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Transcriptomic Insights into the Genetic Regulations of *Leptospira interrogans* within a Mature Biofilm.

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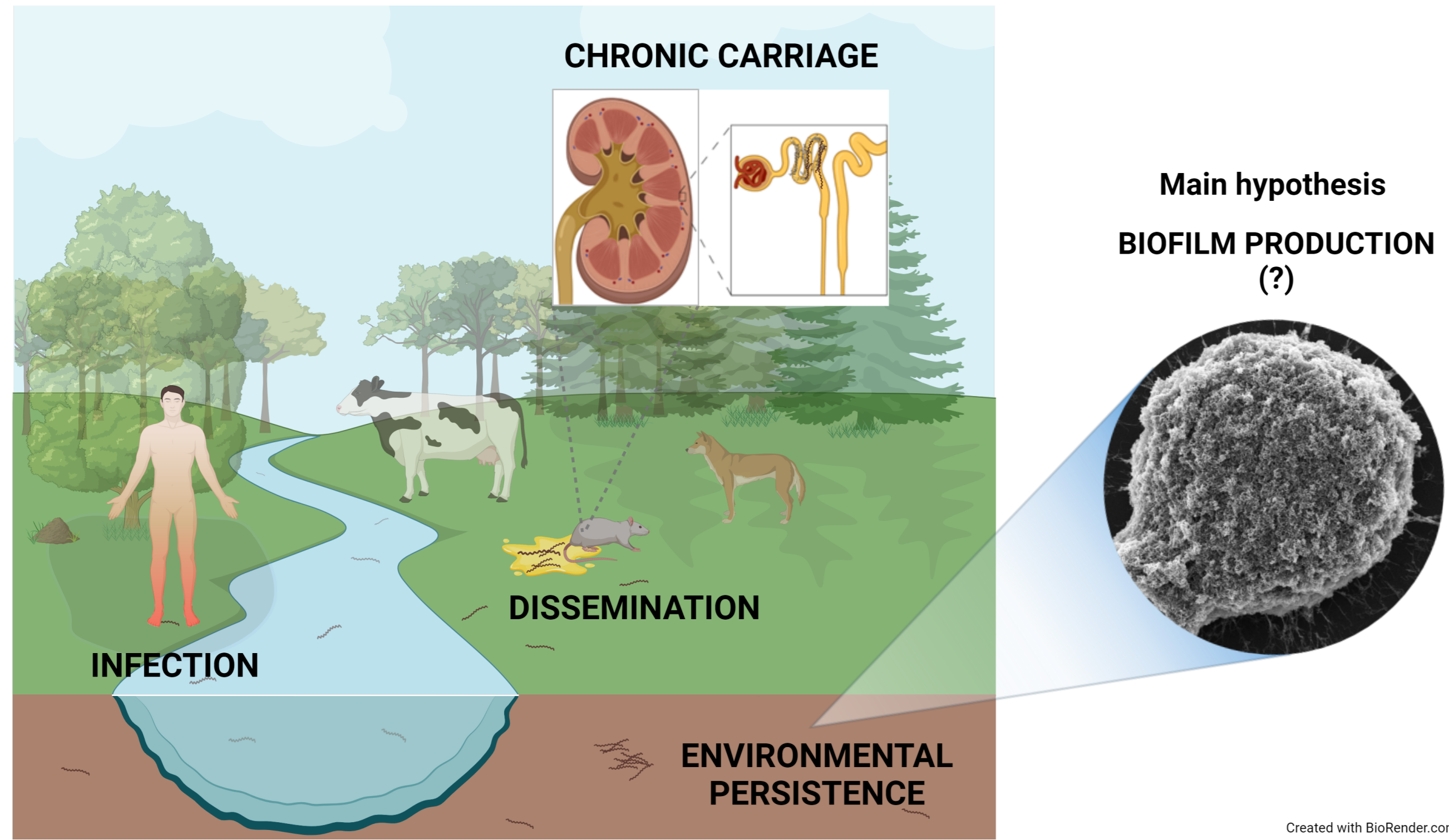
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INTRODUCTION



Could **biofilm** be the missing link in understanding the **environmental persistence** and **chronic carriage** of leptospires?

Leptospira interrogans, the causative agent of leptospirosis, goes through a complex life cycle in which biofilm formation could be one critical survival strategy under adverse environmental conditions. The genetic mechanisms underlying the motile-sessile shifts in *L. interrogans* remain largely unexplored. To unravel the transcriptomic regulation in *L. interrogans* within a mature biofilm, we performed a RNA-seq analysis. We also assessed the metabolic state of biofilm-forming bacteria and their ability to initiate infection.

OBJECTIVES

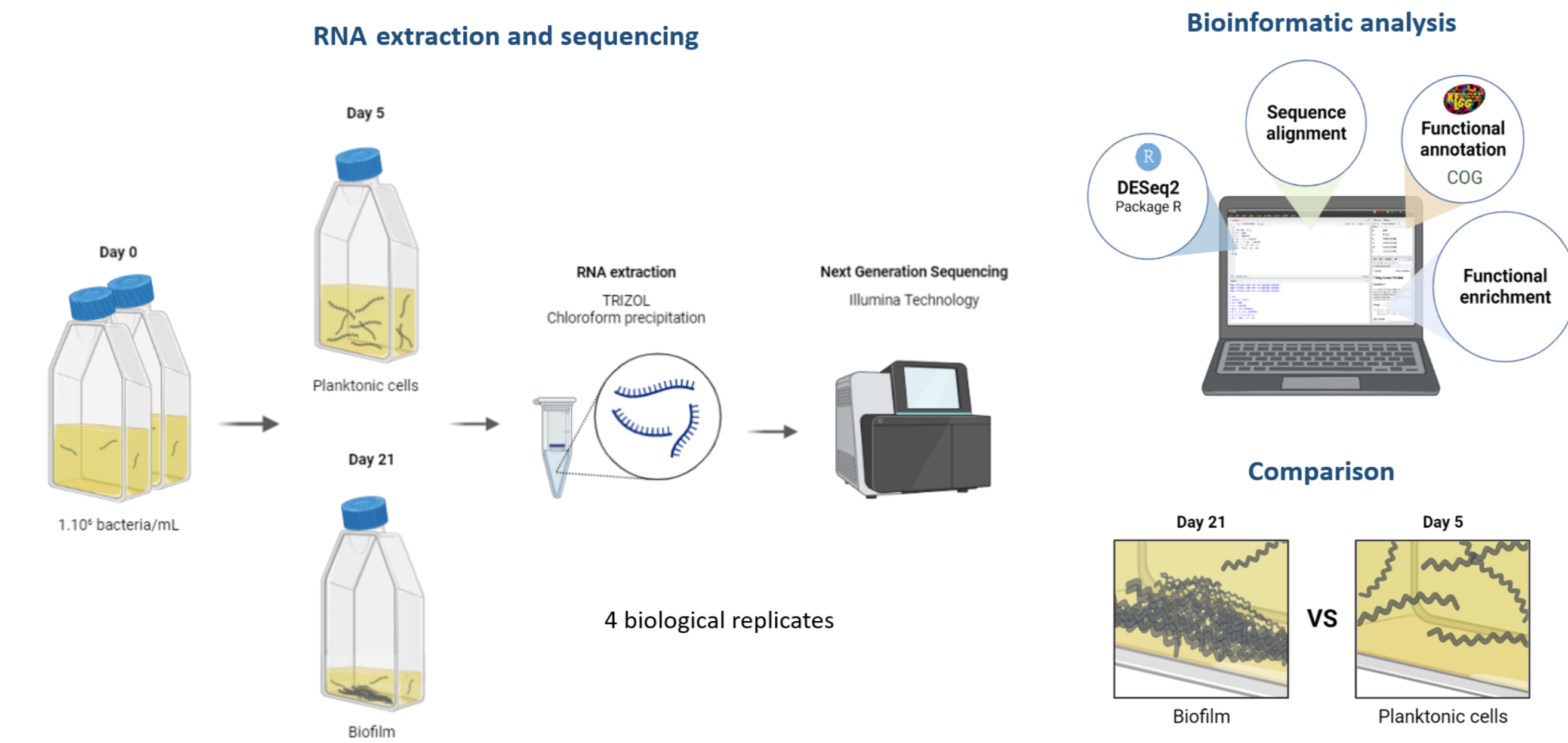
What are the **transcriptomic changes** between planktonic cells and a mature biofilm of a pathogenic strain of *Leptospira interrogans*?

