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The Genome Scale Metabolic Model of Cryptosporidium hominis: iNV209

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THE GEOME SCALE METABOLIC MODEL OF *CRYPTOSPORIDIUM HOMINIS*:

*I*NV213

A thesis submitted in partial fulfillment of the requirements for the degree of Masters of Sciences at Virginia Commonwealth University.

by

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Abstract

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By Niti Vanee, B.Tech.

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The apicomplexan *Cryptosporidium* is a protozoan parasite of humans and other mammals. *Cryptosporidium* species cause acute gastro-enteritis and diarrheal disease in healthy humans and animals, and cause life-threatening infection in immuno-compromised individuals such as people with AIDS. It has a one-host life cycle and invades intestinal epithelial cells causing diarrhea, or more rarely the pulmonary epithelium. *Cryptosporidium* carries out all the asexual reproductive stages like several other apicomplexans. Current annotation of this organism predicts it to contain 3884 genes of which only 1581 genes have predicted functions. By using a combination of bioinformatics

analysis, biochemical evidence, and high-throughput data, a genome-scale metabolic model of *Cryptosporidium hominis* is being constructed. The current model is comprised of approximately 213 gene-associated enzymes involved in major metabolic pathways including carbohydrate, nucleotide, amino acid, and energy metabolism. The approach of constructing a genome-scale model provides a link between the genotype and the phenotypic behavior of the organism, making it possible to study and predict behavior based upon genome content. This modeling approach provides an overview for evaluating missing components in a metabolic network and provides an analytical framework for interpreting data as more research becomes available. The goal of constructing this model is to systematically study and analyze various functional behaviors of *C. hominis* with respect to its stages in life cycle and pathogenicity.

CHAPTER 1 INTRODUCTION

1.1 Cryptosporidium

Cryptosporidium is a protozoan parasite that belongs to the apicomplexa phylum. It causes acute gastroenteritis and diarrhea. Many outbreaks in United States occurred in water parks, community swimming pools and day care centers. Interest in the study of this parasite has increased in the last two decades especially after the outbreak of cryptosporidiosis in Milwaukee, Wisconsin in 1993 where approximately 403,000 people were affected. It was the largest waterborne disease outbreak documented in the history of United States (Kenzie et al., 1994). Transmission of *Cryptosporidium* occurs mainly through contact with the contaminated water (e.g., drinking and recreational water). It is resistant to chemical treatment of water, like chlorination, as it exists in the form of oocysts when outside the host cell and these oocysts pass through the filtration systems of the water supplies as well.

The two most studied species, *C. hominis* and *C. parvum*, which differ in host range, genotype, and pathogenicity, are more relevant to humans. *C.hominis* infects only humans, whereas *C. parvum* also spreads in other mammals. (Xu et al., 2004).

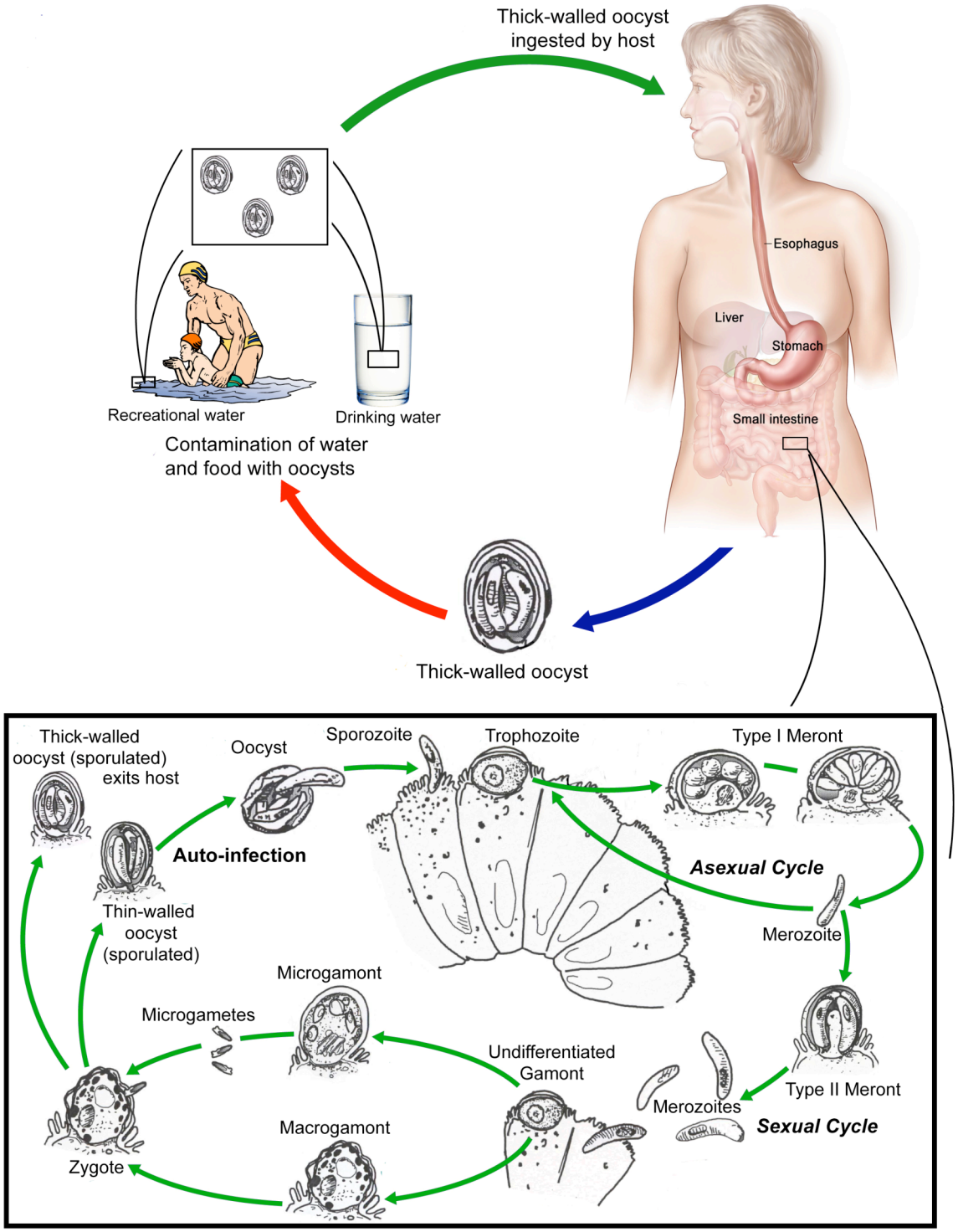

Figure 1: Infection cycle and life cycle of *Cryptosporidium* (adapted from Cryptosporidiosis figure from Department of Health and Human Services)

1.1.1 Infection cycle and life cycle

Cryptosporidium is transmitted be the fecal-oral route via the oocyst stage. These infections increase with close human-to-human contact and by contact with infected livestock, zoo animals, or companion animals (Fayer, 1997).

Transmission of *Cryptosporidium parvum* and *C. hominis* occurs mainly through contact with contaminated water (e.g., drinking or recreational water) as shown in Figure 1. Sometimes it may also be transmitted by food sources, such as chicken salad. Many outbreaks in the United States have occurred in water parks, community swimming pools, and day care centers. Zoonotic and anthroponotic transmission of *C. parvum* and anthroponotic transmission of *C. hominis* occur through exposure to infected animals or exposure to water contaminated by feces of infected animals.

The life cycle of *Cryptosporidium*, shown diagrammatically in Figure 1, is complex as it involves both sexual and asexual developmental stages. It begins upon the inhalation or the ingestion of sporulated oocysts, which is the only exogenous stage, containing 4 sporozoites within a tough layered wall. It is excreted from the body of an infected host in the feces. Following ingestion (and possibly inhalation) by a suitable host, excystation occurs. The sporozoites are released and infect the epithelial cells of the gastrointestinal tract or other tissues such as the respiratory tract. Here the parasites undergo asexual multiplication (schizogony or merogony stages) and then sexual multiplication (gametogony) producing microgamonts (male) and macrogamonts (female). Upon fertilization of the macrogamonts by the microgametes, oocysts are developed that

sporulate in the infected host. Two different types of oocysts are produced –

- Δ The thick-walled, which is commonly excreted from the host, and
- Δ The thin-walled oocyst, which is primarily involved in autoinfection.

Oocysts are infective upon excretion, thus permitting direct and immediate fecal-oral transmission. (Department of Health and Human Services; Thompson et al., 2005)

Oocysts – Thick- as well as thin-walled oocysts are usually recovered from culture after 5 days of inoculation. Approximately 80% of the oocysts formed after the completion of the life cycle are thick- walled oocysts, which are released from the host in the faeces if present in the gastrointestinal tract, or via aerosols or nasal secretions if present in the respiratory tract. However, about 20% of oocysts fails to form a thick oocyst wall and are thus known as thin-walled oocysts. Thin-walled oocysts are important in autoinfection through continuous recycling of sporozoites excysting from ruptures thin-walled oocysts. (Thompson et al., 2005)

Sporozoites – are 5.2 X 1.2 µm in size and are characterized by having a comma shape with a rounded posterior end and a pointed tapered anterior end. They actively move inside the oocysts, excysting and exhibits gliding movement. (Thompson et al., 2005)

1.1.2 Maintenance and amplification of *Cryptosporidium*

Cryptosporidium species are not very well studied because culturing and amplification of the organism of a big challenge. One of the major objectives of many

laboratories is to amplify the parasite and develop reproducible models of infection to facilitate biological, pathological, immunological and molecular and drug evaluation studies. There are two ways by which *Cryptosporidium* can be amplified: *in vivo*, in animal models and *in vitro* using different cell lines.

1.1.2.1 Challenges faced *in vivo*.

The majority of *in vivo* infections have been carried out using the *C. parvum* cattle genotype. Experimental infections with *C. parvum* have been successfully established in a variety of domestic and laboratory animals, especially neonates, immunosuppressed or immunodeficient animals. But there is a high level of difference in infectivity for laboratory animals even between two closely related species of *Cryptosporidium* - *C. parvum* and *C. hominis*. *C. parvum* cattle genotype can readily infect mice and cattle whereas *C.hominis* does not infect them. (Peng et al., 1997)

In summary, *Cryptosporidium* does not support the infection with multiple genotypes. Apart from this, the amplification of *Cryptosporidium* in animal models is labor-intensive, expensive beyond the budget of most of the laboratories, and will not support the growth of the parasite for long period of time. (Thompson et al., 2005)

1.1.2.2 Challenges faced *in vitro*

There are many factors that affect the development and proliferation of *Cryptosporidium* in culture. These include the excystation protocol, age and strain of parasite, stage and size of the inoculum, host cell types and maturity, and culture

conditions such as pH, medium supplements and atmosphere. (Thompson et al., 2005)

Although, major improvements in culturing *Cryptosporidium* in vitro have occurred since 1984, infections could not be maintained for more than a few days and only asexual phases of the parasite life cycle could be consistently maintained for short periods. Efforts are going on in the direction to optimize the conditions for growth in order to increase the number of parasite stages produced and days to maintain the culture for longer period of time. (Thompson et al., 2005)

1.1.3 Host-pathogen interaction - disease caused

Cryptosporidium lives in the intestine of the infected humans and animals, is transmitted by ingestion of oocycsts, and completes its life cycle in a single host (Figure 1). In healthy humans, the parasite is responsible for symptoms such as watery diarrhea, abdominal cramps or pain, dehydration, nausea, vomiting, fever, and weight loss. Its major impact has been among those with weakened immune systems, including, people with HIV or AIDS or Transplant recipients. They may develop serious, chronic, and sometimes fatal version of the illness (P. Xu et al., 2004). There is no therapy available so far to treat patients suffering from cryptosporidiosis.

The time from ingestion of oocysts to the appearance of clinical signs is between 2 and 14 days. The first clinical signs associated with infection is, diarrhea, which may or may not be associated with abdominal cramping. Severity varies from continuous voluminous watery diarrhea to scant or intermittent diarrhea. Blood is infrequently observed in the stool. Other clinical signs include general malaise, fever, and fatigue, loss

of appetite, nausea and vomiting. Dehydration and weight loss are also direct result from the symptoms (Ramirez, et al., 2004).

