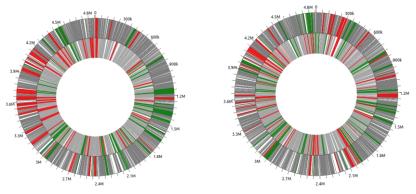
## **Results**

Salmonella enterica is a bacterium known to cause salmonellosis. In enteric bacteria, DNA supercoiling is responsive to environmental conditions and different antibiotics can be used to relax supercoiling and alter the expression of supercoiling-sensitive genes. However, *S. enterica* shows significant resistance to novobiocin antibiotic and relatively small variability of supercoiling response.

Here we analyzed the novobiocin effect on *S. enterica* gene expression and tried to reveal different mechanisms of *S. enterica* antibiotic resistance and transcription-supercoiling coupling. For our study, we used RNA-seq data obtained after incubation of *S. enterica* strain 14028S with various novobiocin concentrations (0, 100 and 500  $\mu$ g/ml) at different time points (10, 20 and 60 min).

Differential expression of genes was visualized in a position-related way using web-server WOPPER.

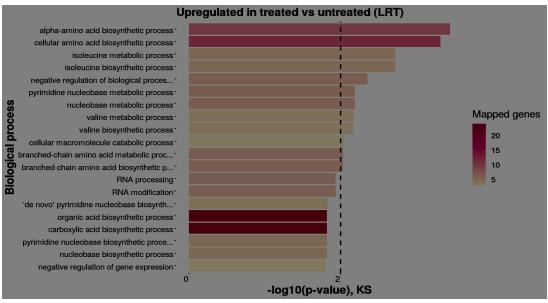


60 minutes without treatment

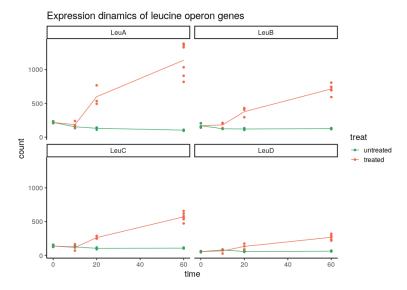
60 minutes with treatment 500 mg

We found that gene expression patterns have become mosaic after novobiocin treatment.

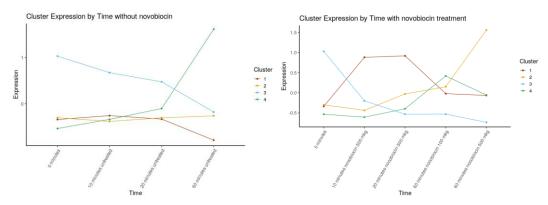
Functional enrichment analysis in GO terms revealed expression changes in groups of genes associated with branch-chain amino acid biosynthesis that can be connected to the regulation of Salmonella pathogenicity island 2.



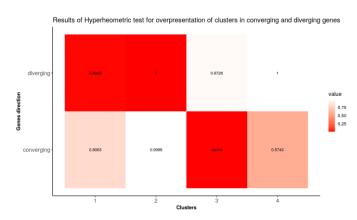
Individual visualization of expression dinamics of genes from Leucine operon revealed this data.



K-means clusterization of co-expressed genes revealed the upregulation of two clusters at different time stages after antibiotic treatment.



These groups were enriched in genes with divergent orientation on the chromosome which may provide the evidence of novobiocin influence on the transcription-supercoiling coupling. This result was used by using the hypergeometric test.



In conclusion, gene expression analysis revealed significant changes in the gene expression patterns of *S. enterica* after novobiocin treatment that can be connected to pathogenicity and transcription-supercoiling coupling.