Could we identify genes involved in **biofilm formation** and **environmental adaptation**?

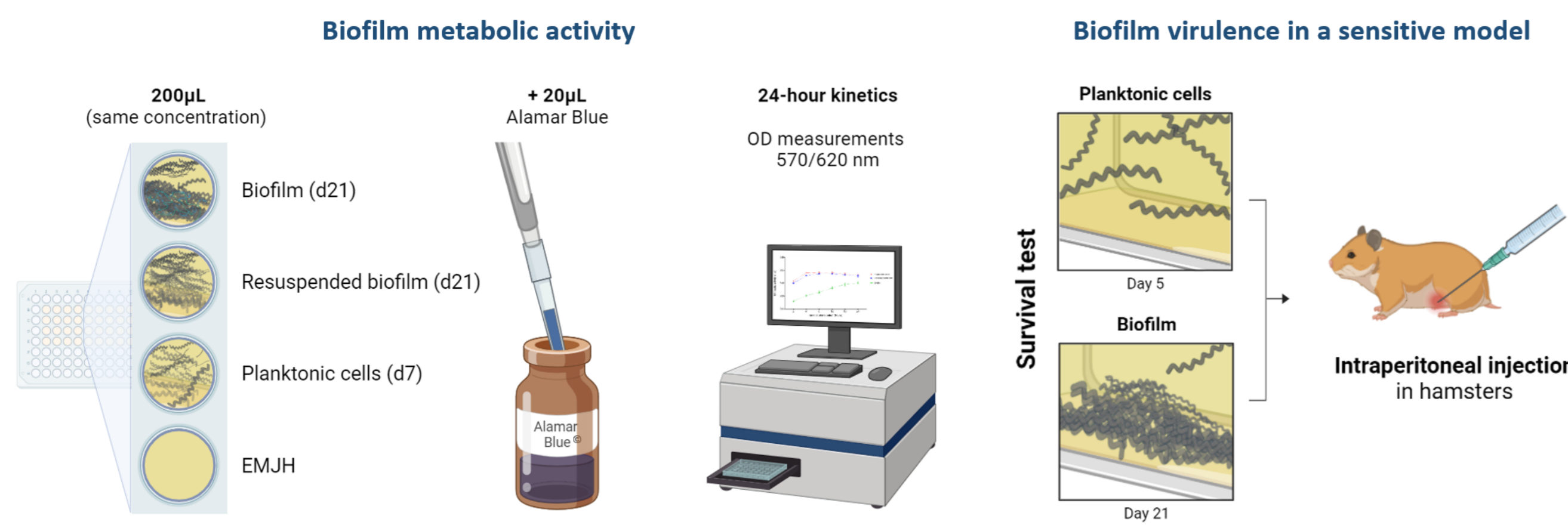
Is *Leptospira interrogans* still **virulent** when in a biofilm state?