In immunocompetent host, clinical signs last for 10-14 days, but in the immunocompromised individuals they can persist for months to years. (Thompson et al., 2005)

It is of particular concern for four reasons:

1. The oocyst is extremely resistant to disinfection and cannot be killed with routine water-disinfection procedures;
2. The disease is not treatable with antibiotics;
3. The mortality from infection in severely immunocompromised patients can be as high as 50-60%; and
4. Animal and human fecal wastes are associated with transmission of the disease to humans. (Bates, 2007)

1.1.4 Genome of *Cryptosporidium hominis*

The parasite genome was sequenced in 2004 by Xu et al. describes that it has eight-chromosome, approximately 9.2 mb genome size and contains an estimated 3994 genes. *In silico* reconstitution of *C.hominis* biochemical properties reveal that basic metabolic pathways are extremely streamlined. The parasite depends mainly on glycolysis for energy production. It supports both aerobic and anaerobic metabolism. However, it shows limited

biosynthetic pathways and mainly relies on transporters. Following figure from Xu et al. explains the major metabolic pathways inside the *C.hominis*. (Xu et al., 2004)

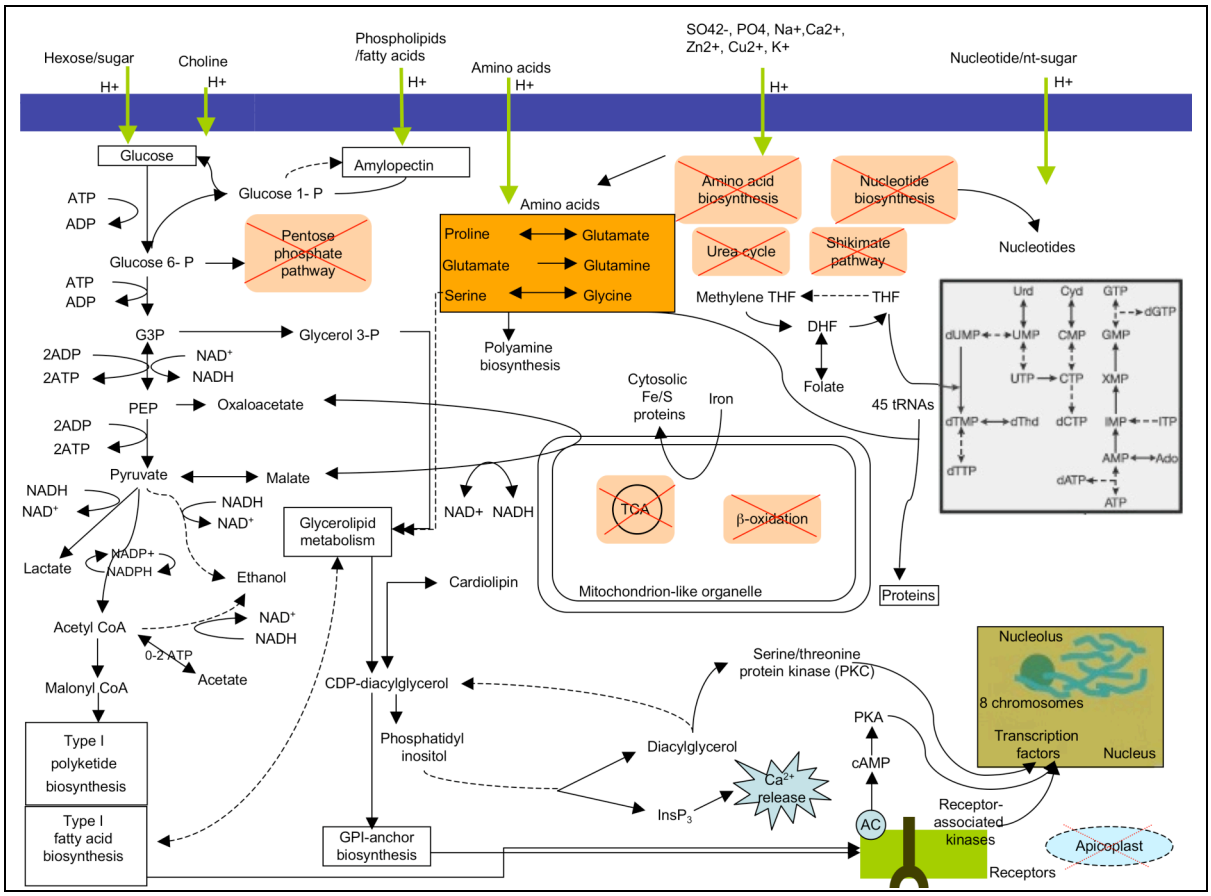

Figure 2: Predicted metabolic network inside *C.hominis* on the basis of genome annotation (Xu et al., 2004)

1.2 Systems Biology

Genome Sequencing has enabled us to determine the biological components that make up a cell or an organism. The new discipline of systems biology examines how these components interact and form networks and how the networks generate the whole cell

functions corresponding to observable phenotypes. The study of whole systems, with the inclusion of genomic, proteomic, metabolomic, and fluxomic data together, is termed Systems Biology (Figure 3).

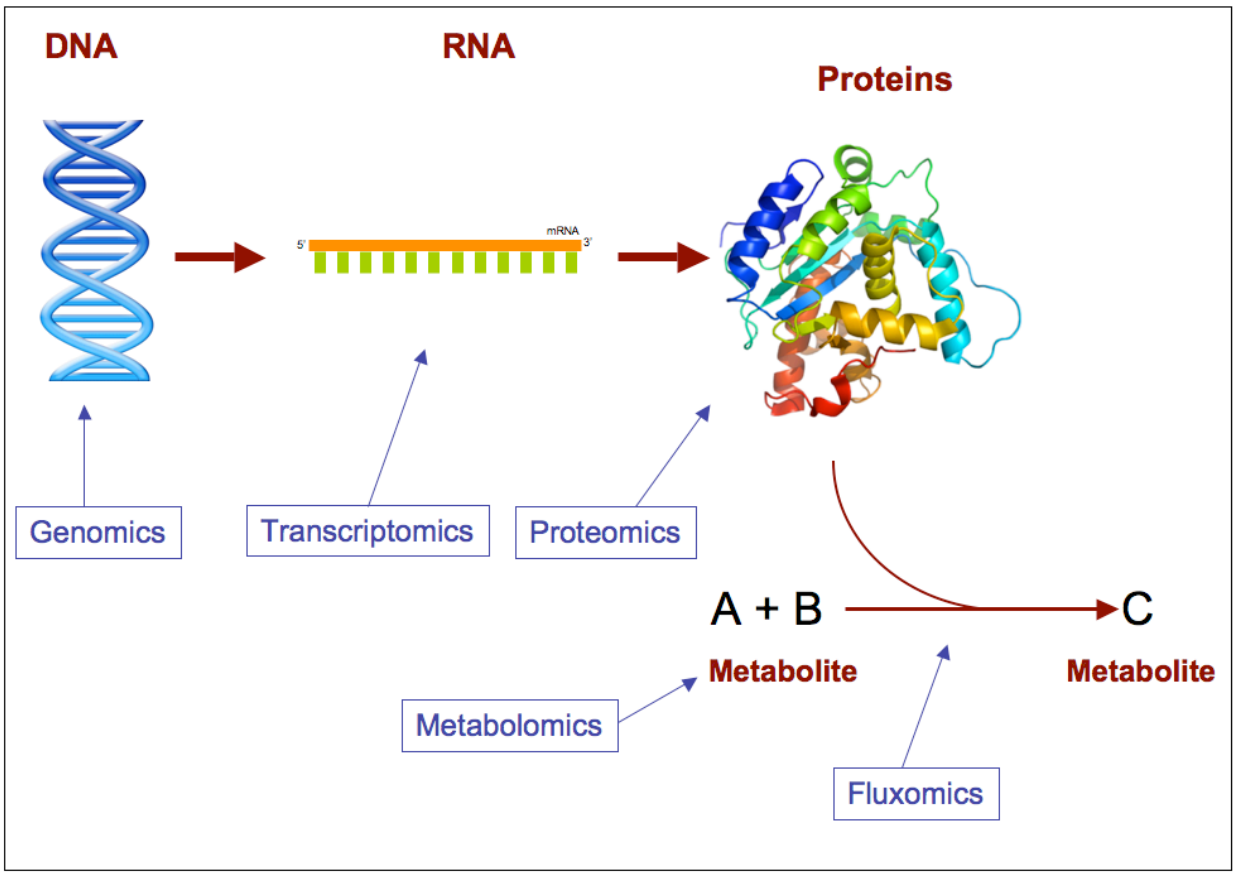

Figure 3: Several elements that describe an organism (Fong, 2008)

This approach focuses on finding the relation between the genotype and phenotype of an organism by using a network model, permitting a better understanding of the cellular processes. Recently, many network models of various organisms have been constructed and validated for use in biological prediction including *Bacillus subtilis, Escherichia coli, Saccharomyces cerevisiae,* Human cardiac mitochondria and Human RBCs. (Joyce &

Palsson, 2007)

1.2.1 Modeling approach - Constraint Based Modeling

Bringing together all the potential biochemical reactions of an organism, builds up a network chart of metabolic pathways however, in the biological world, cells are subjected to various constraints from environmental, physiochemical, evolutionary, and regulatory sources. By incorporating metabolic reactions as well as other above-mentioned properties into the systemic network reconstruction, these models account for the constraints that restrict an organism's phenotypic behavior. Apart from constraints that arise from network topology and stoichiometry, other constraints can be incorporated into these models, e.g. experimentally determined maximum enzyme fluxes, thermodynamic limitation, internal metabolic flux determinations, transcriptional regulation, etc. The constraint-based modeling approach helps distinguish the networks states that a system can achieve from those it cannot achieve rather than exactly predicting the network behavior. (Joyce & Palsson, 2007; Raghunathan et al., 2009)

1.2.2 Mathematical algorithms used for optimization

Once the model is ready in the mathematical form we use mathematical optimization algorithm to investigate the production capabilities and systemic properties of the metabolic network (Joyce & Palsson, 2007; Shlomi et al., 2008).

1.2.2.1 Linear programming algorithm - Flux Balance Analysis

Flux Balance Analysis (FBA) is a type of analysis that imposes mass balance and flux capacity constraints on the network and uses an optimization procedure to find a steady-state flux distribution that maximizes the biomass yield of the cell without the need for measurement of kinetic parameters. FBA relies on Linear programming based optimization. We define an objective function of our network such as biomass production, byproduct secretion, ATP production, etc. and try to optimize that objective. Linear programming works on optimizing the flux distribution for the network model that maximizes the stated objective. (Raman & Chandra, 2009; Roberts et al., 2009)

1.2.2.2 Mixed integer linear programming algorithm – MILP

Another type of optimization algorithm that is used in model analysis is MILP. It is called so because it unlike FBA when we use this algorithm we get the results in terms of integer (-1, 0, 1) that denoting if the reaction is in active state or inactive state and also gives us the flux value of the reaction which may be any decimal value between -1000 to 1000. The flux values are calculated from by linear programming as in FBA.

MILP used in the current work is from Shlomi et al. and the basis for MILP is to optimize the agreement between the two sets of information used (the metabolic model and the proteomic or expression data). (Shlomi et al., 2008)

In the ideal situation, the reactions that are expressed implies that the proteins coding for that specific reaction are active and the reactions that are inactive should mean that the proteins are inactive. In the biological world its not an ideal situation i.e. there is a

possibility that a specific protein is found in the system but reaction is still in affective because of other factors affecting it such as presence of substrate.

To better understand the functioning of MILP consider the following figure where the region of interested is either the active state of reaction and protein or the inactive state of reaction and protein and the aim is to maximize the information related to these 2 regions and minimize the false positive and negative region.

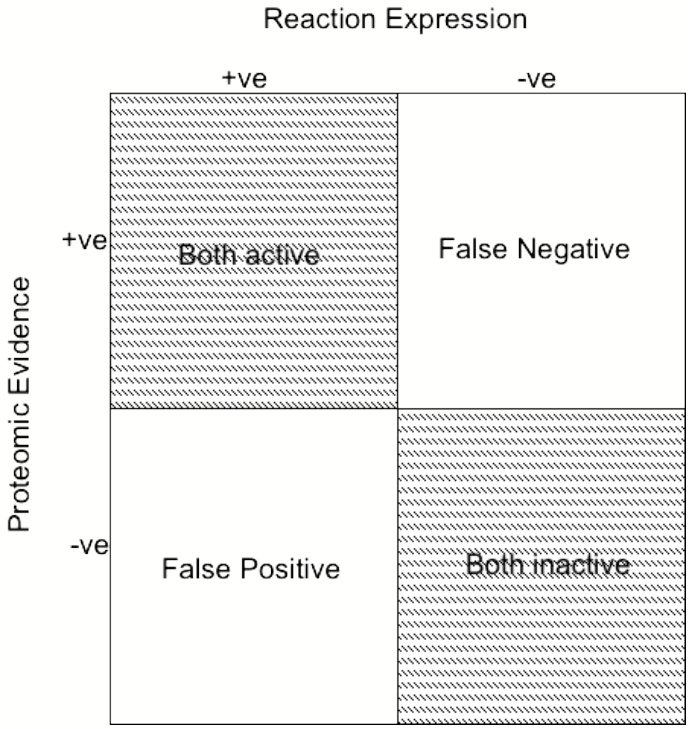

Figure 4: Optimization through MILP algorithm aims at maximizing the information related to the shaded region where reactions and proteins are both found either active or inactive and reducing the other regions. Note: false negative is the region where the protein is found in the systems but the reaction is not present or active where as false positive denotes the case where protein is absent in the system but the reaction is still expressed. The region of false positive exists with the gene expression data where genes are highly expressed or lowly expressed and not with the proteomic data.

1.3 Metabolic modeling

1.3.1 Introduction

Detailed, comprehensive-modeling efforts led to the development of three types of networks: metabolic networks, transcriptional regulatory networks and signaling networks (Palsson, 2007). The most commonly reconstructed and used networks are the metabolic networks that integrate the biochemical interactions present in the organism. Genome annotation provides the basis for the initial prediction of metabolic enzymes and the preliminary genome-scale model. Figure 4 shows the major steps involved construction genome scale metabolic models.

Metabolic network interacts with essentially all other cellular processes. The reconstruction of these processes and the integration of multiple networks will lead to the description of a comprehensive range of cellular functions.

