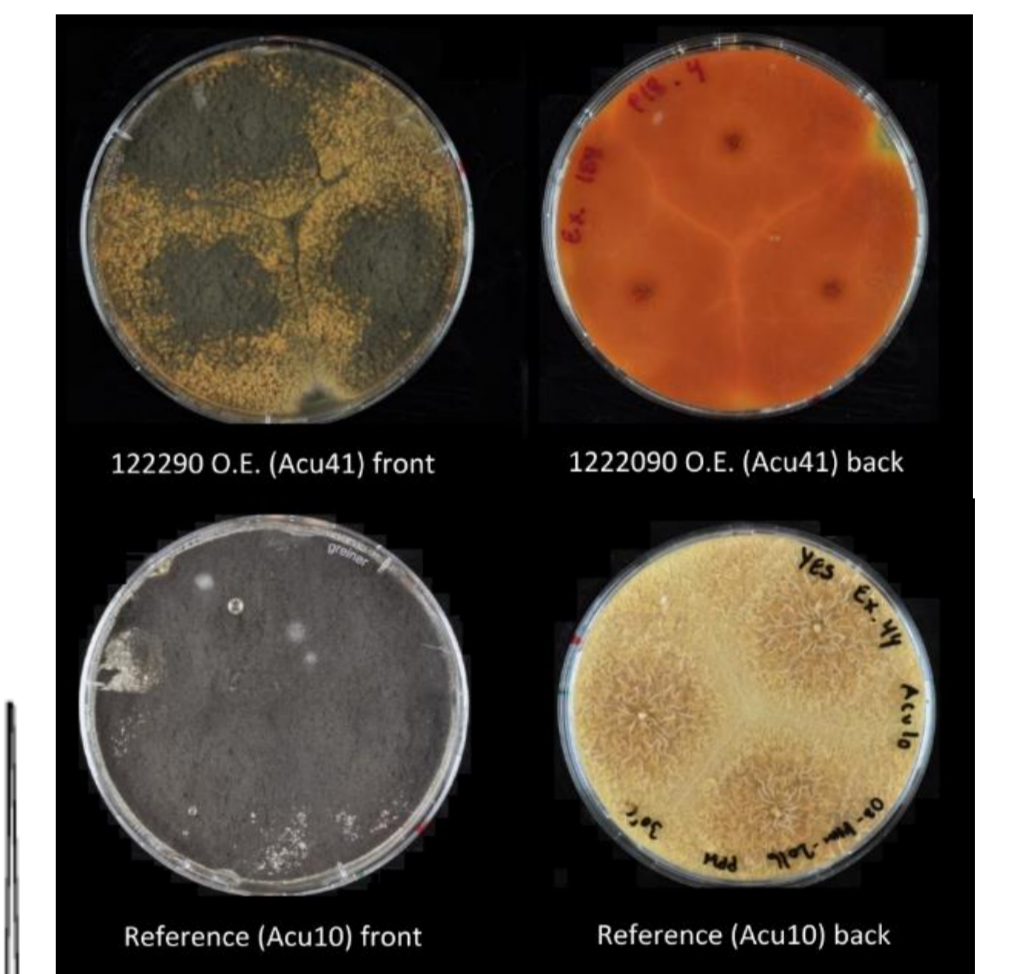
DISCOVERY OF THE ACURIN GENE CLUSTER



**Chemical analysis of deletion strains of the PKS and NRPS in *acr* locus**

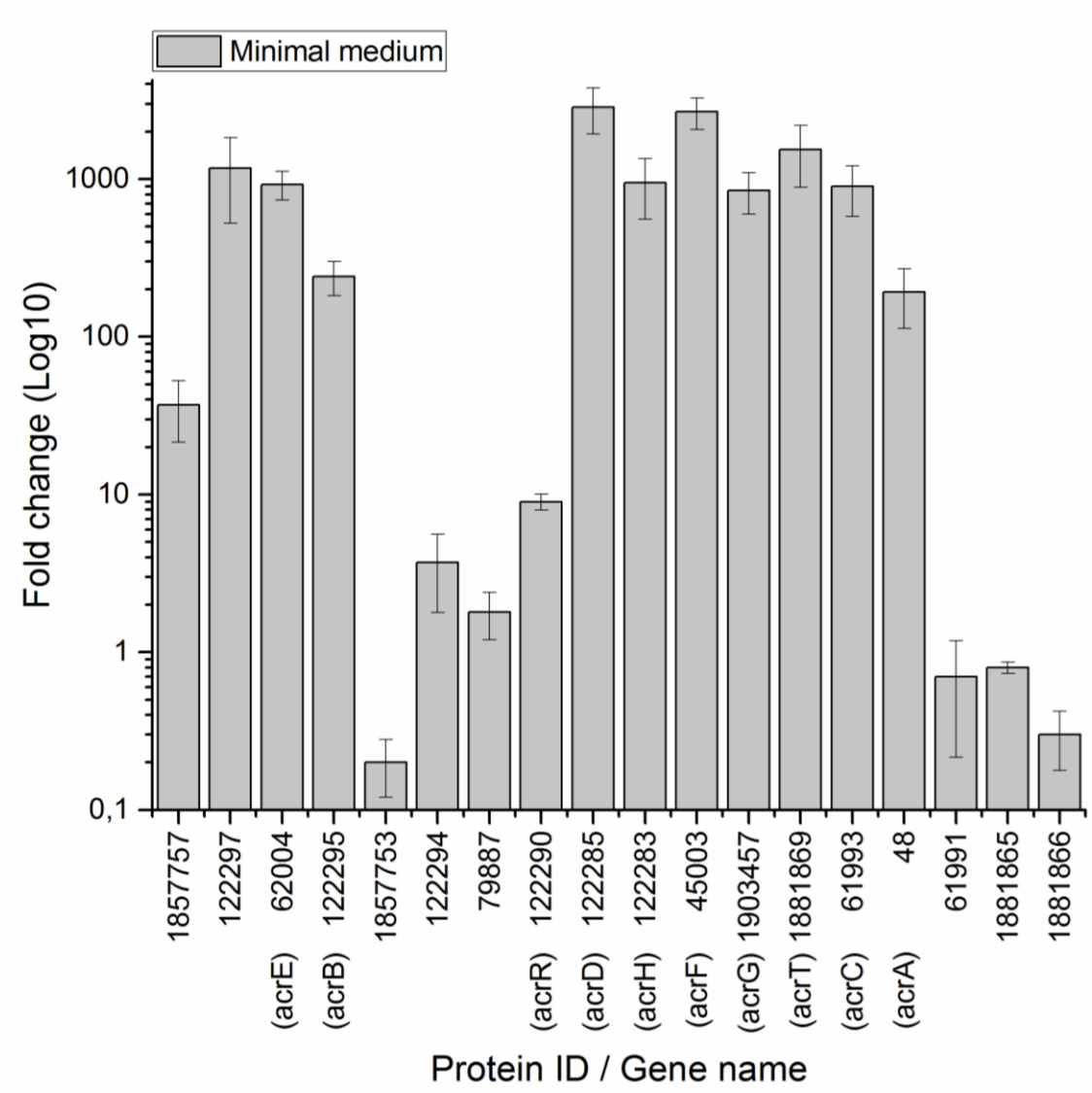


**Global effects**

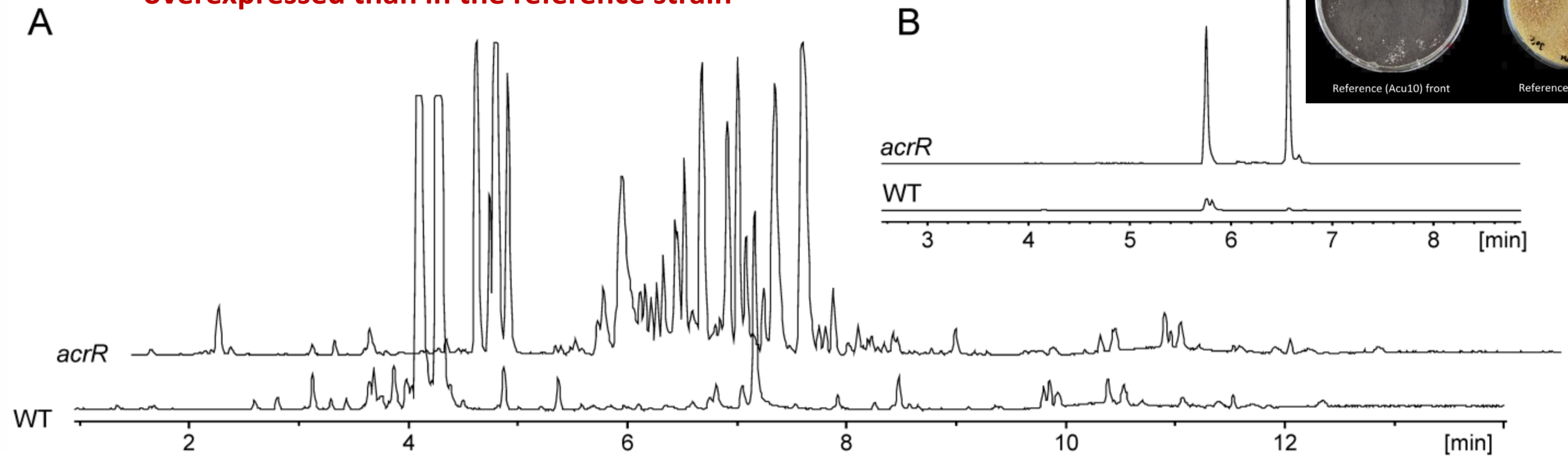


ACURIN TRANSCRIPTIONAL REGULATOR

**RT-qPCR showed local *acr* regulation by *AcrR***

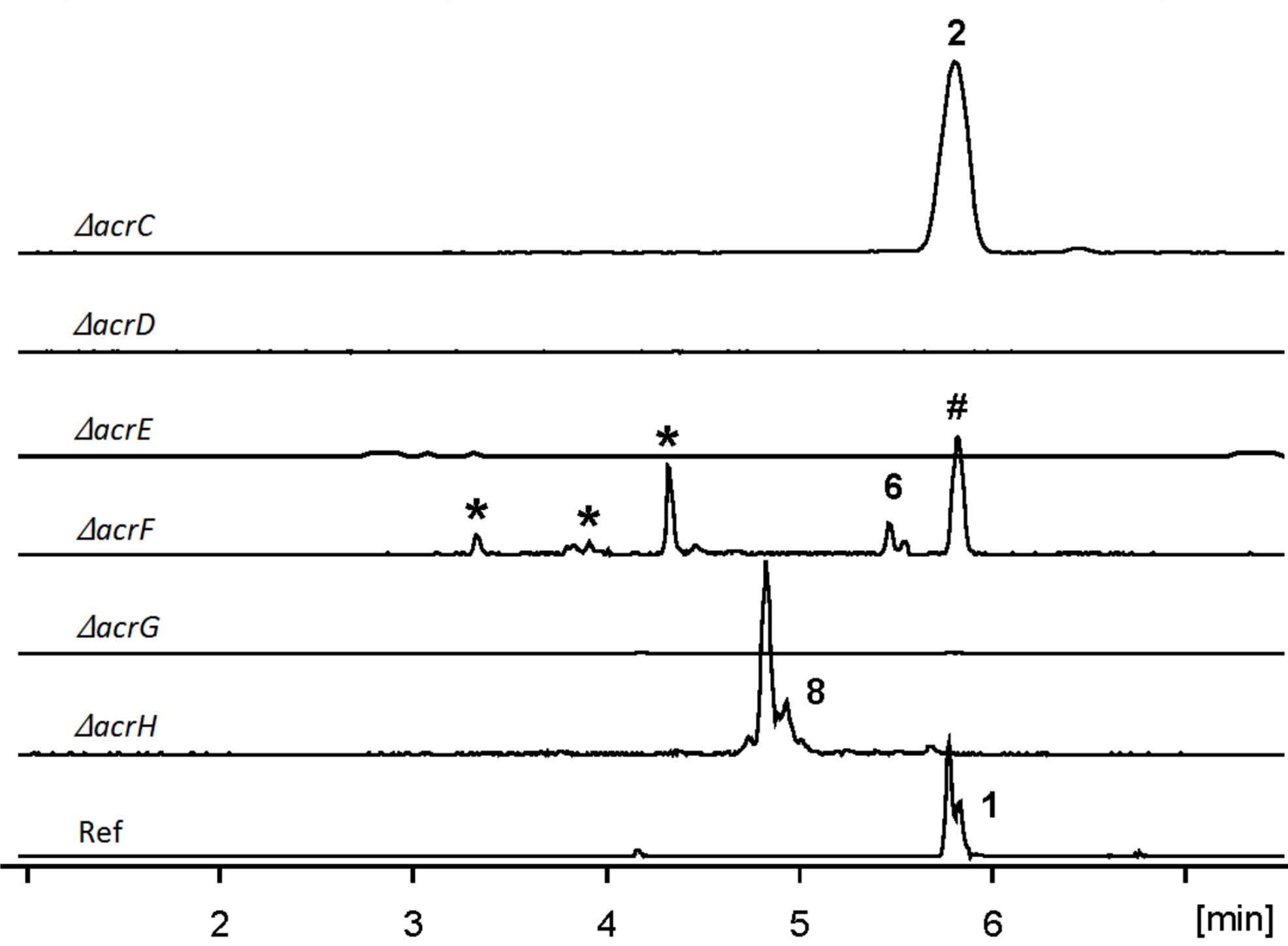