METHODS

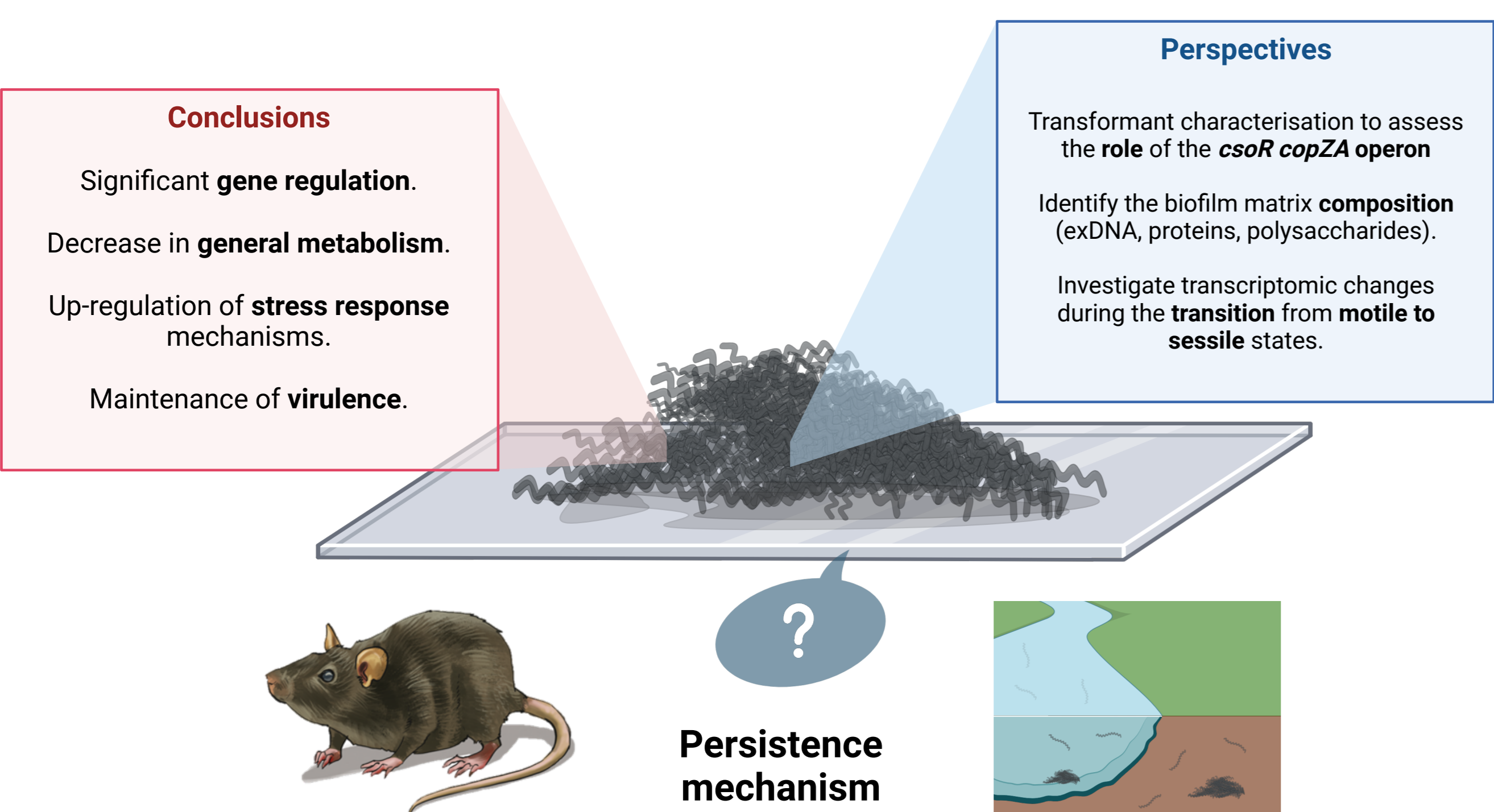
1. COMPARATIVE TRANSCRIPTOMICS



2. BIOFILM ACTIVITY AND VIRULENCE



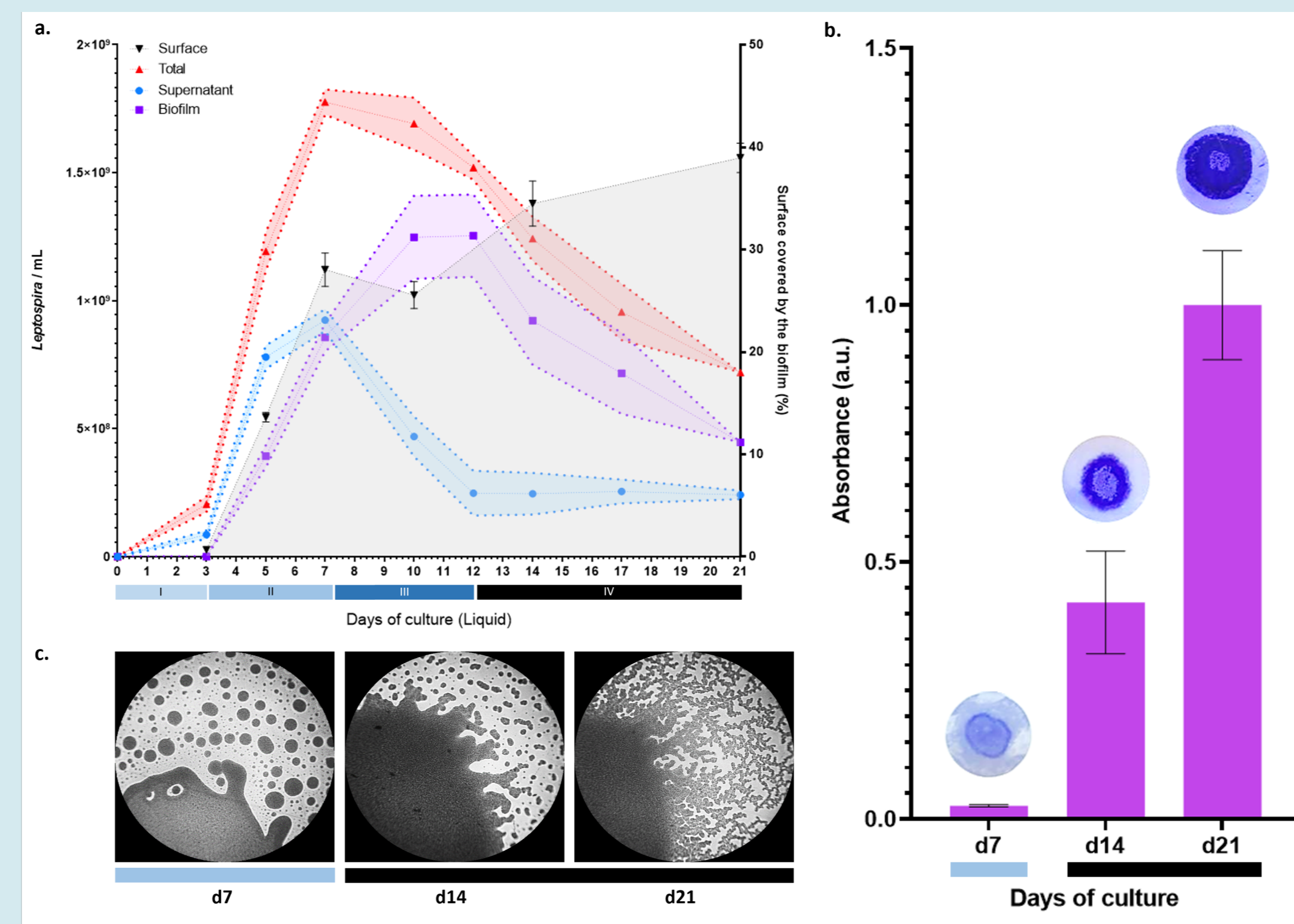
CONCLUSION AND PERSPECTIVES



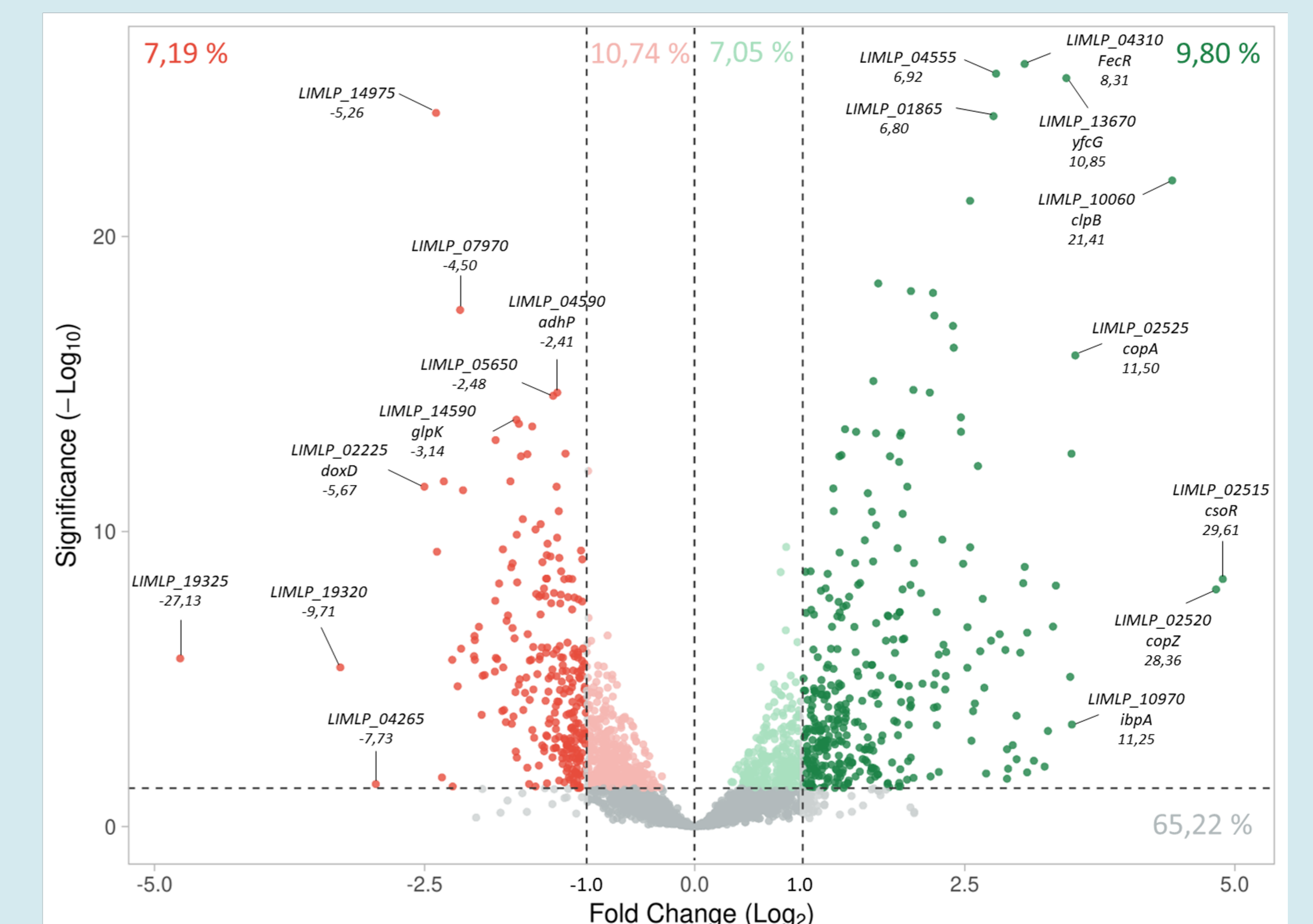
Day 21 likely shows a combination of **biofilm** and **starvation** traits.

RESULTS