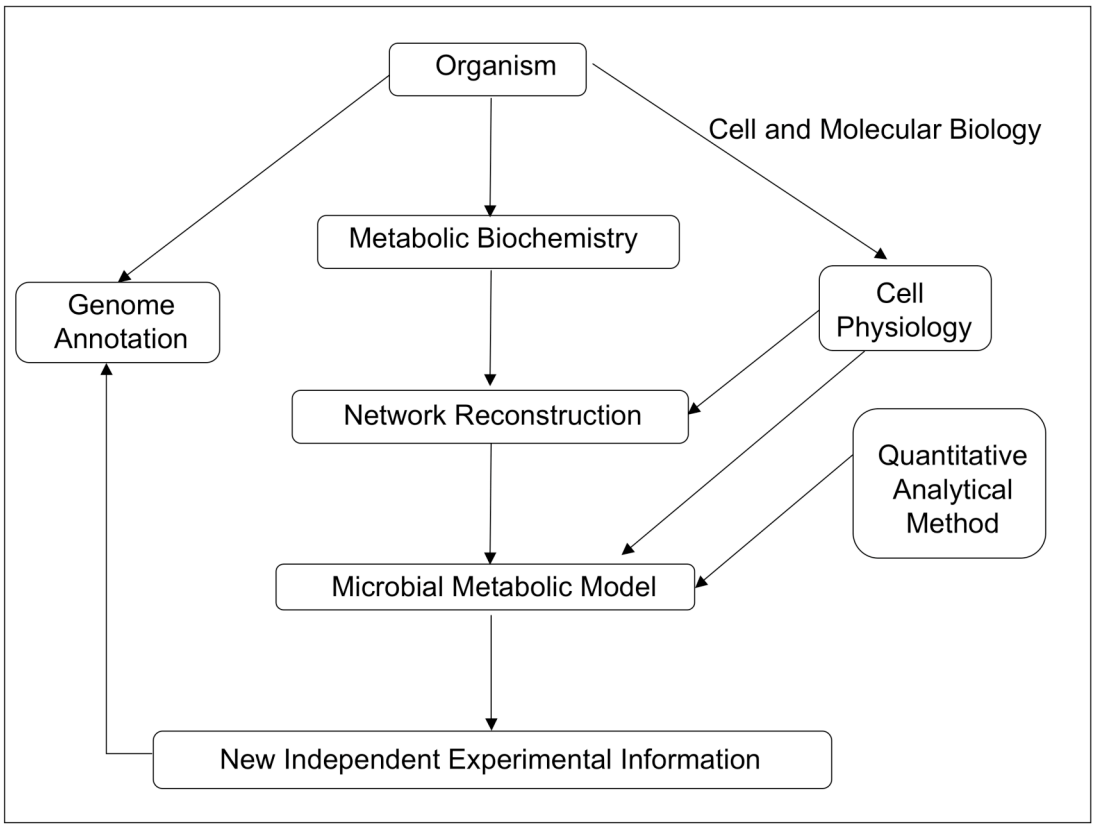

Figure 5: Overall process of genome scale metabolic reconstruction (adapted from Palsson, 2007)

The metabolic reconstruction requires mainly 4 steps:

Step 1: Network reconstruction, i.e. obtaining the genome annotation of the target organism. Genome annotations are available at several only databases such as, IMG (Integrated Microbial Genome), EntrezGene, CMR (Comprehensive Microbial Resource), Genome Reviews (through EBI, European Bioinformatics Institute), etc. Also there are several organism specific sources of genome like EcoCyc for *E.coli*, SGD (*Saccharomyces* Genome Database), etc.

Other databases such as KEGG, MetaCyc, Transport DB can be used to provide metabolic and transport reaction that's have been shown to occur in a range of organisms. (Feist, et al., 2009)

Step 2: Refining the draft reconstruction. The draft reconstruction created in previous step needs to manually curated, ideally with the inputs from organism specific experts. This step of manual curation is labor intensive and sometimes tedious. Organism- specific databases, textbooks, primary publication, review articles, and experts familiar with the legacy data for an organism are the main sources of information for the manual curation step. These sources of information provide direct or indirect evidence for the inclusion of specific reactions in the metabolic reconstruction. (Feist et al., 2009)

Step 3: Mathematical modeling and analysis of the network. Applying mathematical algorithm to the curated biochemical to perform simulations and analysis. Once the network was reconstructed, the list of metabolic reactions was transformed into a stoichiometric matrix (S), i.e., the mathematical representation of the reconstructed network. The S matrix dimensions are m x n, where m is the number of metabolites and n is the number of reactions. Each element S_{ij} represents the stoichiometric coefficient of metabolite i in reaction j. If the metabolite in a particular reaction is a reactant, the coefficient is negative (the metabolite is consumed by the reaction); if it is a product, the coefficient is positive (the

metabolite is produced by the reaction). The S matrix was then used as the basis of further analysis, i.e., Flux Balance Analysis. FBA uses linear programming based optimization to identify a particular flux distribution distribution (a single point in the multidimensional space of possible metabolic behaviors) that optimizes a given metabolic objective (see Biomass Equation, below). The LP optimization problem is formulated as:

Maximize Z,
Subject to $\mathbf{S} \cdot \mathbf{v} = \mathbf{0}$,
$a_i < v_i < b_i$ for all reactions *i*.

Z is the objective function; for this study, Z was defined as the biomass equation. The second two statements are the flux constraints. **S** is the stoichiometric matrix defined above. Each reaction flux is subject to lower and upper bounds, as indicated (in cases where these are not known, a_i and b_i are set to some arbitrary numbers that exceed any feasible internal flux). The solution to this problem is an optimal flux distribution, **v**, a vector that contains flux values for each reaction in the network. The solution is optimal in the sense that it maximizes the flux through the objective Z.

Mathematically, **S** is a transformation of the reaction flux vector, **v**, to a vector of time derivatives for each metabolite concentration:

$$\mathbf{S} \cdot \mathbf{v} = d\mathbf{x}/dt.$$

Since the time constants for metabolic transients are fast (< tens of seconds), but the time constants for cell growth are long (hours to days), the metabolites can be considered as existing in a quasi-steady state (Joyce & Palsson, 2007). This leads to the second equation of the LP optimization problem above. Because of the emphasis on steady states, assumptions regarding reaction kinetics are not needed.

Biomass Equation: In FBA, optimization is used to find a particular flux distribution that maximizes a given metabolic objective. Typical metabolic objectives chosen for optimization include maximization of ATP production, byproduct secretion, or biomass production. In our work, we chose to optimize for biomass production (Roberts et al., 2009). Biomass production is represented in our model by an additional metabolic reaction. Its reactants include such critical metabolites as ATP, acetyl-CoA, and NADPH; its products include ADP, inorganic phosphate, and other metabolites that represent byproducts of anabolic metabolism.

Step 4: Integration of the high-throughput data. Further, the specific experimental or stage specific or tissue specific expression data or proteomic data is integrated with the existing comprehensive reconstructed metabolic network to

study the organisms' performance with respect to the data and thus make further predictions.

1.3.2 Application

Such model once completed can be applied to study the specific growth condition from which the training data were based and can be used to explore additional environmental condition. Network reconstructions help us to build mechanistic genotype-phenotype relationships and thus obtain quantitative (such as, what is the cellular growth rate) and qualitative (such as, will the organism grow in a particular condition) predictions about the organism. (Feist et al., 2009)

In recent year with the growing popularity of the systems biology approach of solving biological problem, researchers from various fields have tried the metabolic reconstructs to analyze the target organism and explain the basis behind some of the previously discovered facts (de Figueiredo et al., 2008). Some of the important applications of metabolic model reconstruction include, optimization of production of certain metabolites (Hjersted & Henson, 2009), study host pathogen interaction (Raghunathan et al., 2009), studying single gene deletions (Xu, Sun, & Yu, 2009) or gene knock out screening (Plaimas et al., 2008) or identifying novel antimicrobial drugs targets (Lee et al., 2009).

1.4 Parasite study and metabolic modeling

In context of pathogenic organisms, a metabolic reconstruction has a potential to

plays important role in drug discovery. With the completion of genome projects of several parasites, there are efforts going on to make sense of that information in terms of genes, their products, interactions in growth and development and survival of parasite. (Wambua, Mcconkey, & Westhead, 2009)

1.4.1 Predicting new drug targets

Genomic information provides an accurate picture of the metabolic reactions that are present in the organism. With the analysis of essential reactions from the whole network we can predict the enzymes or transporters that might be viable targets for few new drug target.

1.4.2 Comparative genomics of host and pathogen metabolism

In the study for potential drug targets against the pathogens, one of the most area of study is the interaction between the host and pathogen. Many parasites are found to have lost pathways that are essential for free-living species. For example, *Mycoplasm genitalium* contains 580 genes (Suthers et al., 2009), *C. parvum* lacks Kreb's cycle enzymes (Fayer, 1997). Often, they depend on the host cell for these incomplete but required missing links. These kinds of interactions between host and pathogen can be compared and studied as potential targets to fight against parasitic disease.

In the current project a metabolic model of parasite *Cryptosporidium hominis* is constructed and integrated with proteomic data, and analyzed to make further predictions.

CHAPTER 2 METHODS

2.1 Reconstruction process – genome to metabolic network

The process of reconstructing the metabolic network of *C.hominis* is shown in Figure 5. The overall process is divided into 4 major steps:

Step 1. Network reconstruction

Step 2. Network refinement

Step 3. Network analysis and simulation

Step 4. Proteomic data integration

In brief, the reconstruction process starts with genome annotation that defines the list of functionally identifiable genes present in *C.hominis* (P. Xu et al., 2004). This serves as the basis for a set of possible reactions that are catalyzed by these annotated gene products (enzymes coded by genes). Tables 1 and 2 contain information on the online genome and pathway databases and key references used for the reconstruction process.

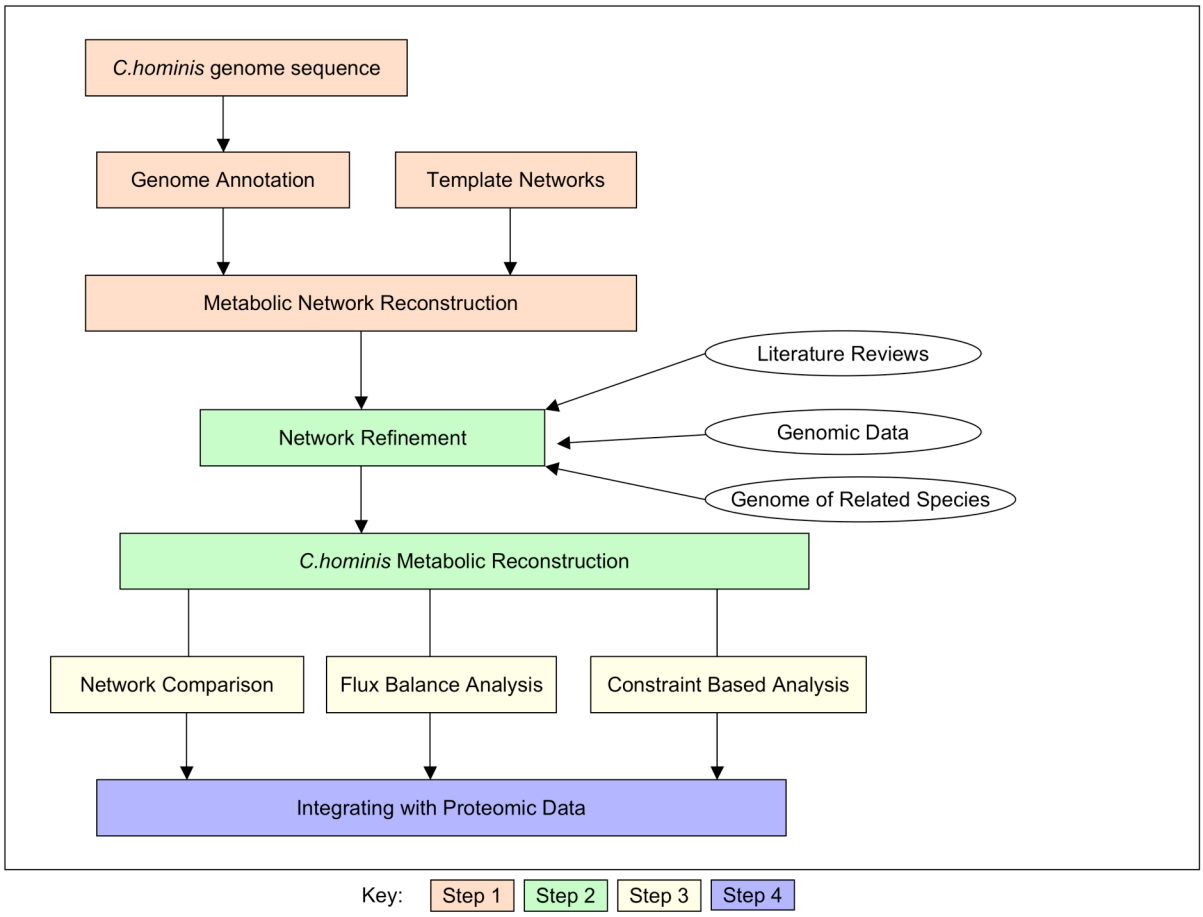

Figure 6: Summary for the *C.hominis* metabolic network reconstruction

Database	Link
Genome Database:	
CSBC *Cryptosporidium hominis* research	http://www.hominis.mic.vcu.edu
Integrated Microbial Genomes (IMG)	http://img.jgi.doe.gov
Pathways and other databases	
KEGG	http://www.genome.jp/kegg/pathway.html
Transport Classification database (TCDB)	http://www.tcdb.org/
Gene Protein Reaction (GPR)	
Uniprot	ftp://ftp.genome.jp/pub/kegg/genes/organisms/cho/cho_xrefall.list

Table 1. Online resources for the reconstruction of metabolic network of *C. hominis*

Metabolism	References
Complete metabolism overview	Thompson et al. 2005
Carbohydrates	Thompson et al. 2005
Energy	Thompson et al. 2005
Nucleic acid	Thompson et al. 2005
Amino acid	
Fatty acids	Fritzler et al. 2007
	Mazumdar et al. 2007
	Thompson et al. 2005

Table 2. Key references consulted additional to the online resources for the reconstruction of metabolic network of *C. hominis*

2.2 Refining the model

EC numbers from the genome annotation were used to look for all possible reactions catalyzed by each enzyme. This created the list of possible reactions in the model. Also the gene IDs were added to the model for each reaction to create **Gene Protein Relation** (GPR) files file for further usage.

