THE GENOME SEQUENCE OF *STREPTOMYCES LIVIDANS* 1326 REVEALS A METAL-RELATED GENOMIC ISLAND, WHICH HARBORS SLP3, LOST DURING LABORATORY ADAPTATION

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Introduction. *Streptomyces lividans* is a widely used host for the heterologous expression of proteins and biosynthetic pathways in both scientific and industrial settings. Previous studies have revealed strain-specific genomic island albeit a similar genomic organization between the industrial strain *S. lividans* TK24 and *S. coelicolor* A3(2) (1,2). Moreover, phenotypic differences between these organisms are well known. A good quality *S. lividans* genome sequence from a parental strain should provide further insights into these intriguing genotypic and phenotypic differences.

Methods. The complete genome sequence of the original isolate of *S. lividans* 1326 was deciphered after a combination of next-generation sequencing platforms (454, Illumina and Pacific Biosystems) and a hybrid assembly pipeline (Celera, PacBioToCA). Comparative analysis of closely related strains was done with Artemis Comparative Tool and manual curation. RNAseq Illumina libraries were used for transcriptomic analysis (BWA and CLC genomics workbench).

Results. The genetic diversity identified included a large genomic island with a mosaic structure, present in *S. lividans* 1326 but not in the laboratory-adapted strain TK24 (Fig. 1). Sequence analyses showed that this genomic island has an anomalous (G + C) content, suggesting recent acquisition, and that it is rich in metal-related genes. Sequences previously linked to a mobile conjugative element, termed plasmid SLP3 (3) and defined here as a 94 Kbp region, could also be identified within this locus. Transcriptional analysis of the response of *S. lividans* 1326 to copper was used to corroborate a role of this large genomic island, including two SLP3-borne 'cryptic' peptide biosynthetic gene clusters, in metal homeostasis.

Conclusions. The genome sequence of *S. lividans* 1326 not only explains long-standing genetic and phenotypic mysteries, but also opens the door for further in-depth comparative genomic analyses of model *Streptomyces* strains, including biotechnology important *S. lividans* strains, as well as for the discovery of novel natural products following genome-mining approaches.

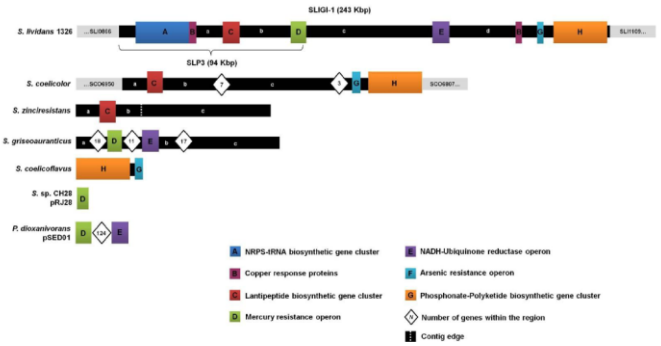

Figure 1. Mosaic structure of Genomic Island 1. SliGI-1 is represented as a thick black continuous line. Synteny blocks encoding for metabolic functions implicated in metal response are shown with different colors and in uppercase letters. Regions that show certain degree of conservation between synteny blocks are marked with lowercase letters. The SLP3 mobile element is highlighted with a key. Conserved similar regions found in the genomes or plasmids of other actinomycetes are shown in the following lines.

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