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P0940 Gain-in omic signatures of colistin-resistant *Acinetobacter baumannii* undergoing colistin therapy

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Background: Colistin (COL) is the last-resort treatment for Multi-Drug-Resistant *Acinetobacter baumannii (Ab),* representing a public health concern. Over the years, computational approaches have become relevant for biology and big-data analysis is a challenge for the processing. Bioinformatics combines biological analysis and informatic technology supporting the researcher biologist's work.

Materials/methods: The genomes and transcriptomes of two isogenic strain-pairs of clinical COL susceptible/resistant (1 and 2 COL-S/R) *Ab* were sequenced using Illumina Mi-Seq and bio-informatically analyzed for traits in single pairwise and in both COL-R strains. The genomic and transcriptomic alignment of the two different libraries (TS and SI) reads was performed on *Ab* ACICU Reference Genome (RefGen) using Bwa and Rockhopper, respectively. CSI-Phylogeny and REALPHY were used to infer phylogeny on genomic SNPs (gSNPs), whilst Nullarbor was used for the phylogenetic analysis on core SNPs (cSNPs). Differential expressed gene (DEG) enrichment, in single pairwise COL-R *vs* COL-S, was carried out by DAVID, and a DEG filtering for common traits in the two COL-R strains was computationally performed. Biological network and pathway were investigated by KEGG, STRING and Expasy.

Results: gSNP phylogenetic-trees showed that the two strain-pairs were closely-related to *Ab* ACICU RefGen. Common genomic non-synonymous SNPs (nsSNPs) were also identified in *proB*, hypothetical proteins, surface adhesion and phage-related minor tail genes in COL-R *Ab*. The Nullarbor generated a core genome alignment showing a close relation in 1 strain-pair (70 cSNP differences) and a very close relation in 2 strain-pair (18 cSNPs). 23 cSNP differences comparing the COL-S *Ab* strains, and 81 cSNP differences between the COL-R ones were detected.
Integrating TS-/SI-library data, the single pairwise enrichment showed 5 affected KEGG-pathways (Butanoate metabolism, Glycolysis/Gluconeogenesis, Benzoate degradation via CoA-ligation, Pyruvate-metabolism, valine/leucine/isoleucine degradation) within the over-expressed gene set in 1 strain-pair (p-value ≤ 0,01). 4 statistically significant over-expressed genes, i.e. Lipid A phosphoethanolamine transferase PmrC, diacylglycerol kinase, ACICU_01518 and ACICU_02436 hypothetical proteins were found. *pmrBC* and new *lpxCD* nsSNPs were found.

Conclusions: Our data define genomic and transcriptomic multilevel signatures of COL-R versus COL-S *Ab* strains directly or indirectly related to COL-resistance and reflecting COL-R *Ab* complexity and adaptive response to antimicrobial pressure.