A list of metabolites required by the set of reactions was compiled within a **Source** file and also there was a compiled list of byproducts, as **Escapes** file were created with literature reviews of closely related species model available. These files were revised with data available for *C.hominis* experimental information and with simulation runs. Also, draft biomass equation was derived based on the existing equation for *B. subtilis* (Oh et al., 2007), as qualitative results of FBA are relatively insensitive to minor mis-specification of the coefficient values. The goal is to eventually have experimental values for *C.hominis.* All these files contain necessary inputs for steady state operation and simulate the availability of certain metabolites in culture medium.

2.3 Analysis of network using Metmodel and FBA

2.3.1 Gap analysis

The Python-based framework, Metmodel (Roberts & Buck, 2007) was used to build and analyze an initial genome scale model of metabolism of *C.hominis*. The model is stored in a series of text file. Metmodel uses these files as input, performs FBA and outputs the predicted fluxes for each reaction in the model, given a set of objective (biomass production). Some of the reactions were added after the first simulation run as the original network/annotation was found to have gaps.

Gap filling, also known as filling pathway holes, is a procedure for including the reactions that might be important and necessary to complete certain pathway for which only one or two reactions are missing. Most of the time it is possible that these reaction are present in the organism but the enzymes responsible for these reactions are not annotated in the genome, as there are several hypothetical proteins that are yet to be studied for their function. There is a possibility that these hypothetical proteins might code for some of these missing reaction.

2.3.2 Essential reaction

Metmodel also helped in finding the essential reaction, i.e. the subset of lethal reactions in the model. The steps of determining them were as follows:

For each reaction, X:

1. Set the upper and lower bounds of reaction X to zero by setting up constrain on the reaction to have zero flux. This simulates the loss of reaction.
2. Run FBA,
   - → If objective value from FBA run comes out to be 0 (or ~ 0), the reaction is predicted to be lethal which means that there is no growth when the reaction is inactivated.
   - → If not, then the reaction is predicted to be non-lethal, i.e. the parasite can still grow, even though reaction is inactivated.
3. Reset the upper and lower bounds of reaction X to their original values.
4. Continue to next reaction.

2.4 Integrating the proteomic data with the model

As mentioned in the figure 1, parasite has a life cycle and the first two stages – oocysts and sporozoite were analyzed in terms of proteomic composition. Unpublished in-house proteomic data that's was used in this project describes the list of active proteins in a specific stage. This information was used to active or inactive the reactions in the model and see how the model will perform. This stage specific proteomic data was integrated with an optimization algorithm from Shlomi et. al (Shlomi et al., 2008).

The graphical representation of the performance of metabolites in the 2 stages was shown using python based program designed in the laboratory. Figure 7 shows the graphical representation of the difference between the 2 stages. The following graph includes the metabolites that are used in highly different way in two stages. To draw this

chart, the difference in the conditions of both the stages was determined; all the metabolites involved in these conditions were listed. A score was assigned to these metabolites depending on the level of difference of usage of these metabolites in both the stages (i.e. highly different manner ~ highest score). Then the score was ranked and a threshold was set. To draw the final chart, the top list of metabolites was used.

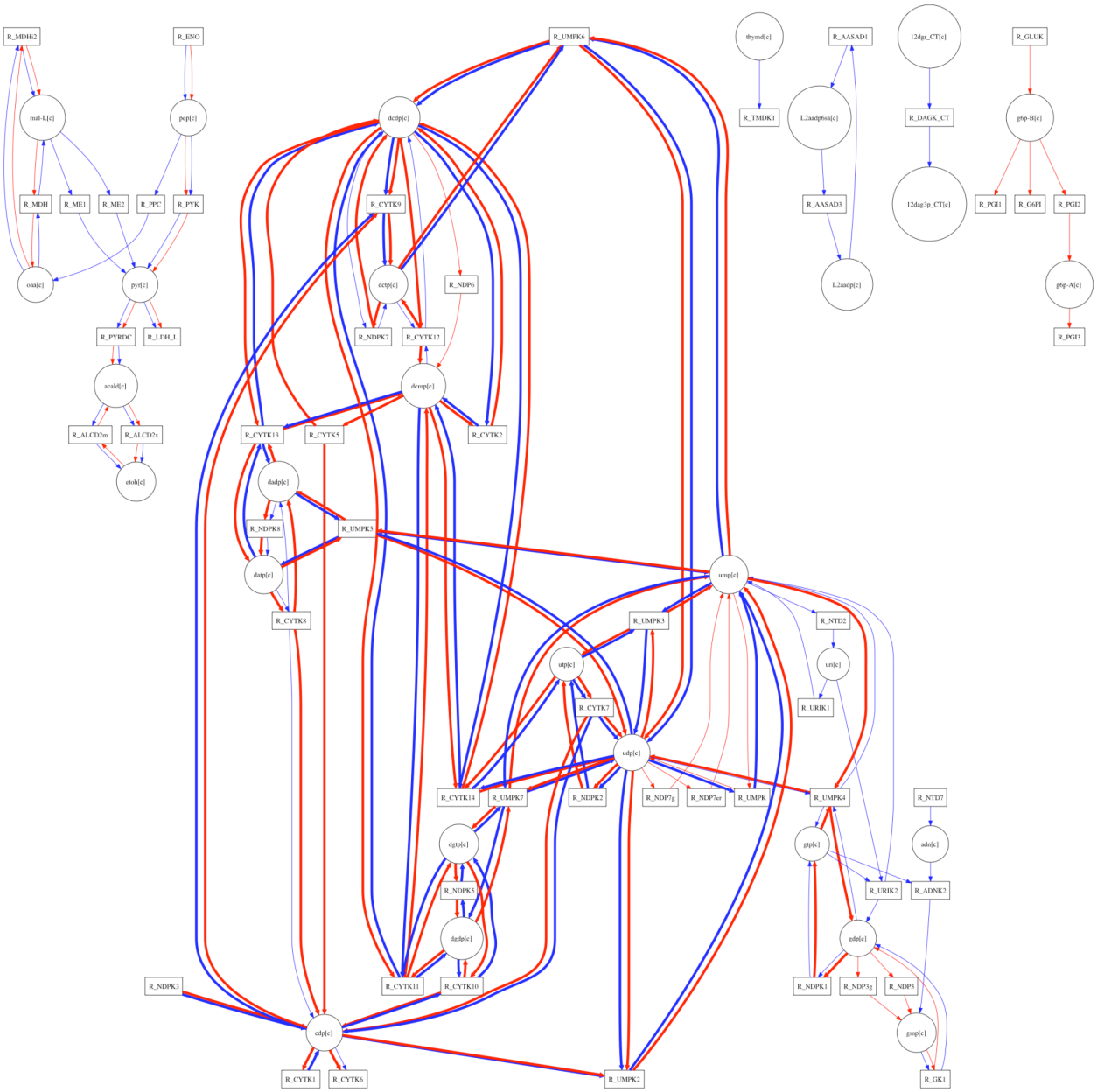

Figure 7: Graphical representation of comparative analysis of 2 stages oocyst and sporozoite in *Cryptosporidium hominis* depending upon the unpublished in-house proteomic data. Blue arrows shows oocyst stage activity and red arrows denote the sporozoite stage activity. This graphical representation only includes the reactions that show maximum level of difference only

CHAPTER 3 RESULTS

3.1 Metabolic Reconstruction

The *i*NV213 network reconstruction accounts for the function of 213 genes and includes 540 reactions with 514 metabolic reaction (including inter-conversion reactions of some metabolites) and 26 are extra-cellular transport reaction. Due to lack of direct biochemical evidences for many reactions, information from genomic data, literature derived conclusions and information from the related organism is used to evidences used to include these reaction in the model. Despite the fact that *C. hominis* is a Eukaryote, the current model contains only one intracellular compartment – the cytosol - as there is not much of information available in terms of compartments and specific pathways that take place inside of the organism.

Figure 8 provides an overview of reactions of *i*NV213. Among, the pathways included in the model, carbohydrate metabolism seem the most functional metabolism network with glycolysis as one of the complete metabolic pathway. However, other metabolic network includes many reactions that are the inter-conversion reactions.

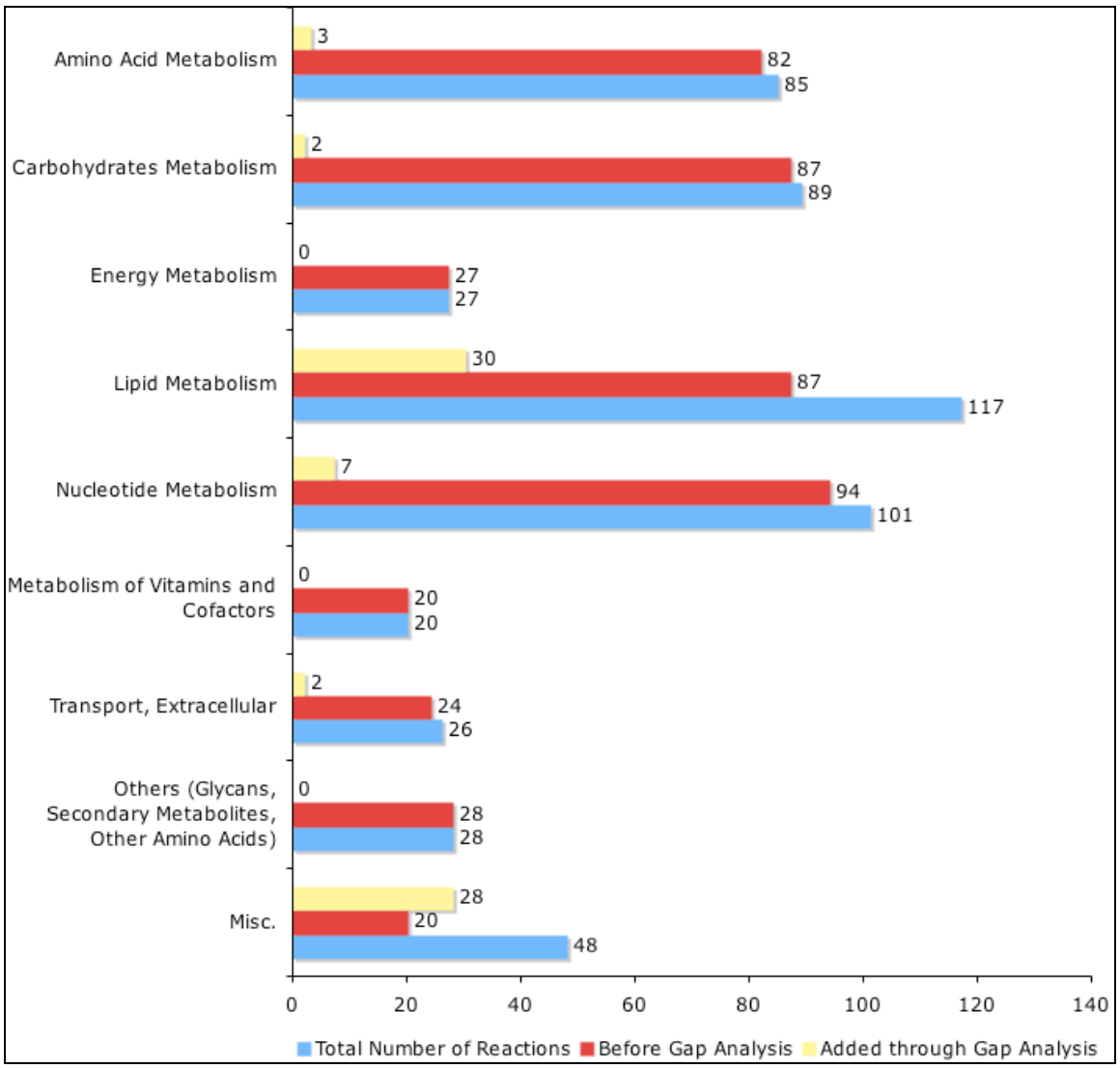

Figure 8: Reactions distribution in the model under several metabolic pathways. Miscellaneous reaction is the set of reactions that were required for the model but could not be categorized under specific metabolism network. Nucleotide metabolism, which is found to have maximum number of reaction in the network, actually comprises of multiple reactions that are coded by single enzymes but exact evidence could not be found to filter them and get the exact minimal set of reactions. Conclusively, carbohydrate metabolism was found to be the most functional and complete network in the model. After completion of reconstruction network a small set of reactions was added to the network to make it functional and yellow bars in each of the metabolic pathways highlights these reaction.

Above figure shows the reaction distribution of each of the metabolic pathway. Genomic evidences support the completeness of metabolic networks such as, Energy

metabolism, glycan metabolism, metabolism of secondary products, and metabolism of other amino acids but some minor additions were required in the amino acid metabolism (3 reactions), carbohydrate metabolism (3 reactions), and nucleotide metabolism (7 reactions). Lipid metabolism accounts for 117 reactions with genomic evidence for 87 reactions. Other 30 reactions were added through gap analysis to complete the metabolic network to of the organism. These reactions are explained in next section of gap analysis.

