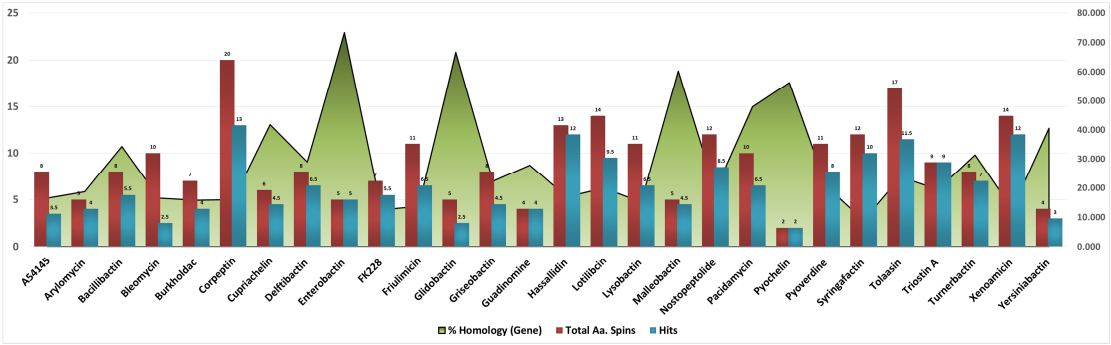
5th BCNP Brazilian Conference on Natural Products
XXXI RESEM
Atibaia – SP – Brazil
ISBN: 978-85-66836-10-3
Oct. 26–29th 2015

REVEALING GENOMIC SECRETS OF MICROORGANISMS

João Luiz Baldim[a], Bruna Lidiane da Silva[a], Daniela Aparecida Chagas-Paula[a], Roger Linington[b], Marisi Gomes Soares[a]

Institute of Chemistry, Federal University of Alfenas, Alfenas, Brazil.
Chemistry & Biochemistry Department, University of California, Santa Cruz, United States
e-mail: jotaelebaldim@gmail.com

Abstract: The great potential of microorganisms in producing compounds of medical interest for the humanity is well known since the first discovery, the most famous antibiotic in fact, Penicillin. Fleming gave birth to a new avenue in Natural Products Compounds and their biological activities. Since then, decades ahead, it is now possible to understand how those small beings, that produce a large variety of compounds, work. Biosynthetic pathways revealed, precise taxonomic and chemotaxonomic classification, cloning, bioinformatics tools turning possible analyzing and interpreting massive amount of information, DNA's peculiarities, all fields merged leading to understand some of the most important classes of compounds known by all of us, NRP and PK compounds [1], [2]. Further scientific and technologic development will come, of course, but nowadays we can make incredible things by using all the available knowledge. In this point of view, make sense doing some calculation to comprehend the potential of a splendid class of microorganisms, called Betaproteobacteria (BPB). Since the discovery of diverse natural compounds from this class, it has been extensively studied. Recently, in January, 2015, a new NRP antibiotic was discovered, teixobactin, from a BPB species and, after substantial analysis, the conclusion taken was that this compound kills pathogens without showing resistance [3]. In July, 2014, Cimermancic and colleagues published a paper showing a huge number of unstudied species harboring large number of Biosynthetic Gene Clusters [4]. These discoveries has driven experiments revealing secrets of biosynthetic machineries and producing systematic information, guiding new natural products discoveries. This facilitate finding patterns in the functionality of these small beings. Based on this knowledge, our group analyzed approximately 450 genomes by their capability of secondary metabolites production. The results obtained in our experiments provided important information about classes and how NRPS modules synthesize compounds in BPB, aiming to find similarities based on genomic homology. In some cases, genomic homology can result in similarities in natural products production [5], [6]. Some homologies from the best hits encountered can be seen at Figure 1 that displays homology of genes, hits of known compounds and hits from our method's predictions. This strategy facilitates NMR and MS analysis saving time and money, by comparing which kind of moieties they can assembly module by module in the NRPS logics.



ISBN: 978-85-66836-10-3

References:

[1] M. Strieker, A. Tanović, and M. a. Marahiel, “Nonribosomal peptide synthetases: Structures and dynamics,” *Curr. Opin. Struct. Biol.*, vol. 20, no. 2, pp. 234–240, 2010.

[2] E. a. Felnagle, E. E. Jackson, Y. a. Chan, A. M. Podevels, A. D. Berti, M. D. McMahon, and M. G. Thomas, “Nonribosomal peptide synthetases involved in the production of medically relevant natural products,” *Mol. Pharm.*, vol. 5, no. 2, pp. 191–211, 2008.

[3] L. L. Ling, T. Schneider, A. J. Peoples, A. L. Spoering, I. Engels, B. P. Conlon, A. Mueller, D. E. Hughes, S. Epstein, M. Jones, L. Lazarides, V. a Steadman, D. R. Cohen, C. R. Felix, K. A. Fetterman, W. P. Millett, A. G. Nitti, A. M. Zullo, C. Chen, and K. Lewis, “A new antibiotic kills pathogens without detectable resistance,” *Nature*, vol. 517, pp. 455–459, 2015.

[4] P. Cimermancic, M. H. H. Medema, J. Claesen, K. Kurita, L. C. W. Brown, K. Mavrommatis, A. Pati, P. A. A. Godfrey, M. Koehrsen, J. Clardy, B. W. W. Birren, E. Takano, A. Sali, R. G. G. Linington, M. A. A. Fischbach, L. C. Wieland Brown, K. Mavrommatis, A. Pati, P. A. A. Godfrey, M. Koehrsen, J. Clardy, B. W. W. Birren, E. Takano, A. Sali, R. G. G. Linington, and M. A. A. Fischbach, “Insights into Secondary Metabolism from a Global Analysis of Prokaryotic Biosynthetic Gene Clusters,” *Cell*, vol. 158, no. 2, pp. 412–421, Jul. 2014.

[5] H. Wang, D. P. Fewer, L. Holm, L. Rouhiainen, and K. Sivonen, “Atlas of nonribosomal peptide and polyketide biosynthetic pathways reveals common occurrence of nonmodular enzymes,” *Proc. Natl. Acad. Sci.*, vol. 111, no. 25, pp. 9259–9264, 2014.

[6] R. R. Forseth, S. Amaike, D. Schwenk, K. J. Affeldt, D. Hoffmeister, F. C. Schroeder, and N. P. Keller, “Homologous NRPS-like gene clusters mediate redundant small-molecule biosynthesis in Aspergillus flavus,” *Angew. Chemie - Int. Ed.*, vol. 52, no. 5, pp. 1590–1594, 2013.