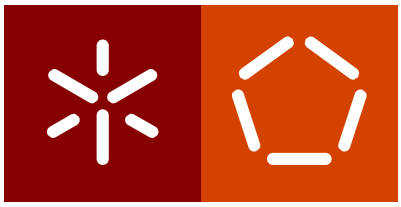

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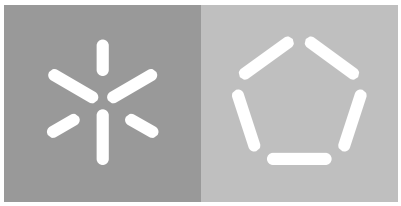

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Reconstructing of the metabolic network of *Lactobacillus rhamnosus*

Master dissertation
Master Degree in Bioinformatics

Dissertation supervised by
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ABSTRACT

With the recent growth in genomics research, complete genomic sequences of a multitude of species are assembled at an unprecedented rate(The Cost of Sequencing a Human Genome n.d.). Therefore, it is evident that full comprehension of encoded functionality is displaced from that increased knowledge rate.

Genome-scale metabolic network reconstructions try to achieve a complete understanding of the metabolic features of an organism by assembly a network of metabolic reactions catalyzed by enzymes and transporters found on the annotations made for the genome sequence(Palsson 2009). Such gene annotations are often generated by applying prior knowledge to the genomic sequence

The reconstruction process of a genome-scale metabolic model encompasses four steps, namely: (1) Genome Sequencing; (2) assembling the genome-wide metabolic network; (3) Conversion of the network to a stoichiometric model ; (4)metabolic model validation(Merlin Homepage n.d.).

In this thesis, the main aim is to use the genome sequence of *Lactobacillus rhamnosus GG* and data generated at LNEG to reconstruct the metabolic network of *L. rhamnosus*. The main tasks was the accomplishment of the metabolically annotate the genome and perform a preliminary analysis of the resulting metabolic network(Lin, Bennett, and San 2005; Lopes da Silva et al. 2013).

In spite of the work done, there is still a long way to go until the construction of a functional model. The main steps still to be taken are the Transport prediction, removal of the dead ends, compartmentalization and the assembly of model.

Another improvement for this work would be the validation of the model whit real data for *L. rhamnosus GG*, instead of the data from the *Lactobacillus rhamnosus strain C83*.

RESUMO

Com o recente crescimento da pesquisa ao nível genómico, tem levado ao aparecimento inúmeras sequencias genómicas completas das mais variadas espécies(The Cost of Sequencing a Human Genome n.d.). Portanto, é evidente que a compreensão completa da funcionalidade do genoma é desproporcional à taxa que se gera o conhecimento.

As reconstruções de redes metabólicas à escala genómica tentam alcançar uma compreensão completa das características metabólicas de um organismo através da montagem de uma rede de reações metabólicas catalisadas por enzimas e transportadores encontradas nas anotações feitas para o genoma(Palsson 2009).

O processo de construção de um modelo metabólico à escala genómica abrange quatro etapas: (1) Sequenciamento do Genoma/Anotação; (2) montagem da rede metabólica do genoma; (3) Conversão da rede para um modelo estequiométrico; (4) validação do modelo metabólico(Merlin Homepage n.d.).

O principal objetivo desta tese é usando a sequência genómica d *Lactobacillus rhamnosus GG* e os dados gerados na LNEG para construir a rede metabólica de *L. rhamnosus*. As principais tarefas foram a anotação do genoma e realização uma análise preliminar da rede metabólica resultante(Lin, Bennett, and San 2005; Lopes da Silva et al. 2013).

Apesar do trabalho realizado, ainda há um longo caminho a percorrer até a construção de um modelo funcional. Os principais passos a serem tomados são a previsão dos transportes, a remoção dos dead ends, a compartimentalização e a criação do modelo.

Outra melhoria para este trabalho seria a validação do modelo com dados reais para *L. rhamnosus GG*, ao invés dos dados *da strain Lactobacillus rhamnosus* C83.

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1. INTRODUCTION

1.1. Context

It is apparent that full perception of encoded functionality is displaced from that expanded learning rate. An example of this discrepancy is the Polaromonas sp. strain JS666 whose genome is totally sequenced although few biochemical evidences were further obtained (Jennings et al. 2009; Mattes et al. 2008).

Genome-scale metabolic network reconstructions endeavor to accomplish a global comprehension of the metabolic features of a life form by assembling a network of metabolic reactions catalyzed by enzymes and transporters found on the annotations made for the genome sequence (Palsson 2009). Such gene annotations are frequently obtained by applying prior knowledge to the genomic sequence, utilizing algorithms like for example BLAST or HMMER, which analyze the sequence similarity to previously known enzymes and identify best matching homologs.

There are a few open databases that can be used in these organism specific gene annotations to uncover the functionality of the encoded enzymes, in a manual or automated way, such as KEGG, BRENDA or MetaCyc. Since the fundamental goal is the remaking of metabolic networks, usually the data are arranged and stored in various leveled Gene-Protein-Reaction affiliations, although the storage of transcriptional and regulatory associations/networks could also be included. Although every one of those databases could be utilized in the generation of metabolic networks, they have altogether different proprieties and incorporated information. KEGG does not give solid quality gene annotations for metabolic network reconstruction purposes for many organisms (Green and Karp 2006), but has some of the most complete pathway schemes and can still serve as a reference framework for network modeling and network gap filling. BRENDA is an enzyme database which contains manually curated information from organism-specific enzyme assays or protein structure studies (Scheer et al. 2011) being, in this manner adequate for high confidence reconstructions. MetaCyc is a metabolic network database with more than 2260 pathways from 2600 distinct organisms having a portrayal of each reaction, metabolite, gene association on each pathways.

With the expanding number of entire sequenced genomes, there was additionally an expanding number of recently annotated genes and pathways found. The

quantity of genome-scale metabolic network is accordingly expanding despite the fact that at much slower rate.(Palsson 2009).

To help scientist in the notorious task of building genome-scale metabolic networks, automated reconstruction software packages were created. These bioinformatics tools recover the stored data and assemble automatically a draft reconstruction of the metabolism of a specific life form. Some product like Model SEED and PathwayTools have the capacity of automatically predicting the GPRs based solo in the annotation (Peter D Karp, Latendresse, and Caspi 2011), filling up network gaps and even converting the network to functional models (Peter D Karp et al. 2010).

However, since a considerable sample of the gene products are anticipated from earlier learning got from orthologous genes, a few forecasts result in unannotated or even missing annotated enzymes. Moreover, regardless of enzyme annotation being right, a portion of those enzymes can utilize different substrates simultaneously. Additionally, with the expanding number of annotated genes on those databases the predictions made by programming that use those same databases have lesser certainty about explicit functionality.

Currently produced genome-scale reconstructions often have genome coverage around 20%, because of the huge rate (30-40%) of hypothetical proteins unannotated in the genome and since a large number of the anticipated coding sequences belong with non-physiologically pertinent proteins. That implies that it is important to supplement the list of enzymes with different sources of biochemical data, to fill holes, including new pathways that have a high certainty level in the reproduced metabolic network. In occurrences where the metabolic network is missing at least one reaction to finish a metabolic pathway, the researcher must choose whether to incorporate a biochemical reaction lacking (Wittig and De Beuckelaer 2001).

A genome-scale metabolic network can be adjusted into a mathematical model, to try simulate biological behavior. One way to deal with metabolic modeling is to use conventional ordinary differential equations (ODEs) to assess the dynamics of the metabolites in the model. Nonetheless, such methodology is practically impracticable for modeling large complex systems with little *a priori* knowledge, since it requires a lot of pre-determined dynamic parameters and intracellular concentrations. A few enhancements for foreseeing thermodynamic parameters of those reactions were accomplished utilizing algorithms that incorporate the reaction of Gibbs free energy (Feist et al. 2007). Another methodology, increasingly reasonable for modeling genome-scale metabolic networks, is constraint-based modeling, which forces zero-order kinetic requirements (mass balanced reactions) to restrict the potential behaviors of a reactional network and at the same time enhances for the maximization of a flux rate or a metabolite generation, usually biomass for growth (Thiele and Palsson 2010). The most utilized procedures are the Flux Balance Analysis (FBA) and Flux Variability Analysis (FVA).

Currently there are a few different ways to construct a metabolic model, some more automated than others. The main tools used to aid this task are presented in table 1.

Table 1 - Online tools and databases for in silico model construction. A variety of tools are available to aid the automated construction, validation and verification of in silico models. These include tools for genome annotation, Open Reading Frames function assessment, pathway design, and optimization routines

Systems metabolic engineering online databases and computational tools(Blazeck and Alper 2010; Copeland et al. 2013)	
Databases for automated and manual genome annotation	TRANSPORT DB, WIT, SGD, KEGG, LIGAND, BioCYC, EcoCYC, MetaCYC, and BRENDA, UniProt, SWISS-PROT.
Elucidating gene function for unknown ORF	**Gene Finders** (GLIMMER, GlimmerM, Exonomy and Unveil or GENSCAN) **Homology based** (BLAST, FASTA or HMMER) **Non-homology** based (Prolinks database)
Pathway completion tools	REBIT, BNICE, FMM, PathBLAST
In silico modeling tools	MOMA, ROOM, OptKnock, OptStrain, OptReg, OMNI, COBRA Toolbox, COPASI, GrowMatch.
Automatic reconstruction tools	merlin, pathway tools, raven, SEED

1.2. Objectives

Given the described context, the main aim of this work is to use the genome sequence of *Lactobacillus rhamnosus* (*L. rhamnosus*) *GG* to reconstruct the metabolic network of *L. rhamnosus*. The main tasks will be to metabolically annotate the genome and perform a preliminary analysis of the resulting metabolic network.

2

2. STATE OF THE ART

2.1. Molecular biology

Molecular biology is a branch of science concerning biological activity at the molecular level represented in figure 1.

The field of molecular biology is related whit biology, genetics and chemistry. A key area of molecular biology concerns seeing how different cell systems cooperate as far as the way DNA, RNA and protein synthesis function.

Molecular biology takes a gander at the molecular instruments behind procedures of transcription, replication and cell work. One approach to describe molecular biology is to state it concerns seeing how genes are transcribed into RNA and how RNA is then translated into protein (sciencedaily n.d.).

A great part of the work in molecular biology is quantitative, and recently work has been done at the interface of molecular biology and software engineering in bioinformatics and bio computation (Biologia Molecular n.d.; infoescola n.d.; sciencedaily n.d.).

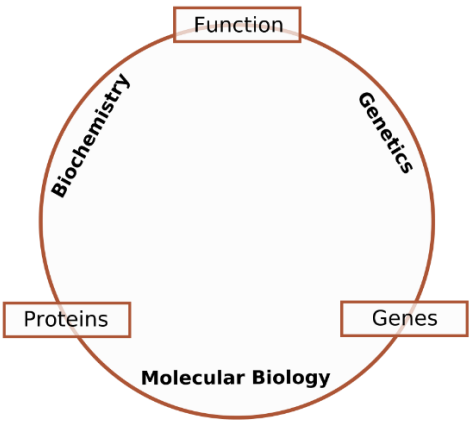

Figure 1- This scheme shows the main fields in which Molecular Biology play a role. The field of molecular biology overlaps with biology, genetics and biochemistry, where molecular biology will consider the genes, the proteins they encode and their functions.

2.2. Metabolic engineering

Metabolic Engineering can be describe as the redirection, manipulation and construction of cellular metabolism to obtain biocatalysis or biosynthesis of desired compounds (Stephanopoulos 2000).

The bases of Metabolic Engineering have started being developed in the 1970s with the advancement of one important tool in the field of genetic engineering - recombinant DNA technology (Woolston, Edgar, and Stephanopoulos 2013). This new approach permitted to consider the organisms in its integrate, as one of the characterizing parts of ME is the attention paid to systems-level understanding rather than to individual responses, which implies analyzing whole biochemical reaction networks.

Another part of Metabolic Engineering is the cell improvement, contrasted with arbitrary mutagenesis. Metabolic Engineering is the coordinated improvement of cell properties through the alteration of explicit biochemical responses, with the utilization of recombinant DNA innovation (George Stephanopoulos, Aristos Aristidou 1998; Stephanopoulos 2000).

The main goal of Metabolic Engineering is the production of useful biochemical products. This principle objective is accomplished by control of biochemical pathways , that decide the cell physiology, prompting the over-generation of target compound (Kulkarni 2016). This objective can be achieved by various means:

1- By overexpressing the gene encoding the enzyme that participates in the pathway of the target product;
2- By inhibiting the competing metabolic reactions that use the same precursor of the target product for another biochemical;
3- By carrying out the production of the desired biochemical in a non-native organism;

2.3. Systems Biology

Systems biology is a holistic approach to decoding the complexity of biological systems that starts from the understanding that the networks that form the living organisms are more than the sum of their parts. It is a collaborative field, coordinating numerous fields of science, biology, computer science, engineering, bioinformatics, physics, to anticipate how these systems change along time and under differing conditions (Breitling 2010; wikipedia n.d.).

These fields have reformed the manner in which biological research is led, including the study of several omics. There are three noteworthy omics that are relevant for the achievement of systems-level understanding of biological systems: metabolomics, proteomics and transcriptomics

Transcriptomics is the investigation of the transcriptome, the total arrangement of RNA transcripts that are generated from the genome, under explicit conditions or in a particular cell. Transcriptome analysis can be performed utilizing techniques,

for example, RNA-Seq or microarray analysis (Jongeneel et al. 2001; R. Lowe et al. 2017; wikipedia n.d.).

Proteomics is the analysis of the entire protein complement of a cell, tissue, or organism under a specific, defined set of conditions. This field uses various techniques and technologies such as protein fractionation techniques, mass spectrometry and bioinformatics (Tomislav Meštrović; Graves and Haystead 2002; Husi, Albalat, and Albalat 2014).

Metabolomics is a recently rising field of "omics", focusing on the characterization of the small molecule metabolites in biological systems. It can provide a global view of the biochemical events associated with a cellular or biological system. (Clish 2015; Roessner and Bowne 2009).

2.4. Genome scale metabolic models

The exploitation of microorganisms in medical, industrial, food and environmental biotechnology requires an extensive understanding of their physiology (Lin, Bennett, and San 2005; Lopes da Silva et al. 2013; Wendisch, Bott, and Eikmanns 2006). The accessibility of information on genome sequencing permits an increased comprehension of organism physiology at the systems level, and genome-scale metabolic (GSM) models are valuable for performing integrate analysis of metabolism (Liu, Ma, and Goryanin 2013). *GSM* models are produced from a combination of genome sequence information and detailed biochemical data and these recreated models can be utilized for dissecting and simulating operation of metabolism in response to different stimuli (Dias et al. 2015; Lin, Bennett, and San 2005; Schaffrath and Breunig 2000).

Stoichiometric models of metabolism are representations of the full or part of the metabolism of a cell.

They can be represented using a formal mathematical description:

1- A stoichiometric matrix is build according to the metabolic reactions;
2- Each row of the matrix represents one metabolite and each column represents one reaction;
3- Each element of the matrix is the stoichiometric coefficient of the correspondent reaction and metabolite(s)

This matrix, together with other linear constraints, allows performing analyses to predict flux distributions, by using tools such as Flux Balance Analysis (FBA), Parsimonious Flux Balance Analysis (pFBA), Flux Variability Analysis (FVA) or others methods(Dias et al. 2015).

The most used methodologies are the Flux Balance Analysis (*FBA*).

The reconstruction process of a genome-scale metabolic model encompasses four steps, namely:

1- Genome Sequencing and annotation;
2- Assembling the genome-wide metabolic network;
3- Conversion of the network to a stoichiometric model;

4- Metabolic model validation(Dias et al. 2015).

At first, the genome of the organism is recovered from an open database of genomic information. The following stage is the determination of coding sequences and the functional annotation of genes, which can be retrieved by finding homologous protein sequences. Here, retrieved data includes Enzyme Commission and Transporter Classification numbers and the gene associations. The part of the genome that will be used in the model is only the genes encoding enzymes or membrane transporters.

This step can be accomplished by performing a Basic Local Alignment Search Tool (*BAST*) or a HMMER.

Another step is the identification of the metabolic reactions associated with the organism. To retrieve candidate biochemical reactions, the EC numbers are matched to biochemical reaction databases, such as KEGG or BRENDA and to already existing curated GSM models for phylogenetically close organisms (e.g. the models in BIGG database).

A crucial step in the reconstruction of *GSM* models is the inclusion of reactions which are not inferred from genome annotation. Such reactions include spontaneous reactions and their addition will decrease the number of dead-end metabolites and improve network connectivity (Dias et al. 2015).

Another requirement of these models is the inclusion of reactions that represent a drain of building blocks into the biomass (Dias et al. 2015; Eremina et al. 2010; Moses et al. 2008). Growth-associated energy requirements, which represent the amount of energy depleted during replication, should also be included in the biomass equation.

The third stage of the reconstruction process involves converting the reactions list to a constraint-based mathematical model, including by assuming a steady-state condition. If no constraints are imposed on the model, it can take up or excrete compounds at any arbitrary rate, which is clearly not representative of living cells (Dias et al. 2015; Schaffrath and Breunig 2000; Scheer et al. 2011).

Once a metabolic network is obtained, the following step is to verify and evaluate the reconstructed *GSM* model. The first step is to check its consistency, to identify metabolic gaps and to track how different substrates are catabolized into different metabolites (Dias et al. 2015; Schaffrath and Breunig 2000).

The last step of the reconstruction process is testing the models metabolic capacity at three distinct levels: the ability to produce biomass precursors; the growth rate on different types of media; and whether the model is able to secrete by-products and whether the specific production rates of metabolites are correct when compared to environmental data (Dias et al. 2015; Schaffrath and Breunig 2000).

2.5. merlin tool

merlin is an open-source tool, currently available for Unix and Windows. The application is fully implemented in Java.

merlin uses several Java libraries to access web services, namely BioJava(Prlić et al. 2012), NCBI Utilities Web Service Java Application Programming Interface (API), UniProtJAPI (Patient et al. 2008), and the KEGG Representational State Transfer (REST) API, among others.

This tool has the ability to annotate a genome with both enzymatic and transport functions, and build a draft *GSM* model, with minimum user interactions (Dias et al. 2015; Merlin Homepage n.d.).

merlin tool performs several steps of the reconstruction process in a semiautomatic manner, including the functional genomic annotations. For performing the annotation of the genome it utilizes Basic Local Alignment Search Tool (BLAST) and HMMER. The results from BLAST or HMMER are evaluated and an automatic annotation of the genome is showed. The tool assigns annotations to each gene of the target organism, using an internal score that weights the frequency of functions and the taxonomy of every homologue of each gene of the genome (Merlin Homepage n.d.).

merlin is helpful for other steps of the reconstruction of models such as the transporters annotation, assembling the genome scale metabolic models, model curation and validation of the model.