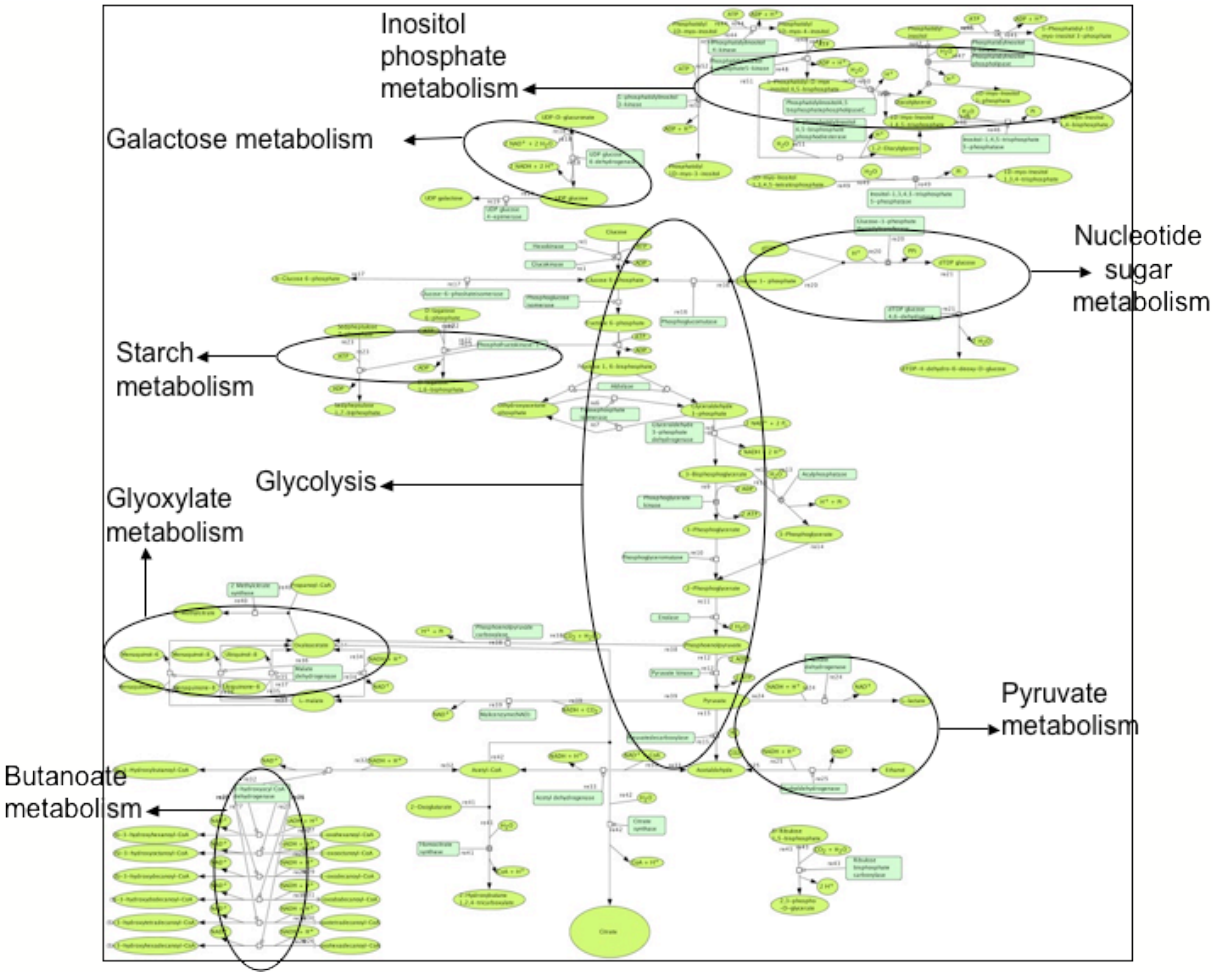

Figure 9: Graphical representation of carbohydrate metabolism network that was found to be the active

3.2 Gap analysis – filling the missing links

The next important step in completion of the model was filling up the missing links - the gaps. There were some of the reactions added to the original *i*NV213 after performing the FBA simulation. This process is termed as gap analysis in network modeling. These reactions are required in order to complete certain pathways e.g., lipid metabolism cannot be functional if these 30 reactions (Supplementary file 2) are absent in the network. Similarly, there is a small set of reaction added to many other pathways including fructose mannose metabolism, glycolysis / gluconeogenesis, aminosugar metabolism, tyrosine metabolism, extra-cellular transport reactions, valine, leucine and isoleucine biosynthesis, pyrimidine metabolism and purine metabolism. There is a set of 29 reactions added to the model through gap analysis but their exact sub systems were not studied. These reactions are listed in the supplement data file 2 but are not included in the following figure of gap analysis reactions chart.

For some of these reaction filled in lipid metabolism by gap analysis, the enzymes responsible for them were further checked in genome of *C. hominis.* This was done by isolating the hypothetical protein sequences from the whole genome of *C.hominis* and performing the translated nucleotide BLAST against non-redundant protein sequences to see if there genome annotation can be updated after the developments since 2004 when this genome was last annotated. This might help us answer some of the questions about the reactions added through the gap analysis. At the current stage of this procedure, no significant matches were found but efforts are going on to optimize the search process.

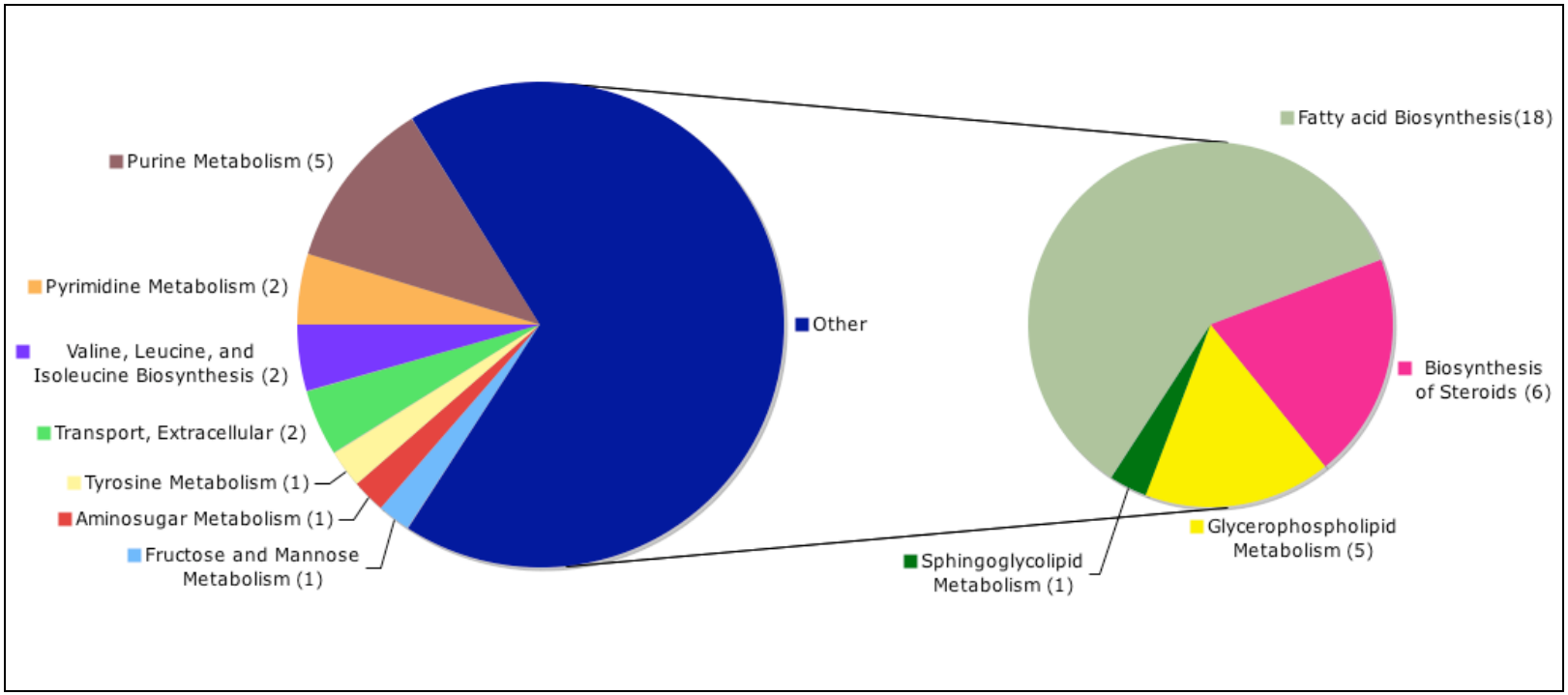

Figure 9: Distribution of reactions added to the known metabolic networks by gap analysis algorithm. Almost 50% of the reactions are found to fill the gaps in lipid metabolism with most of the reaction in fatty acid biosynthesis, biosynthesis of steroids, glycerophospholipid metabolism and sphingolipid metabolism

3.3 Essential reaction

Simulation runs using Metmodel also helped in predicting the lethal reactions from the model. 52 reactions were found to be essential using the deletion prediction algorithm (described above). Summary of those lethal/essential reactions is shown in figure 10. When performing the iterative flux balance analysis to study for reaction deletions it was observed that eliminating reaction either reduces the optimal flux value or does not affects it at all. However, when any of these 52 reaction were removed or masked in the model the optimal flux value became negative which denotes there is no growth seen in the model if these reactions are absent from the pathway network.

Figure 10 shows the lethal reaction distribution among the respective pathways. Individual analysis of each of these reactions and comparing them with the ones added through gap analysis showed that some of these reactions that were found lethal were added in the process of gap analysis eg. in the fatty acid metabolism, 16 reaction were found lethal out of which 9 reactions were added to the model by gap analysis algorithm. Also, among the 3 important reactions of the glycerophospholipid metabolism all of them were added in the above step to complete the metabolic network chart. Other predicted lethal reaction include 5 reactions (out of 10) were found to be lethal. This prediction is well supported by all the previous literature about importance of glycolysis in *Cryptosporidium.* Glycolysis is the fully functional and active pathway in the organism and the major source of energy production as well (Thompson et al., 2005). The lethal reactions found in glycolysis are listed in table 3.

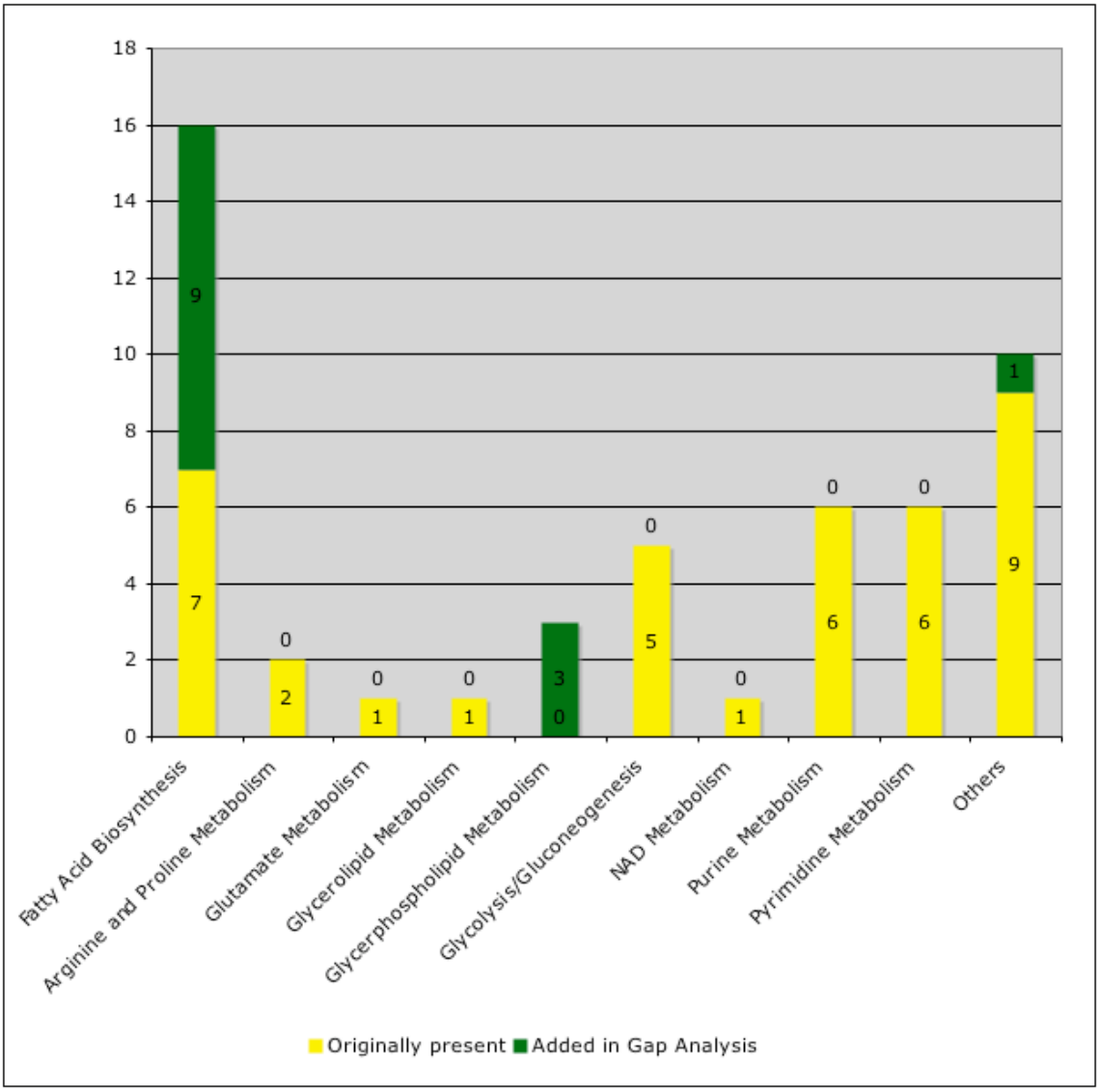

Figure 10: Predicted number of essential reaction in the respective pathway. Green bars denote the lethal reactions found in each of the metabolic pathway where as the yellow bar shows the subset of those lethal reactions, which were included in the model by gap analysis algorithm

Apart from these, other lethal reactions were from some of the amino acid metabolism (arginine and proline metabolism, glutamate metabolism), lipid metabolism (glycerolipid, and glycerophospholipid metabolism), NAD metabolism, and nucleotide metabolism.

