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Consecutive Master Theses in Bioinformatics and Nano-Science

Interactions of *Corynebacterium striatum* with its environment

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1 Background and Motivation

Corynebacterium striatum, a gram-positive and non-sporulating rod, has recently been discovered for its pathogenic properties. Even though it has been known since the early 20th century, *C. striatum* was often disregarded as a pathogen since it is part of the typical human skin microbiota [1]. Nevertheless, it was found that, especially in immunocompromised patients, *C. striatum* can be the source for diseases such as Chronic Obstructive Pulmonary Disease, also known as COPD or pneumonia [2]. Not only is *C. striatum* active within the respiratory tract, but it was also attributed to long-standing open wound infections [3] and prolonged hospitalizations [4].

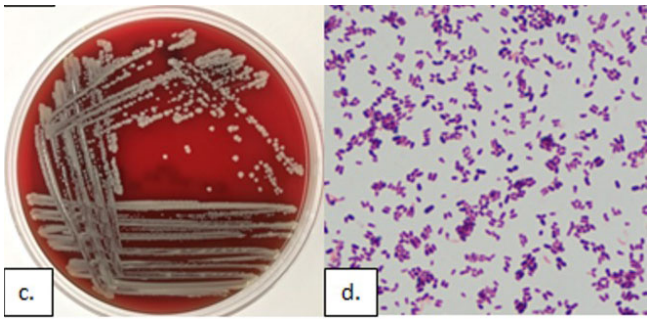

Figure 1 | C. Colony morphology *C. striatum*. D. Coryneform morphology of *C. striatum* with Gram stain [1].

Furthermore, compared to other gram-positive skin flora, *C. striatum* is relatively resistant to various antibiotics [1]. A non-exhaustive list includes resitance towards ampicillin, gentamicin, cefoperazone sulbactam, ciprofloxacin, clindamycin, erythromycin, nitrofurantoin, oxacillin, penicillin, tetracycline, vancomycin, imipenem, linezolid, and chloramphenicol [3].

One reason for *C. striatum*'s resistance towards antibiotics and immune responses might be its ability to form biofilms [1, 3, 5]. Biofilms are complex bacterial communities with distinct architecture which show resistance to biocides, antimicrobial treatments, and immune defense responses [6]. In a 2019 study, de Souza et al. investigated the virulence potential of *C. striatum* using *Caenorhabditis elegans* as a model host. They found that the formation of biofilms acts as a virulence mechanism that allows *C. striatum* to adhere to surfaces (for example medical instruments) and resist both host immune factors and antibiotics. Furthermore, it was established that infections often needed to be removed fully to enable a cure [5].

Another highly relevant bacterium due to its pathogenic properties is *Staphylococcus aureus*. Since it causes infections in a wide variety of organ systems, it is considered one of the most dangerous of the many staphy-

lococcal bacteria [7]. A 2016 study by Ramsey et al. concluded that microbe-microbe interactions between *S. aureus* and *C. striatum* affect both the fitness and behavior of *S. aureus*. They found that *S. aureus* increased its adhesion to epithelial cells, which reflects a commensal state, and that it decreased its hemolysin activity, which can be connected to attenuation of virulence [8]. Thus, while still being a respectable pathogen itself, *C. striatum* might offer a possibilty to counteract the virulence and pathogenicity of *S. aureus*.

Aside from studies on *C. elegans* infection [5] and microbe interactions with *S. aureus* [8], not many studies on microbial behavior of *C. striatum* exist. Still, there is no published genome-scale metabolic model (GEM) available and metabolic requirements of *C. striatum* for growth remain largely unknown. For these reasons, research towards a better understanding of *C. striatum* and investigation of reseasons for its pathogenicity are of high interest.

2 Aim and Approach

This project of two consecutive theses aims to understand *C. striatum*, its metabolic behavior, its virulence and potential microbic treatment for *S. aureus* infections. In order to uncover the secrets of *C. striatum*, multiple routes are open for investigation:

A general lack of laboratory data makes it difficult to confirm the existing models' correctness. Thus, a fundamental approach to gain experimental data is necessary for all further *in silico* investigations. An important step would be to find a chemically defined medium on which *C. striatum* grows both *in silico* and *in vivo*.

Further experiments to gain insight into interactions of *C. striatum* with other bacteria, including *S. aureus* and *P. aeruginosa*, can be planned based on *in silico* simulations of interactions of those bacteria. Microbe-microbe interactions of *C. striatum* with *S. aureus* were already published [8]. For other bacteria suitable experimental data must be gathered.

Due to the pathogenic properties and antibiotic resistances of *C. striatum*, any insight into possible treatments can be of value. A study of necessary metabolites or necessary reaction pathways which could be blocked using already existing drugs is possible with GEM. Afterwards, hypotheses created *in silico* can be confirmed by testing those *in vivo* in the lab.

Ribaudo et al. shown in their study from 2016 that the formation of biofilms can be simulated using a modified genome-scale metabolic model, which includes reactions necessary for the formation of an extracellular biofilm matrix. Their work is based on *Salmonella typhimurium* [9]. Xu et al. conducted a similar study in 2015 using a model of *P. aeruginosa*. They identified vital key metabolites which need to be present to enable biofilm instead of planktonic growth [10]. Since both approaches are based on GEMs and a curated model of *C. striatum* was already created in a research project prior to this master theses project, an adaption of their methodology should be possible.

Another appealing route could be the recreation of *C. striatum* infection of *C. elegans in silico*, following the paper by de Souza et al. [5]. A well-curated GEM of *C. elegans* exists [11]. This approach could lead to both a further refinement of the *C. striatum* model and a deeper understanding of the infection mechanism.

3 Requirements

(1) Fundamental understanding of biochemistry (2) interest in systems biology thinking (3) microbiology laboratory work (4) python programming.

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