

# nature REVIEWS

## NATURE REVIEWS MICROBIOLOGY

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**M**icrobial secondary metabolites represent some of the most useful and important molecules in human medicine. The fungal kingdom includes many species that produce secondary metabolites with important medicinal value, including penicillin, cyclosporin and the statins. Although chemically diverse, all secondary metabolites are produced using a few common biosynthetic pathways, and the genes involved in their production are clustered, a recent finding that has important implications for gene regulation and evolution. In this issue, Nancy Keller and colleagues review the field of fungal secondary metabolism, assess the insights that have been gained from recent advances in molecular biology, bioinformatics and comparative genomics, and ask whether these advances will accelerate the discovery of new pharmacologically active natural products.

Polyketides are the most abundant fungal secondary metabolites, and pharmaceuticals derived from them account for 20% of the world's top-selling drugs. Not surprisingly, there is intense interest in discovering new variations of polyketide products that have new or improved pharmaceutical activity. One successful approach — known as 'combinatorial biosynthesis' — involves genetically engineering new polyketides by exploiting the modular architecture of bacterial multienzyme polyketide synthases (PKSs). On page 925, Kira Weissman and Peter Leadlay review recent progress in PKS genetic engineering and the challenges that remain to transform this strategy into a routine and effective component of modern drug discovery.

Finally, on behalf of everyone at *Nature Reviews Microbiology*, we would also like to take this opportunity to sincerely thank our authors, readers and referees for their support in 2005, and to extend to all our best wishes for a happy holiday season and a successful New Year.



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