Reaction number in Glycolysis	Enzyme	Reaction	Function
Reaction # 4	Fructose bisphosphate	Split Molecule in half: fdp <==> dhap + g3p	The six-carbon fructose diphophate is split into two three-carbon compounds, an aldehyde and a ketone.
Reaction # 5	Glyceraldehyde-3-phosphate dehydrogenase	Oxidation/Phosphate Ester Synthesis: g3p + nad + pi <==> 13dpg + h + nadh	This reaction is first an oxidation involving the coenzyme NAD+. The aldehyde is oxidized to an acid as an intermediate through the conversion of NAD+ to NADH + H+. Then an inorganic phosphate is added in a phosphate esteer synthesis.
Reaction # 7	Phosphoglycero mutase	Isomerization: 2pg <==> 3pg	In this reaction the phosphate group moves from the 3rd position to the 2nd position in an isomerization reaction.
Reaction # 8	Enolase	Alcohol Dehydration: 2pg <==> h2o + pep	In this reaction, which is the dehydration of an alcohol, the -OH on C-3 and the -H on C-2 are removed to make a water molecule. At the same time a double bond forms between C-2 and C-3. This change makes the compound somewhat unstable, but energy for the final step of glycolysis.
Reaction # 9	Pyruvate kinase	Phosphate Ester Hydrolysis; Synthesis of ATP: adp + h + pep --> atp + pyr	This is the final reaction in glycolysis. Again one of the phosphate groups undergoes hydrolysis to form the acid and a phosphate ion, giving off energy. This first energy producing reaction is coupled with the next endothermic reaction making ATP. The phosphate is transferred directly to an ADP to make ATP.

Table 3: Lethal reactions predicted in glycolysis and their function in the pathway (Ophardt, 2003)

3.4 Integrating the proteomic data

Summary of integration of proteomic data with metabolic network can be found in the attached supplementary data file (Appendix D). Out of all the predicted reactions, it was found that 48 reactions were common between both the stages oocyst and sporozoite but 12 reactions were found to be present only in oocyst stage and 14 reactions were listed under sporozoite stage only. An important point to be noticed in the result was that glucokinase is active in sporozoite stage but not in oocyst stage on the other hand hexokinase is active in oocyst stage. Hexokinase in known to have more affinity for glucose where as glucokinase shows less affinity for glucose. This is justified observation as during the sporozoite stage when parasite if inside host cell it has sufficient supply of glucose and thus can afford to have active glucokinase activity where as when in oocyst stage the supply of glucose is not sufficient and thus hexokinase is active instead to make the carbohydrate metabolism work during minimal glucose concentration. Glucokinase activity can be rapidly amplified or damped in response to changes in the glucose supply. Graphical representation of difference in metabolite performance in 2 stages is shown in figure 7.

CHAPTER 4 DISCUSSION

4.1 Model

Previous research has shown that *C. hominis* relies mainly on glycolysis for its energy metabolism (Thompson et al., 2005; Zhu & Rider Jr, 2009). The current annotation of its genome, (P. Xu et al., 2004; *Integrated microbial genome.*) suggests the absence of several biosynthetic capabilities such as synthesis of major amino acids and nucleotides and appears to rely mainly on the extra cellular transport reactions (approximately 69 proteins are annotated as transporters (P. Xu et al., 2004)). Nucleotide and amino acid includes salvage and inter-conversion pathways, but not the reactions for *de novo* synthesis since the parasite lacks that capability. Also, uptake of sugar, and amino acids in the model are facilitated by set transport reactions but the nucleotide and fatty acid uptake mechanism is not well understood and is therefore not completely discussed in the model. Fully functional glycolysis pathway as seen in *i*NV213 is supported by previous biochemical evidence (Fayer, 1997; Thompson et al., 2005; Zhu & Rider Jr, 2009), however some aspects of lipid in *C. hominis* are still not well understood. There is an ongoing analysis of the model to predict more such biochemical facts about the parasite to understand the

systems better and develop new, testable hypotheses.

4.2 Filling the gaps

Cryptosporidium lacks many important links in the minimal set of metabolic pathway that is required for its successful replication and thus, the first simulation runs showed that the reconstructed model is incomplete and lacks some metabolic reactions. Resolving these metabolic gaps entails expanding the model by identifying and including missing biochemical activities. This process basically consists of two steps: (1) identifying plausible candidate reactions that could complete the model and (2) finding genes that could catalyze the hypothesized activities. The current work completes the filling of gaps however, finding gene for the hypothesized activity is one of the future directions for the project.

Lipid metabolism was the metabolic network where most of the reactions were inserted to complete the reaction flow and get the optimal flux. These 30 reactions were in several categories respectively fatty acid metabolism, biosynthesis of steroids, glycerophospholipids, and shingolipids. Many previous and ongoing research suggest that these reactions, especially the glycerophosphlipids metabolism and biosynthesis of steroids are putative drug targets sites for apicomplexans. (Clastre et al., 2007; Ralph, D'Ombrain, & McFadden, 2001; Wambua et al., 2009) It is predicted that the reactions that are added through gap analysis in lipid metabolism might be the required reaction for completion of lipid metabolism but literature suggests that *Cryptosporidium* lacks the MEP pathway (Clastre et al., 2007) and therefore it can be predicted that they depend on the host cell for

these set of reaction. This opens up a prospect to individually analyze the subset of reaction added to the lipid metabolism to study the host – parasite interaction. As these reactions specially the ones added in glycerophospholipid mechanism are well-studied putative drug targets is other apicomplexans. Also, this information may be useful in determining minimal culture media requirement for the in vitro culturing of organism.

A noticeable addition to the glycerolipid pathways in this step was a phospholipase A2 catalyzed hydrolysis of phosphatidyl choline. However, there is a patent pending regarding use of phosphlipase A2 as biocides that neutralizes *C. parvum* sporozoite. (Homan, Imboden, Riggs, Carryn, & Schaefer, 2006) Thus, accuracy and eligibility of this addition of this reaction could not be established.

In a recent review, Zhu et al. (2009) explain the lipid metabolism to a great extent but still there is no evidence for the biosynthetic capabilities of fatty acids in the *C. hominis*. But since these reactions are predicted to be required for the metabolic network to complete it might be possible that the parasite depends on host cell for some of these reactions. This finding again leads to these questions: If the parasite needs these reactions for the metabolic network to complete can any of its hypothetical proteins code for any of these reactions? If not, then is it possible to answer question related to the transport mechanism to support the entry of these lipids into the pathogen?

To answer the first question, some of these functional proteins that coded for the newly added reaction were searched in the *C. hominis* genome. So far, no significant matches were found hence with the current understanding of model, no information could be added to the current genome annotation. This however opens up a prospect to perform

homology search for the specific proteins to reanalyze the subset of hypothetical proteins and also to study the transport mechanism of these lipids to update the list of transporter proteins in the parasite.

Another interesting link added to the model was in amino sugar metabolism pathway. UDP acetylglucosamine epimerase catalyzes the reaction involving UDP-N-acetyl-D-glucosamine. This reaction and enzyme is important in cyst-wall formation and Jarroll et al. suggest that this can be a putative drug target for cyst-walled protozoan. (Jarroll & Sener, 2003)

4.3 Essential reactions

The analysis of the essential reactions in the model is the most important outcome as this expected to determine the major potential drug target sites specific to *C.hominis*. From the subset of 52 reactions, Table 3 lists the 5 essential reactions of the glycolysis pathway, which accounts for almost 50% of the glycolysis reaction. But since glycolysis is an active pathway for all the host cells also, it does not prove to be a right direction to look for drug targets. An important extension of the work is to determine which of these lethal reactions are not affecting the human metabolic network. Attacking those sites might be useful in determining the weak link for the parasite.

This reaction deletion approach can be used to find the performance of the cell in presence of enzyme inhibitors. Thus, if reaction X is predicted to be lethal, and an inhibitor of that enzyme is available, then the model can predict what will be the probability of growth of parasite in the presence of inhibitor. And this can be useful find the infection

neutralization chemicals (the enzyme inhibitors).

4.4 From reaction deletion to gene knock out

The ultimate aim of such model reconstruction is to extend the analysis to study gene knockout experiments *in silico.* The reaction deletion approach is useful to find out important reactions in the metabolic network. The GPR (Gene Protein Relation) file was used to study the relation of genes and proteins (enzymes) to determine which gene were important in the metabolism network of parasite.

The supplement data file 3 provides the list of important genes that code for the lethal reactions in the metabolic network. These genes can be computationally switched on and off to study how the flux distribution would change in the presence or absence of a particular gene. Gene knockout experiments may again be useful to find putative drug targets for *Cyrptosporidium*. Some previous studies have shown how this approach can be made useful in predicting essential genes (Lee et al., 2009; Oh et al., 2007; Pinney et al., Nov 2007; Plaimas et al., 2008; Wambua et al., 2009). These genes will then be studied as potential drug targets that could be used to develop novel antibodies.

4.5 Conclusion

Genome-scale models integrate various types of data (genomic, expression and proteomic) and allow modeling of the integrated functions of an organism. It is a powerful tool that facilitates understanding of the whole system of an organism rather than focusing on a particular component or segment. This model-based study can be used to help

researchers prioritize experimental projects and save considerable time at the bench. Beyond serving as a tool for basic biological research, this computational approach also has potential medical and drug development relevance, e.g.: in pathogenic microbial models, each gene that is predicted to be essential by constraint based modeling and analysis, represents a potential drug target that could be used to develop novel antibiotics in future. Also, the network analysis of human biology may help us in detecting several therapeutic targets and thus provide a platform for assessing potentially adverse effects of novel treatments (Mo & Palsson, 2009). The flexibility of constraint-based models will lead to exploration of countless exciting biological questions in the future.

CHAPTER 5 FUTURE DIRECTIONS

5.1 Refining model

There are lot of questions unanswered in terms of nucleotide metabolism, and lipid metabolism. The metabolic networks needs to be more refined with some more literature, biochemical or experimental evidences that individually focus on each of these reactions. For example, in nucleotide metabolism there are many enzymes that work in multiple ways and catalyze more than one reaction (in some cases around 20 reaction) but there were no evidences how so ever to include or exclude any of those multiple reaction. Similar cases were found in lipid metabolism as well. These reactions can be selected by studying the parasite specifically in terms of nucleotide and lipid composition. This question can be answered by some of the facts such as preference of substrate, behavior of organism under specific condition or stages.

5.2 Finding the hypothesized function related gene

With the gap analysis there are several hypothetical functions added to the metabolic network of the parasite. From the pool of hypothetical proteins these function

related genes could be determined. A specific enzyme codes each of the reaction added by gap analysis. If we can find out all the possible nucleotide sequence that may code for these protein and compare it with the hypothetical proteins of *C.hominis* it is possible that this may help to update the genome annotation for the organism

5.3 Host pathogen interaction

This pathogen depends on its host for various essential nutrients that support life, and experimental determination of its growth requirements has proven difficult. As seen in the gap analysis and essential reaction analysis there are several reactions related to lipid metabolism which suggest the presence of fatty acid, steroid, glycerolipid biosynthetic capabilities however, previous biochemical findings do not support this result. It might be possible that the pathogen uses the host cell's biosynthetic capabilities for its survival in these cases. Analysis of this subset of reaction can be done in host cell to study how parasite might get this support of lipid metabolism to complete its growth requirement. This narrows down the list of reaction or pathways to focus on.

