ANALYSIS OF *SALMONELLA* TYPHIMURIUM GROWTH IN THE MOUSE INTESTINE USING METABOLIC NETWORK RECONSTRUCTION

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ABSTRACT

Nontyphoidal *Salmonellae* (NTS) are important foodborne pathogens that cause millions of cases of gastroenteritis, bacteremia, and subsequent focal infection, yearly, and impose a large burden on the health care system[1]. The increasing antibiotic resistance of NTS bacteria requires better understanding of their complex metabolism during infection. Genome-scale metabolic models (GEMs) and computational methods constitute powerful tools to study metabolism[2].

In this study, we reconstructed a thermodynamically constrained GEM for *S.* Typhimurium SL1344, starting with genome annotation using the KEGG database. Growth data on 190 single carbon and 95 single nitrogen sources under aerobic and anaerobic conditions were used to curate the draft metabolic network, while the extracellular space of the model was enriched using metabolite measurements from the murine gut. We further amended the genome annotation of the model by suggesting catalyzing sequences for more than 40 orphan reactions by applying advanced bioinformatics methods.

We use the model to explore the metabolic pathway usage of NTS bacteria in the murine gut environment and gain insight into the nutritional requirements and metabolic bottlenecks of *S.* Typhimurium. Our analysis identifies key metabolic genes and substrates for NTS growth in the initial phase of gut lumen colonization.

Our work expands our knowledge about the biochemical capabilities of SL1344 beyond the information from the conventional sequence annotation. The hypotheses presented here can guide further experimental studies to facilitate a better understanding of the NTS metabolism and, thus, the identification of targets for efficient treatment.

KEYWORDS: genome-scale metabolic reconstruction, Salmonella Typhimurium, metabolic network curation, murine gut lumen, colonization

REFERENCES

[1] Kirk, M. D. et al. (2015). *PLOS Med*. 12(12):e1001940.
[2] Gu, C. et al. (2019*). Genome Biol*. 20:121