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Master Thesis

Workflow Toward a Consensus Metabolic Network Model of *Klebsiella* Species

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1 Background

The human nasal microbiome plays a crucial role in human health and is associated with numerous diseases. Surprisingly, the contribution of many nasal microorganisms to human health remains undiscovered. Between them, *Klebsiella pneumoniae* is a Gram-negative bacterium and of the six most dangerous pathogens known today [1]. This is a multi-drug resistant bacterium that not only threatens immunocompromised individuals but can also lead to severe damage in healthy individuals [2]. It can colonize different human mucosal surfaces and spread to other tissues like the respiratory tract [3].

Figure 1 | *Klebsiella pneumoniae* pathogenesis. Source: microbewiki

There are currently three manually curated genome-scale metabolic models (GEMs) for *K. pneumoniae*. Liao et al. [4] reconstructed and experimentally validated the MGH78578 strain by mapping the current GEM for *E. coli* onto the genome of MGH78578 and improving the model with the help of experimental data. In 2017, a metabolic network was built for the KPPR1 strain of *K. pneumoniae* using the Propagate Model to New Genome application and Gap-filling on the glucose minimal medium [5]. Of note, these two models do not pass the current community standards [6] and FAIR Data Principles (findable, accessible, interoperable, reusable)[7]. The latest metabolic reconstruction available for *K. pneumoniae* is the first GEM built for the strain HS11286. It is a high-quality model with high prediction accuracy created within our group. Currently, multiple strains of *K. pneumoniae* have been isolated, and knowledge of their functional roles and interspecies interactions is crucial for improving the understanding of the human nose microbiome in health and disease on one side. On the other side, reconstructing high-quality genome-scale metabolic models, specifically with limited annotation resources, still remains challenging. Although GEMs of metabolism are potent tools that can be deployed to investigate similarities and differences between strains of the same species and save time and money in laborious experiments by providing predictions and promising hypotheses that can be further evaluated.

2 Aim

Therefore, this thesis aims to find how one can derive strain-specific genome-scale metabolic models of *K. pneumoniae* using one high-quality model of the same species and characterizing the pan and core metabolic capabilities. In addition, the genetic basis behind strain-specific auxotrophies will be explored. The latest high-quality generated model of *K. pneumoniae* will be independently combined with previously published GEMs. Besides, the similarities and differences between strains using the organism's genome sequence from the experimental lab will be leveraged to develop a path for constructing models of the same species and different strains. This construction will be done using information from curated models of related organisms, pan and core identifications, and reviewed gene annotations. Due to less availability of data gathered in the human swab, we used the genome sequence of *K. pneumoniae* gathered from human feces. Therefore, the validation of the models will be based on the results extracted from these data. Since *Klebsiella oxytoca* is also available in the human nose [8], in the end, the workflow will be expanded on different species of *Klebsiella* by using data from healthy human feces.

3 Requirements

This work requires the collection and combination of multiple information from different sources, including the organism's genome sequence, biological databases, and scientific literature. Experience in Python programming and familiarity with COBRApy [9] and libSBML [10] for the reconstruction process is necessary. High motivation to learn more about systems biology and constrained-based modeling, as well as exploring biochemistry and microbiology, is also vital.

References

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