5.4 Culturing condition optimization

It is known that perfect culturing media composition could not be established for *C.hominis* growth (explained in section 1). From the gap analysis we have found some of the proteins that may be required by the organism but are not present in it. Experiments can be performed to see if addition of these enzymes in the culture media affects the growth in

some way. If the minimal media list can be derived by all these analysis it is possible to optimize its growth initially *in silico* then *in vitro.*

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Appendices

Appendix A: Metabolic Network Reactions included in the Model *i*NV213

REACTION IDs	GENE IDs	EC NUMBER	ENZYME NAME	PATHWAY	REACTION
R_BIOMASS	**.**	**.**	**biomass**	**Biomass Equation**	**[c] : 0.257980584 ala-L + 0.176597196 arg-L + 0.218152121 asn-L**
R_ALAR	Chro.50329	5.1.1.1	alaninera cemase	Alanine and Aspartate Metabolism	[c] : ala-L <==> ala-D
R_ASPTRS	Chro.80047 or Chro.70182 or	6.1.1.12	Aspartyl-tRNAsynthetase	Alanine and Aspartate Metabolism	[c] : asp-L + atp + trnaasp --> amp + asptrna + ppi
R_ASNTRS	Chro.80047	6.1.1.22	Asparaginyl-tRNAsynthetase	Alanine and Aspartate Metabolism	[c] : asn-L + atp + trnaasn --> amp + asntrna + ppi
R_ALATRS	Chro.60075	6.1.1.7	Alanyl-tRNAsynthetase	Alanine and Aspartate Metabolism	[c] : ala-L + atp + trnaala --> alatrna + amp + ppi
R_PETHCT	Chro.70332	2.7.7.14	phosphoethanolaminecytidyltransferase	Aminophosphonate Metabolism	[c] : ctp + ethamp + h --> cdpea + ppi
R_CHLP	Chro.80135	2.7.7.15	cholinephosphatephosphatase	Aminophosphonate Metabolism	[c] : cholp + h2o --> chol + pi
R_CYANST	Chro.40314	2.8.1.1	Cyanidesulfurtransferase	Aminophosphonate Metabolism	[c] : cyan + tsul --> h + so3 + tcynt
R_GF6PTA	Chro.10420	2.6.1.16	glutamine-fructose-6-phosphatetransaminase	Aminosugar Metabolism	[c] : f6p + gln-L --> gam6p + glu-L
R_UDPACGLP	Chro.40100 or Chro.70213	2.7.7.23	UDP-N-acetylglucosaminediphosphorylase	Aminosugar Metabolism	[c] : acgam1p + h + utp <==> ppi + udpacgal
R_UAGDP	Chro.40100 or Chro.70213	2.7.7.23	UDP-N-acetylglucosaminediphosphorylase	Aminosugar Metabolism	[c] : acgam1p + h + utp --> ppi + uacgam
R_UAG4E	.	5.1.3.7	R_UDP_N_acetylglucosamine_4_epimerase	Aminosugar Metabolism	[c] : 1.0 uacgam --> 1.0 uacgala
R_ACGAMPM	Chro.40374	5.4.2.3	phosphoacetylglucosaminemutase	Aminosugar Metabolism	[c] : acgam6p <==> acgam1p
R_PROAKGOX1	Chro.30441	1.14.11.2	L-Proline,2-oxoglutarate:oxygenoxidoreductase(4-hydrox	Arginine and Proline Metabolism	[c] : akg + o2 + pro-L --> 4hpro-LT + co2 + succ
R_NOS2	Chro.40304	1.14.13.39	NitricOxideSynthase(NOforming)	Arginine and Proline Metabolism	[c] : nadph + 2 nwharg + 2 o2 --> 2 citr-L + h + 2 h2o + nadp + 2 no
R_NOS1	Chro.40304	1.14.13.39	NitricOxideSynthase(intermediateforming)	Arginine and Proline Metabolism	[c] : arg-L + h + nadph + o2 --> h2o + nadp + nwharg
R_3MOXTYROX	Chro.21000	1.4.3.4	3-Methoxytyramine:oxygenoxidoreductase(deaminating	Arginine and Proline Metabolism	[c] : 3moxtyr + h2o + o2 --> 3mox4hpac + h2o2 + nh4
R_APRTO2	Chro.21000	1.4.3.4	N-acetylputrescine:oxygenoxireductase(deaminating)	Arginine and Proline Metabolism	[c] : aprut + h2o + o2 --> h2o2 + n4abutn + nh4
R_MHISOR	Chro.21000	1.4.3.4	N-Methylhistamine:oxygenoxidoreductase(deaminating)	Arginine and Proline Metabolism	[c] : h2o + mhista + o2 --> 3mldz + h2o2 + nh4
R_MAOLNOR	Chro.21000	1.4.3.4	monoamineoxidase(L-Normetanephrine)	Arginine and Proline Metabolism	[c] : h2o + normete-L + o2 --> 3m4hpga + h2o2 + nh4
R_4HGLSD	Chro.70551	1.5.1.12	L-4-hydroxyglutamatesemialdehydedehydrogenase,mito	Arginine and Proline Metabolism	[c] : 4hglusa + h2o + nad <==> e4hglu + 2 h + nadh
R_HPROym	Chro.70551	1.5.1.12	L-hydroxyprolinedehydrogenase(NADP),mitochondrial	Arginine and Proline Metabolism	[c] : 4hpro-LT + nadp --> 1p3h5c + 2 h + nadph
R_PHCD	Chro.70551	1.5.1.12	L-1-pyrroline-3-hydroxy-5-carboxylatedehydrogenase	Arginine and Proline Metabolism	[c] : 1p3h5c + 2 h2o + nad --> e4hglu + h + nadh
R_4HGLSDm	Chro.70551	1.5.1.12	L-4-hydroxyglutamatesemialdehydedehydrogenase,mito	Arginine and Proline Metabolism	[c] : 4hglusa + h2o + nad <==> e4hglu + 2 h + nadh
R_PYR5CDm	Chro.70551	1.5.1.12	D1-pyrroline-5-carboxylatedehydrogenase,mitochondrial	Arginine and Proline Metabolism	[c] : glu5sa + h2o + nadp --> glu-L + 2 h + nadph
R_PUTA3	Chro.70551	1.5.1.12	puta3	Arginine and Proline Metabolism	[c] : glu5sa + h2o + nad --> glu-L + 2 h + nadh
R_P5CR	Chro.60426	1.5.1.2	pyrroline-5-carboxylatereductase	Arginine and Proline Metabolism	[c] : 1pyr5c + 2 h + nadph --> nadp + pro-L
R_HPROb	Chro.60426	1.5.1.2	L-hydroxyprolinereductase(NADP)	Arginine and Proline Metabolism	[c] : 1p3h5c + 2 h + nadph --> 4hpro-LT + nadp
R_HPROa	Chro.60426	1.5.1.2	L-hydroxyprolinereductase(NAD)	Arginine and Proline Metabolism	[c] : 1p3h5c + 2 h + nadh --> 4hpro-LT + nad
R_P5CRm	Chro.60426	1.5.1.2	pyrroline-5-carboxylatereductase(m)	Arginine and Proline Metabolism	[c] : 1pyr5c + 2 h + nadph --> nadp + pro-L
R_P5CRx	Chro.60426	1.5.1.2	pyrroline-5-carboxylatereductase	Arginine and Proline Metabolism	[c] : 1pyr5c + 2 h + nadh --> nad + pro-L
R_PRO1x	Chro.60426	1.5.1.2	prolineoxidase(L-proline,NAD)	Arginine and Proline Metabolism	[c] : nad + pro-L --> 1pyr5c + 2 h + nadh
R_PROTRS	Chro.60505 or Chro.80098	6.1.1.15	Prolyl-tRNAsynthetase	Arginine and Proline Metabolism	[c] : atp + pro-L + trnapro --> amp + ppi + protrna
R_ARGTRS	Chro.50402	6.1.1.19	Arginyl-tRNAsynthetase	Arginine and Proline Metabolism	[c] : arg-L + atp + trnaarg --> amp + argtrna + ppi
R_DXPS	.	2.2.1.7	1-deoxy-D-xylulose5-phosphatesynthase	Biosynthesis of Steroids	[c] : g3p + h + pyr --> co2 + dxyl5p
R_CDPMEK	.	2.7.1.148	4-(cytidine5'-diphospho)-2-C-methyl-D-erythritolkinase	Biosynthesis of Steroids	[c] : 4c2me + atp --> 2p4c2me + adp + h
R_MEPCT	.	2.7.7.60	2-C-methyl-D-erythritol4-phosphatecytidylyltransferase	Biosynthesis of Steroids	[c] : 2me4p + ctp + h --> 4c2me + ppi
R_BACCL	Chro.20303	6.3.4.15	biotin-[acetyl-CoA-carboxylase]ligase	Biotin Metabolism	[c] : atp + btn + h --> btamp + ppi
R_HACD1	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(acetoacetyl-CoA)	Butanoate Metabolism	[c] : aacoa + h + nadh <==> 3hbcoa + nad
R_HACD2	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(3-oxohexanoyl-CoA)	Butanoate Metabolism	[c] : 3ohcoa + h + nadh <==> 3hhcoa + nad
R_HACD3	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(3-oxooctanoyl-CoA)	Butanoate Metabolism	[c] : 3oocoa + h + nadh <==> 3hocoa + nad
R_HACD4	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(3-oxodecanoyl-CoA)	Butanoate Metabolism	[c] : 3odcoa + h + nadh <==> 3hdcoa + nad
R_HACD5	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(3-oxododecanoyl-Co	Butanoate Metabolism	[c] : 3oddcoa + h + nadh <==> 3hddcoa + nad
R_HACD6	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(3-oxotetradecanoyl-	Butanoate Metabolism	[c] : 3otdcoa + h + nadh <==> 3htdcoa + nad
R_HACD7	Chro.30048	1.1.1.35	3-hydroxyacyl-CoAdehydrogenase(3-oxohexadecanoyl-	Butanoate Metabolism	[c] : 3ohdcoa + h + nadh <==> 3hhdcoa + nad
R_PGK	Chro.70113	2.7.2.3	phosphoglyceratekinase	Carbon Fixation	[c] : 3pg + atp <==> 13dpg + adp
R_RPI	Chro.10337	5.3.1.6	ribose-5-phosphateisomerase	Carbon Fixation	[c] : r5p <==> ru5p-D
R_OIVD1		1.2.4.4	R_2_oxoisovalerate_dehydrogenase__acylating_4_meth	Cofactor and Prosthetic Group Biosynthes	[c] : 1.0 4mop + 1.0 coa + 1.0 nad <==> 1.0 co2 + 1.0 ivcoa + 1.0 nadh
R_MECDPS	.	4.6.1.12	2-C-methyl-D-erythritol2,4-cyclodiphosphatesynthase	Cofactor and Prosthetic Group Biosynthes	[c] : 2p4c2me --> 2mecdp + cmp
R_CYSTRS	Chro.60125	6.1.1.16	Cysteinyl-tRNAsynthetase	Cysteine Metabolism	[c] : atp + cys-L + trnacys --> amp + cystrna + ppi
R_MCOATA	Chro.40326 or Chro.30258	2.3.1.39	Malonyl-CoA-ACPtransacylase	Fatty Acid Biosynthesis	[c] : ACP + malcoa <==> coa + malACP
R_KAS2	.	2.3.1.41	R_b_ketoacyl_synthetase__n_C140	Fatty Acid Biosynthesis	[c] : 1.0 accoa + 17.0 h + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa
R_KAS8	.	2.3.1.41	R_b_ketoacyl_synthetase__palmitate__n_C160	Fatty Acid Biosynthesis	[c] : 1.0 accoa + 20.0 h + 7.0 malcoa + 14.0 nadph --> 7.0 co2 + 8.0 coa
R_KAS13	.	2.3.1.41	R_b_ketoacyl_synthetase__n_C180	Fatty Acid Biosynthesis	[c] : 1.0 accoa + 23.0 h + 8.0 malcoa + 16.0 nadph --> 8.0 co2 + 9.0 coa
R_KAS141	.	2.3.1.41	R_b_ketoacyl_synthetase__n_C141	Fatty Acid Biosynthesis	[c] : 1.0 accoa + 16.0 h + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa
R_KAS7	.	2.3.1.41	R_b_ketoacyl_synthetase__n_C161	Fatty Acid Biosynthesis	[c] : 1.0 accoa + 19.0 h + 7.0 malcoa + 13.0 nadph --> 7.0 co2 + 8.0 coa
R_KAS17	.	2.3.1.41	R_b_ketoacyl_synthetase__n_C181	Fatty Acid Biosynthesis	[c] : 1.0 accoa + 22.0 h + 8.0 malcoa + 15.0 nadph --> 8.0 co2 + 9.0 coa
R_KAS100iso	.	2.3.1.41	R_b_ketoacyl_synthetase__branched(iso)_C100	Fatty Acid Biosynthesis	[c] : 8.0 h + 1.0 ibcoa + 3.0 malcoa + 6.0 nadph --> 3.0 co2 + 4.0 coa +
R_KAS130iso	.	2.3.1.41	R_b_ketoacyl_synthetase__branched(iso)_C130	Fatty Acid Biosynthesis	[c] : 11.0 h + 1.0 ivcoa + 4.0 malcoa + 8.0 nadph --> 4.0 co2 + 5.0 coa +
R_KAS1	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C140_	Fatty Acid Biosynthesis	[c] : 14.0 h + 1.0 ibcoa + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 coa
R_KAS3	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C150	Fatty Acid Biosynthesis	[c] : 14.0 h + 1.0 ivcoa + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 coa
R_KAS6	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C160	Fatty Acid Biosynthesis	[c] : 17.0 h + 1.0 ibcoa + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa
R_KAS11	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C170	Fatty Acid Biosynthesis	[c] : 17.0 h + 1.0 ivcoa + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa
R_KAS180iso	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C180	Fatty Acid Biosynthesis	[c] : 20.0 h + 1.0 ibcoa + 7.0 malcoa + 14.0 nadph --> 7.0 co2 + 8.0 coa
R_KAS5	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C161	Fatty Acid Biosynthesis	[c] : 16.0 h + 1.0 ibcoa + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa
R_KAS9	.	2.3.1.41	R_b_ketoacyl_synthetase__Iso_C171	Fatty Acid Biosynthesis	[c] : 16.0 h + 1.0 ivcoa + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa
R_KAS4	.	2.3.1.41	R_b_ketoacyl_synthetase__Anteiso_C150	Fatty Acid Biosynthesis	[c] : 1.0 2mbcoa + 14.0 h + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 c
R_KAS12	.	2.3.1.41	R_b_ketoacyl_synthetase__Anteiso_C170	Fatty Acid Biosynthesis	[c] : 1.0 2mbcoa + 17.0 h + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 c
R_KAS10	.	2.3.1.41	R_b_ketoacyl_synthetase__Anteiso_C171	Fatty Acid Biosynthesis	[c] : 1.0 2mbcoa + 16.0 h + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 c
R_ALCD19	Chro.80199 or Chro.80198	1.1.1.1	alcoholdehydrogenase(glycerol)	Fatty Acid Metabolism	[c] : glyald + h + nadh <==> glyc + nad
R_34DHOXPEGOX	Chro.80199 or Chro.80198	1.1.1.1	3,4-Dihydroxyphenylethyleneglycol:NAD+oxidoreductas	Fatty Acid Metabolism	[c] : 34dhmald + h + nadh <==> 34dhoxpeg + nad
R_LNS14DM	Chro.21001	1.14.14.1	cytochromeP450lanosterol14-alpha-demethylase(NADP)	Fatty Acid Metabolism	[c] : 2 h + lanost + 3 nadph + 3 o2 --> 44mctr + for + 4 h2o + 3 nadp
R_MELATNOX	Chro.21001	1.14.14.1	Melatonin:NADPoxidoreductase	Fatty Acid Metabolism	[c] : h + melatn + nadph + o2 --> 6hoxmelatn + h2o + nadp
R_FACOAL1813	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + elaid <==> amp + od2coa + ppi
R_FACOAL1812	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + vacc <==> amp + ppi + vacccoa
R_FACOAL150	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + ptdca <==> amp + ppi + ptdcacoa
R_FACOAL2042	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + eicostet <==> amp + eicostetcoa + ppi
R_FACOAL1831	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + lnlncg <==> amp + lnlncgcoa + ppi
R_FACOAL1832	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + lnlnca <==> amp + lnlncacoa + ppi
R_FACOAL241	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + nrvnc <==> amp + nrvnccoa + ppi
R_FACOAL170	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + hpdca <==> amp + hpdcacoa + ppi
R_FACOAL244_1	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + tetteto6 <==> amp + ppi + tetteto6coa
R_FACOAL182	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(octadecynoate)	Fatty Acid Metabolism	[c] : atp + coa + ocdcya <==> amp + ocdycacoa + ppi
R_FACOAL181	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(octadecenoate)	Fatty Acid Metabolism	[c] : atp + coa + ocdcea <==> amp + odecoa + ppi
R_FACOAL180	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(octadecanoate)	Fatty Acid Metabolism	[c] : atp + coa + ocdca <==> amp + ppi + stcoa
R_FACOAL184	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + strdnc <==> amp + ppi + strdnccoa
R_FACOAL141	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(tetradecenoate)	Fatty Acid Metabolism	[c] : atp + coa + ttdcea <==> amp + ppi + tdecoa
R_FACOAL140	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(tetradecanoate)	Fatty Acid Metabolism	[c] : atp + coa + ttdca <==> amp + ppi + tdcoa
R_FACOAL226i	Chro.50052 or Chro.30084	6.2.1.3	C226fattyacidactivation	Fatty Acid Metabolism	[c] : atp + coa + crvnc --> amp + c226coa + ppi
R_FACOAL1822	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + lneldc <==> amp + lneldccoa + ppi
R_FACOAL1821	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + lnlc <==> amp + lnlccoa + ppi
R_FACOAL161	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(hexadecenoate)	Fatty Acid Metabolism	[c] : atp + coa + hdcea <==> amp + hdcoa + ppi
R_FACOAL160	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(hexadecanoate)	Fatty Acid Metabolism	[c] : atp + coa + hdca <==> amp + pmtcoa + ppi
R_FACOAL200	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : arach + atp + coa <==> amp + arachcoa + ppi
R_FACOAL203	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + dlnlcg <==> amp + dlnlcgcoa + ppi
R_FACOAL204	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : arachd + atp + coa <==> amp + arachdcoa + ppi
R_FACOAL205	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + tmndnc <==> amp + ppi + tmndnccoa
R_FACOAL206	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + phyt <==> amp + phytcoa + ppi
R_FACOAL226	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + crvnc <==> amp + c226coa + ppi
R_FACOAL224	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : adrn + atp + coa <==> adrncoa + amp + ppi
R_FACOAL240	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + lgnc <==> amp + lgnccoa + ppi
R_FACOAL260	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase(n-C26:0)	Fatty Acid Metabolism	[c] : atp + coa + hexc <==> amp + hexccoa + ppi
R_FACOAL245_2	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + tetpent3 <==> amp + ppi + tetpent3coa
R_FACOAL245_1	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + tetpent6 <==> amp + ppi + tetpent6coa
R_FACOAL191	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + prist --> amp + ppi + pristcoa
R_FACOAL246_1	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + tethex3 <==> amp + ppi + tethex3coa
R_FACOAL2251	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + coa + dcsptn1 <==> amp + dcsptn1coa + ppi
R_FACOAL2252	Chro.50052 or Chro.30084	6.2.1.3	fatty-acid--CoAligase	Fatty Acid Metabolism	[c] : atp + clpnd + coa <==> amp + clpndcoa + ppi
R_DHFR	Chro.40506	1.5.1.3	dihydrofolatereductase	Folate-Vit B9 Metabolism	[c] : dhf + h + nadph <==> nadp + thf
R_FOLR2	Chro.40506	1.5.1.3	folatereductase	Folate-Vit B9 Metabolism	[c] : fol + nadph --> dhf + nadp
R_AKP1	Chro.70170	3.1.3.1	alkalinephosphatase(Dihydroneopterin)	Folate-Vit B9 Metabolism	[c] : ahdt + 3 h2o --> dhnpt + 2 h + 3 pi
R_HEX7	Chro.60435	2.7.1.1	hexokinase(D-fructose:ATP)	Fructose and Mannose Metabolism	[c] : atp + fru --> adp + f6p + h
R_HEX10	Chro.60435	2.7.1.1	hexokinase(D-glucosamine:ATP)	Fructose and Mannose Metabolism	[c] : atp + gam --> adp + gam6p + h
R_PFK26	Chro.50115	2.7.1.105	6-phosphofructo-2-kinase	Fructose and Mannose Metabolism	[c] : atp + f6p --> adp + f26bp + h
R_MAN1PT	Chro.20192	2.7.7.13	mannose-1-phosphateguanylyltransferase	Fructose and Mannose Metabolism	[c] : gtp + h + man1p --> gdpmann + ppi
R_MAN1PT2r	.	2.7.7.22	mannose-1-phosphateguanylyltransferase(GDP)reversibl	Fructose and Mannose Metabolism	[c] : gdp + h + man1p <==> gdpmann + pi
R_FBA4	Chro.10335	4.1.2.13	D-Fructose1-phosphateD-glyceraldehyde-3-phosphate-N	Fructose and Mannose Metabolism	[c] : xu1p-D <==> dhap + gcald
R_FBA5	Chro.10335	4.1.2.13	D-Tagatose1-phosphateD-glyceraldehyde-3-phosphate-N	Fructose and Mannose Metabolism	[c] : tag1p-D <==> dhap + glyald

