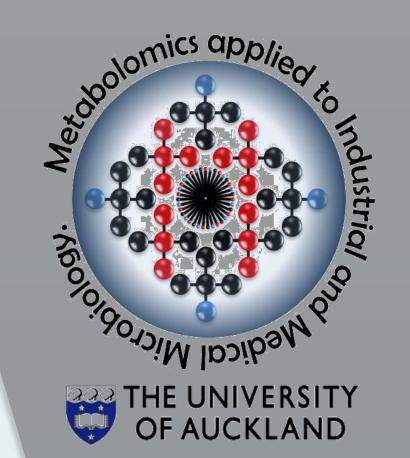


Metabolic network reconstruction of the central carbon metabolism of Enterococcus faecalis

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Introduction

E. faecalis is a gram-positive bacterium that is receiving more attention due to its "two-face" behavior. This natural inhabitant of the mammalian gastrointestinal tract is also an opportunistic pathogen responsible for urinary tract infections, nosocomial infections, bacteremia and infective endocarditis. Its intrinsic physiological properties such as inherent antibiotic resistance and exceptional ability to adapt to harsh conditions provide this organism with an enormous advantage during the infection process.

Objectives

We propose to reconstruct the metabolic network of the central carbon metabolism of *E. faecalis*. The reconstruction is based on the genome sequencing information available, as well as online databases and literature. Later, the model will be tested and validated in the laboratory, by performing experiments based on the simulations. The model will support the interpretation and better understanding of the metabolomic and proteomic data generated in our labs.