L. interrogans biofilm development and expansion



One-third of the genome is regulated within a mature biofilm

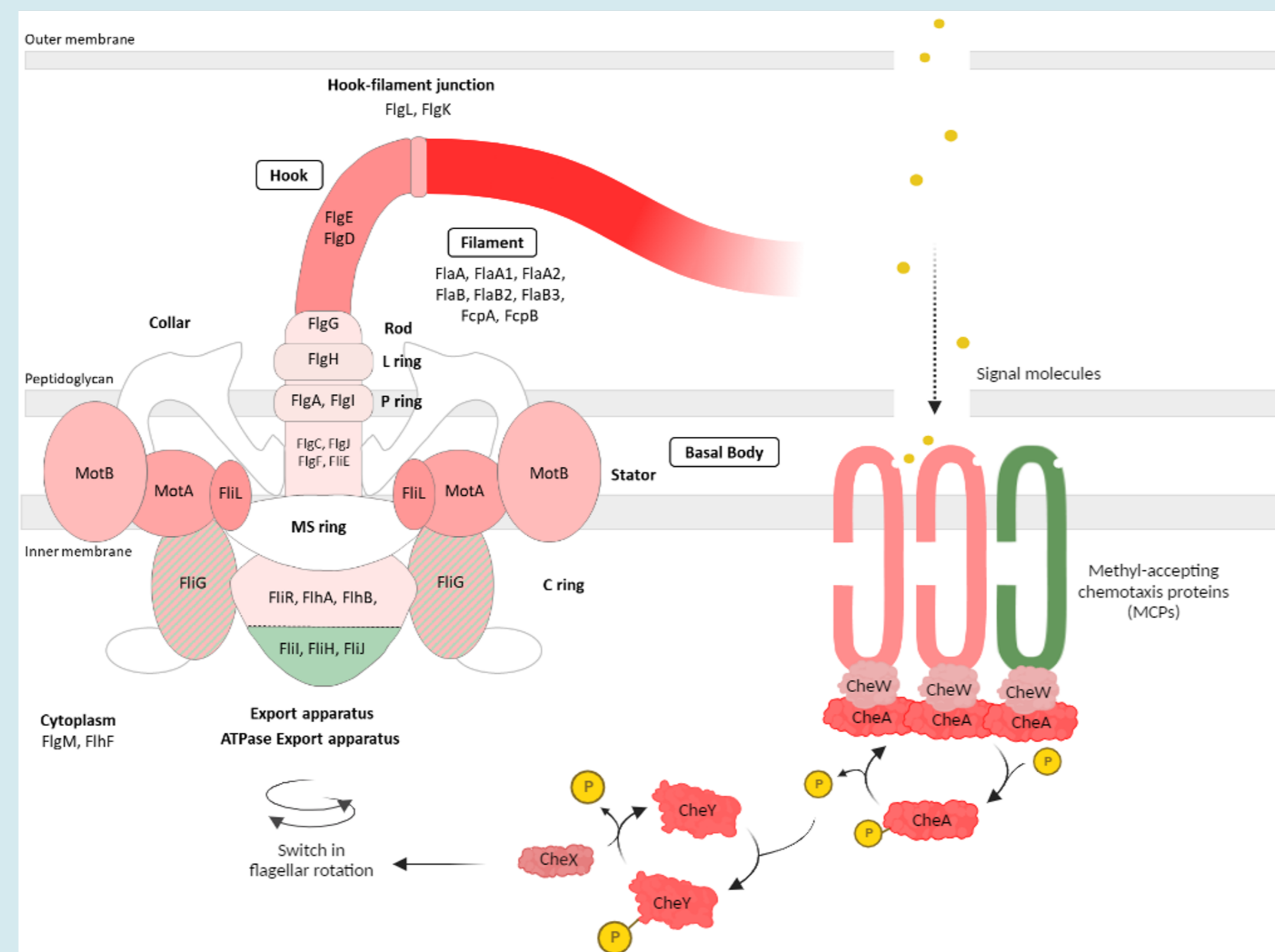


Although the **biofilm surface expands for up to 21 days**, the **number of bacterial cells decreases over time**, probably giving way to a larger portion of matrix or dead cells.

