

Analysis of subject- and bacteria-specific metabolic models in Necrotizing Soft Tissue Infection patients.

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Type of thesis: Computational

Required competences: Basic statistics, Basic knowledge of R and possibly Python, Basic of dynamic modelling (differential equations)

Acquired competences: Dynamic modelling, Network analysis, Multivariate statistics, analysis of (metabol)omics data, Phenotyping of human metabolism, characterization of host-bacteria interactions

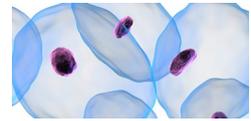
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Description

Early detection and appropriate treatment are crucial in Necrotizing Soft Tissue Infections (NSTI, sometimes called flesh eating bacterial infection), a devastating type of bacterial infection (Hansen, Rasmussen et al. 2017, Stevens and Bryant 2017). NSTI is becoming increasingly more common, and continue to be associated with a fulminant course and high mortality rates. These infections comprise a spectrum of diseases ranging from necrosis of the skin to life-threatening infections involving the fascia and muscle with systemic toxicity. They vary in predisposing and causative factors, anatomic location, offending bacteria, and tissue level of involvement.

How host (human) and NSTI causing bacteria interacts to give origin to the infection is largely unknown: different people responds differently to different bacteria and this make very complicate to define optimal treatment for different patient.

Using gene expression derived from patient samples constraint metabolic models have been build for each patient and the infecting bacteria. Compartment based meta models have been created for each -bacteria and human cells, and for each meta-model



Flux variability analysis have been performed for each reaction in the model while trying to maximize the biomass of the bacteria

Scope of the thesis is the analysis of a pool of (already existing) subject and bacteria-specific metabolic models to investigate whether (and which) NSTI patient clinical characteristics can be associated to the model parameters. The ultimate goal is to provide alternative and more tailored stratification of patient for better diagnosis and therapy.

The project is in collaboration with the Weizmann Institute, Tel Aviv

References

Hansen, M. B., L. S. Rasmussen, M. Svensson, B. Chakrakodi, T. Bruun, M. B. Madsen, A. Perner, P. Garred, O. Hyldegaard, A. Norrby-Teglund, I. s. group, M. Nekludov, P. Arnell, A. Rosén, N. Oscarsson, Y. Karlsson, O. Oppegaard, S. Skrede, A. Itzek, A. M. Wahl, M. Hedetoft, N. F. Børnthsén, R. Müller and T. Nedrebø (2017). "Association between cytokine response, the LRINEC score and outcome in patients with necrotising soft tissue infection: a multicentre, prospective study." Scientific Reports **7**: 42179.

Stevens, D. L. and A. E. Bryant (2017). "Necrotizing Soft-Tissue Infections." New England Journal of Medicine **377**(23): 2253-2265.