Methods

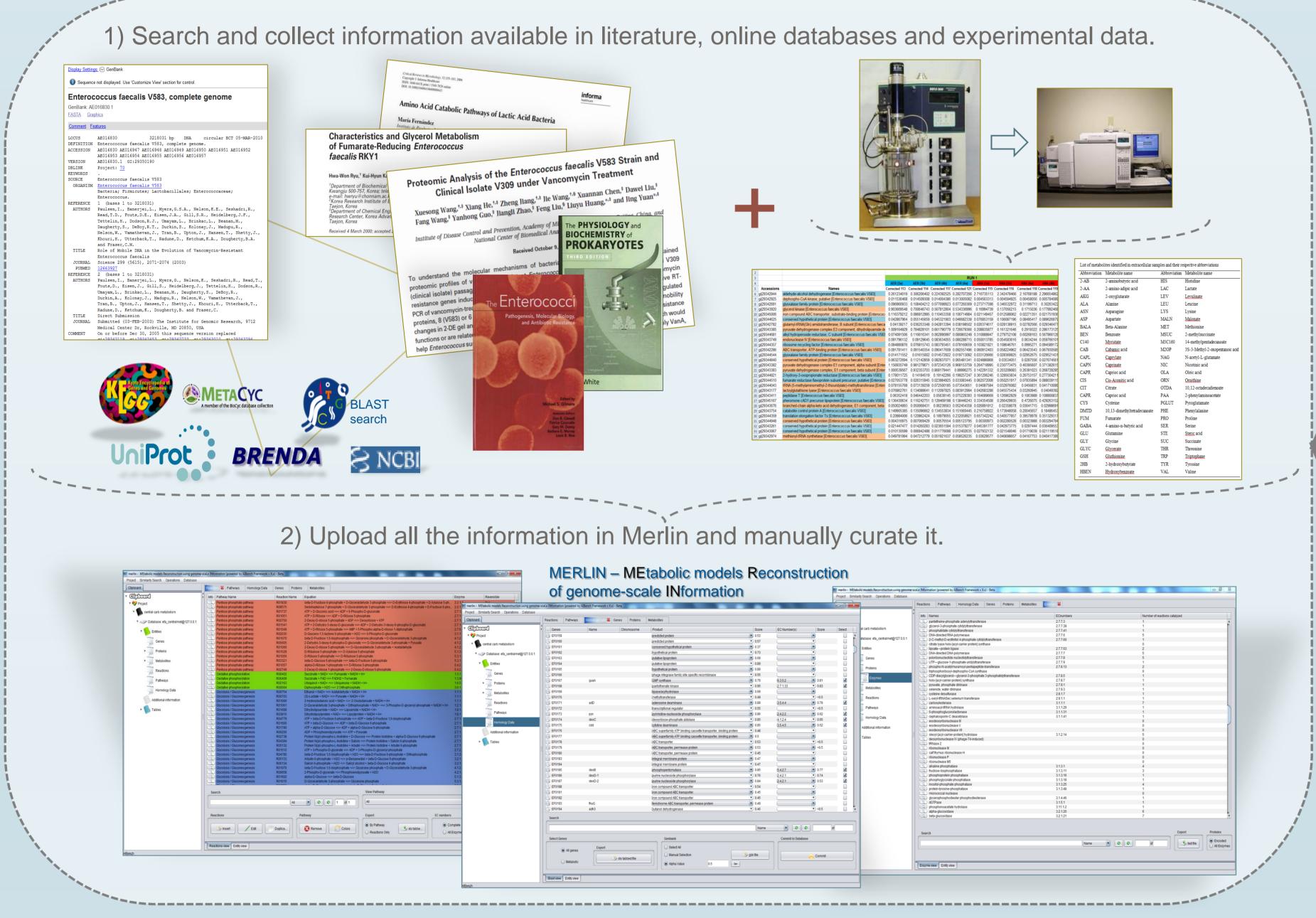
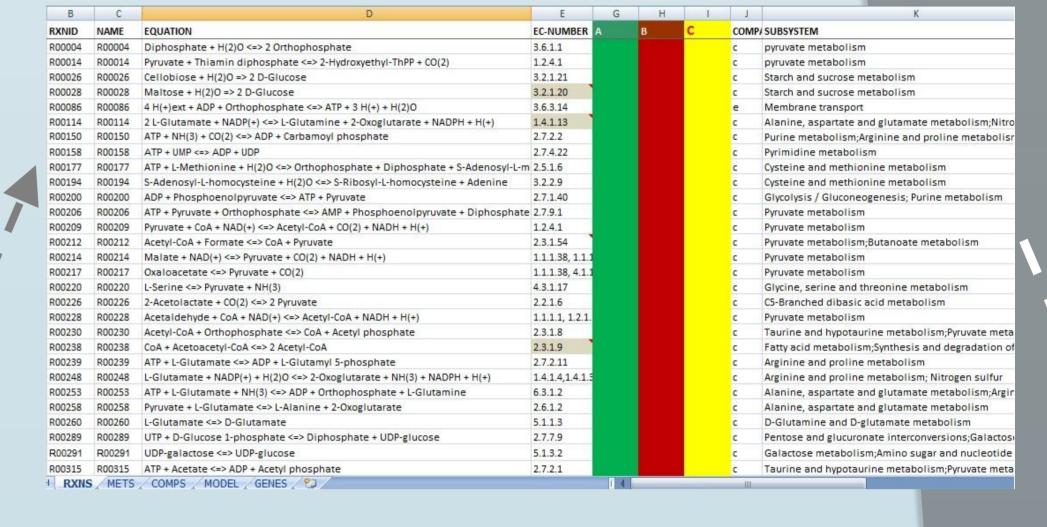
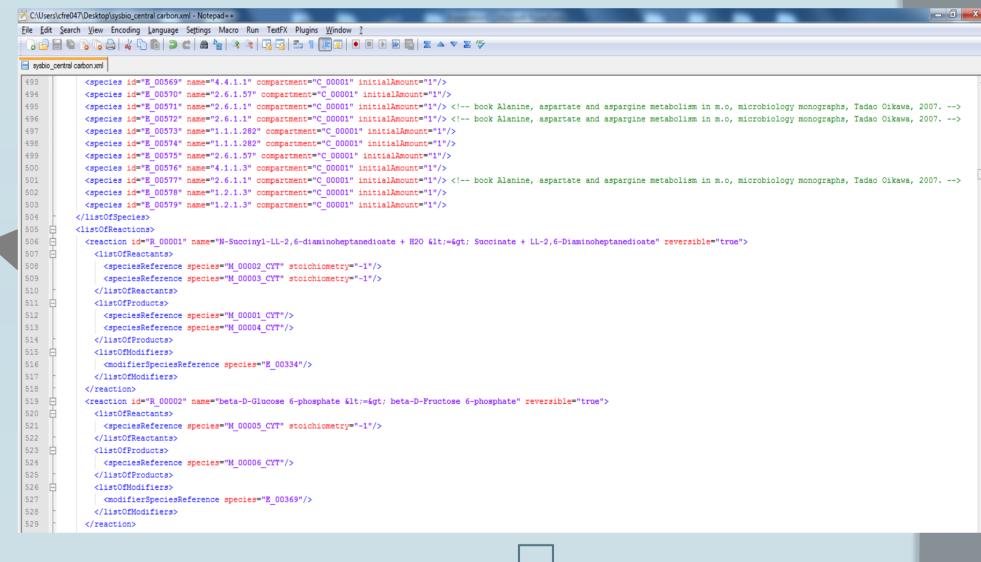