**Not only local regulation -> More production of compounds in *acrR* overexpressed than in the reference strain**



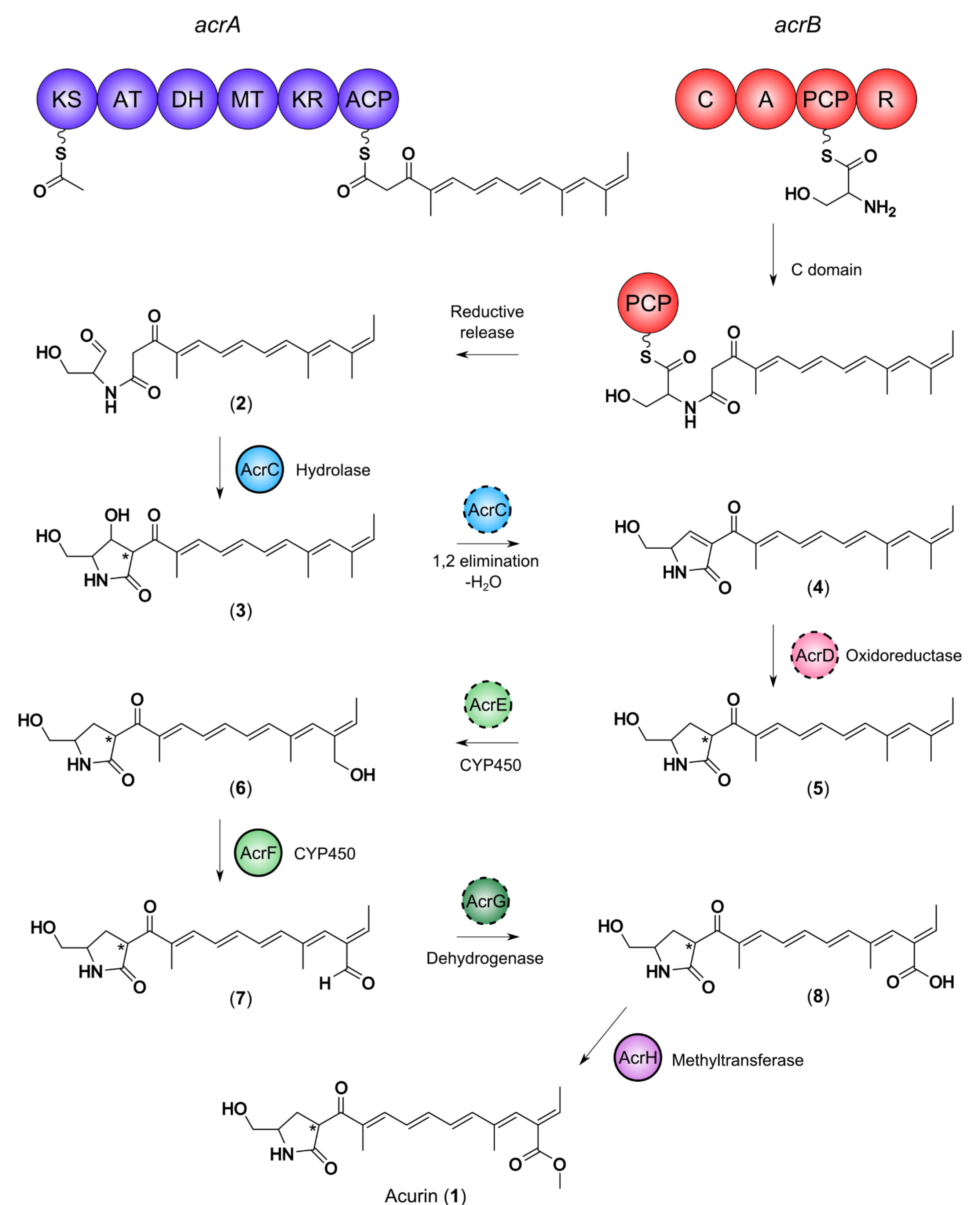
**Elevated acurin production was confirmed**

**Deletion of all genes showing increased expression in the *acrR*↑ strain revealed that six additional genes were required for acurin production (see model for compounds)**



REMOVAL OF TAILORING ACTIVITIES

**We propose this model for biosynthesis of acurin. Not all deletion strains revealed intermediates, and in these cases enzymes will be shown with dashed lines to illustrate that the step is speculative. Other structures are verified by HPLC-MS, and acurin additionally by NMR. *AcrF* loss also produces compounds that we have not identified yet, and cannot couple to acurin biosynthesis**



BIOSYNTHETIC ROUTE TO ACURIN

LITT.

<sup>1</sup>Nødvig, C.S.,..., and Mortensen, U.H. 2015. PLOS One. DOI:10.371/journal.pone.0133085

<sup>2</sup>Niehaus, E. ... Humpf, H., 2013. Chemistry & Biology 20, 1055-66.