Indian J Microbiol (July–Sept 2011) 51(3):414
DOI 10.1007/s12088-011-0188-0

NEWS AND VIEWS

Discovering Metabolic Products of Cryptic Biosynthetic Pathways

Devi Lal · Rup Lal

Genome sequencing has accelerated our understanding about organization of biosynthetic clusters in bacterial genomes which are responsible for the production of secondary metabolites. These metabolites are sources of important drugs and act like anticancer, antibacterial and anti-infective agents. In this context actinomycetes are notable as nearly 70% of the economically important metabolites are produced by them. Genome sequences of many actinomycetes have suggested the presence of many cryptic biosynthetic gene clusters that are not expressed or poorly expressed [1]. These cryptic gene clusters may encode for novel products that can prove to be beneficial for mankind. In a recent study published in PNAS [2] Laureti et al. have identified one such cryptic gene cluster in genome of *Streptomyces ambofaciens* (producer of antibiotics-spiramycine and congocidine). This cluster is not associated with any metabolite production and is found to be poorly expressed. These workers expressed this cryptic gene cluster using large ATP-binding regulator of the LuxR family (LAL) protein, the members of which are known to be activator of pikromycin [3] and rapamycin [4]. NMR analysis of the expressed product suggested that the product is a novel macrolide which was named stambomycin. These workers identified four such macrolides-stambomycin A to D. Bioactivity of the novel macrolide suggested that the product can provide new insights into anticancer therapy owing to its antiproliferative activities against adenocarcinoma, human breast, lung and prostate cancer cell lines. Researchers have been looking for better drugs for treatment of antibiotic resistant strains and different types of cancers. This study has opened up new realms in the discovery of several novel natural products that find application in medicine.

References

1. Zerikly M, Challis GL (2009) Strategies for the discovery of new natural products by genome mining. ChemBioChem 10:625–633
2. Laureti L, Song L, Huang S, Corre C, Leblond P, Challis GL, Aigle B (2011) Identification of a bioactive 51-membered macrolide complex by activation of a silent polyketide synthase in *Streptomyces ambofaciens*. Proc Natl Acad Sci USA. doi: 10.1073/pnas.1019077108
3. Wilson DJ, Xue Y, Reynolds KA, Sherman DH (2001) Characterization and analysis of the PikD regulatory factor in the pikromycin biosynthetic pathway of *Streptomyces venezuelae*. J Bacteriol 183:3468–3475
4. Kuscer E, Coates N, Challis I, Gregory M, Wilkinson B, Sheridan R, Petković H (2007) Roles of *rapH* and *rapG* in positive regulation of rapamycin biosynthesis in *Streptomyces hygroscopicus*. J Bacteriol 189:4756–4763

D. Lal · R. Lal (✉)
Department of Zoology, University of Delhi, Delhi 110007, India
e-mail: ruplal@gmail.com