2.6. *Lactobacillus rhamnosus GG* (ATCC 53103)

L. rhamnosus is a Gram-positive, non-motile, non-sporulating rod-shaped facultative anaerobic lactic acid bacterium and can be isolate from the human gastrointestinal mucosa.

L. rhamnosus GG, was originally isolated from fecal samples by Sherwood Gorbach and Barry Goldwin, which can explain its typical surname GG. It was distinguished as a potential probiotic strain in light of its protection from acid and bile and adhesion capacity to the intestinal epithelial layer (Doron S., Snydman DR. 2005). From that point forward, it has been a standout amongst the most broadly examined probiotic strains, utilized in an assortment of probiotic items. The beneficial effects of this strain have been studied in clinical trials and human intervention studies (Doron S., Snydman DR. 2005; Lebeer, Vanderleyden, and De Keersmaecker 2008).

This microorganism demonstrated a high capacity of lactic acid production in industrial environments(Bernardo et al. 2016; Lopes da Silva et al. 2013).

Lactic acid fermentation in *L. rhamnosus* is relatively fast, has high yields, and can lead, selectively, to one of its two stereoisomers or the racemic mixture.

Lactic acid is a multifunctional profitable natural acid and as of recently has been described to have the most encouraging application in assembling of biodegradable

and biocompatible polymers, for example, poly(lactic acid) (PLA), an ecologically correct alternative to conventional non-biodegradable plastics derived from petrochemicals (Axelsson et al. 2012; Datta and Henry 2006).

2.6.1. Genome

The genome of strain GG is constituted by a single circular chromosome 3.01 Mbp in size; the genome is one of the largest sized of the *Lactobacilli* genomes, which typically average ≈ 2 Mbp.

Fosmid library of the strain GG genome was constructed using the CopyControl Fosmid Library Production Kit (Epicentre). Genomic DNA was sheared by several passages through a hypodermic needle, the purified DNA fragments (40–45 kb) were ligated into the Copy Control pCC1FOS vector, and the ligated vector was packaged according to the manufacturer protocol. Fosmid end and plasmid sequencing was performed using an ABI BigDye Terminator Cycle Sequencing Kit and a 96-capillary 3730xl DNA Analyzer (Applied Biosystems).

Portions of genome missing from the fosmid libraries were sequenced directly from GG (18.5 Mbp with 6.1-fold coverage) genomic DNA using the Genome Sequencer GS 20 (Roche Applied Science). Direct sequencing of PCR-amplified fragments from genomic DNA was performed to fill in remaining sequence gaps and confirm contig order. The GG genome sequences were assessed for quality (Phred), assembled (Phrap), and edited (Gap4) using the Staden software package (Staden, Beal, and Bonfield 1999). Sequence data obtained from the Genome Sequencer GS 20 were assembled by the gsAssembler (Roche Applied Science) (Kankainen et al. 2009).

The rough number of identified genes was ≈ 3000. The genome of strain GG shows a high degree of synteny that is unexpectedly interrupted by several genomic islands. The five genomic islands in strain GG (designated GGISL1-5) are anticipated to encode 80 unique proteins with lengths of 100 residues or more(Kankainen et al. 2009). All the genomic islands were identified, as those DNA sequences deviate in codon usage, base composition and dinucleotide frequency from the rest of the genome (Tu and Ding 2003). The GG-specific islands included genes coding for bacteriophage components, sugar metabolism and transport, and exopolysaccharide biosynthesis. Moreover, these genomic islands were not conserved between closely related strains, suggesting that they originated by horizontal gene transfer (Kankainen et al. 2009).

For the GG genome, the prediction and annotation of genes were accomplished using similar methodologies. ORF predictions were performed by Glimmer3 (Arthur L Delcher et al. 2007) using the iteration mode, threshold (score >50), minimum gene length (150 bp), and maximum overlap (50 bp) adjusted parameter settings. Potential start codons were verified manually by evaluating the location and motif alignment scores for ribosomal binding sites and by comparing BLASTP alignments of similar proteins (Altschul et al. 1997; D. L. Wheeler et al. 2008). Intergenic sequences (with 50-bp flanking regions) were re-examined for ORFs using BLASTX (Altschul et al. 1997). Putative tRNA and rRNA loci were detected using tRNAscan-

SE (T. M. Lowe and Eddy 1997) in the COVE-only mode and RNAmmer (Lagesen et al. 2007) with default settings, respectively. Manual primary annotations were determined by comparing the predicted and translated ORFs with the public protein sequence database using BLASTP with default parameter settings (Altschul et al. 1997; D. L. Wheeler et al. 2008) and based on protein sequences that aligned with more than 35% amino-acid identity and 80% coverage threshold. Additional annotation information was obtained using InterPro (Mulder et al. 2007) (default settings), KAAS (Moriya et al. 2007) (set at bidirectional best-hit default mode against all known enzymes), and COGni assigned annotations accordingly. All matches obtained from searches of the Super Family database having e-value cutoffs of >0.01 were accepted (Kankainen et al. 2009).

The genome encodes a ubiquitous set of phosphotransferase system (PTS) transporters as well as many carbohydrate-metabolizing enzymes depicted in a metabolic network reconstruction. The ability to use lactose was lost in strain GG because of frameshifts in the antiterminate (lacT) and 6-phospho-β-galactosidase (lacG) genes (Kankainen et al. 2009). Other experimentally verified metabolic differences, including the inability of strain GG to use rhamnose, ribose, and maltose, were explained by genetic variations in enzymes or transporters. Also, 40 and 49 genes predicted to encode potential glycosidases in the genomes of strains GG were identified (Kankainen et al. 2009). Because of their annotation and predicted cellular location 10 of these genes may participate in peptidoglycan hydrolysis and conversion of complex polysaccharides and prebiotics to simple carbohydrates (Kankainen et al. 2009).

Other features of the genome are shown in Table 2 (Kankainen et al. 2009).

Carbohydrate utilization assays showed that strains GG use a variety of mono- and disaccharide substrates (Table 3), a metabolic activity considered advantageous for bacteria residing in the carbohydrate-rich proximal region of the small intestine (Lebeer, Vanderleyden, and De Keersmaecker 2008).

Table 2- General genomic features of L. rhamnosus GG (Kankainen et al. 2009).

Organism	*L. rhamnosus* GG
Genome size, Mbp	3.01
No. genes	2944
Plasmids	0
rRNA operons	5
tRNA genes	57
GC content, %	47
Coding efficiency, %	85
Average gene size, bp	873
Transposases	69
Prophage clusters	3
CRISPR	1

Table 3- Summary of the utilization of key carbohydrates by L. rhamnosus GG (Sugar utilization was measured according to the API 50 CH (Biomerieux®) test. ND (not determined).)(Kankainen et al. 2009).

Substrate	Sugar Utilization	Predictive transport system
Cellobiose	+	PTS
Fructose	+	PTS
Galactose	+	Galactose proton symporter?
Glucose	+	PTS
Lactose	-	PTS
Maltose	-	ABC transporter / PTS
Mannose	+	PTS
Rhamnose	-	L-rhamnose-proton symport
Trehalose	+	PTS
Ribose	+	?
Sucrose	+	PTS
Sorbose	-	-
ß-glucoside	ND	PTS
N-acetyl-glucosamine	+	PTS
Sorbitol	+	PTS
Glucitol	ND	PTS
Galactitol	ND	PTS
Mannitol	+	PTS

2.7. Systems metabolic engineering online databases and computational tools.

2.7.1. Databases for automated and manual genome annotation.

- The **BioCyc** is a group of Pathway or Genome DataBases (PGDB) that presents information on genomes and cellular networks, as well as allows powerful computational analysis and exploitation of the database(Peter D Karp et al. 2002).

  The **EcoCyc** and **MetaCyc** databases (DBs) are online reference hotspots for metabolic information. They are comparable in describing metabolic pathways, enzymes, reactions and substrate compounds. Both DBs use the same DB schema. Both are accessed using the same software environment, called the Pathway Tools (Peter D Karp et al. 2000).
  MetaCyc is a well-known metabolic pathway database that contains information on organism enzymes and pathways involved in primary and secondary metabolism and its associated compounds, enzymes, and genes (P D Karp et al. 1999; Peter D Karp et al. 2000).

- **BRENDA**, Braunschweig Enzyme Database is a protein function database, which contains a huge amount of enzymatic and metabolic data and is updated and evaluated by extracting information from primary literature.(BRENDA n.d.; Scheer et al. 2011).

- **UniProtKB** Universal Protein Resource Knowledgebase (UniProtKB) is a collection of accurate and rich information on proteins. It consists of two sections: the first section contains manually annotated proteins with information extracted from literature and computational analysis (referred to as UniProtKB/Swiss-Prot) and the second section with computationally analyzed proteins to be fully manually annotated yet (UniProtKB/TrEMBL) (Apweiler et al. 2004).

2.7.2. Elucidating gene function for unknown ORF.

- ***Glimmer*** is a framework for discovering genes in DNA, particularly the genomes of microscopic organisms, virus, and archaea. Glimmer utilizes Markov models (IMMs) to recognize the coding genes and separate them from noncoding DNA (A L Delcher et al. 1999).

- The ***BLAST*** developed by Altschul (1990) (Altschul et al. 1990). The *BLAST* is a set of algorithms that attempt to find a short fragment of a query sequence that aligns perfectly with a fragment of a sequence found in a database. For the original *BLAST* algorithm, the fragment is then used as a seed to extend the alignment in both directions. Said another way,

BLAST looks for short sequences in the query that match short sequences found in the database, allowing the annotation of the unknown genome by comparing with the genomes already studied (BLAST n.d.).

- Profile hidden Markov models (profile ***HMMER***) (Krogh et al. 1994) represent an important advance in terms of sensitivity of sequence searches for remote homology. They provide a formal probabilistic framework for sequence comparison and improve detection of remote homologs by enabling position-specific residue and gap scoring based on a query profile, and calculating the signal of homology based on the more powerful 'Forward/Backward' *HMM* algorithm that computes not just one best-scoring alignment, but a sum of support over all possible alignments (T. J. Wheeler and Eddy 2013).

2.7.3. Pathway completion tools

- ***PathBLAST*** is a network alignment and search tool for comparing protein interaction networks across species to identify protein pathways and complexes that have been conserved by evolution. The basic method searches for high-scoring alignments between pairs of protein interaction paths, for which proteins of the first path are paired with putative orthologs occurring in the same order in the second path. This technique discriminates between true- and false-positive interactions and allows for functional annotation of protein interaction pathways based on similarity to the network of another, well-characterized species (Feist et al. 2007; pathblast n.d.).

2.7.4. *In silico* modeling tools.

Validation of Genome-scale Metabolic Models

The GSM model should be validated by comparing computer simulations to laboratory data. This assessment allows improving the model as it measures the accuracy of the model (Dias et al. 2015).

- The **FBA** identifies flux distributions under steady state assuming a given optimal condition. This algorithm usually uses the maximization of the biomass flux as objective function to simulate the cellular growth, or the maximization of ATP to simulate the natural objectives of the cell (Orth, Thiele, and Palsson 2010).

- Method Of Minimization of Metabolic Adjustment (**MOMA**) is good at predicting sub-optimal growth immediately after a reaction knockout.

MOMA is based on the same stoichiometric constraints as FBA, but has a relaxed display for optimal growth flux when genes are deleted. Therefore, MOMA mimics with higher accuracy the metabolic networks of a mutant cell to determine its growth than FBA(Vitkup and Church 2002).

- ***OptFlux*** is an open-source user-friendly software, implemented in Java, that applies steady-state stoichiometric models to study the phenotype of microorganisms, under different environmental and genetic conditions. this tool incorporate strain optimization tasks, the identification of Metabolic Engineering targets, using Evolutionary Algorithms/Simulated Annealing metaheuristics or the previously proposed OptKnock algorithm (Rocha et al. 2010).

3

3. METHODS AND DEVELOPMENT

In this chapter, merlin will be used to reconstruct the metabolic network of *Lactobacillus rhamnosus*, as mentioned before. Overall, through an iterative process, with validation from data obtained through wet-lab experiments, the metabolic model is increasingly improved until the results approximate with the simulations performed with the model (Figure 2). In the present work, the main tasks of metabolic annotation have been performed.

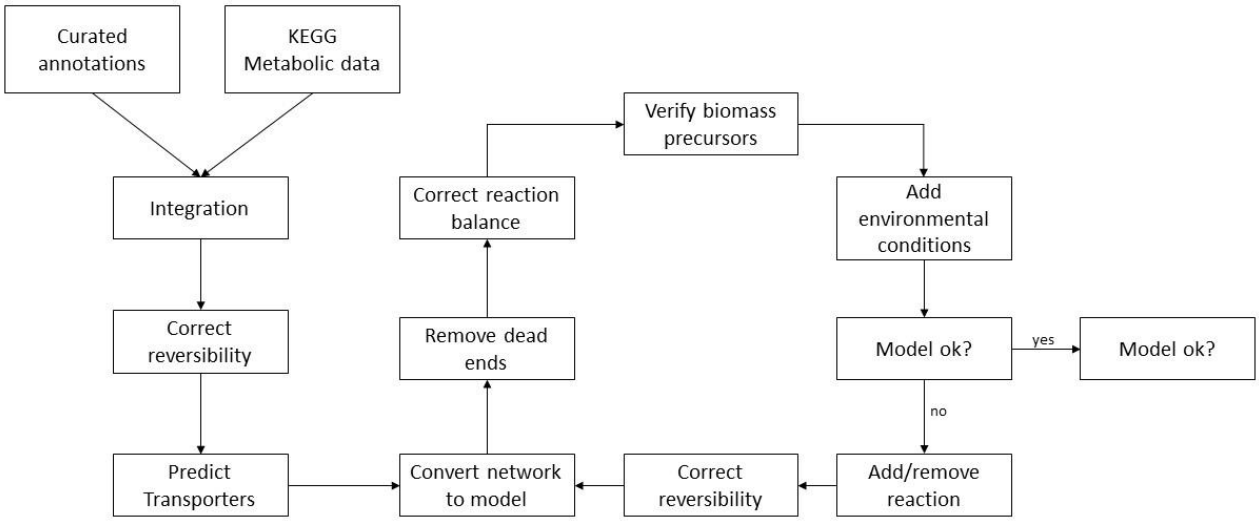

Figure 2- Scheme of the methodology used to reconstruct the GSM model of L. Rhamnosus

3.1. Reconstruction of the draft network

The first step was to create a new project in Merlin regarding the organism *L. rhamnosus* GG (tax. ID 568703). To carry out this step, we followed the instructions present in the merlin page (Merlin Homepage n.d.).

3.1.1. Finding organisms for comparison

The method used to find the organism for comparison during BLAST and HMMER annotations consisted in searching in the genus of the species gathered during BLAST, for species with a high percentage of curated data. Each species of the genus *Bacillus* was assessed in UniProt to find the better organism for this purpose. The organism with the most curated genes was selected (*Bacillus subtilis*).

3.1.2. Automatic annotation using merlin

After the project has been created, an automatic annotation through Merlin's tools was performed for the enzymes present in the genome. This annotation was performed through a BLAST of the target genome against the Uni-ProtKB/TrEMBL database. After a preliminary analysis of the results obtained, it was concluded that the data obtained did not have the best quality. In order to try to obtain better results it was decided to change the pipeline and perform the automatic annotation in two stages. Firstly, a BLAST was performed of the target genome against the UniProt database UniProtKB/Swiss-Prot and then a second BLAST was performed against the UniProtKB/TrEMBL database, using only the genes that did not obtain results on the BLAST against the Swiss-Prot.

3.1.3. Manual curation

Since the results obtained by the automatic annotation performed by merlin did not contain a high rate of genes with curated annotations i. e., functions obtained by comparing against Swiss-Prot data), it was decided to carry out a manual curation of all annotations with EC number.

For the execution of manual curation, the pipeline represented in Figure 3 was used.

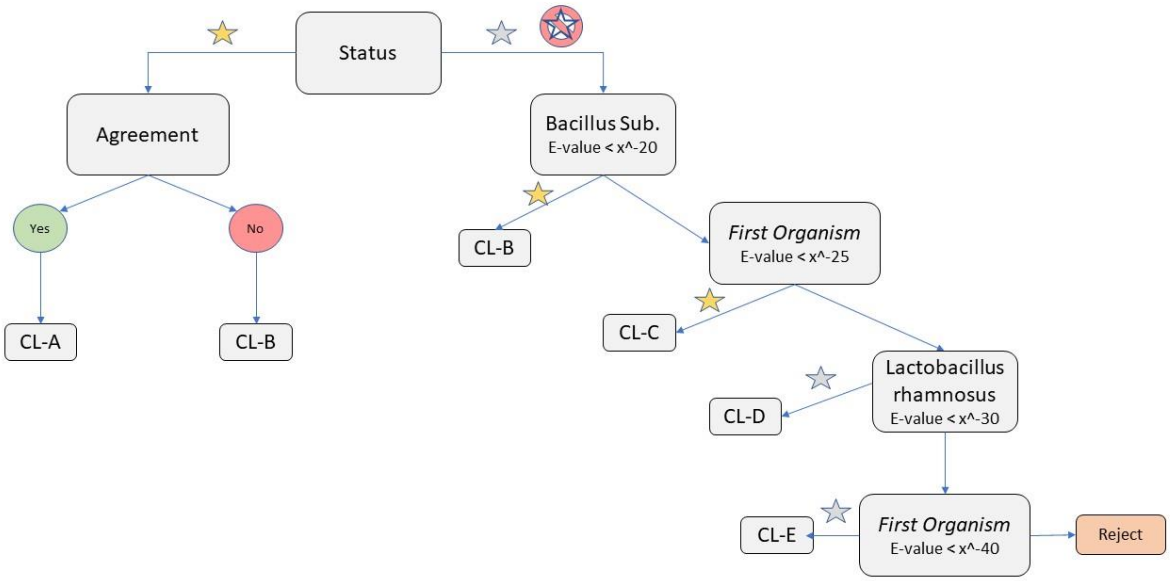

Figure 3 -Pipeline used for manual curation for the genome functional annotation of the microorganism Lactobacillus rhamnosus using merlin. ***Yellow star*** *- reviewed record on UniProtKB;* ***grey star*** *- unreviewed record on UniProtKB;* ***Bacillus sub.-*** *taxonomically closest organism, the model organism;* ***First Organism*** *- organism of first hit in the list of homologous genes;* ***Lactobacillus rhamnosus*** *- Organism for which the sequence is being annotated;* ***CL-A/B/C/D/E*** *- Annotation Confidence Levels. A, B and C stands for Very High, High and Medium Confidences, while D and E stands for Low and Very Low Confidences, respectively.*

Phylogenetically close organisms are more prone to have similar protein functions than distant ones. From this premise, an annotation workflow based on the phylogeny of some organisms relatively close to *L. Rhamnosus*, was developed. The phylogenetic distance between *L. Rhamnosus* and other organisms will influence the curation confidence level. Likewise, the curation status of the homologous gene was also taken into account for the confidence level. In summary, manually curated homologous genes from organisms phylogenetically close to *L. Rhamnosus* or the ones that have an annotation against Swiss-Prot have a greater confidence level, as opposed to homologous genes from organisms phylogenetically distant or that have an annotation against TrEMBL.