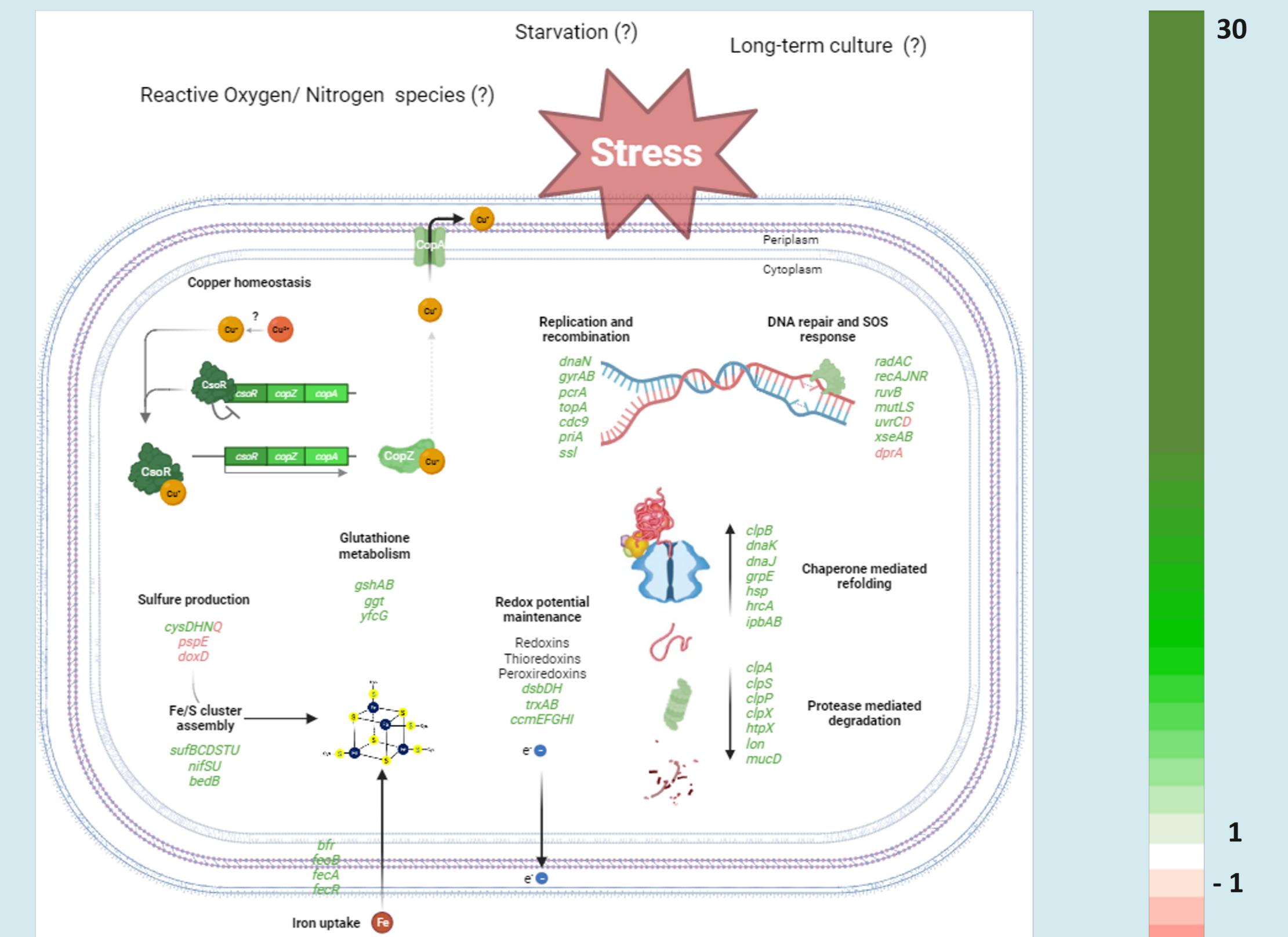
1263 modulated genes out of 3651
612 up-regulated genes and **651** down-regulated genes
Evenly distributed on the chromosomes and the plasmid

While the general metabolism is down-regulated, the stress response is up-regulated in the biofilm state