Figure 1: Data integration of different levels of information.

3) Export the information to a stardard format, either an excel spreadsheet or XML. Excel spreadsheets can also be converted to an XML format.





4) Outcome: Model reconstruction of central carbon metabolism of *E. faecalis*, ready to be tested in OptFlux and later validated in the laboratory.

Results

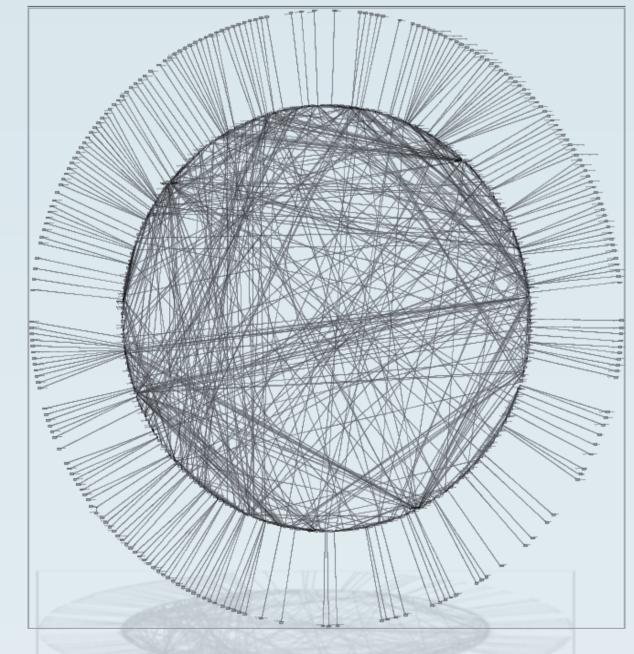


www.optflux.org

Figure 2: Snapshots of Optflux Overview network conditions EX_M_PUTRext_e Non-Essential aminoacids FluxLimits (limitation of fluxes) FluxLimits (no limitation of fluxes) Project Elements: Essential aminoacids ▼ Reactions Constraints

Overall reaction:

 $0.147328\ M_ILEext_e + 2.0\ M_ASNext_e + 0.082117\ M_CYSext_e + 5.10867\ M_GLUCext_e + 0.0603801\ M_METext_e + 0.156988\ M_PHEext_e + 0.173895\ M_VALext_e + 0.147328$ 0.0362281 M_HISext_e + 981.732 M_PPiext_e + 0.210123 M_LEUext_e + 0.0410585 M_TRPext_e + 0.512349 M_ORNext_e --> 1.92625 M_NH3ext_e + 328.409 M_Hext_e + 0.574912 M_BIOMASSext_e + 1000.0 M_H2Oext_e + 4.39983 M_GLCNext_e + 2.87125 M_FORMext_e



Conclusions and future directions

The metabolic model generated for this bacterium allows the correlation of flux distributions with different environmental conditions. It is also possible to determine the minimal medium required for growth. As an example, the overall conversion reaction shown above indicates that given a minimal medium specific for E. faecalis, it is able to produce biomass and bi-products. Additionally, metabolomic data generated by our group allowed the identification of key compounds/reactions in E. faecalis metabolism that were previously unclear, adding valuable information to the model. In the future, this model will be expanded to a genome scale and validated in the laboratory. As it has been previously shown for other organisms, the genome scale network reconstruction may serve as a valuable tool to predict the phenotypic behaviour under various genetic and environmental conditions, as well as to perform metabolic engineering simulations (e.g. gene deletion experiments) and drug target identification.

Figure 3: Graphical representation of the complex network of the cental carbon metabolism of Enterococcus faecalis – Cell designer

Acknowledgements





results.

conversion

environmental