The first step of this workflow is the identification of the type of BLAST made to the gene that originated the collected results: if it was a BLAST against the database TrEMBL or the database Swiss-Prot. If the annotation of the gene was done through a comparison with Swiss-Prot, a confidence level of A or B was given, depending or on if the annotation already existed (and coincided) for *L. rhamnosus* in Swiss-Prot. If no curated annotation existed for *L. rhamnosus* for the gene in question, the results obtained by comparing with the model organism (*Bacillus subtilis* strain 168) were analyzed. If a gene exists in Swiss-Prot for the model organism similar to the target gene, the confidence level B was also given. If no similarity existed with the model organism, then the next step was to verify if there was some annotation

cured for this gene regardless of the organism and the first annotation is accepted with a confidence level C.

If the annotations of the gene in question were obtained through a BLAST against TrEMBL, the first step is to check if there is any uncurated classification of the target gene, and, if so, the annotation will be accepted with a level of confidence D. If this is not verified, uncurated annotations of similar genes for other organism will be sought and accepted with a confidence level E.

3.1.4. Integration with the metabolic data

The next step was to integrate the annotation in the model database. merlin retrieved all metabolic information from KEGG (enzymes, pathways, metabolites and reactions). Then, merlin uses the data collected, together with the annotation, to assemble the draft network. This way, it was possible to use KEGG pathways as a template to ease this reconstruction and the curation of network.

3.1.5. Correct the reversibility of reactions

The reversibility of the reactions in the network was automatically corrected using merlin. However, during the process of curation some reactions needed to be manually confirmed by comparing with the information in KEGG pathways or using other tools like metaCyc or eQuilibrator for more confirmation(Flamholz et al. 2011).

3.2. Curation of the genomic-scale metabolic model

The model curation is an iterative process, that constantly updates the GSM model. Each iteration comprises several steps that improve the model qualitatively and quantitatively. Some of the steps performed in this phase were the addition and removal of some of the reactions, complementing metabolic pathways, among other things (Dias et al. 2015; Merlin Homepage n.d.).

3.2.1. Reactions balance

merlin has a tool that allows to detect unbalanced reactions in the model. KEGG was used to assess the reason for the unbalancing of the reactions and to fix these issues. Often, the problem was associated with generic compounds that have a repetitive monomer. In these cases, the problem was solved by adjusting the stoichiometry of such monomers in the reactants or in the products of the reaction.

3.2.2. Verify biomass precursors

An equation for biomass formation was developed to account for the drain of precursors and building blocks into biomass. Biomass synthesis was set as a linear combination of seven macromolecular components – proteins, DNA, RNA, lipids,

cofactor, polysaccharides – which were considered to account for the cell overall biomass composition (Oliveira, Nielsen, and Förster 2005).

Another important component incorporated in the biomass is ATP, though in this case it represents the amount of energy required to biosynthesize one gram of biomass.

When compiling the biomass composition, data was retrieved from literature (Oliveira, Nielsen, and Förster 2005). As there is insufficient information for *L. rhamnosus* it was decided that *Lactococcus lactis* would be used to complete the information.

3.2.3. Culture medium for validation.

The culture medium chosen to test the metabolic model is described in table 4.

This culture medium was used to perform the growth of *Lactobacillus rhamnosus strain* C83 that will serve as a comparison term for our organism (Gamar, Blondeau, and Simonet 1997).

Table 4 – Composition of growth media(Gamar, Blondeau, and Simonet 1997).

Macroelement	**Concentration ($mg.L^{-1}$)**	**Bases**	**Concentration ($mg.L^{-1}$)**
$MgSO_4.7H_2O$	2	Adenine	2,5
$MnSO_4.7H_2O$	0,2	Uracil	2,5
$FeSO_4.7H2O$	0,08	Xanthine	10
L-amino acids	**Concentration ($g.L^{-1}$)**	**Vitamins**	**Concentration ($mg.L^{-1}$)**
Alanine	0,1	D-Biotin	0,01
Aspatic acid	0,1	Thiamine	0,2
Glutamine	0,1	**Oligoelements**	**Concentration ($\mu g.L^{-1}$)**
Glycine	0,1	$CoCl_2.6H_2O$	95
Histidine	0,2	$ZnCl_2$	35
Isoleucine	0,05	H_3BO_3	3
Methionine	0,05	$NiCl_2$	12
Phenylalanine	0,2	$CuSO_4.5H_2O$	1
Proline	0,1		
Threonine	0,05		
Tryptophan	0,05		
Tyrosine	0,2		

4

4. Results and discussion

In this section, all the results regarding the reconstruction of the metabolic network are presented.

4.1.1. Genome annotation

4.1.1.1. Analysis of annotations with a EC number after manual curation (genes gone be considered in the constructions of the first draft).

After curation the automatic annotation made by merlin, table 5 was constructed. For better understand of the distribution of the annotations by the respective confidence levels an analysis of the table 8 was performed. After the analysis was possible to conclude that we have 2 annotations with confidence level of CL-A (0,36% of total annotations), 241 annotations with confidence level of CL-B (43,03% of total annotations), 118 annotations with confidence level of CL-C (21,07% of total annotations) and 199 annotations with confidence level of CL-C (35,54% of total annotations). In the total was performed the curation of 1237 genes from the L. Rhamnosus from the total only 560 annotations were used to performing the first draft.

Table 5- Distribution of genes annotations by the respective confidence levels.

Distribution of genes by confidence levels					
confi. Level	CL-A	CL-B	CL-C	CL-D	Total genes
Nº of annotations	2	241	118	199	560
%	0,36	43,03	21,07	35,54	100%

In the table 6 we have the distribution of annotations by the categories reviewed and data base. Initiating with the data base swissprot it was obtained a total of 308 annotations reviewed representing 85% of the total of all reviewed annotations. In the uniport data base have a total of 53 annotations reviewed representing the remaining 15%.

Table 6- Distribution of the genes annotations by the categories reviewed and data base.

Table 6- Distribution of annotations by the categories reviewed and data base		
	total	%
reviewed/swissprot	308	85%
reviewed/uniprotkb	53	15%

4.1.2. Correction of the reversibility of reactions and of EC numbers in the model.

The reversibility, along with the direction correction of reactions (in irreversible cases) was done to solve various problems within model.

4.1.3. Biomass precursors.

All the macromolecules are represented in the following equation, and these are resultant of the biomass composition, in the metabolic model. This quantitative study was done through multiple sources(Oliveira, Nielsen, and Förster 2005).

1- Biomass equation.

0.136 e-RNA + 0.01 e-Cofactor + 0.027 e-DNA + 0.032 e-Lipid + 0.064 e-Carbohydrate + 0.533 e-Protein + 18.15 ATP => 1.0 e-Biomass + 18.15 ADP + 18.15 Phosphate

2- Carbohydrate equation.

5.5 UDP-glucose + UDP-galactose + 5.6 dTDP-rhamnose -> 1.0 e-Carbohydrate + 6.5 UDP + 5.6 dTDP

3- Cofactor equation.

1.0E-6 Glutathione + 1.0E-6 NAD + 1.0E-6 SAM + 1.0E-6 heme + 1.0E-6 NADP + 1.0E-6 CoA + 1.0E-6 FMN + 1.0E-6 FAD + 1.0E-6 THF + 1.0E-6 Riboflavin + 1.0E-6 thiamine + 1.0E-6 ubiquinone + 1.0E-6 Pyridoxal phosphate => 1.0 e-Cofactor

4- DNA equation.

0.5465765898588533 dTTP + 0.48953803330216883 dGTP + 0.5479844722298137 dATP + 0.4688228210580573 dCTP => 3.2372809934738105 PPI + 3.23728099347381 e-DNA

5- Lipid equetion.

18.9 phosphatidylglycerol + 42.5 cardiolipin + 4.3 lysophosphatidylglycerol + 30.3 diglucosyl diacylglycerol + 4 monoglucosyl diacylglycerol -> 100 e-Lipid

6- Protein equation.

0.26459651144173313 L-Tyrosyl-tRNA(Tyr) + 0.4485609840261761 L-Lysyl-tRNA + 0.7104669599600648 L-Alanyl-tRNA + 0.34091712381854355 L-Phenylalanyl-tRNA(Phe) + 0.37275236971985237 L-Glutamyl-tRNA(Glu) + 0.18742615748547115 L-Histidyl-tRNA(His) + 0.09137271436906821 L-Tryptophanyl-tRNA(Trp) + 0.7989056405722051 L-Leucyl-tRNA + 0.5013311526624874 L-Isoleucyl-tRNA(Ile) + 0.4137330978892393 L-Seryl-tRNA(Ser) + 0.029736295377768333 L-Cysteinyl-tRNA(Cys) + 0.46891093440574605 Glycyl-tRNA(Gly) + 0.49823706278775465 L-Threonyl-tRNA(Thr) + 0.5440372065049127 L-Valyl-tRNA(Val) + 0.21058572743394274 L-Methionyl-tRNA + 0.44936642455446013 L-Aspartyl-tRNA(Asp) + 0.31418295799560686 L-Asparaginyl-tRNA(Asn) + 0.3642249057830923 L-Arginyl-tRNA(Arg) + 0.3151588206145171 L-Prolyl-tRNA(Pro) + 0.3824400149402909 Glutaminyl-tRNA => 0.21058572743394274 tRNA(Met) + 0.09137271436906821 tRNA(Trp) + 0.49823706278775465 tRNA(Thr) + 0.18742615748547115 tRNA(His) + 0.7104669599600648 tRNA(ala) + 0.7989056405722051 tRNA(Leu) + 0.5013311526624874 tRNA(Ile) + 0.3151588206145171 tRNA(Pro) + 0.31418295799560686 tRNA(Asn) + 0.3824400149402909 tRNA(Gln) + 0.3642249057830923 tRNA(Arg) + 0.34091712381854355 tRNA(Phe) + 0.029736295377768333 tRNA(Cys) + 0.46891093440574605 tRNA(Gly) + 0.44936642455446013 tRNA(Asp) + 0.4485609840261761 tRNA(Lys) + 0.37275236971985237 tRNA(Glu) + 0.4137330978892393 tRNA(Ser) + 9.04310433512522 H2O + 0.5440372065049127 tRNA(Val) + 0.26459651144173313 tRNA(Tyr) + 9.04310433512522 e-Protein

7- RNA equation.

0.6124617338259931 GTP + 0.4362891303847912 UTP + 0.5041748840447573 ATP + 0.4401031379389717 CTP => 3.091632944116432 e-RNA + 3.0916329441164323 PPI

4.1.4. Draft model

A draft model was created to evaluate the integrity of the different pathways in order to carry out a manual curation in order to be present the growth of the biomass. This first draft was constituted by 837 reactions from cured genome annotations.

These reactions are part of the main metabolic pathway, such as Biosynthesis of unsaturated fatty acids, Fatty acid biosynthesis and degradation, Carbohydrate metabolism, Amino acid metabolism among others.

5

5. Conclusions and Future work

In this chapter, a summary of the work done in the GSM model is presented, in the context of this work, as well as future work to continue to improve this model.

5.1.1. Conclusions.

A robust genome-wide annotation was performed in this work, which allowed providing a reliable representation of the metabolism of this organism for the construction of model.

During this work it was also possible to identify the main constituents of the biomass so that a biomass reaction could be created as close to reality as possible.

5.1.2. Future work

In spite of the work done, there is still a long way to go until the construction of a functional model.

The main steps still to be taken are the Transport prediction, removal of the dead ends, compartmentalization and the assembly of model.

One of them is the compartmentalization of the model, by adding new compartments in which reactions can take place.

Another improvement for this work would be the validation of the model whit real data for L. rhamnosus GG, instead of the data from the *Lactobacillus rhamnosus strain* C83.

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Attachments

The table 7 shows all the genes used in the construction of the first draft. In the first column is the identification of the gene, in the second column the gene product is identified, in the third column is the e-value of the gene product, the fourth column represents the EC number, then the e-value in relation to the EC number and finally the annotation attributed.

Table 7- all the gene used in the construction of the draft.

Genes	Product	score	EC number	score	notes
CAR85897.1	Beta sliding clamp	0.79	2.7.7.7	0.21	CL-B
CAR85900.1	DNA gyrase subunit B	0.67	5.99.1.3	0.79	CL-B
CAR85901.1	DNA gyrase subunit A	0.67	5.99.1.3	0.79	CL-B
CAR85910.1	Putative cysteine protease YraA	0.17	3.2.-.-	0.23	CL-B
CAR85911.1	Cytochrome bd ubiquinol oxidase subunit 1	0.26	1.10.3.-	0.33	CL-B
CAR85912.1	Cytochrome bd ubiquinol oxidase subunit 2	0.27	1.10.3.-	0.27	CL-B
CAR85925.1	Baeyer-Villiger flavin-containing monooxygenase	0.65	1.14.13.-	0.65	CL-C
CAR85928.1	Uncharacterized ABC transporter ATP-binding protein YknY	0.15	3.6.3.-	0.63	CL-B
CAR85934.1	Probable maltose O-acetyltransferase	0.18	2.3.1.79	0.17	CL-B
CAR85936.1	Probable dipeptidase A	0.47	3.4.-.-	0.88	CL-C
CAR85945.1	Beta-glucuronidase	0.43	3.2.1.31	0.43	CL-C
CAR85947.1	KHG/KDPG aldolase	0.4	4.1.3.16, 4.1.2.14	0.4	CL-B
CAR85948.1	2-dehydro-3-deoxygluconokinase	0.62	2.7.1.45	0.62	CL-B
CAR85949.1	Uronate isomerase	0.83	5.3.1.12	0.83	CL-B
CAR85950.1	Uronate isomerase	0.83	5.3.1.12	0.83	CL-B

CAR85951.1	Mannonate dehydratase	0.81	4.2.1.8	0.83	CL-B
CAR85966.1	5-methylthioadenosine/S-adenosylhomocysteine deaminase	0.59	3.5.4.31, 3.5.4.28	0.61	CL-C
CAR85977.1	Zinc-transporting ATPase	0.13	3.6.3.-	0.35	CL-B
CAR85985.1	PTS system fructose-specific EIIABC component	0.26	2.7.1.191	0.2	CL-B
CAR85988.1	Mannosylglycerate hydrolase	0.3	3.2.1.170	0.62	CL-C
CAR85990.1	6-phospho-beta-glucosidase GmuD	0.15	3.2.1.86	0.18	CL-B
CAR85993.1	Tryptophan synthase alpha chain	0.86	4.2.1.20	0.86	CL-C
CAR85994.1	Tryptophan synthase beta chain	0.9	4.2.1.20	0.93	CL-B
CAR85995.1	N-(5'-phosphoribosyl)anthranilate isomerase	0.93	5.3.1.24	0.93	CL-C
CAR85996.1	Indole-3-glycerol phosphate synthase	0.92	4.1.1.48	0.93	CL-C
CAR85997.1	Anthranilate phosphoribosyltransferase	0.93	2.4.2.18	0.93	CL-C
CAR86003.1	4-hydroxy-tetrahydrodipicolinate reductase	0.93	1.17.1.8	0.93	CL-B
CAR86004.1	4-hydroxy-tetrahydrodipicolinate synthase	0.92	4.3.3.7	0.93	CL-B
CAR86005.1	N-acetyldiaminopimelate deacetylase	0.8	3.5.1.47	0.8	CL-B
CAR86006.1	2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-acetyltransferase	0.93	2.3.1.89	0.93	CL-B
CAR86007.1	Diaminopimelate decarboxylase	0.67	4.1.1.20	0.7	CL-B
CAR86008.1	Aspartokinase 3	0.2	2.7.2.4	0.32	CL-B
CAR86009.1	Diaminopimelate epimerase	0.88	5.1.1.7	0.88	CL-C
CAR86010.1	Aspartate-semialdehyde dehydrogenase	0.62	1.2.1.11	0.64	CL-B
CAR86016.1	Cyclic-di-AMP phosphodiesterase GdpP	0.38	3.1.4.-	0.51	CL-B

CAR86018.1	Replicative DNA helicase	0.52	3.6.4.12	0.56	CL-B
CAR86020.1	Putative PTS system EIIBC component YbbF	0.16	2.7.1.-	0.58	CL-B
CAR86021.1	N-acetylmuramic acid 6-phosphate etherase	0.84	4.2.1.126	0.93	CL-B
CAR86025.1	Uncharacterized ABC transporter ATP-binding protein MT1014	0.05	3.6.3.-	0.58	CL-B
CAR86027.1	Decarboxylase yanB	0.5	4.1.1.-	0.5	CL-C
CAR86028.1	Adenylosuccinate synthetase	0.93	6.3.4.4	0.93	CL-B
CAR86030.1	Zinc-transporting ATPase	0.13	3.6.3.-	0.34	CL-B
CAR86033.1	Anaerobic ribonucleoside-triphosphate reductase	0.57	1.1.98.6	0.57	CL-C
CAR86043.1	D-alanine--D-alanine ligase	0.89	6.3.2.4	0.93	CL-C
CAR86050.1	Heme sensor protein HssS	0.65	2.7.13.3	0.65	CL-C
CAR86052.1	Methylated-DNA--protein-cysteine methyltransferase, inducible	0.65	2.1.1.63	0.65	CL-B
CAR86053.1	D-2-hydroxyisocaproate dehydrogenase	0.31	1.1.1.-	0.42	CL-C
CAR86054.1	PTS system cellobiose-specific IIB component	0.53	2.7.1.69	0.55	CL-D
CAR86058.1	Aryl-phospho-beta-D-glucosidase BglA	0.15	3.2.1.86	0.26	CL-B
CAR86067.1	Taurine import ATP-binding protein TauB	0.54	3.6.3.36	0.45	CL-C
CAR86070.1	Coenzyme A disulfide reductase	0.59	1.8.1.14	0.59	CL-C
CAR86073.1	Putative ring-cleaving dioxygenase MhqE	0.32	1.13.11.-	0.71	CL-B
CAR86085.1	Acetate kinase	0.87	2.7.2.1	0.9	CL-B
CAR86087.1	Xylulose kinase	0.41	2.7.1.17	0.41	CL-B
CAR86088.1	Probable fructose-bisphosphate aldolase	0.15	4.1.2.13	0.43	CL-B