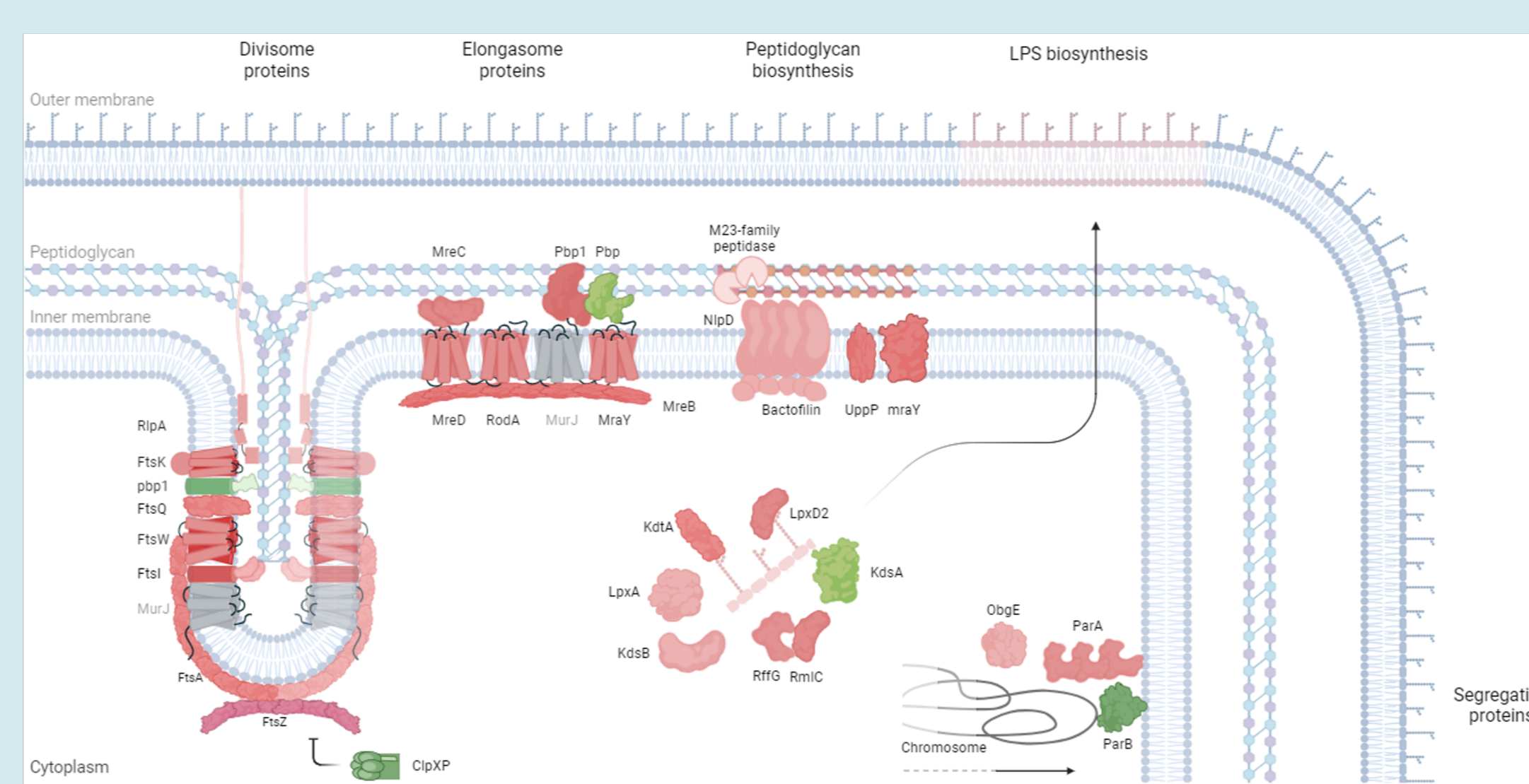
Loss of motility and chemotaxis



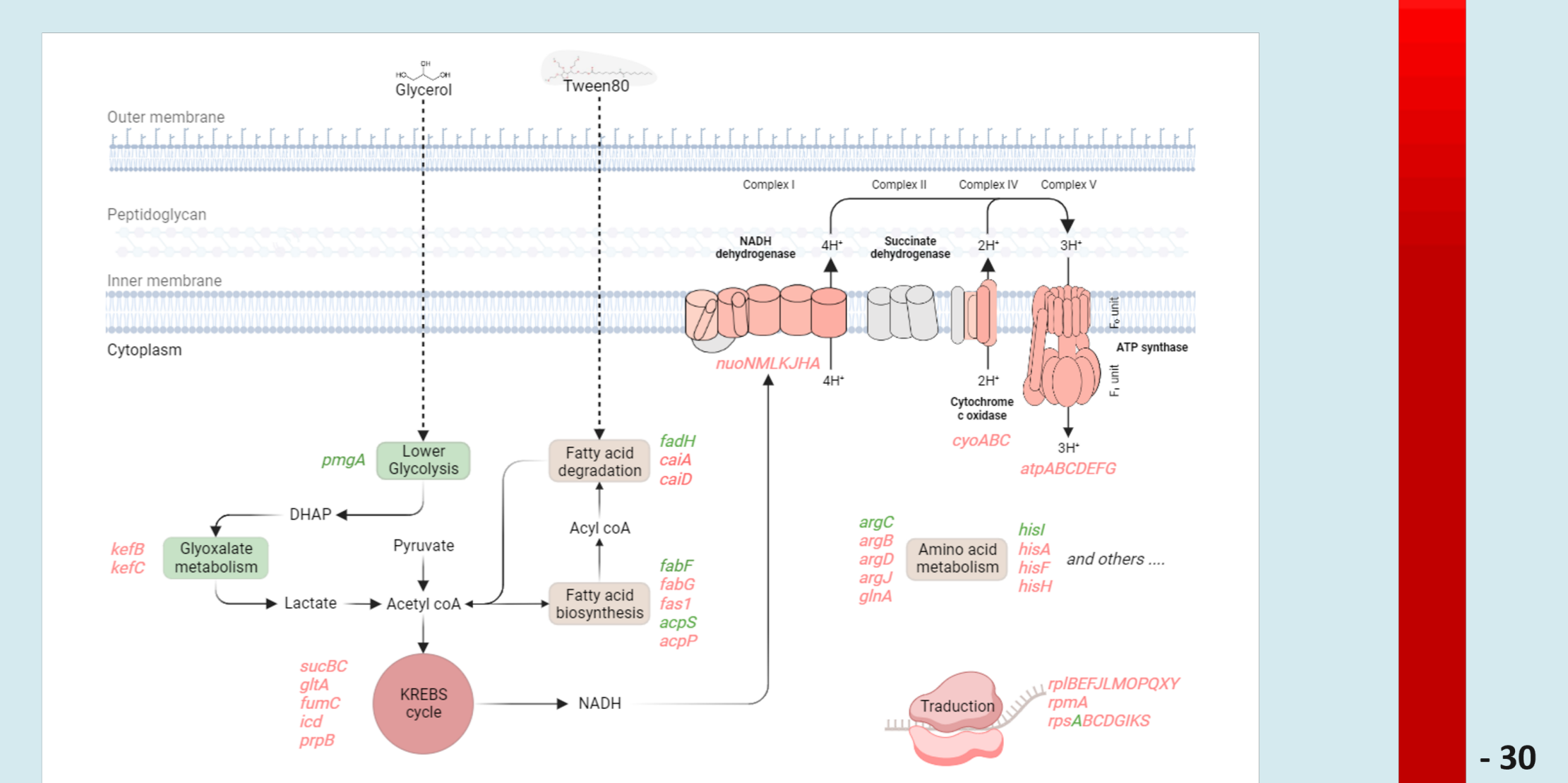
Up-regulation of repair mechanisms and management of intracellular stress



