
Breaking transcriptional locks to discover novel microbial antibiotics

Christophe Corre

Department of Chemistry and School of Life Sciences, University of Warwick,
Gibbet Hill Road, CV4 7AL Coventry, UK
C.Corre@warwick.ac.uk

More than 70% of clinically approved antibiotics originate from *Streptomyces* bacteria.¹ And, over the last ten years, sequencing of their genomes has revealed the presence of a vast number of unsuspected gene clusters that are predicted to direct the biosynthesis of new natural products.² Thus new strategies for natural product discovery have been developed.^{3,4} However, many of these gene clusters remained silent in the laboratory environment due to the presence of pathway-specific transcriptional regulators.⁵ By investigating the detailed molecular mechanisms of the regulation of antibiotic production in *Streptomyces* bacteria, additional approaches for antibiotic discovery are being developed.⁶ In particular inactivation of specific transcriptional repressor genes or overexpression of specific transcriptional activators have successfully resulted in the production of novel bioactive metabolites.^{7,8}

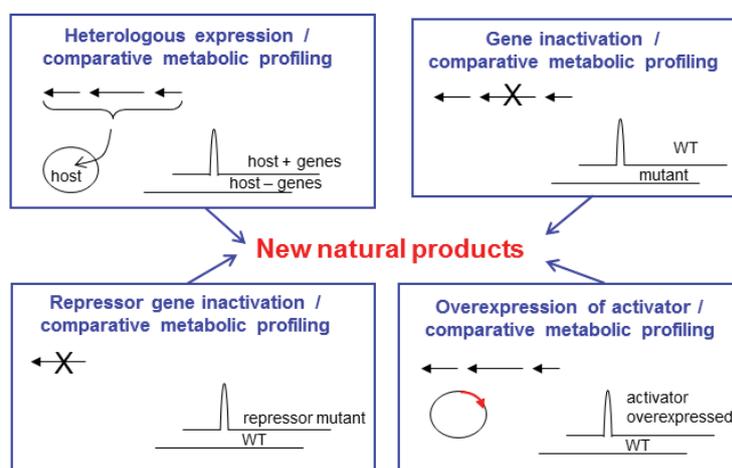


Fig. 1: Novel approaches for natural product discovery.

References

1. D.A. Hopwood, "Streptomyces in Nature and Medicine: The Antibiotic Makers" 2007, New York, Oxford University Press;
2. S.D. Bentley, *et al.*, *Nature*, 2002, **417**, 141.
3. C. Corre and G.L. Challis, *Nat. Prod. Rep.*, 2009, **26**, 977.
4. C. Corre and G.L. Challis, "Exploiting genomics for new natural product discovery in prokaryotes". In *Comprehensive Natural Products Chemistry II Chemistry and Biology*; L. Mander, H.-W. Liu, Eds.; Elsevier: Oxford, 2010, Vol. 2, pp 429-453.
5. C. Corre, L. Song, S. O'Rourke, K.F. Chater, G.L. Challis, *Proc Natl Acad Sci USA*, 2008, **105**, 17510.
6. B. Aigle and C. Corre, *Methods in Enzymol.*, 2012, **517**, 343-366.
7. L. Laureti, L. Song, S. Huang, C. Corre, P. Leblond, G.L. Challis and B. Aigle, *Proc. Natl. Acad. Sci. USA*, 2011, **108**, 6258.
8. J.D. Sidda, L. Song, V. Poon, M. Al-Bassam, O. Lazos, M.J. Buttner, G.L. Challis and C. Corre, *Chem. Sci.*, 2014, **5**, 86.