CAR86095.1	Probable phosphoketolase	0.76	4.1.2.-	0.9	CL-C
CAR86104.1	Lipid A export ATP-binding/permease protein MsbA	0.38	3.6.3.-	0.63	CL-B
CAR86107.1	NADH oxidase	0.28	1.6.99.3	0.4	CL-C
CAR86120.1	Probable 2-ketogluconate reductase	0.15	1.1.1.215	0.15	CL-B
CAR86133.1	Pyrrolidone-carboxylate peptidase	0.9	3.4.19.3	0.93	CL-C
CAR86137.1	Ribosomal RNA small subunit methyltransferase G	0.93	2.1.1.-	0.93	CL-C
CAR86139.1	Sporulation initiation inhibitor protein Soj	0.25	3.6.-.-	0.3	CL-B
CAR86144.1	Inosine-5'-monophosphate dehydrogenase	0.62	1.1.1.205	0.72	CL-B
CAR86148.1	Sensor protein kinase WalK	0.67	2.7.13.3	0.74	CL-C
CAR86149.1	D-alanyl-D-alanine carboxypeptidase DacA	0.43	3.4.16.4	0.71	CL-B
CAR86152.1	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate--2,6-diaminopimelate ligase	0.57	6.3.2.13	0.58	CL-B
CAR86153.1	Aspartate racemase	0.74	5.1.1.13	0.74	CL-C
CAR86154.1	Glyoxal reductase	0.15	1.1.1.283, 1.1.1.-	0.15	CL-B
CAR86157.1	Malonate-semialdehyde dehydrogenase	0.38	1.2.1.-, 1.2.1.27	0.49	CL-B
CAR86158.1	5-deoxy-glucuronate isomerase	0.79	5.3.1.30	0.79	CL-B
CAR86159.1	5-dehydro-2-deoxygluconokinase	0.65	2.7.1.92	0.67	CL-B
CAR86160.1	3D-(3,5/4)-trihydroxycyclohexane-1,2-dione hydrolase	0.53	3.7.1.22	0.55	CL-B
CAR86161.1	Inositol 2-dehydrogenase	0.45	1.1.1.369, 1.1.1.18	0.41	CL-B
CAR86162.1	Inositol 2-dehydrogenase/D-chiro-inositol 3-dehydrogenase	0.33	1.-.-.-	0.18	CL-B
CAR86163.1	Inosose dehydratase	0.89	4.2.1.44	0.92	CL-B

CAR86164.1	6-phospho-5-dehydro-2-deoxy-D-gluconate aldolase	0.24	4.1.2.29	0.24	CL-B
CAR86165.1	Probable tautomerase YolI	0.4	5.3.2.-	0.68	CL-B
CAR86169.1	6-phosphogluconate dehydrogenase, decarboxylating	0.65	1.1.1.-	0.16	CL-B
CAR86170.1	Gluconokinase	0.19	2.7.1.12	0.19	CL-B
CAR86176.1	Glycosyltransferase, group 2 family protein	0.48	2.4.-.-	0.37	CL-D
CAR86180.1	Zinc import ATP-binding protein ZnuC	0.53	3.6.3.-	0.54	CL-C
CAR86182.1	Metallophosphoesterase	0.53	3.-.-.-	0.46	CL-D
CAR86183.1	Uncharacterized oxidoreductase YkwC	0.16	1.1.-.-	0.23	CL-B
CAR86185.1	Polyisoprenyl-teichoic acid--peptidoglycan teichoic acid transferase TagU	0.5	2.7.8.-	0.54	CL-B
CAR86190.1	Putative glycosyltransferase EpsH	0.65	2.4.-.-	0.65	CL-B
CAR86193.1	Signal peptidase I	0.92	3.4.21.89	0.92	CL-D
CAR86195.1	Uncharacterized ABC transporter ATP-binding protein YfmM	0.16	3.6.3.-	0.2	CL-B
CAR86216.1	Deoxyribose-phosphate aldolase	0.75	4.1.2.4	0.83	CL-B
CAR86217.1	Phosphopentomutase	0.92	5.4.2.7	0.93	CL-B
CAR86218.1	Purine nucleoside phosphorylase DeoD-type	0.9	2.4.2.1	0.93	CL-B
CAR86223.1	ATP-dependent helicase	0.61	3.6.4.12	0.3	CL-D
CAR86226.1	Mannose-6-phosphate isomerase	0.32	5.3.1.8	0.74	CL-B
CAR86228.1	D-galactosamine-6-phosphate deaminase AgaS	0.37	3.5.99.-	0.47	CL-C
CAR86229.1	N-acetylglucosamine-6-phosphate deacetylase	0.6	3.5.1.25	0.6	CL-B
CAR86231.1	Beta-galactosidase	0.11	3.2.1.23	0.47	CL-C

CAR86232.1	PTS mannose transporter subunit IIAB	0.53	2.7.1.69	0.48	CL-D
CAR86236.1	Tagatose-6-phosphate kinase	0.7	2.7.1.144	0.72	CL-C
CAR86237.1	Sorbitol-6-phosphate 2-dehydrogenase	0.09	1.1.1.140	0.09	CL-C
CAR86240.1	PTS galactitol transporter subunit IIA	0.6	2.7.1.69	0.46	CL-D
CAR86244.1	Glycosyltransferase Gtf1	0.79	2.4.1.-	0.79	CL-C
CAR86246.1	Cystathionine beta-lyase PatB	0.4	4.4.1.8	0.62	CL-B
CAR86247.1	Uncharacterized peptidase YqhT	0.17	3.4.-.-	0.47	CL-B
CAR86251.1	Glutamyl aminopeptidase	0.26	3.4.11.-	0.58	CL-B
CAR86253.1	Peptidase T	0.93	3.4.11.4	0.93	CL-B
CAR86259.1	Energy-coupling factor transporter ATP-binding protein EcfA1	0.6	3.6.3.-	0.88	CL-B
CAR86261.1	Aminopyrimidine aminohydrolase	0.65	3.5.99.2	0.65	CL-B
CAR86263.1	Hydroxyethylthiazole kinase 2	0.6	2.7.1.50	0.88	CL-C
CAR86264.1	Thiamine-phosphate synthase	0.85	2.5.1.3	0.86	CL-C
CAR86265.1	Hydroxymethylpyrimidine/phosphomethylpyrimidine kinase	0.49	2.7.1.49, 2.7.4.7	0.55	CL-B
CAR86268.1	Bifunctional ribokinase/ribose-5-phosphate isomerase A	0.34	2.7.1.15, 5.3.1.6	0.34	CL-C
CAR86270.1	Peptidase, S54 family	0.42	3.4.21.-	0.42	CL-D
CAR86288.1	Probable licABCH operon regulator	0.65	2.7.1.-	0.65	CL-B
CAR86292.1	PTS system fructose-specific EIIB'BC component	0.27	2.7.1.202	0.37	CL-B
CAR86293.1	Transaldolase	0.15	2.2.1.2	0.83	CL-B
CAR86294.1	Ribulose-phosphate 3-epimerase	0.49	5.1.3.1	0.59	CL-C

CAR86300.1	Transketolase	0.54	2.2.1.1	0.72	CL-B
CAR86301.1	Putative transketolase C-terminal section	0.01	2.2.1.1	0.04	CL-C
CAR86302.1	Fructokinase	0.71	2.7.1.4	0.81	CL-B
CAR86305.1	PTS fructose transporter subunit IIB	0.48	2.7.1.69	0.48	CL-D
CAR86306.1	PTS system fructose-specific EIIABC component	0.23	2.7.1.202	0.43	CL-B
CAR86308.1	Fructose-bisphosphate aldolase	0.41	4.1.2.13	0.41	CL-B
CAR86309.1	Fructose-bisphosphate aldolase	0.41	4.1.2.13	0.43	CL-B
CAR86310.1	PTS system, mannose-specific IIB component	0.48	2.7.1.69	0.49	CL-D
CAR86313.1	Transaldolase	0.93	2.2.1.2	0.92	CL-D
CAR86325.1	Energy-coupling factor transporter ATP-binding protein EcfA1	0.59	3.6.3.-	0.93	CL-B
CAR86328.1	o-succinylbenzoate synthase	0.4	4.2.1.113	0.4	CL-B
CAR86329.1	Beta-hexosaminidase	0.32	3.2.1.52	0.45	CL-B
CAR86344.1	DNA helicase	0.91	3.6.4.12	0.91	CL-D
CAR86351.1	Calcium-transporting ATPase 1	0.2	3.6.3.8	0.51	CL-B
CAR86362.1	Beta-Ala-His dipeptidase	0.5	3.4.13.20	0.5	CL-C
CAR86365.1	Beta-galactosidase	0.82	3.2.1.23	0.93	CL-C
CAR86373.1	Methionine import ATP-binding protein MetN	0.63	3.6.3.-	0.82	CL-B
CAR86381.1	Lysozyme	0.72	3.2.1.17	0.73	CL-D
CAR86385.1	Lipoprotein-releasing system ATP-binding protein LolD	0.39	3.6.3.-	0.66	CL-B
CAR86386.1	NADH peroxidase	0.22	1.11.1.1	0.22	CL-C

CAR86387.1	Putative phosphatase YxeH	0.25	3.1.3.-	0.41	CL-B
CAR86389.1	Streptomycin 3''-adenylyltransferase	0.64	2.7.7.47	0.63	CL-D
CAR86396.1	Penicillin acylase	0.65	3.5.1.11	0.65	CL-C
CAR86398.1	Oleate hydratase	0.69	4.2.1.53	0.69	CL-C
CAR86401.1	PTS-dependent dihydroxyacetone kinase, phosphotransferase subunit DhaM	0.45	2.7.1.121	0.71	CL-C
CAR86403.1	PTS-dependent dihydroxyacetone kinase, ADP-binding subunit DhaL	0.32	2.7.1.121	0.57	CL-C
CAR86404.1	PTS-dependent dihydroxyacetone kinase, dihydroxyacetone-binding subunit DhaK	0.22	2.7.1.121	0.33	CL-C
CAR86417.1	Probable GMP synthase [glutamine-hydrolyzing]	0.22	6.3.5.2	0.22	CL-C
CAR86419.1	Fructose-bisphosphate aldolase	0.41	4.1.2.13	0.43	CL-B
CAR86425.1	L-Ala-D/L-Glu epimerase	0.25	5.1.1.20	0.25	CL-B
CAR86431.1	Glutamine synthetase	0.75	6.3.1.2	0.76	CL-B
CAR86436.1	Glyoxal reductase	0.15	1.1.1.283, 1.1.1.-	0.15	CL-B
CAR86444.1	Histidine kinase	0.88	2.7.13.3	0.87	CL-D
CAR86445.1	Uncharacterized ABC transporter ATP-binding protein YxlF	0.15	3.6.3.-	0.87	CL-B
CAR86449.1	Aminopeptidase N	0.52	3.4.11.2	0.56	CL-C
CAR86457.1	Dihydroanticapsin 7-dehydrogenase	0.26	1.1.1.385	0.26	CL-B
CAR86459.1	Shikimate dehydrogenase (NADP(+))	0.6	1.1.1.25	0.6	CL-C
CAR86461.1	Shikimate dehydrogenase (NADP(+))	0.65	1.1.1.25	0.65	CL-C
CAR86462.1	Homoserine O-acetyltransferase	0.63	2.3.1.31	0.63	CL-B
CAR86463.1	Cysteine synthase	0.39	2.5.1.47	0.52	CL-B

CAR86466.1	Cystathionine beta-lyase	0.37	4.4.1.2, 4.4.1.1	0.16	CL-B
CAR86491.1	5,10-methylenetetrahydrofolate reductase	0.33	1.5.1.20	0.57	CL-C
CAR86492.1	5-methyltetrahydropteroyltriglutamate--homocysteine methyltransferase	0.8	2.1.1.14	0.83	CL-C
CAR86497.1	Trehalose-6-phosphate hydrolase	0.14	3.2.1.93	0.14	CL-B
CAR86498.1	PTS system glucose-specific EIIA component	0.3	2.7.1.-	0.51	CL-B
CAR86501.1	L-lactate dehydrogenase	0.72	1.1.1.27	0.93	CL-C
CAR86502.1	NAD-specific glutamate dehydrogenase	0.28	1.4.1.2	0.3	CL-B
CAR86509.1	Uncharacterized sugar epimerase YhfK	0.65	4.-.-.-	0.65	CL-B
CAR86524.1	Sensor histidine kinase YcbM	0.65	2.7.13.3	0.65	CL-B
CAR86538.1	Aerobic glycerol-3-phosphate dehydrogenase	0.38	1.1.5.3	0.63	CL-B
CAR86539.1	Glycerol kinase	0.92	2.7.1.30	0.93	CL-B
CAR86545.1	6-phospho-beta-galactosidase	0.65	3.2.1.85	0.67	CL-C
CAR86546.1	6-phospho-beta-galactosidase	0.87	3.2.1.85	0.91	CL-A
CAR86548.1	Galactokinase	0.93	2.7.1.6	0.93	CL-B
CAR86549.1	UDP-glucose 4-epimerase	0.69	5.1.3.2	0.71	CL-B
CAR86550.1	Galactose-1-phosphate uridylyltransferase	0.87	2.7.7.12	0.93	CL-B
CAR86552.1	Aldose 1-epimerase	0.63	5.1.3.3	0.63	CL-C
CAR86559.1	1-phosphofructokinase	0.19	2.7.1.56	0.19	CL-B
CAR86560.1	Tagatose 1,6-diphosphate aldolase	0.6	4.1.2.40	0.79	CL-C
CAR86561.1	Galactose-6-phosphate isomerase subunit LacB	0.67	5.3.1.26	0.79	CL-C

CAR86562.1	Galactose-6-phosphate isomerase subunit LacA	0.65	5.3.1.26	0.79	CL-C
CAR86571.1	Adenine DNA glycosylase	0.67	3.2.2.31	0.67	CL-B
CAR86576.1	Hydroxymethylpyrimidine/phosphomethylpyrimidine kinase	0.58	2.7.1.49, 2.7.4.7	0.6	CL-B
CAR86580.1	Thermostable beta-glucosidase B	0.1	3.2.1.21	0.58	CL-C
CAR86587.1	Putative quinone oxidoreductase YhfP	0.27	1.6.5.-	0.27	CL-B
CAR86588.1	Calcium-transporting ATPase 1	0.2	3.6.3.8	0.54	CL-B
CAR86590.1	Undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase	0.5	2.4.-.-	0.25	CL-B
CAR86591.1	Putative mannosyltransferase YkcB	0.4	2.4.1.-	0.68	CL-B
CAR86596.1	Sensor protein CiaH	0.74	2.7.13.3	0.74	CL-C
CAR86601.1	Putative NAD(P)H nitroreductase YdgI	0.65	1.-.-.-	0.65	CL-B
CAR86602.1	L-lactate dehydrogenase	0.41	1.13.12.4	0.16	CL-C
CAR86612.1	LexA repressor	0.93	3.4.21.88	0.93	CL-B
CAR86617.1	5-formyltetrahydrofolate cyclo-ligase	0.93	6.3.3.2	0.9	CL-D
CAR86621.1	NAD-dependent malic enzyme	0.51	1.1.1.38	0.65	CL-B
CAR86623.1	Thiol peroxidase	0.92	1.11.1.15	0.91	CL-D
CAR86626.1	Lipid A export ATP-binding/permease protein MsbA	0.55	3.6.3.-	0.55	CL-C
CAR86627.1	Oligoendopeptidase F homolog	0.44	3.4.24.-	0.79	CL-B
CAR86628.1	Nucleoside diphosphate kinase	0.76	2.7.4.6	0.67	CL-D
CAR86630.1	Copper-exporting P-type ATPase	0.29	3.6.3.54	0.31	CL-B
CAR86631.1	Proline iminopeptidase	0.69	3.4.11.5	0.69	CL-C

CAR86635.1	5'-nucleotidase	0.55	3.1.3.5	0.55	CL-C
CAR86639.1	Uncharacterized oxidoreductase YtbE	0.15	1.-.-.-	0.25	CL-B
CAR86645.1	S-ribosylhomocysteine lyase	0.92	4.4.1.21	0.93	CL-C
CAR86647.1	Holliday junction ATP-dependent DNA helicase RuvA	0.93	3.6.4.12	0.93	CL-B
CAR86648.1	Holliday junction ATP-dependent DNA helicase RuvB	0.92	3.6.4.12	0.93	CL-C
CAR86649.1	S-adenosylmethionine:tRNA ribosyltransferase-isomerase	0.93	2.4.99.17	0.93	CL-C
CAR86650.1	Queuine tRNA-ribosyltransferase	0.9	2.4.2.29	0.9	CL-B
CAR86652.1	Alcohol dehydrogenase	0.17	1.1.1.1	0.26	CL-B
CAR86655.1	Glucose-6-phosphate 1-dehydrogenase	0.59	1.1.1.49	0.65	CL-B
CAR86656.1	DNA polymerase IV	0.82	2.7.7.7	0.83	CL-C
CAR86658.1	Bifunctional oligoribonuclease and PAP phosphatase NrnA	0.42	3.1.-.-, 3.1.3.7	0.59	CL-B
CAR86659.1	DEAD-box ATP-dependent RNA helicase CshA	0.38	3.6.4.13	0.81	CL-B
CAR86661.1	Uncharacterized protein	0.64	2.1.2.3, 3.5.4.10	0.44	CL-D
CAR86662.1	Alanine--tRNA ligase	0.92	6.1.1.7	0.93	CL-B
CAR86665.1	Putative pre-16S rRNA nuclease	0.93	3.1.-.-	0.93	CL-B
CAR86669.1	Endonuclease MutS2	0.93	3.1.-.-	0.93	CL-B
CAR86672.1	D-alanine--D-alanyl carrier protein ligase	0.79	6.2.1.-	0.79	CL-B
CAR86677.1	Glutamate racemase	0.91	5.1.1.3	0.92	CL-B
CAR86678.1	Phosphoesterase	0.92	3.1.4.-	0.91	CL-D
CAR86687.1	Putative dipeptidase YkvY	0.17	3.4.13.-	0.19	CL-B