Down-regulation of cell division and biogenesis

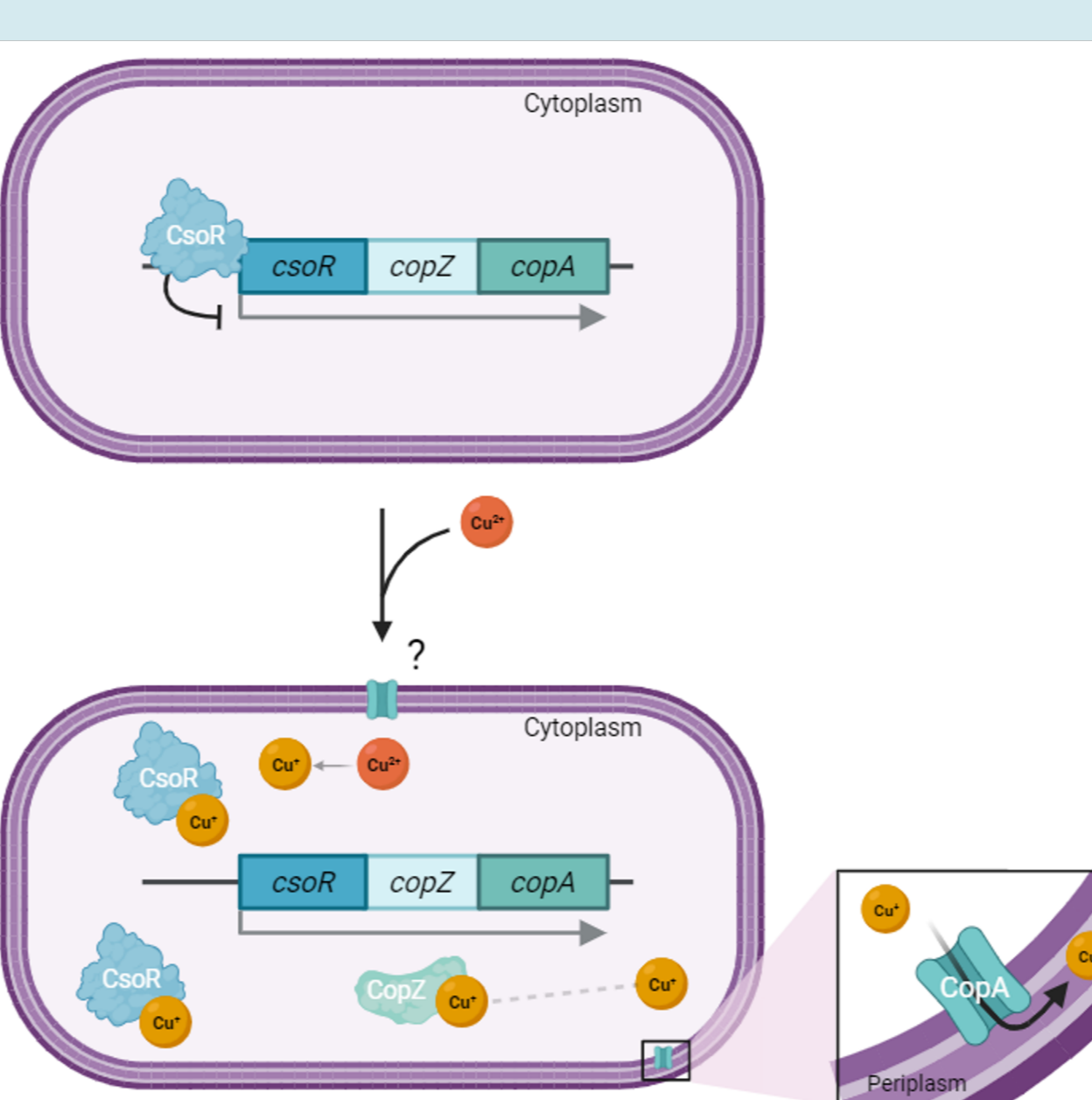


Significant changes in intracellular metabolism

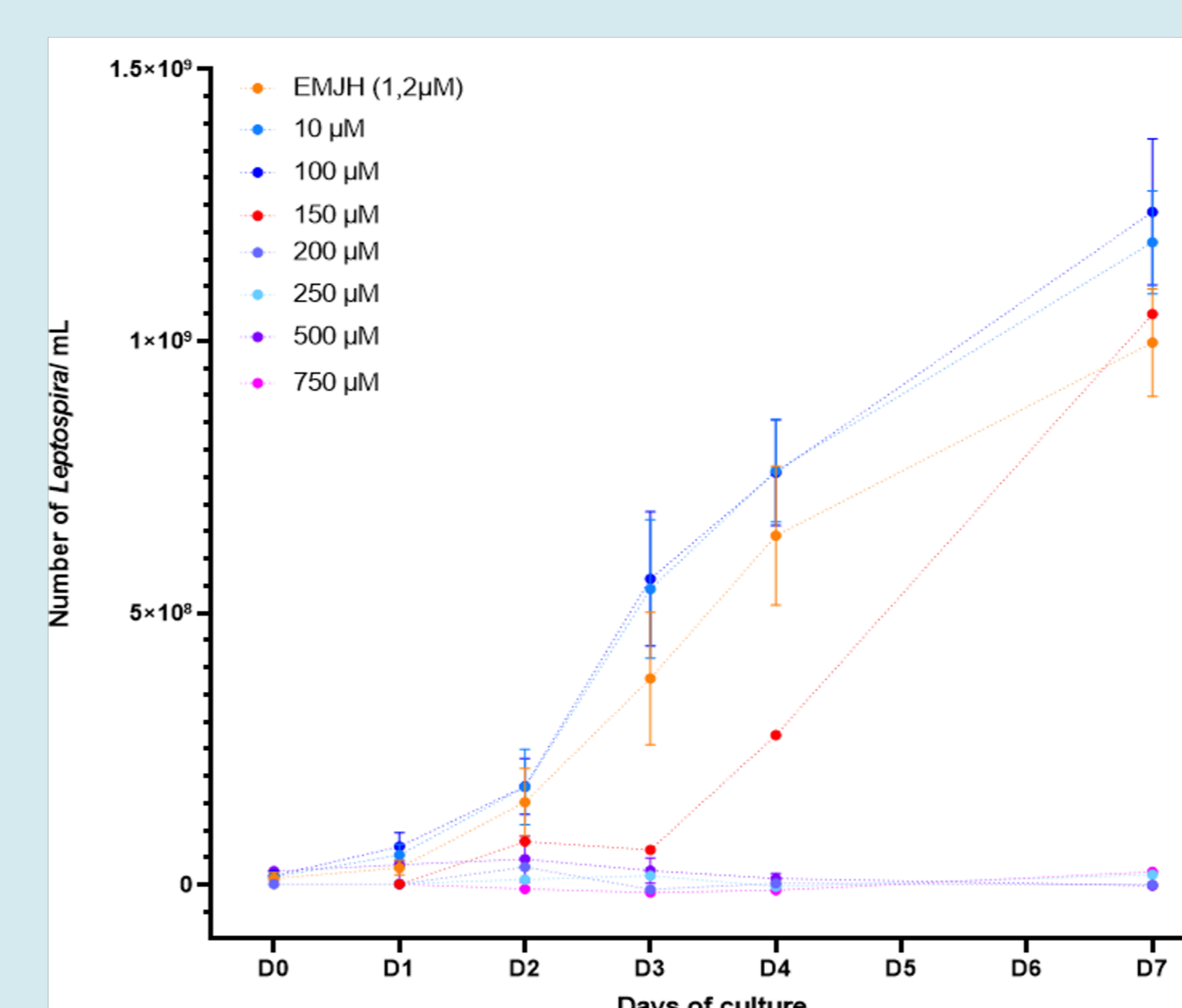


Focus on the *csoR-copZ* operon

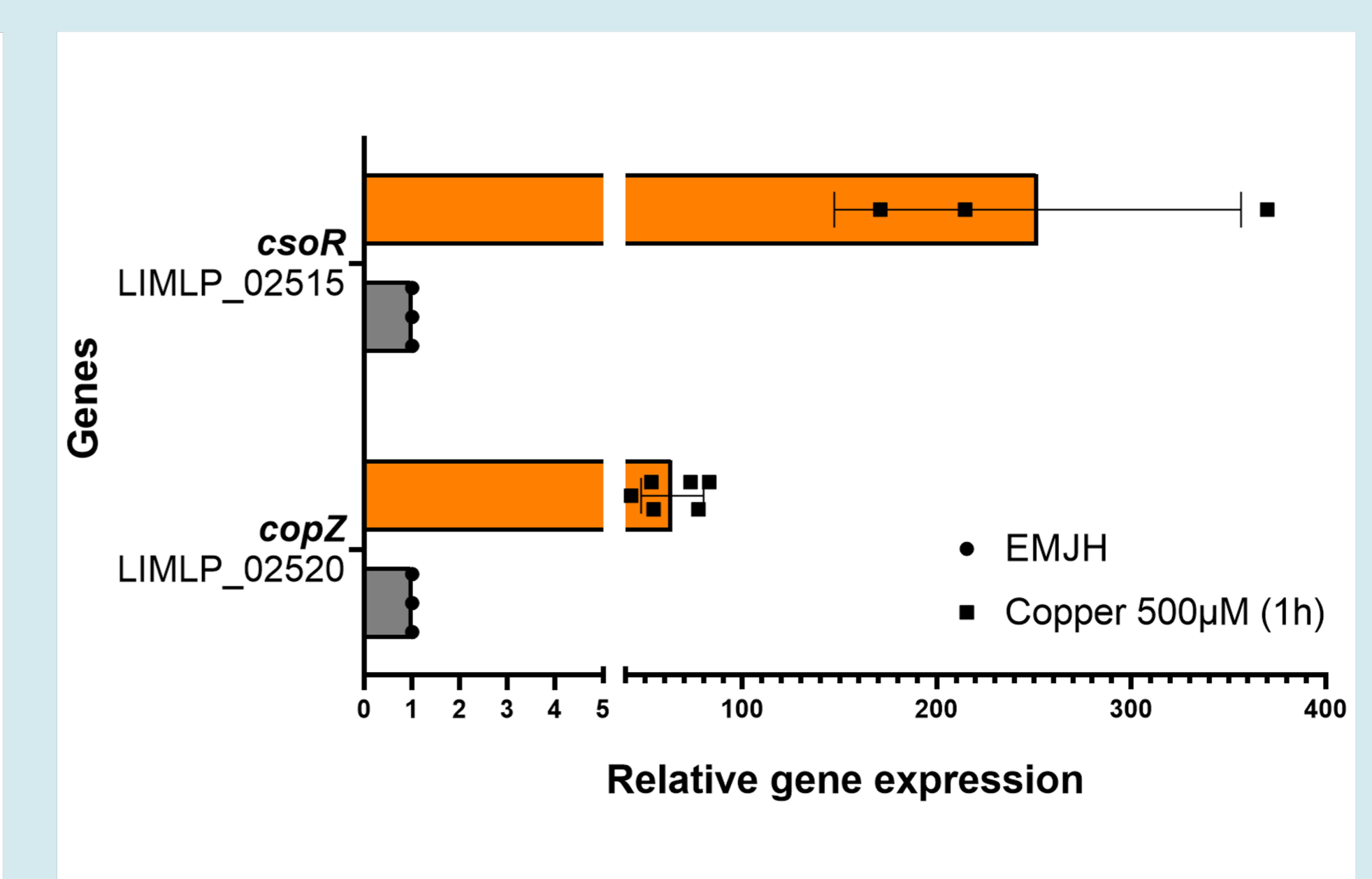
csoR-copZ is required for copper detoxification in other bacteria



