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Bachelorthesis

Reconstruction of a genome-scale metabolic network of *Staphylococcus lugdunensis* N920143

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1 Background and Motivation

Staphylococcus lugdunensis is a Gram-positive and coagulase-negative human commensal [1]. Like all members of the staphylococcus genus, it is a spherical cell that forms clusters. It was first isolated and described by Freney et al. in 1988 and is named after the French city Lyon (lat. Lugdunum) [2]. *S. lugdunensis* can produce a non-ribosomally synthesized cyclic peptide antibiotic named lugdunin [3]. Lugdunin is effective against major pathogens, especially *Staphylococcus aureus*, which is known to cause aggressive infections in humans. It has been shown that nasal colonization by *S. lugdunensis* was associated with a significantly reduced *S. aureus* carriage rate. Thus, the use of *S.lugdunensis* as a probiotic to inhibit *S. aureus* in affected patients is being investigated [4]. However, this process is contraindicated by *S. lugdunensis* being an opportunistic pathogen with a high degree of virulence, unlike other Coagulase-Negative Staphylococcal species (CoNS) [5]. Although *S. lugdunensis* is a commensal and part of the normal skin flora, it has been found to cause aggressive infections similar to *S. aureus* [6]. These are often SSTIs, but the bacteria can also cause infections with high mortality, such as endocarditis [7].

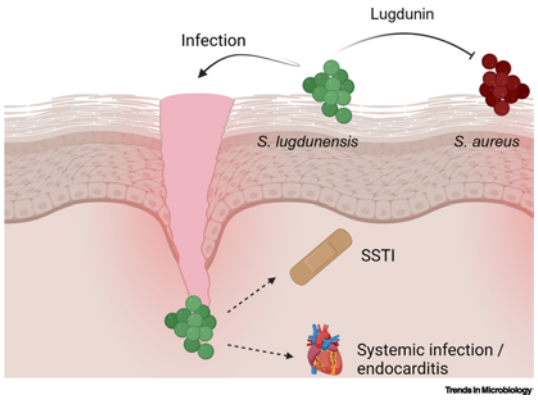

Figure 1 | *Staphylococcus lugdunensis* is found in the normal skin flora of humans. It can produce lugdunin and inhibit other bacteria like *Staphylococcus aureus*. But it also can cause skin- and soft-tissue infections (SSTIs) or more severe systemic infections (e.g., endocarditis). Image source: `https://www.cell.com/trends/microbiology/fulltext/S0966-842X(21)00184-0`

The strain N920143 was isolated from a breast abscess in 1992 [5]. The genome consists of a chromosome of 2.6 Mb and no plasmids. Currently, there is no genome-scale metabolic model (GEM) for this strain, which makes the reconstruction of such a promising microbe of keen interest.

2 Aim and Approach

This thesis focuses on manually improving an automated draft of a genome-scale model. For the first draft, automated tools like CarveMe [8] will be used, which then will be refined using different databases and literature on *S. lugdunensis*. The aim is to create a high-quality systems biology model of *Staphylococcus lugdunensis* N920143. The quality will be assured by following the protocol for generating a high-quality genome-scale metabolic reconstruction [9]. The aim is to understand this unique bacteria's metabolic processes better and compare it to models of other strains (e.g., *Staphylococcus lugdunensis* HKU09-01). The model will be validated by testing the growth for different carbon and nitrogen sources, and testing the biomass yield.

3 Requirements

(a) Fundamental understanding of biochemistry, (b) interest in systems biology, particularly in constraint-based modeling, (c) Python programming using packages (e.g., COBRApy [10], libSBML [11]), and (d) interest in learning the usage of tools to improve the model gradually (e.g., CarveMe [8], MEMOTE [12]).

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