CAR86689.1	Penicillin-binding protein 1A	0.66	3.4.16.4, 2.4.1.129	0.79	CL-B
CAR86691.1	Putative HAD-hydrolase YfnB	0.32	3.-.-.-	0.32	CL-B
CAR86693.1	Beta-Ala-Xaa dipeptidase	0.33	3.4.13.-	0.79	CL-B
CAR86701.1	Acid sugar phosphatase	0.6	3.1.3.-	0.63	CL-B
CAR86705.1	Ferredoxin--NADP reductase	0.79	1.18.1.2	0.93	CL-B
CAR86706.1	Putative peptidyl-prolyl cis-trans isomerase	0.29	5.2.1.8, 3.1.3.-	0.21	CL-C
CAR86720.1	Alpha-monoglucosyldiacylglycerol synthase	0.65	2.4.1.337	0.65	CL-C
CAR86721.1	Alpha-galactosylglucosyldiacylglycerol synthase	0.7	2.4.1.-	0.7	CL-C
CAR86722.1	Phosphatidylglycerol lysyltransferase	0.91	2.3.2.3	0.91	CL-D
CAR86723.1	Putative N-acetyl-LL-diaminopimelate aminotransferase	0.16	2.6.1.-	0.26	CL-B
CAR86725.1	Lipoteichoic acid synthase	0.6	2.7.8.-	0.66	CL-B
CAR86737.1	S-adenosylmethionine synthase	0.93	2.5.1.6	0.93	CL-C
CAR86743.1	Leucine--tRNA ligase	0.93	6.1.1.4	0.93	CL-B
CAR86747.1	Ribosomal small subunit pseudouridine synthase A	0.45	5.4.99.-	0.21	CL-B
CAR86749.1	ADP-dependent (S)-NAD(P)H-hydrate dehydratase	0.72	4.2.1.136	0.72	CL-C
CAR86751.1	Glutathione peroxidase homolog BsaA	0.33	1.-.-.-	0.26	CL-B
CAR86752.1	Cystathionine beta-lyase PatB	0.21	4.4.1.8	0.62	CL-B
CAR86760.1	GTP pyrophosphokinase YjbM	0.4	2.7.6.5	0.68	CL-B
CAR86761.1	NAD kinase 1	0.28	2.7.1.23	0.93	CL-B
CAR86762.1	Uncharacterized RNA pseudouridine synthase YjbO	0.17	5.4.99.-	0.35	CL-B

CAR86763.1	FAD:protein FMN transferase	0.57	2.7.1.180	0.57	CL-C
CAR86765.1	Undecaprenyl-diphosphatase	0.91	3.6.1.27	0.93	CL-C
CAR86766.1	6-phosphogluconolactonase	0.49	3.1.1.31	0.49	CL-B
CAR86769.1	GMP reductase	0.93	1.7.1.7	0.93	CL-B
CAR86771.1	Putative 23S rRNA (guanine-N(1)-)-methyltransferase YxjB	0.65	2.1.1.-	0.65	CL-B
CAR86773.1	Putative tRNA (cytidine(34)-2'-O)-methyltransferase	0.49	2.1.1.207	0.83	CL-B
CAR86779.1	Uncharacterized zinc protease YmfH	0.65	3.4.24.-	0.65	CL-B
CAR86780.1	Uncharacterized oxidoreductase YmfI	0.32	1.-.-.-	0.32	CL-B
CAR86782.1	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase	0.71	2.7.8.5	0.71	CL-B
CAR86787.1	Ribonuclease Y	0.92	3.1.-.-	0.93	CL-B
CAR86789.1	ComF operon protein 1	0.65	3.6.4.12	0.65	CL-B
CAR86800.1	Sensor protein kinase WalK	0.45	2.7.13.3	0.71	CL-B
CAR86804.1	Phosphate import ATP-binding protein PstB 2	0.58	3.6.3.27	0.93	CL-B
CAR86805.1	Phosphate import ATP-binding protein PstB	0.55	3.6.3.27	0.93	CL-C
CAR86812.1	HPr kinase/phosphorylase	0.92	2.7.11.-, 2.7.4.-	0.93	CL-B
CAR86813.1	Prolipoprotein diacylglyceryl transferase	0.92	2.4.99.-	0.93	CL-B
CAR86814.1	Glycerol-3-phosphate dehydrogenase [NAD(P)+]	0.92	1.1.1.94	0.93	CL-B
CAR86815.1	Thioredoxin reductase	0.51	1.8.1.9	0.57	CL-B
CAR86816.1	Phosphoglucomutase	0.47	5.4.2.2	0.49	CL-B
CAR86826.1	ATP-dependent Clp protease proteolytic subunit	0.89	3.4.21.92	0.93	CL-C

CAR86828.1	Glyceraldehyde-3-phosphate dehydrogenase	0.68	1.2.1.12	0.83	CL-B
CAR86829.1	Phosphoglycerate kinase	0.92	2.7.2.3	0.92	CL-C
CAR86830.1	Triosephosphate isomerase	0.91	5.3.1.1	0.93	CL-B
CAR86831.1	Enolase	0.9	4.2.1.11	0.93	CL-B
CAR86836.1	Carboxylesterase	0.65	3.1.1.1	0.65	CL-C
CAR86837.1	Exoribonuclease 2	0.38	3.1.13.1	0.62	CL-B
CAR86839.1	Intracellular maltogenic amylase	0.23	3.2.1.-	0.23	CL-B
CAR86840.1	Maltose phosphorylase	0.27	2.4.1.8	0.27	CL-B
CAR86841.1	Beta-phosphoglucomutase	0.69	5.4.2.6	0.69	CL-B
CAR86849.1	Fe(3+) ions import ATP-binding protein FbpC	0.14	3.6.3.30	0.15	CL-C
CAR86853.1	Uracil-DNA glycosylase	0.9	3.2.2.27	0.93	CL-B
CAR86854.1	Phosphate acetyltransferase	0.66	2.3.1.8	0.66	CL-B
CAR86859.1	Exodeoxyribonuclease	0.36	3.1.11.2	0.36	CL-B
CAR86861.1	UDP-N-acetylenolpyruvoylglucosamine reductase	0.9	1.3.1.98	0.93	CL-C
CAR86864.1	Spermidine/putrescine import ATP-binding protein PotA	0.93	3.6.3.31	0.93	CL-C
CAR86871.1	Calcium-transporting ATPase 1	0.19	3.6.3.8	0.47	CL-B
CAR86875.1	Diadenylate cyclase	0.43	2.7.7.85	0.71	CL-B
CAR86877.1	Phosphoglucosamine mutase	0.93	5.4.2.10	0.93	CL-B
CAR86878.1	Glutamine--fructose-6-phosphate aminotransferase [isomerizing]	0.83	2.6.1.16	0.83	CL-B
CAR86896.1	Alpha-galactosidase Mel36A	0.33	3.2.1.22	0.85	CL-C

CAR86899.1	Sensor histidine kinase YclK	0.32	2.7.13.3	0.67	CL-B
CAR86910.1	ATP-dependent helicase/nuclease subunit A	0.43	3.6.4.12	0.69	CL-B
CAR86911.1	DNA ligase	0.93	6.5.1.2	0.93	CL-B
CAR86913.1	Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit C	0.93	6.3.5.-	0.93	CL-D
CAR86914.1	Glutamyl-tRNA(Gln) amidotransferase subunit A	0.91	6.3.5.7	0.92	CL-C
CAR86915.1	Aspartyl/glutamyl-tRNA(Asn/Gln) amidotransferase subunit B	0.93	6.3.5.-	0.93	CL-B
CAR86916.1	Diacylglycerol kinase	0.71	2.7.1.107	0.71	CL-B
CAR86917.1	23S rRNA (uracil(1939)-C(5))-methyltransferase RlmD	0.17	2.1.1.189, 2.1.1.190	0.15	CL-B
CAR86918.1	Type III restriction-modification system EcoP15I enzyme mod	0.22	2.1.1.72	0.55	CL-C
CAR86921.1	Type III restriction-modification system StyLTI enzyme mod	0.55	2.1.1.72	0.55	CL-C
CAR86922.1	Type III restriction-modification system Bce10987IP enzyme res	0.32	3.1.21.5	0.6	CL-C
CAR86927.1	Polyphosphate:ADP phosphotransferase	0.2	2.7.4.1	0.29	CL-C
CAR86928.1	Neutral endopeptidase	0.38	3.4.24.-	0.54	CL-C
CAR86938.1	scyllo-inositol 2-dehydrogenase (NADP(+)) IolU	0.4	1.1.1.371	0.4	CL-B
CAR86939.1	DEAD-box ATP-dependent RNA helicase CshA	0.38	3.6.4.13	0.83	CL-B
CAR86944.1	Probable ATP-dependent DNA helicase RecQ	0.16	3.6.4.12	0.61	CL-B
CAR86949.1	Ribonuclease BN	0.69	3.1.-.-	0.47	CL-D
CAR86951.1	Methionine aminopeptidase	0.49	3.4.11.18	0.71	CL-B
CAR86956.1	Phosphomevalonate kinase	0.55	2.7.4.2	0.55	CL-C
CAR86957.1	UTP--glucose-1-phosphate uridylyltransferase	0.63	2.7.7.9	0.79	CL-B

CAR86959.1	Aryl-phospho-beta-D-glucosidase BglH	0.15	3.2.1.86	0.26	CL-B
CAR86960.1	PTS system sucrose-specific EIIBCA component	0.3	2.7.1.-	0.69	CL-B
CAR86964.1	Putative glycosyltransferase CsbB	0.16	2.4.-.-	0.26	CL-B
CAR86970.1	Exo-glucosaminidase LytG	0.65	3.2.1.-	0.65	CL-B
CAR86971.1	Xanthine phosphoribosyltransferase	0.93	2.4.2.22	0.93	CL-B
CAR86973.1	N5-carboxyaminoimidazole ribonucleotide synthase	0.71	6.3.4.18	0.71	CL-B
CAR86974.1	Adenylosuccinate lyase	0.66	4.3.2.2	0.66	CL-B
CAR86977.1	Lipoteichoic acid synthase	0.6	2.7.8.-	0.66	CL-B
CAR86980.1	Glucose-6-phosphate isomerase	0.92	5.3.1.9	0.93	CL-B
CAR87043.1	Putative oxidoreductase YceM	0.56	1.-.-.-	0.56	CL-C
CAR87044.1	Guanine deaminase	0.4	3.5.4.3	0.4	CL-B
CAR87053.1	Probable dipeptidase A	0.47	3.4.-.-	0.88	CL-C
CAR87064.1	Thymidine kinase	0.93	2.7.1.21	0.93	CL-C
CAR87067.1	Release factor glutamine methyltransferase	0.76	2.1.1.297	0.76	CL-B
CAR87068.1	Threonylcarbamoyl-AMP synthase	0.57	2.7.7.87	0.57	CL-B
CAR87069.1	Serine hydroxymethyltransferase	0.93	2.1.2.1	0.93	CL-B
CAR87070.1	Uracil phosphoribosyltransferase	0.93	2.4.2.9	0.93	CL-B
CAR87076.1	ATP synthase subunit alpha	0.91	3.6.3.14	0.93	CL-B
CAR87079.1	ATP synthase subunit beta	0.91	3.6.3.14	0.93	CL-C
CAR87087.1	Probable peptidoglycan glycosyltransferase FtsW	0.63	2.4.1.129	0.71	CL-B

CAR87089.1	Probable succinyl-diaminopimelate desuccinylase	0.51	3.5.1.18	0.71	CL-C
CAR87092.1	Methionine import ATP-binding protein MetN	0.74	3.6.3.-	0.93	CL-B
CAR87096.1	Probable cysteine desulfurase	0.39	2.8.1.7	0.4	CL-B
CAR87097.1	Iron-sulfur cluster assembly scaffold protein IscU	0.45	2.-.-.-	0.4	CL-B
CAR87108.1	Glutathione biosynthesis bifunctional protein GshAB	0.83	6.3.2.2, 6.3.2.3	0.83	CL-C
CAR87111.1	Probable L-serine dehydratase, beta chain	0.4	4.3.1.17	0.65	CL-B
CAR87112.1	Probable L-serine dehydratase, alpha chain	0.35	4.3.1.17	0.76	CL-B
CAR87114.1	Peptide methionine sulfoxide reductase MsrA	0.92	1.8.4.11	0.92	CL-D
CAR87117.1	Deoxyguanosine kinase	0.7	2.7.1.113	0.7	CL-C
CAR87133.1	Sensor histidine kinase YvfT	0.4	2.7.13.3	0.68	CL-B
CAR87135.1	Nod factor export ATP-binding protein I	0.48	3.6.3.-	0.54	CL-B
CAR87153.1	Cysteine desulfurase IscS	0.56	2.8.1.7	0.69	CL-B
CAR87154.1	Probable tRNA sulfurtransferase	0.93	2.8.1.4	0.93	CL-C
CAR87156.1	Valine--tRNA ligase	0.93	6.1.1.9	0.93	CL-B
CAR87157.1	Dihydrofolate synthase/folylpolyglutamate synthase	0.29	6.3.2.17, 6.3.2.12	0.29	CL-B
CAR87169.1	Cardiolipin synthase A	0.41	2.7.8.-	0.71	CL-B
CAR87173.1	Ribosomal RNA small subunit methyltransferase H	0.93	2.1.1.199	0.93	CL-B
CAR87176.1	Phospho-N-acetylmuramoyl-pentapeptide-transferase	0.93	2.7.8.13	0.93	CL-B
CAR87177.1	UDP-N-acetylmuramoylalanine--D-glutamate ligase	0.93	6.3.2.9	0.93	CL-C
CAR87178.1	UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase	0.9	2.4.1.227	0.93	CL-B

CAR87186.1	Isoleucine--tRNA ligase	0.9	6.1.1.5	0.93	CL-B
CAR87192.1	ADP-ribose pyrophosphatase	0.4	3.6.1.13	0.4	CL-B
CAR87194.1	5'-methylthioadenosine/S-adenosylhomocysteine nucleosidase	0.71	3.2.2.9	0.71	CL-C
CAR87195.1	Cysteine desulfurase IscS	0.58	2.8.1.7	0.67	CL-B
CAR87199.1	tRNA-specific 2-thiouridylase MnmA	0.92	2.8.1.13	0.93	CL-B
CAR87203.1	RecBCD enzyme subunit RecD	0.4	3.1.11.5	0.4	CL-B
CAR87205.1	Putative lipid kinase YtlR	0.65	2.7.1.-	0.65	CL-B
CAR87206.1	Ribonuclease J 2	0.39	3.1.-.-	0.73	CL-B
CAR87210.1	Peptide deformylase	0.9	3.5.1.88	0.93	CL-B
CAR87215.1	Pyruvate dehydrogenase E1 component subunit alpha	0.4	1.2.4.1	0.56	CL-B
CAR87216.1	Pyruvate dehydrogenase E1 component subunit beta	0.46	1.2.4.1	0.59	CL-B
CAR87217.1	Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex	0.38	2.3.1.12	0.45	CL-B
CAR87218.1	Dihydrolipoyl dehydrogenase	0.47	1.8.1.4	0.58	CL-B
CAR87221.1	Inositol-1-monophosphatase	0.65	3.1.3.25	0.65	CL-B
CAR87223.1	Probable peptidoglycan glycosyltransferase FtsW	0.69	2.4.1.129	0.73	CL-B
CAR87224.1	Pyruvate carboxylase	0.12	6.4.1.1	0.19	CL-B
CAR87226.1	Putative rRNA methyltransferase YlbH	0.65	2.1.1.-	0.65	CL-B
CAR87227.1	Phosphopantetheine adenylyltransferase	0.93	2.7.7.3	0.93	CL-C
CAR87235.1	Ribonuclease J 2	0.39	3.1.-.-	0.73	CL-B
CAR87243.1	Carboxymuconolactone decarboxylase	0.65	4.1.1.44	0.5	CL-D

CAR87246.1	Trigger factor	0.93	5.2.1.8	0.93	CL-B
CAR87254.1	PTS system fructose-specific EIIABC component	0.21	2.7.1.202	0.35	CL-B
CAR87255.1	1-phosphofructokinase	0.2	2.7.1.56	0.2	CL-B
CAR87257.1	GTPase Obg	0.93	3.6.5.-	0.93	CL-B
CAR87258.1	Putative peptidoglycan O-acetyltransferase YrhL	0.19	2.3.1.-	0.71	CL-B
CAR87259.1	Ribonuclease Z	0.88	3.1.26.11	0.88	CL-B
CAR87260.1	Uncharacterized oxidoreductase YqjQ	0.65	1.-.-.-	0.65	CL-B
CAR87265.1	Trifunctional nucleotide phosphoesterase protein YfkN	0.25	3.1.3.5, 3.1.3.6, 3.1.4.16	0.25	CL-B
CAR87268.1	DNA polymerase III subunit alpha	0.59	2.7.7.7	0.79	CL-B
CAR87269.1	ATP-dependent 6-phosphofructokinase	0.93	2.7.1.11	0.93	CL-B
CAR87270.1	Pyruvate kinase	0.62	2.7.1.40	0.81	CL-B
CAR87277.1	Ribosomal large subunit pseudouridine synthase B	0.28	5.4.99.22	0.28	CL-B
CAR87281.1	Probable ATP-dependent DNA helicase RecQ	0.16	3.6.4.12	0.61	CL-B
CAR87283.1	Cytidylate kinase	0.93	2.7.4.25	0.93	CL-B
CAR87289.1	CCA-adding enzyme	0.92	2.7.7.72	0.92	CL-B
CAR87291.1	Uncharacterized ABC transporter ATP-binding protein YfmM	0.16	3.6.3.-	0.2	CL-B
CAR87292.1	Thymidylate synthase	0.93	2.1.1.45	0.93	CL-C
CAR87293.1	Dihydrofolate reductase	0.8	1.5.1.3	0.8	CL-C
CAR87298.1	Peptide methionine sulfoxide reductase MsrA	0.83	1.8.4.11	0.92	CL-B
CAR87300.1	Carboxy-terminal processing protease CtpA	0.17	3.4.21.102	0.42	CL-B

CAR87304.1	Ribonuclease HII	0.92	3.1.26.4	0.93	CL-B
CAR87306.1	DNA topoisomerase 1	0.54	5.99.1.2	0.66	CL-B
CAR87307.1	Methylenetetrahydrofolate--tRNA-(uracil-5-)-methyltransferase TrmFO	0.93	2.1.1.74	0.93	CL-B
CAR87309.1	ATP-dependent protease subunit HslV	0.91	3.4.25.2	0.91	CL-C
CAR87313.1	Glycerol-3-phosphate acyltransferase	0.88	2.3.1.n3	0.93	CL-B
CAR87314.1	DNA gyrase subunit B	0.66	5.99.1.3	0.79	CL-B
CAR87315.1	DNA gyrase subunit A	0.66	5.99.1.3	0.79	CL-B
CAR87316.1	Formate acetyltransferase	0.63	2.3.1.54	0.67	CL-C
CAR87317.1	Pyruvate formate-lyase-activating enzyme	0.62	1.97.1.4	0.74	CL-C
CAR87319.1	Probable manganese-dependent inorganic pyrophosphatase	0.91	3.6.1.1	0.93	CL-B
CAR87323.1	Sensor protein BceS	0.68	2.7.13.3	0.68	CL-B
CAR87328.1	Putative NAD(P)H nitroreductase YdgI	0.65	1.-.-.-	0.65	CL-B
CAR87330.1	Histidinol-phosphate aminotransferase	0.71	2.6.1.9	0.87	CL-B
CAR87331.1	Phosphoribosyl-ATP pyrophosphatase	0.93	3.6.1.31	0.93	CL-C
CAR87332.1	Histidine biosynthesis bifunctional protein HisIE	0.29	3.6.1.31, 3.5.4.19	0.29	CL-B
CAR87333.1	Imidazole glycerol phosphate synthase subunit HisF	0.93	4.1.3.-	0.93	CL-B
CAR87334.1	1-(5-phosphoribosyl)-5-[(5-phosphoribosylamino)methylideneamino] imidazole-4-carboxamide isomerase	0.92	5.3.1.16	0.93	CL-B
CAR87335.1	Imidazole glycerol phosphate synthase subunit HisH	0.88	2.4.2.-	0.92	CL-B
CAR87336.1	Imidazoleglycerol-phosphate dehydratase	0.93	4.2.1.19	0.93	CL-B
CAR87338.1	Histidinol dehydrogenase	0.79	1.1.1.23	0.83	CL-B