Copper becomes lethal above 150µM

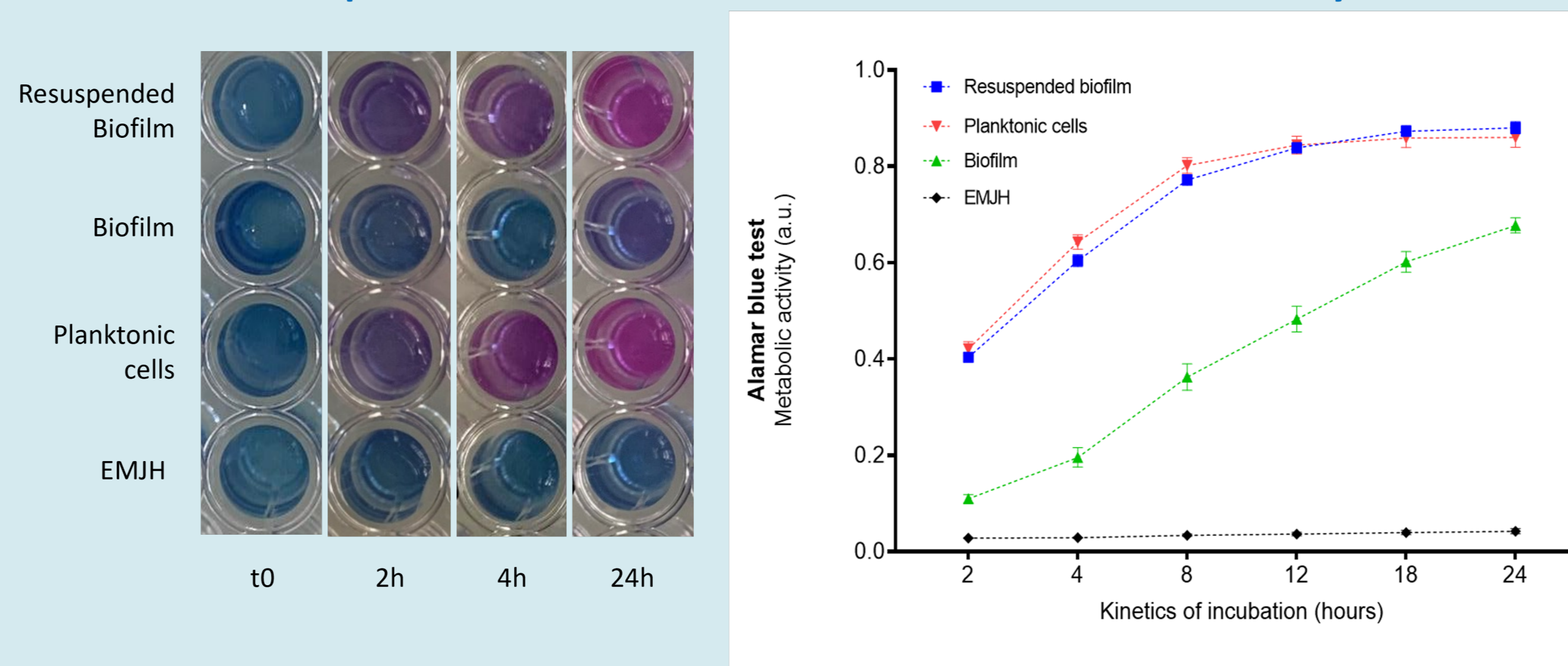


A copper stress similarly leads to over-expression of the operon



Leptospira interrogans metabolic activity and virulence in a biofilm state

Resuspension of the biofilm reactivates the metabolic activity



Leptospira interrogans remains virulent when in a biofilm state

