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# GENOME SCALE METABOLIC NETWORK RECONSTRUCTION OF PATHOGEN – *ENTEROCOCCUS FAECALIS*

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**ABSTRACT**

*Enterococcus faecalis* is a Gram-positive bacterium that is getting more attention due to its "two-face" behavior. This natural inhabitant of the gastrointestinal mammalian tract is also an opportunist pathogen responsible for urinary tract infections, nosocomial infections, bacteremia and infective endocarditis (1).
Since the metabolic reconstruction of *Haemophilus influenzae* was published in 1999 (2), many other researchers have focused their attention into the possibilities that the new era of genome-scale metabolic models could bring to the scientific scene, both in prokaryotic and eukaryotic organisms.

## INTRODUCTION

Genome scale models consist on a set of chemical reactions that are inter-connected to represent the metabolic transformations that occur in the organism. They are valuable tools that allow the better understanding of the physiology of an organism while allowing the prediction of the behaviour given certain constraints.
We have formulated a genome scale reconstruction (GENRE) with 682 reactions, 655 metabolites, 516 genes (with associated metabolic function) and 584 reactions with gene association as shown in table 1.
Table 1 depicts the basic properties of GENRE of *Enterococcus faecalis*.

Table 1: Basic network properties of GENRE of pathogen *Enterococcus faecalis*

| **Basic Network Properties** | | | Total |
|---|---|---|---|
| Reactions | cytosol | 600 | 682 |
| | external | 82 | |
| Metabolites | cytosol | 577 | 655 |
| | external | 78 | |
| Genes | | 516 | 516 |
| Reactions with gene association | | 584 | 584 |

Most of the reactions in the GENRE (86%) have one or more genes associated while 14% do not have any gene associated. These are mainly transport reactions.

## RESULTS AND CONCLUSION

From the total of the 682 reactions, 496 reaction (73%) have flux while 186 reaction (27%) do not carry any flux, meaning that they are not connected to the system. These reactions are in the model since there is some evidence (in literature, databases) that justifies their presence, however, it is not possible yet to connect them to the network already assembled.
A matrix generated by this set of reactions can be solved by linear programming using a Flux Balance analysis (FBA) approach. To solve a linear programming problem it is necessary to have an objective function. For bacteria the main purpose is to grow and therefore, biomass equation is our objective function. Using FBA approach is possible to determine the set of fluxes that lead to an optimal growth subject to constrains.
Doing a GENRE of any organism is not a straightforward process as it requires the collection of all the available data, curate that information (with literature and databases and blast searches), analyze flux distribution and fill the gaps of the system until biomass is being formed. The data already available (from metabolomic, fluxomic and proteomic experiments) allowed the better understanding of some key control

points of the network as well as to fill some gaps in the model.
Currently, the model is able to do simulations and produce biomass. The validation of the model is initially acomplished by trying to make the predictions match what is experimentally observed. Once the model predicts with accuracy it is possible to test different experimental designs (from different growth media to gene deletions) and analyze if it is also observable in a laboratory scale.

## REFERENCES

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## AUTHORS' BIOGRAPHIES

**CARLA PORTELA** was born in Porto, Portugal and went to the University of Minho, where she studied biological engineering and obtained her degree in 2006. After her degree she has worked in Lyngby, Denmark and Lisbon, Portugal as a research assistant before enrolling in her PhD. Since 2009 she is working in her PhD project in Chemical and Biological Engineering under the Supervision of Eugénio C. Ferreira (IBB - UM), Isabel Rocha (IBB - UM) and Silas Villas-Bôas (UoA – New Zealand). Her e-mail address is: portela.carla@deb.uminho.pt.