CAR87339.1	ATP phosphoribosyltransferase	0.92	2.4.2.17	0.93	CL-C
CAR87341.1	Histidinol-phosphate aminotransferase	0.71	2.6.1.9	0.85	CL-B
CAR87342.1	Hydrolase, NUDIX family	0.45	3.6.1.13	0.49	CL-D
CAR87348.1	Orotate phosphoribosyltransferase	0.93	2.4.2.10	0.93	CL-B
CAR87349.1	Orotidine 5'-phosphate decarboxylase	0.93	4.1.1.23	0.93	CL-B
CAR87350.1	Dihydroorotate dehydrogenase B (NAD(+)), catalytic subunit	0.77	1.3.1.14	0.77	CL-B
CAR87351.1	Carbamoyl-phosphate synthase large chain	0.9	6.3.5.5	0.93	CL-B
CAR87352.1	Carbamoyl-phosphate synthase small chain	0.75	6.3.5.5	0.83	CL-B
CAR87353.1	Dihydroorotase	0.93	3.5.2.3	0.93	CL-B
CAR87354.1	Aspartate carbamoyltransferase	0.93	2.1.3.2	0.93	CL-B
CAR87356.1	Bifunctional protein PyrR	0.9	2.4.2.9	0.92	CL-B
CAR87358.1	Uncharacterized RNA pseudouridine synthase YlyB	0.16	5.4.99.-	0.34	CL-B
CAR87359.1	Lipoprotein signal peptidase	0.93	3.4.23.36	0.93	CL-C
CAR87360.1	Formate--tetrahydrofolate ligase	0.86	6.3.4.3	0.93	CL-C
CAR87362.1	Ribonuclease HI	0.72	3.1.26.4	0.48	CL-D
CAR87363.1	Putative nitroreductase HBN1	0.5	1.-.-.-	0.5	CL-C
CAR87364.1	Cardiolipin synthase A	0.4	2.7.8.-	0.71	CL-B
CAR87369.1	Ribonucleoside-diphosphate reductase subunit alpha	0.29	1.17.4.1	0.67	CL-B
CAR87370.1	Ribonucleoside-diphosphate reductase subunit beta	0.35	1.17.4.1	0.67	CL-B
CAR87373.1	Neutral endopeptidase	0.38	3.4.24.-	0.54	CL-C

CAR87374.1	Lipoate-protein ligase A	0.53	6.3.1.20	0.74	CL-B
CAR87376.1	Uncharacterized protein in mprR 3'region	0.17	1.-.-.-	0.45	CL-C
CAR87377.1	Putative RNA methyltransferase YpsC	0.15	2.1.1.-	0.13	CL-B
CAR87381.1	Holliday junction resolvase RecU	0.93	3.1.22.-	0.93	CL-C
CAR87382.1	Penicillin-binding protein 1A	0.67	3.4.16.4, 2.4.1.129	0.79	CL-B
CAR87383.1	ComE operon protein 2	0.65	3.5.-.-	0.65	CL-B
CAR87384.1	Endonuclease III	0.59	4.2.99.18	0.59	CL-B
CAR87386.1	Asparagine--tRNA ligase	0.91	6.1.1.22	0.93	CL-B
CAR87387.1	Aspartate aminotransferase	0.36	2.6.1.1	0.41	CL-B
CAR87390.1	3'-5' exonuclease DinG	0.58	3.1.-.-	0.58	CL-B
CAR87391.1	ATP-dependent helicase/nuclease subunit A	0.93	3.1.-.-, 3.6.4.12	0.93	CL-B
CAR87392.1	ATP-dependent helicase/deoxyribonuclease subunit B	0.93	3.1.-.-, 3.6.4.12	0.93	CL-B
CAR87393.1	Mevalonate kinase	0.5	2.7.1.36	0.5	CL-C
CAR87394.1	Diphosphomevalonate decarboxylase	0.43	4.1.1.33	0.5	CL-C
CAR87395.1	Isopentenyl-diphosphate delta-isomerase	0.93	5.3.3.2	0.93	CL-C
CAR87396.1	Ribosomal RNA small subunit methyltransferase F	0.56	2.1.1.178, 2.1.1.-	0.06	CL-C
CAR87401.1	Tautomerase	0.89	5.3.2.-	0.9	CL-D
CAR87405.1	tRNA (adenine(22)-N(1))-methyltransferase	0.65	2.1.1.217	0.65	CL-B
CAR87407.1	DNA primase	0.76	2.7.7.-	0.76	CL-B
CAR87408.1	Glycine--tRNA ligase beta subunit	0.93	6.1.1.14	0.93	CL-B

CAR87409.1	Glycine--tRNA ligase alpha subunit	0.93	6.1.1.14	0.93	CL-B
CAR87446.1	Cytidine deaminase	0.71	3.5.4.5	0.71	CL-B
CAR87447.1	Diacylglycerol kinase	0.73	2.7.1.107	0.53	CL-D
CAR87448.1	Endoribonuclease YbeY	0.93	3.1.-.-	0.93	CL-B
CAR87452.1	Putative pyruvate, phosphate dikinase regulatory protein	0.83	2.7.4.27, 2.7.11.32	0.93	CL-B
CAR87453.1	Probable endonuclease 4	0.9	3.1.21.2	0.9	CL-C
CAR87455.1	Peptide methionine sulfoxide reductase MsrB	0.77	1.8.4.12	0.78	CL-B
CAR87456.1	Aspartate--tRNA ligase	0.82	6.1.1.12	0.83	CL-B
CAR87457.1	Histidine--tRNA ligase	0.9	6.1.1.21	0.93	CL-C
CAR87461.1	Putative N-acetylmuramoyl-L-alanine amidase YrvJ	0.19	3.5.1.28	0.19	CL-B
CAR87464.1	GTP pyrophosphokinase	0.39	2.7.6.5	0.58	CL-B
CAR87466.1	Ribosomal RNA small subunit methyltransferase E	0.65	2.1.1.193	0.65	CL-B
CAR87467.1	Ribosomal protein L11 methyltransferase	0.93	2.1.1.-	0.93	CL-B
CAR87469.1	Putative 3-methyladenine DNA glycosylase	0.91	3.2.2.-	0.91	CL-B
CAR87481.1	Glycosyltransferase Gtf1	0.79	2.4.1.-	0.79	CL-C
CAR87491.1	Putative Cys-tRNA(Pro)/Cys-tRNA(Cys) deacylase EbsC	0.7	4.2.-.-	0.7	CL-C
CAR87492.1	Adenine phosphoribosyltransferase	0.93	2.4.2.7	0.93	CL-B
CAR87493.1	Single-stranded-DNA-specific exonuclease RecJ	0.62	3.1.-.-	0.62	CL-B
CAR87497.1	Elongation factor 4	0.92	3.6.5.n1	0.93	CL-C
CAR87502.1	Oxygen-independent coproporphyrinogen-III oxidase-like protein LL1139	0.23	1.3.99.-	0.62	CL-B

CAR87503.1	Riboflavin biosynthesis protein	0.9	2.7.1.26, 2.7.7.2	0.91	CL-D
CAR87504.1	tRNA pseudouridine synthase B	0.93	5.4.99.25	0.93	CL-B
CAR87512.1	DNA polymerase III PolC-type	0.91	2.7.7.7	0.93	CL-B
CAR87513.1	Proline--tRNA ligase	0.9	6.1.1.15	0.93	CL-B
CAR87514.1	Zinc metalloprotease RasP	0.29	3.4.24.-	0.79	CL-B
CAR87515.1	Phosphatidate cytidylyltransferase	0.71	2.7.7.41	0.71	CL-B
CAR87516.1	Isoprenyl transferase	0.73	2.5.1.-	0.74	CL-B
CAR87520.1	Uridylate kinase	0.93	2.7.4.22	0.93	CL-B
CAR87526.1	1-acyl-sn-glycerol-3-phosphate acyltransferase	0.71	2.3.1.n4	0.71	CL-B
CAR87529.1	Lipid A export ATP-binding/permease protein MsbA	0.42	3.6.3.-	0.63	CL-B
CAR87530.1	Probable multidrug resistance ABC transporter ATP-binding/permease protein YheI	0.15	3.6.3.-	0.58	CL-B
CAR87535.1	tRNA (guanine-N(1)-)-methyltransferase	0.93	2.1.1.228	0.93	CL-B
CAR87541.1	Uncharacterized protein	0.6	2.1.2.3, 3.5.4.10	0.49	CL-D
CAR87546.1	Ribonuclease 3	0.93	3.1.26.3	0.93	CL-B
CAR87554.1	Phosphate acyltransferase	0.93	2.3.1.n2	0.93	CL-B
CAR87555.1	ATP-dependent DNA helicase RecG	0.46	3.6.4.12	0.48	CL-B
CAR87559.1	Thiamine pyrophosphokinase	0.65	2.7.6.2	0.65	CL-B
CAR87560.1	Ribulose-phosphate 3-epimerase	0.51	5.1.3.1	0.6	CL-B
CAR87561.1	Small ribosomal subunit biogenesis GTPase RsgA	0.9	3.6.1.-	0.93	CL-B
CAR87562.1	Serine/threonine-protein kinase StkP	0.31	2.7.11.1	0.73	CL-B

CAR87563.1	Protein phosphatase PrpC	0.2	3.1.3.16	0.79	CL-B
CAR87564.1	Ribosomal RNA small subunit methyltransferase B	0.48	2.1.1.176	0.54	CL-B
CAR87565.1	Methionyl-tRNA formyltransferase	0.93	2.1.2.9	0.93	CL-C
CAR87566.1	Primosomal protein N'	0.62	3.6.4.-	0.62	CL-B
CAR87567.1	Probable coenzyme A biosynthesis bifunctional protein CoaBC	0.18	6.3.2.5, 4.1.1.36	0.59	CL-B
CAR87568.1	DNA-directed RNA polymerase subunit omega	0.93	2.7.7.6	0.93	CL-C
CAR87569.1	Guanylate kinase	0.93	2.7.4.8	0.93	CL-B
CAR87574.1	Putative rRNA methyltransferase YqxC	0.27	2.1.1.-	0.27	CL-B
CAR87575.1	Farnesyl diphosphate synthase	0.28	2.5.1.10	0.31	CL-B
CAR87576.1	Exodeoxyribonuclease 7 small subunit	0.93	3.1.11.6	0.93	CL-D
CAR87577.1	Exodeoxyribonuclease 7 large subunit	0.93	3.1.11.6	0.93	CL-B
CAR87578.1	Bifunctional protein FolD	0.89	1.5.1.5, 3.5.4.9	0.93	CL-C
CAR87582.1	Uncharacterized peptidase YqhT	0.17	3.4.-.-	0.48	CL-B
CAR87590.1	Xaa-Pro dipeptidyl-peptidase	0.9	3.4.14.11	0.93	CL-C
CAR87591.1	Glutamine synthetase	0.72	6.3.1.2	0.73	CL-B
CAR87593.1	Inducible ornithine decarboxylase	0.3	4.1.1.17	0.37	CL-C
CAR87595.1	tRNA dimethylallyltransferase	0.93	2.5.1.75	0.93	CL-C
CAR87598.1	Glucokinase	0.46	2.7.1.2	0.46	CL-B
CAR87600.1	Rhomboid protease GluP	0.65	3.4.21.105	0.65	CL-B
CAR87606.1	Sensor protein VraS	0.64	2.7.13.3	0.68	CL-B

CAR87609.1	Uridine kinase	0.93	2.7.1.48	0.93	CL-B
CAR87610.1	Endolytic murein transglycosylase	0.71	4.2.2.-	0.71	CL-B
CAR87612.1	Phenylalanine--tRNA ligase beta subunit	0.93	6.1.1.20	0.93	CL-B
CAR87613.1	Phenylalanine--tRNA ligase alpha subunit	0.93	6.1.1.20	0.93	CL-B
CAR87616.1	Uncharacterized tRNA/rRNA methyltransferase YsgA	0.65	2.1.1.-	0.65	CL-B
CAR87618.1	Acylphosphatase	0.8	3.6.1.7	0.8	CL-C
CAR87620.1	Sensor protein kinase WalK	0.47	2.7.13.3	0.76	CL-B
CAR87622.1	6-phosphogluconate dehydrogenase, decarboxylating	0.66	1.1.1.44	0.73	CL-B
CAR87628.1	Putative methyltransferase GWCH70_2453	0.4	2.1.1.-	0.68	CL-B
CAR87631.1	Probable nicotinate-nucleotide adenylyltransferase	0.83	2.7.7.18	0.83	CL-B
CAR87635.1	Putative ring-cleaving dioxygenase MhqE	0.32	1.13.11.-	0.71	CL-B
CAR87636.1	Putative ring-cleaving dioxygenase MhqE	0.32	1.13.11.-	0.71	CL-B
CAR87637.1	Putative hydrolase MhqD	0.65	3.1.-.-	0.65	CL-B
CAR87638.1	Chloroplast envelope quinone oxidoreductase homolog	0.5	1.3.1.-	0.5	CL-C
CAR87646.1	NAD-dependent protein deacetylase	0.64	3.5.1.-	0.64	CL-C
CAR87649.1	Threonine--tRNA ligase	0.92	6.1.1.3	0.93	CL-B
CAR87654.1	Dephospho-CoA kinase	0.89	2.7.1.24	0.89	CL-B
CAR87655.1	Formamidopyrimidine-DNA glycosylase	0.93	3.2.2.23, 4.2.99.18	0.93	CL-B
CAR87656.1	DNA polymerase I	0.55	2.7.7.7	0.68	CL-B
CAR87663.1	UDP-N-acetylmuramate--L-alanine ligase	0.93	6.3.2.8	0.93	CL-B

CAR87669.1	tRNA (guanine-N(7)-)-methyltransferase	0.93	2.1.1.33	0.93	CL-C
CAR87675.1	Foldase protein PrsA	0.71	5.2.1.8	0.93	CL-B
CAR87676.1	3'-5' exoribonuclease YhaM	0.71	3.1.-.-	0.71	CL-B
CAR87678.1	Penicillin-binding protein 1A	0.64	3.4.16.4, 2.4.1.129	0.77	CL-B
CAR87679.1	Uncharacterized RNA pseudouridine synthase YhcT	0.17	5.4.99.-	0.32	CL-B
CAR87681.1	Arginine--tRNA ligase	0.86	6.1.1.19	0.93	CL-C
CAR87684.1	Dihydroorotate dehydrogenase (Fumarate)	0.2	1.3.98.1	0.22	CL-C
CAR87688.1	Probable metallo-hydrolase YhfI	0.65	3.-.-.-	0.65	CL-B
CAR87694.1	Sensor protein BceS	0.43	2.7.13.3	0.71	CL-B
CAR87695.1	Anaerobic ribonucleoside-triphosphate reductase-activating protein	0.57	1.97.1.-	0.57	CL-C
CAR87696.1	Copper-exporting P-type ATPase	0.36	3.6.3.54	0.53	CL-B
CAR87698.1	Phosphoribosylamine--glycine ligase	0.77	6.3.4.13	0.78	CL-B
CAR87700.1	Bifunctional purine biosynthesis protein PurH	0.93	2.1.2.3, 3.5.4.10	0.93	CL-C
CAR87701.1	Phosphoribosylglycinamide formyltransferase	0.67	2.1.2.2	0.67	CL-B
CAR87702.1	Phosphoribosylformylglycinamidine cyclo-ligase	0.92	6.3.3.1	0.92	CL-D
CAR87703.1	Amidophosphoribosyltransferase	0.72	2.4.2.14	0.79	CL-B
CAR87704.1	Phosphoribosylformylglycinamidine synthase subunit PurL	0.93	6.3.5.3	0.93	CL-B
CAR87705.1	Phosphoribosylformylglycinamidine synthase subunit PurQ	0.93	6.3.5.3, 3.5.1.2	0.93	CL-B
CAR87706.1	Phosphoribosylformylglycinamidine synthase subunit PurS	0.92	6.3.5.3	0.92	CL-D
CAR87707.1	Phosphoribosylaminoimidazole-succinocarboxamide synthase	0.93	6.3.2.6	0.93	CL-B

CAR87708.1	N5-carboxyaminoimidazole ribonucleotide synthase	0.54	6.3.4.18	0.54	CL-B
CAR87709.1	N5-carboxyaminoimidazole ribonucleotide mutase	0.45	5.4.99.18	0.45	CL-B
CAR87715.1	Phosphoenolpyruvate-protein phosphotransferase	0.65	2.7.3.9	0.68	CL-B
CAR87729.1	Uncharacterized RNA methyltransferase LJ_1698	0.3	2.1.1.-	0.81	CL-B
CAR87732.1	Hydroxymethylglutaryl-CoA synthase	0.23	2.3.3.-	0.2	CL-B
CAR87733.1	3-hydroxy-3-methylglutaryl-coenzyme A reductase	0.36	1.1.1.88	0.39	CL-C
CAR87734.1	Probable acetyl-CoA acyltransferase	0.27	2.3.1.9	0.48	CL-B
CAR87741.1	Probable succinyl-diaminopimelate desuccinylase	0.71	3.5.1.18	0.71	CL-C
CAR87746.1	Phosphonates import ATP-binding protein PhnC 2	0.32	3.6.3.28	0.52	CL-C
CAR87750.1	Calcium-transporting ATPase 1	0.19	3.6.3.8	0.52	CL-B
CAR87753.1	NH(3)-dependent NAD(+) synthetase	0.93	6.3.1.5	0.93	CL-C
CAR87755.1	Nicotinate phosphoribosyltransferase	0.37	6.3.4.21	0.62	CL-B
CAR87757.1	N-acetylglucosamine-6-phosphate deacetylase	0.6	3.5.1.25	0.6	CL-B
CAR87758.1	Pyrroline-5-carboxylate reductase	0.32	1.5.1.2	0.71	CL-B
CAR87759.1	Uncharacterized peptidase YuxL	0.4	3.4.21.-	0.4	CL-B
CAR87764.1	Macrolide export ATP-binding/permease protein MacB	0.39	3.6.3.-	0.63	CL-B
CAR87769.1	Alpha-L-fucosidase	0.25	3.2.1.51	0.5	CL-C
CAR87788.1	Serine--tRNA ligase	0.91	6.1.1.11	0.93	CL-B
CAR87793.1	Alpha-acetolactate decarboxylase	0.79	4.1.1.5	0.79	CL-B
CAR87794.1	Pyruvate oxidase	0.31	2.2.1.6	0.51	CL-B

CAR87801.1	Uncharacterized RNA pseudouridine synthase YjbO	0.17	5.4.99.-	0.35	CL-B
CAR87805.1	Probable 2-(5''-triphosphoribosyl)-3'-dephosphocoenzyme-A synthase	0.59	2.4.2.52	0.82	CL-C
CAR87807.1	Pyruvate carboxylase	0.24	6.4.1.1	0.45	CL-B
CAR87808.1	Probable apo-citrate lyase phosphoribosyl-dephospho-CoA transferase	0.74	2.7.7.61	0.74	CL-C
CAR87809.1	Citrate lyase alpha chain	0.64	2.8.3.10, 4.1.3.6	0.64	CL-C
CAR87812.1	[Citrate [pro-3S]-lyase] ligase	0.64	6.2.1.22	0.64	CL-C
CAR87813.1	Oxaloacetate decarboxylase beta chain	0.16	4.1.1.3	0.47	CL-C
CAR87818.1	Probable RNA 2'-phosphotransferase	0.74	2.7.1.-	0.74	CL-C
CAR87824.1	FMN reductase (NADPH)	0.18	1.5.1.38	0.18	CL-B
CAR87842.1	Lactococcin transport/processing ATP-binding protein LcnC-like	0.32	3.6.3.-	0.31	CL-C
CAR87863.1	GMP synthase [glutamine-hydrolyzing]	0.92	6.3.5.2	0.93	CL-B
CAR87864.1	Pantothenate kinase	0.93	2.7.1.33	0.93	CL-C
CAR87867.1	Probable dipeptidase A	0.47	3.4.-.-	0.88	CL-C
CAR87870.1	DNA helicase IV	0.65	3.6.4.12	0.65	CL-B
CAR87874.1	Proline iminopeptidase	0.57	3.4.11.5	0.57	CL-C
CAR87877.1	Ferrochelatase	0.93	4.99.1.1	0.93	CL-C
CAR87879.1	Rhamnulose-1-phosphate aldolase	0.93	4.1.2.19	0.92	CL-D
CAR87883.1	Diacylglycerol kinase	0.67	2.7.1.107	0.67	CL-B
CAR87886.1	UDP-N-acetylglucosamine 2-epimerase	0.45	5.1.3.14	0.64	CL-B
CAR87887.1	UDP-N-acetylglucosamine 2-epimerase	0.45	5.1.3.14	0.64	CL-B

CAR87891.1	dTDP-4-dehydrorhamnose reductase	0.46	1.1.1.133	0.49	CL-B
CAR87892.1	dTDP-glucose 4,6-dehydratase	0.46	4.2.1.46	0.58	CL-B
CAR87893.1	dTDP-4-dehydrorhamnose 3,5-epimerase	0.57	5.1.3.13	0.57	CL-C
CAR87894.1	Glucose-1-phosphate thymidylyltransferase	0.56	2.7.7.24	0.67	CL-B
CAR87899.1	UDP-glucose:undecaprenyl-phosphate glucose-1-phosphate transferase	0.23	2.-.-.-	0.2	CL-B
CAR87900.1	Uncharacterized UDP-glucose epimerase YtcB	0.25	4.-.-.-	0.25	CL-B
CAR87904.1	Methionine import ATP-binding protein MetN	0.36	3.6.3.-	0.65	CL-B
CAR87912.1	Tyrosine--tRNA ligase	0.85	6.1.1.1	0.93	CL-B
CAR87916.1	FAD:protein FMN transferase	0.56	2.7.1.180	0.56	CL-C
CAR87917.1	Intracellular maltogenic amylase	0.24	3.2.1.-	0.24	CL-B
CAR87918.1	Glycogen phosphorylase	0.25	2.4.1.1	0.64	CL-B
CAR87919.1	Glycogen synthase	0.89	2.4.1.21	0.93	CL-B
CAR87921.1	Glucose-1-phosphate adenylyltransferase	0.92	2.7.7.27	0.93	CL-B
CAR87922.1	1,4-alpha-glucan branching enzyme GlgB	0.9	2.4.1.18	0.93	CL-B
CAR87923.1	Probable branched-chain-amino-acid aminotransferase	0.32	2.6.1.42	0.66	CL-B
CAR87927.1	Fructose-1,6-bisphosphatase class 3	0.91	3.1.3.11	0.93	CL-B
CAR87931.1	Putative tyrosine-protein phosphatase CapC	0.4	3.1.3.48	0.68	CL-B
CAR87932.1	Polyisoprenyl-teichoic acid--peptidoglycan teichoic acid transferase TagU	0.67	2.7.8.-	0.7	CL-B
CAR87933.1	dTDP-glucose 4,6-dehydratase	0.46	4.2.1.46	0.58	CL-B
CAR87934.1	dTDP-4-dehydrorhamnose 3,5-epimerase	0.57	5.1.3.13	0.57	CL-C

CAR87935.1	Glucose-1-phosphate thymidylyltransferase	0.57	2.7.7.24	0.69	CL-B
CAR87937.1	Glucose-1-phosphate thymidylyltransferase	0.57	2.7.7.24	0.64	CL-C
CAR87938.1	Uncharacterized sugar transferase EpsL	0.21	2.-.-.-	0.31	CL-B
CAR87940.1	Beta-1,6-galactofuranosyltransferase Wbbl	0.55	2.4.1.-	0.55	CL-C
CAR87945.1	UDP-galactopyranose mutase	0.45	5.4.99.9	0.51	CL-C
CAR87947.1	Tyrosine-protein kinase CpsD	0.4	2.7.10.2	0.48	CL-B
CAR87953.1	2-dehydro-3-deoxy-D-gluconate 5-dehydrogenase	0.15	1.1.1.127	0.15	CL-B
CAR87969.1	PTS cellobiose transporter subunit IIA	0.54	2.7.1.69	0.53	CL-D
CAR87974.1	Alpha-galactosidase Mel36A	0.33	3.2.1.22	0.85	CL-C
CAR87977.1	ATP-dependent RecD-like DNA helicase	0.65	3.6.4.12	0.65	CL-B
CAR87979.1	Alpha-galactosidase	0.55	3.2.1.22	0.55	CL-D
CAR87983.1	Putative D-/L-hydantoinase subunit A	0.55	3.5.2.-	0.55	CL-C
CAR87998.1	PTS system sucrose-specific EIIBCA component	0.37	2.7.1.-	0.69	CL-B
CAR87999.1	PTS system sucrose-specific EIIBC component	0.55	2.7.1.-	0.55	CL-C
CAR88000.1	Glucan 1,6-alpha-glucosidase	0.32	3.2.1.10	0.36	CL-B
CAR88002.1	Sucrose-6-phosphate hydrolase	0.63	3.2.1.26	0.81	CL-B
CAR88003.1	NAD(P)H azoreductase	0.55	1.7.-.-	0.55	CL-C
CAR88004.1	Probable fatty acid methyltransferase	0.07	2.1.1.-	0.29	CL-C
CAR88005.1	Acetyl-coenzyme A carboxylase carboxyl transferase subunit alpha	0.77	2.1.3.15	0.79	CL-B
CAR88006.1	Acetyl-coenzyme A carboxylase carboxyl transferase subunit beta	0.9	2.1.3.15	0.93	CL-C

CAR88007.1	Biotin carboxylase	0.17	6.4.1.2, 6.3.4.14	0.44	CL-B
CAR88008.1	3-hydroxyacyl-[acyl-carrier-protein] dehydratase FabZ	0.93	4.2.1.59	0.93	CL-B
CAR88010.1	3-oxoacyl-[acyl-carrier-protein] synthase 2	0.37	2.3.1.179	0.34	CL-B
CAR88011.1	3-oxoacyl-[acyl-carrier-protein] reductase FabG	0.38	1.1.1.100	0.44	CL-B
CAR88012.1	Malonyl CoA-acyl carrier protein transacylase	0.66	2.3.1.39	0.71	CL-B
CAR88013.1	Probable nitronate monooxygenase	0.68	1.13.12.16	0.71	CL-B
CAR88015.1	3-oxoacyl-[acyl-carrier-protein] synthase 3	0.91	2.3.1.180	0.91	CL-C
CAR88017.1	3-hydroxyacyl-[acyl-carrier-protein] dehydratase FabZ	0.93	4.2.1.59	0.93	CL-C
CAR88019.1	Probable NADH-dependent butanol dehydrogenase 2	0.2	1.1.1.-	0.44	CL-B
CAR88033.1	2,3-bisphosphoglycerate-dependent phosphoglycerate mutase	0.82	5.4.2.11	0.93	CL-C
CAR88043.1	Glycine betaine transport ATP-binding protein OpuAA	0.22	3.6.3.32	0.26	CL-B
CAR88047.1	D-aspartate ligase	0.7	6.3.1.12	0.7	CL-C
CAR88048.1	Homoserine kinase	0.79	2.7.1.39	0.79	CL-C
CAR88050.1	Homoserine dehydrogenase	0.76	1.1.1.3	0.76	CL-C
CAR88051.1	Aspartokinase 3	0.22	2.7.2.4	0.43	CL-B
CAR88058.1	D-3-phosphoglycerate dehydrogenase	0.17	1.1.1.95, 1.1.1.399	0.14	CL-B
CAR88059.1	Putative N-acetyl-LL-diaminopimelate aminotransferase	0.16	2.6.1.-	0.26	CL-B
CAR88070.1	Asparagine synthetase [glutamine-hydrolyzing] 1	0.15	6.3.5.4	0.7	CL-B
CAR88072.1	Uncharacterized protease YdeA	0.65	3.2.-.-	0.65	CL-B
CAR88077.1	Heptaprenyl diphosphate synthase component 2	0.23	2.5.1.30	0.23	CL-B

CAR88078.1	Acetate kinase	0.86	2.7.2.1	0.9	CL-B
CAR88084.1	Glucose 1-dehydrogenase	0.18	1.1.1.47	0.26	CL-B
CAR88085.1	6-phospho-beta-galactosidase	0.37	3.2.1.86	0.52	CL-B
CAR88086.1	Aryl-phospho-beta-D-glucosidase BglC	0.19	3.2.1.86	0.5	CL-B
CAR88087.1	PTS system sucrose-specific EIIBCA component	0.29	2.7.1.-	0.56	CL-B
CAR88090.1	Lipid A export ATP-binding/permease protein MsbA	0.34	3.6.3.-	0.54	CL-B
CAR88098.1	CRISPR-associated endonuclease Cas1	0.65	3.1.-.-	0.65	CL-C
CAR88099.1	CRISPR-associated endonuclease Cas9	0.56	3.1.-.-	0.79	CL-C
CAR88102.1	Cytochrome bd-I ubiquinol oxidase subunit 2	0.32	1.10.3.-	0.29	CL-B
CAR88103.1	Cytochrome bd-I ubiquinol oxidase subunit 1	0.26	1.10.3.-	0.42	CL-B
CAR88104.1	Thymidine phosphorylase	0.5	2.4.2.4	0.5	CL-B
CAR88105.1	Adenosine deaminase	0.87	3.5.4.4	0.88	CL-C
CAR88110.1	Probable GMP synthase [glutamine-hydrolyzing]	0.22	6.3.5.2	0.22	CL-C
CAR88116.1	Epoxyqueuosine reductase	0.75	1.17.99.6	0.75	CL-B
CAR88137.1	Polyisoprenyl-teichoic acid--peptidoglycan teichoic acid transferase TagU	0.61	2.7.8.-	0.68	CL-B
CAR88145.1	tRNA N6-adenosine threonylcarbamoyltransferase	0.93	2.3.1.234	0.93	CL-C
CAR88151.1	Probable L-asparaginase	0.21	3.5.1.1	0.51	CL-B
CAR88153.1	Ribosomal RNA small subunit methyltransferase I	0.79	2.1.1.198	0.79	CL-B
CAR88155.1	DNA polymerase III subunit delta'	0.65	2.7.7.7	0.65	CL-B
CAR88157.1	Thymidylate kinase	0.93	2.7.4.9	0.93	CL-C

CAR88161.1	DNA polymerase III subunit gamma/tau	0.3	2.7.7.7	0.47	CL-B
CAR88162.1	tRNA-specific adenosine deaminase	0.79	3.5.4.33	0.79	CL-B
CAR88165.1	Phosphatidylglycerol lysyltransferase	0.71	2.3.2.3	0.71	CL-B
CAR88169.1	Minor extracellular protease vpr	0.19	3.4.21.-	0.19	CL-B
CAR88170.1	Foldase protein PrsA	0.72	5.2.1.8	0.93	CL-B
CAR88180.1	Poly(glycerol-phosphate) alpha-glucosyltransferase	0.27	2.4.1.52	0.27	CL-B
CAR88181.1	Succinate-semialdehyde dehydrogenase [NADP(+)]	0.15	1.2.1.79	0.18	CL-B
CAR88185.1	Calcium-transporting ATPase 1	0.19	3.6.3.8	0.34	CL-B
CAR88187.1	Glutamyl-tRNA(Gln) amidotransferase subunit A	0.81	6.3.5.7	0.84	CL-B
CAR88188.1	Cob(I)yrinic acid a,c-diamide adenosyltransferase	0.65	2.5.1.17	0.65	CL-B
CAR88191.1	Adenosylcobalamin-dependent ribonucleoside-triphosphate reductase	0.75	1.17.4.2	0.93	CL-C
CAR88192.1	Nucleoside 2-deoxyribosyltransferase	0.66	2.4.2.6	0.53	CL-D
CAR88199.1	FAD:protein FMN transferase	0.56	2.7.1.180	0.56	CL-C
CAR88203.1	NADH dehydrogenase-like protein SAR0903	0.18	1.6.99.-	0.63	CL-B
CAR88206.1	Heptaprenyl diphosphate synthase component 2	0.22	2.5.1.30	0.22	CL-B
CAR88219.1	23S rRNA (guanosine-2'-O-)-methyltransferase RlmB	0.34	2.1.1.-	0.44	CL-B
CAR88220.1	Mini-ribonuclease 3	0.83	3.1.26.-	0.83	CL-B
CAR88221.1	Cysteine--tRNA ligase	0.93	6.1.1.16	0.93	CL-B
CAR88227.1	Glutamate--tRNA ligase	0.9	6.1.1.17	0.93	CL-B
CAR88234.1	Uncharacterized PIN and TRAM-domain containing protein Lin0266	0.25	3.1.-.-	0.71	CL-B

CAR88235.1	DNA repair protein RadA	0.79	3.6.4.-	0.79	CL-B
CAR88236.1	Deoxyuridine 5'-triphosphate nucleotidohydrolase	0.7	3.6.1.23	0.7	CL-C
CAR88240.1	Aminopeptidase G	0.32	3.4.22.-	0.5	CL-C
CAR88241.1	Aminopeptidase C	0.55	3.4.22.40	0.81	CL-C
CAR88246.1	Pyruvate, phosphate dikinase	0.27	2.7.9.1	0.45	CL-C
CAR88248.1	2,3-bisphosphoglycerate-dependent phosphoglycerate mutase	0.79	5.4.2.11	0.93	CL-C
CAR88251.1	Lactate 2-monooxygenase	0.16	1.13.12.4	0.16	CL-C
CAR88260.1	Gamma-glutamyl phosphate reductase	0.93	1.2.1.41	0.93	CL-C
CAR88261.1	Glutamate 5-kinase	0.87	2.7.2.11	0.88	CL-C
CAR88281.1	SPBc2 prophage-derived sublancin-168-processing and transport ATP-binding protein SunT	0.15	3.4.22.-	0.37	CL-B
CAR88296.1	Uncharacterized oxidoreductase YcsN	0.4	1.-.-.-	0.62	CL-B
CAR88298.1	Uncharacterized oxidoreductase MW2403	0.17	1.-.-.-	0.49	CL-C
CAR88299.1	Probable NADH-dependent flavin oxidoreductase YqiG	0.16	1.-.-.-	0.28	CL-B
CAR88301.1	Fumarate hydratase class II	0.62	4.2.1.2	0.71	CL-B
CAR88307.1	Calcium-transporting ATPase 1	0.19	3.6.3.8	0.48	CL-B
CAR88331.1	Long-chain-fatty-acid--CoA ligase	0.21	6.2.1.3	0.22	CL-B
CAR88333.1	Aliphatic sulfonates import ATP-binding protein SsuB	0.33	3.6.3.-	0.66	CL-B
CAR88337.1	Lipid A export ATP-binding/permease protein MsbA	0.27	3.6.3.-	0.51	CL-B
CAR88338.1	Lipid A export ATP-binding/permease protein MsbA	0.37	3.6.3.-	0.57	CL-B
CAR88346.1	Lipoprotein-releasing system ATP-binding protein LolD	0.31	3.6.3.-	0.67	CL-B

CAR88350.1	tRNA pseudouridine synthase A	0.9	5.4.99.12	0.93	CL-C
CAR88352.1	Energy-coupling factor transporter ATP-binding protein EcfA2	0.85	3.6.3.-	0.93	CL-B
CAR88353.1	Energy-coupling factor transporter ATP-binding protein EcfA1	0.88	3.6.3.-	0.93	CL-B
CAR88356.1	DNA-directed RNA polymerase subunit alpha	0.93	2.7.7.6	0.93	CL-B
CAR88361.1	Adenylate kinase	0.93	2.7.4.3	0.93	CL-B
CAR88385.1	Alkyl hydroperoxide reductase C	0.38	1.11.1.15	0.71	CL-B
CAR88392.1	DNA-directed RNA polymerase subunit beta'	0.93	2.7.7.6	0.93	CL-B
CAR88393.1	DNA-directed RNA polymerase subunit beta	0.93	2.7.7.6	0.93	CL-B
CAR88403.1	Lysine--tRNA ligase	0.93	6.1.1.6	0.93	CL-B
CAR88404.1	tRNA-dihydrouridine synthase B	0.37	1.3.1.-	0.62	CL-B
CAR88409.1	ATP-dependent zinc metalloprotease FtsH	0.77	3.4.24.-	0.88	CL-B
CAR88410.1	Hypoxanthine-guanine phosphoribosyltransferase	0.66	2.4.2.8	0.74	CL-B
CAR88411.1	tRNA(Ile)-lysidine synthase	0.82	6.3.4.19	0.82	CL-B
CAR88416.1	Transcription-repair-coupling factor	0.49	3.6.4.-	0.49	CL-B
CAR88417.1	Peptidyl-tRNA hydrolase	0.93	3.1.1.29	0.93	CL-B
CAR88418.1	L-lactate dehydrogenase	0.75	1.1.1.27	0.93	CL-B
CAR88424.1	Putative L,D-transpeptidase YciB	0.65	2.-.-.-	0.65	CL-B
CAR88425.1	Glutamate synthase [NADPH] small chain	0.26	1.4.1.13	0.3	CL-B
CAR88426.1	Glutamate synthase [NADPH] large chain	0.21	1.4.1.13	0.33	CL-B
CAR88429.1	Endoribonuclease EndoA	0.18	3.1.27.-	0.18	CL-B

CAR88431.1	Alanine racemase	0.86	5.1.1.1	0.92	CL-B
CAR88432.1	Holo-[acyl-carrier-protein] synthase	0.93	2.7.8.7	0.93	CL-C
CAR88433.1	DEAD-box ATP-dependent RNA helicase CshA	0.38	3.6.4.13	0.83	CL-B
CAR88434.1	UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase	0.62	6.3.2.10	0.62	CL-B
CAR88440.1	UDP-N-acetylglucosamine 1-carboxyvinyltransferase 2	0.59	2.5.1.7	0.93	CL-B
CAR88441.1	CTP synthase	0.93	6.3.4.2	0.93	CL-B
CAR88442.1	NADH dehydrogenase-like protein YumB	0.18	1.6.-.-	0.22	CL-B
CAR88449.1	Octanoyl-[GcvH]:protein N-octanoyltransferase	0.68	2.3.1.204	0.68	CL-B
CAR88456.1	Ribose-phosphate pyrophosphokinase	0.52	2.7.6.1	0.88	CL-B
CAR88457.1	Bifunctional protein GlmU	0.93	2.3.1.157, 2.7.7.23	0.93	CL-B
CAR88460.1	Probable iron export ATP-binding protein FetA	0.17	3.6.3.-	0.17	CL-C
CAR88463.1	4-diphosphocytidyl-2-C-methyl-D-erythritol kinase	0.8	2.7.1.148	0.93	CL-B
CAR88466.1	Ribosomal RNA small subunit methyltransferase A	0.93	2.1.1.182	0.93	CL-B
CAR88467.1	Ribonuclease M5	0.7	3.1.26.8	0.93	CL-B
CAR88468.1	Uncharacterized metal-dependent hydrolase YabD	0.16	3.1.-.-	0.31	CL-B
CAR88470.1	Tagatose 1,6-diphosphate aldolase	0.6	4.1.2.40	0.79	CL-C
CAR88475.1	Lipid A export ATP-binding/permease protein MsbA	0.35	3.6.3.-	0.54	CL-B
CAR88476.1	Lipid A export ATP-binding/permease protein MsbA	0.46	3.6.3.-	0.51	CL-B
CAR88479.1	Methionine--tRNA ligase	0.76	6.1.1.10	0.83	CL-B
CAR88482.1	Proline iminopeptidase	0.88	3.4.11.5	0.88	CL-C

CAR88486.1	L-lactate dehydrogenase	0.71	1.1.1.27	0.92	CL-B
CAR88488.1	NAD-dependent protein deacetylase	0.81	3.5.1.-	0.81	CL-C
CAR88495.1	Polyphosphate kinase	0.77	2.7.4.1	0.79	CL-C
CAR88496.1	Exopolyphosphatase	0.89	3.6.1.11	0.51	CL-D
CAR88497.1	Uncharacterized oxidoreductase YcsN	0.32	1.-.-.-	0.45	CL-B
CAR88499.1	Putative phosphinothricin acetyltransferase YwnH	0.65	2.3.1.183	0.65	CL-B
CAR88504.1	Tryptophan--tRNA ligase	0.77	6.1.1.2	0.79	CL-C
CAR88510.1	Dihydrolipoyl dehydrogenase	0.39	1.8.1.4	0.43	CL-B
CAR88514.1	DNA helicase IV	0.65	3.6.4.12	0.65	CL-B
CAR88525.1	Uncharacterized oxidoreductase YrpG	0.17	1.1.1.-	0.37	CL-B
CAR88532.1	Ribonuclease H	0.64	3.1.26.4	0.64	CL-C
CAR88542.1	PTS system fructose-specific EIIABC component	0.23	2.7.1.202	0.43	CL-B
CAR88543.1	1-phosphofructokinase	0.25	2.7.1.56	0.25	CL-B
CAR88545.1	Glycerol kinase	0.92	2.7.1.30	0.93	CL-B
CAR88548.1	PTS system mannose-specific EIIAB component	0.64	2.7.1.191	0.64	CL-C
CAR88551.1	Gallate decarboxylase	0.4	4.1.1.59, 4.1.1.63	0.4	CL-C
CAR88552.1	Flavin prenyltransferase UbiX	0.55	2.5.1.129	0.79	CL-B
CAR88559.1	D-galactonate dehydratase	0.29	4.2.1.6	0.3	CL-C
CAR88565.1	PTS cellobiose transporter subunit IIA	0.55	2.7.1.69	0.51	CL-D
CAR88566.1	PTS system cellobiose-specific IIB component	0.53	2.7.1.69	0.54	CL-D

CAR88567.1	6-phospho-beta-glucosidase GmuD	0.15	3.2.1.86	0.24	CL-B
CAR88570.1	Mannosylglycerate hydrolase	0.55	3.2.1.170	0.55	CL-C
CAR88572.1	Mannosylglycerate hydrolase	0.55	3.2.1.170	0.55	CL-C
CAR88577.1	L-fucose mutarotase	0.54	5.1.3.29	0.57	CL-C
CAR88579.1	Rhamnulokinase	0.84	2.7.1.5	0.85	CL-C
CAR88580.1	L-fucose isomerase	0.79	5.3.1.25	0.78	CL-C
CAR88582.1	Rhamnulose-1-phosphate aldolase	0.8	4.1.2.19	0.81	CL-C
CAR88583.1	L-rhamnose isomerase	0.8	5.3.1.14	0.8	CL-C
CAR88584.1	L-rhamnose mutarotase	0.88	5.1.3.32	0.88	CL-C
CAR88585.1	Rhamnulokinase	0.87	2.7.1.5	0.87	CL-B
CAR88588.1	Aryl-alcohol dehydrogenase	0.05	1.1.1.90	0.05	CL-C
CAR88591.1	Glucan 1,6-alpha-glucosidase	0.32	3.2.1.10	0.36	CL-B
CAR88594.1	Ribose-5-phosphate isomerase A	0.92	5.3.1.6	0.92	CL-C
CAR88596.1	6-phospho-alpha-glucosidase 1	0.34	3.2.1.122	0.56	CL-B
CAR88597.1	PTS system maltose-specific EIICB component	0.14	2.7.1.208	0.14	CL-B
CAR88600.1	PTS system glucose-specific EIICBA component	0.49	2.7.1.199	0.49	CL-B
CAR88602.1	2-dehydro-3-deoxy-phosphogluconate aldolase	0.55	4.1.2.14	0.55	CL-C
CAR88603.1	D-glucosaminate-6-phosphate ammonia lyase	0.3	4.3.1.29	0.3	CL-C
CAR88604.1	Deacetylase EF_0837	0.37	3.1.1.-	0.64	CL-C
CAR88611.1	Transaldolase	0.93	2.2.1.2	0.92	CL-D

CAR88613.1	PTS system glucitol/sorbitol-specific EIIB component	0.6	2.7.1.198	0.6	CL-C
CAR88617.1	3-oxoacyl-[acyl-carrier-protein] reductase FabG	0.4	1.1.1.100	0.4	CL-B
CAR88618.1	L-ribulose-5-phosphate 4-epimerase UlaF	0.46	5.1.3.4	0.7	CL-C
CAR88619.1	Putative phosphatase YxeH	0.27	3.1.3.-	0.27	CL-B
CAR88620.1	L-ribulose-5-phosphate 3-epimerase UlaE	0.52	5.1.3.22	0.57	CL-C
CAR88623.1	3-keto-L-gulonate-6-phosphate decarboxylase UlaD	0.54	4.1.1.85	0.57	CL-C
CAR88625.1	PTS ascorbate transporter subunit IIB	0.56	2.7.1.69	0.48	CL-D
CAR88628.1	Probable L-ascorbate-6-phosphate lactonase UlaG	0.57	3.1.1.-	0.57	CL-C
CAR88629.1	PII-type proteinase	0.5	3.4.21.96	0.73	CL-C
CAR88632.1	Isoaspartyl peptidase/L-asparaginase	0.12	3.5.1.26	0.27	CL-C
CAR88633.1	Beta-Ala-Xaa dipeptidase	0.33	3.4.13.-	0.79	CL-B
CAR88636.1	Alpha-L-fucosidase	0.8	3.2.1.51	0.49	CL-D
CAR88638.1	Xylulose kinase	0.59	2.7.1.17	0.59	CL-B
CAR88639.1	Sorbitol dehydrogenase	0.29	1.1.1.14	0.29	CL-B
CAR88646.1	Probable fructose-bisphosphate aldolase	0.16	4.1.2.13	0.41	CL-B
CAR88649.1	PTS sugar transporter subunit IIB	0.54	2.7.1.69	0.54	CL-D
CAR88650.1	Uncharacterized protein	0.47	2.7.1.69	0.36	CL-D
CAR88651.1	Probable fructose-bisphosphate aldolase	0.16	4.1.2.13	0.41	CL-B
CAR88654.1	Putative ADP-ribose pyrophosphatase YjhB	0.65	3.6.1.-	0.65	CL-B
CAR88657.1	Alpha-glucosidase 2	0.65	3.2.1.20	0.65	CL-C

CAR88659.1	Uncharacterized isochorismatase family protein PncA	0.65	3.-.-.-	0.65	CL-B
CAR88660.1	Nicotinate phosphoribosyltransferase	0.37	6.3.4.21	0.62	CL-B
CAR88662.1	Arsenate reductase	0.61	1.20.4.4	0.71	CL-B
CAR88666.1	Maltodextrin import ATP-binding protein MsmX	0.15	3.6.3.-	0.14	CL-B
CAR88670.1	N-acetylmuramic acid 6-phosphate etherase	0.89	4.2.1.126	0.93	CL-C
CAR88678.1	Glyoxal reductase	0.15	1.1.1.283, 1.1.1.-	0.15	CL-B
CAR88692.1	Ribosomal RNA large subunit methyltransferase H	0.93	2.1.1.177	0.93	CL-B
CAR88695.1	Beta-Ala-His dipeptidase	0.15	3.4.13.20	0.15	CL-C
CAR88698.1	Zinc-transporting ATPase	0.13	3.6.3.-	0.34	CL-B
CAR88701.1	Uncharacterized serine protease YyxA	0.16	3.4.21.-	0.41	CL-B
CAR88704.1	Putative metallo-hydrolase YycJ	0.65	3.-.-.-	0.65	CL-B
CAR88707.1	Sensor protein kinase WalK	0.41	2.7.13.3	0.71	CL-B
CAR88712.1	Argininosuccinate synthase	0.93	6.3.4.5	0.93	CL-B
CAR88713.1	Argininosuccinate lyase	0.92	4.3.2.1	0.93	CL-B
CAR88719.1	PTS cellobiose transporter subunit IIA	0.54	2.7.1.69	0.52	CL-D
CAR88725.1	Probable hydrolase YcaC	0.55	4.-.-.-	0.55	CL-C
CAR88728.1	Aldo-keto reductase YhdN	0.21	1.1.1.-	0.44	CL-B
CAR88733.1	PTS system fructose-specific EIIB component	0.21	2.7.1.202	0.21	CL-B
CAR88747.1	Alpha-galactosidase	0.53	3.2.1.22	0.48	CL-D
CAR88756.1	Glutamine transport ATP-binding protein GlnQ	0.18	3.6.3.-	0.68	CL-B

CAR88767.1	Fumarate hydratase class II	0.58	4.2.1.2	0.65	CL-B
CAR88770.1	Probable NAD-dependent malic enzyme 1	0.2	1.1.1.38	0.36	CL-B
CAR88771.1	Probable NAD-dependent malic enzyme 1	0.22	1.1.1.38	0.43	CL-B
CAR88773.1	Probable C4-dicarboxylate sensor kinase	0.29	2.7.13.3	0.71	CL-B
CAR88801.1	Ribose-phosphate pyrophosphokinase	0.52	2.7.6.1	0.88	CL-B
CAR88804.1	Mannitol-1-phosphate 5-dehydrogenase	0.93	1.1.1.17	0.93	CL-B
CAR88806.1	Transcriptional regulator MtlR	0.4	2.7.1.197	0.4	CL-B
CAR88807.1	PTS system mannitol-specific EIICB component	0.61	2.7.1.197	0.79	CL-B
CAR88808.1	Glucosamine-6-phosphate deaminase	0.92	3.5.99.6	0.93	CL-B
CAR88815.1	Macrolide export ATP-binding/permease protein MacB	0.38	3.6.3.-	0.65	CL-B
CAR88819.1	Transaminase MtnE	0.16	2.6.1.-	0.26	CL-B
CAR88820.1	Hydrolase MtnU	0.22	3.5.-.-	0.32	CL-B
CAR88823.1	Hydroxycarboxylate dehydrogenase A	0.11	1.1.1.-	0.11	CL-C
CAR88826.1	Putative amidohydrolase YhaA	0.15	3.5.1.-	0.15	CL-B
CAR88833.1	tRNA modification GTPase MnmE	0.93	3.6.-.-	0.93	CL-B
CAR88837.1	Ribonuclease P protein component	0.93	3.1.26.5	0.93	CL-C
LGG_02202	CRISPR-associated endoribonuclease Cas2	0.89	3.1.-.-	0.89	CL-A

The table 8 shows the identified biomass precursors considered for the construction of the draft.

Table 8- Constitution of the biomass used in the construction of the draft.

Macromuleculas	Metabolites	Formula	KEGG ID	stoichiometry		mass %	MW
				mmol M/ gMM	mmol M/ gDW	g MM/ gDW	gM/molM
Cofactors	Glutathione	C10H17N3O6S	C00051	0,0001			307.3235
	FMN	C17H21N4O9P	C00061	0,0001			456.3438
	NADPH	C21H30N7O17P3	C00005	0,0001			745.4209
	Pyridoxal phosphate	C8H10NO6P	C00018	0,0001			247.1419
	Ubiquinone	C14H18O4(C5H8)n	C00399	0,0001			
	CoA	C21H36N7O16P3S	C00010	0,0001			767.5341
	NAD+	C21H28N7O14P2	C00003	0,0001			664.433
	S-Adenosyl-L-methionine	C15H22N6O5S	C00019	0,0001			398.4374
	FAD	C27H33N9O15P2	C00016	0,0001			785.5497
	Thiamine	C12H17N4OS	C00378	0,0001			265.3546
	Heme	C34H32FeN4O4	C00032	0,0001			616.4873
	Tetrahydrofolate	C19H23N7O6	C00101	0,0001			445.4292
	Riboflavin	C17H20N4O6	C00255	0,0001			376.3639
e-DNA	dCTP	C9H16N3O13P3	C00458	0,562440419	0,013098	0,03602689	467,1569
	dTTP	C10H17N2O14P3	C00459	1,026374325	0,023902		482,1683
	dGTP	C10H16N5O13P3	C00286	0,562440419	0,013098		507,181
	dATP	C10H16N5O12P3	C00131	1,026374325	0,023902		491,1816
e-RNA	ATP	C10H16N5O13P3	C00002	0,807147258	0,019388	0,03718879	507,181
	UTP	C9H15N2O15P3	C00075	0,665434381	0,015984		484,1411
	CTP	C9H16N3O14P3	C00063	0,616142945	0,0148		483,1563
	GTP	C10H16N5O14P3	C00044	0,991990142	0,023828		523,1804
Lipoteichoid acid	Glycerol phosphate	C3H9O6P(C3H7O5P)n	C02768	0,162312998	0,009813478	0,03177717	2637.00

	diglucosyl diacylglycerol	C17H26O15R2	C06040	0,076935869	0,004651559		1249,93
	L-alanine	C3H7NO2	C00041	0,002083892	0,000125993		89,094
	D-galactose	C6H12O6	C00124	0,006764282	0,00040897		180,156
Lipid	Phosphatidylglycerol	C8H13O10PR2	C00344	0,175748559	0,002835	0,00948534	1017,58
	3-O-L-Lysyl-1-O-phosphatidylglycerol	C14H25N2O11PR2	C04482	0,039985122	0,000645		497,58
	Diacylglycerol	C5H6O5R2	C00165	0,037195462	0,0006		997,71
	Diglucosyldiacylglycerol	C17H26O15R2	C06040	0,281755626	0,004545		1249,93
	Cardiolipin	C13H18O17P2R4	C05980	0,395201785	0,006375		2801,23
Protein	Glycine	C2H5NO2	C00037	0,839416058	0,386492	0,53669646	75,0666
	L-Alanine	C3H7NO2	C00041	0,784671533	0,361286		89,932
	L-Arginine	C6H14N4O2	C00062	0,374087591	0,172241		174,201
	L-Asparagine	C4H8N2O3	C00152	0,538321168	0,247859		132,1179
	L-Aspartate	C4H7NO4	C00049	0,282846715	0,130231		133,1027
	L-Cysteine	C3H7NO2S	C00097	0,310218978	0,142834		121,1582
	L-Glutamate	C5H9NO4	C00025	0,328467153	0,151236		147,1293
	L-Glutamine	C5H10N2O3	C00064	0,583941606	0,268864		146,1445
	L-Histidine	C6H9N3O2	C00135	0,136861314	0,063015		155,1546
	L-Isoleucine	C6H13NO2	C00407	0,556569343	0,256261		131,1729
	L-Leucine	C6H13NO2	C00123	0,79379562	0,365487		131,1729
	L-Lysine	C6H14N2O2	C00047	0,656934307	0,302472		146,1876
	L-Phenylalanine	C9H11NO2	C00079	0,346715328	0,159638		165,1891
	L-Proline	C5H9NO2	C00148	0,319343066	0,147035		115,1305
	L-Serine	C3H7NO3	C00065	0,465328467	0,214251		105,0926
	L-Threonine	C4H9NO3	C00188	0,510948905	0,235256		119,1192
	L-Tryptophan	C11H12N2O2	C00078	0,155109489	0,071417		204,2252
	L-Tyrosine	C9H11NO3	C00082	0,246350365	0,113427		181,1885
	L-Valine	C5H11NO2	C00183	0,656934307	0,302472		117,1463
	L-Methionine	C5H11NO2S	C00073	0,237226277	0,109226		149,2113

Draft LR.xml

The “Draf LR”t document refers to the result of the construction of the model.