R_FBA2	Chro.10335	4.1.2.13	D-Fructose1-phosphateD-glyceraldehyde-3-phosphate-ly	Fructose and Mannose Metabolism	[c] : f1p <==> dhap + glyald
R_FBA3	Chro.10335	4.1.2.13	Sedoheptulose1,7-bisphosphateD-glyceraldehyde-3-phos	Fructose and Mannose Metabolism	[c] : s17bp <==> dhap + e4p
R_TPI	Chro.10337	5.3.1.1	triose-phosphateisomerase	Fructose and Mannose Metabolism	[c] : dhap <==> g3p
R_FCI	Chro.20165	5.3.1.25	L-fucoseisomerase	Fructose and Mannose Metabolism	[c] : fuc-L <==> fcl-L
R_MAN6PI	Chro.80224	5.3.1.8	mannose-6-phosphateisomerase	Fructose and Mannose Metabolism	[c] : man6p <==> f6p
R_PMANM	Chro.40115	5.4.2.8	phosphomannomutase	Fructose and Mannose Metabolism	[c] : man1p <==> man6p
R_MALT	Chro.30190	3.2.1.20	alpha-glucosidase	Galactose metabolism	[c] : h2o + malt --> 2 glc-D
R_UDPG4E	Chro.40292	5.1.3.2	UDPglucose4-epimerase	Galactose metabolism	[c] : udpg <==> udpgal
R_P5CD	Chro.60426	1.5.1.12	1-pyrroline-5-carboxylatedehydrogenase	Glutamate metabolism	[c] : 1pyr5c + 2 h2o + nad --> glu-L + h + nadh
R_GLUTRS	Chro.60505 or Chro.80098 or	6.1.1.17	Glutamyl-tRNAsynthetase	Glutamate metabolism	[c] : atp + glu-L + trnaglu --> amp + glutrna + ppi
R_GLNTRS	Chro.10244	6.1.1.18	Glutaminyl-tRNAsynthetase	Glutamate metabolism	[c] : atp + gln-L + trnagln --> amp + glntrna + ppi
R_GMPS2	Chro.50499	6.3.5.2	GMPsynthase	Glutamate metabolism	[c] : atp + gln-L + h2o + xmp --> amp + glu-L + gmp + 2 h + ppi
R_G6PDH3	Chro.40088 or Chro.60425	1.1.1.49	glucose6-phosphatedehydrogenase(F420-Dependent)	Glutathione Metabolism	[c] : f420-2 + g6p --> 6pgl + f420-2h2
R_G6PDH2r	Chro.40088 or Chro.60425	1.1.1.49	glucose6-phosphatedehydrogenase	Glutathione Metabolism	[c] : g6p + nadp <==> 6pgl + h + nadph
R_GTHP	Chro.30063	1.11.1.9	glutathioneperidoxase	Glutathione Metabolism	[c] : 2 gthrd + h2o2 <==> gthox + 2 h2o
R_AMPTASECG	Chro.80395	3.4.11.2	alanylaminopeptidase(cys-gly)	Glutathione Metabolism	[c] : cgly + h2o --> cys-L + gly
R_G3PD1ir	Chro.20028	1.1.1.8	glycerol-3-phosphatedehydrogenase(NAD)	Glycerolipid Metabolism	[c] : dhap + h + nadh --> glyc3p + nad
R_G3PD6	Chro.80050	1.1.99.5	glycerol-3-phosphatedehydrogenase(menaquinone-8)	Glycerolipid Metabolism	[c] : glyc3p + mqn8 --> dhap + mql8
R_G3PD7	Chro.80050	1.1.99.5	glycerol-3-phosphatedehydrogenase(demethylmenaquin	Glycerolipid Metabolism	[c] : 2dmmq8 + glyc3p --> 2dmmql8 + dhap
R_G3PD5	Chro.80050	1.1.99.5	glycerol-3-phosphatedehydrogenase(ubiquinone-8)	Glycerolipid Metabolism	[c] : glyc3p + q8 --> dhap + q8h2
R_GPAM_hs	Chro.60161	2.3.1.15	glycerol-3-phosphateacyltransferase	Glycerolipid Metabolism	[c] : Rtotalcoa + glyc3p --> alpa_hs + coa
R_AGPAT1	Chro.80165	2.3.1.51	1-acylglycerol-3-phosphateO-acyltransferase1	Glycerolipid Metabolism	[c] : Rtotal2coa + alpa_hs --> coa + pa_hs
R_DAGK_SA	Chro.80280	2.7.1.107	Diacylglycerolkinase	Glycerolipid Metabolism	[c] : 0.02 12dgr_SA + atp --> adp + h + 0.02 pa_SA
R_DAGK_EC	Chro.80280	2.7.1.107	Diacylglycerolkinase	Glycerolipid Metabolism	[c] : 0.02 12dgr_EC + atp --> adp + h + 0.02 pa_EC
R_CHOLK	Chro.30240	2.7.1.32	Cholinekinase	Glycerolipid Metabolism	[c] : atp + chol --> adp + cholp + h
R_ETHAK	Chro.50319	2.7.1.82	Ethanolaminekinase	Glycerolipid Metabolism	[c] : atp + etha --> adp + ethamp + h
R_EPCTX	Chro.70332	2.7.7.14	ethanolamine-phosphatecytidylyltransferase	Glycerolipid Metabolism	[c] : 2ameph + ctp + h --> cmp2amep + ppi
R_CHLPCTD	Chro.80135	2.7.7.15	cholinephosphatecytididylyltransferase	Glycerolipid Metabolism	[c] : cholp + ctp + h --> cdpchol + ppi
R_CPCTDTX	Chro.80135	2.7.7.15	choline-phosphatecytidylyltransferase	Glycerolipid Metabolism	[c] : ctp + h + ntm2amep --> cmpntm2amep + ppi
R_DASYNm_SC	Chro.70059 or Chro.20170	2.7.7.41	CDP-Diacylglycerolsynthetase,yeast-specific,mitochondri	Glycerolipid Metabolism	[c] : ctp + h + 0.01 pa_SC <==> 0.01 cdpdag_SC + ppi
R_DASYN_HP	Chro.70059 or Chro.20170	2.7.7.41	CDP-DiacylglycerolsynthetaseHpspecific	Glycerolipid Metabolism	[c] : ctp + h + pa_Hp <==> cdpdag_HP + ppi
R_CDGGGS	Chro.70059 or Chro.20170	2.7.7.41	CDP-2,3-di-O-geranylgeranyl-sn-glycerolsynthase	Glycerolipid Metabolism	[c] : ctp + dgggp + h --> cdgggp + ppi
R_DASYN_TC	Chro.70059 or Chro.20170	2.7.7.41	CDP-Diacylglycerolsynthetase,cruzi-specific	Glycerolipid Metabolism	[c] : ctp + h + 0.01 pa_TC <==> 0.01 cdpdag_TC + ppi
R_CDSm	Chro.70059 or Chro.20170	2.7.7.41	phosphatidatecytidylyltransferase	Glycerolipid Metabolism	[c] : ctp + h + pa_hs --> cdpdag_hs + ppi
R_DASYN_EC	Chro.70059 or Chro.20170	2.7.7.41	CDP-Diacylglycerolsynthetase(Ecoli)	Glycerolipid Metabolism	[c] : ctp + h + 0.02 pa_EC <==> 0.02 cdpdag_EC + ppi
R_DASYN_SC	Chro.70059 or Chro.20170	2.7.7.41	CDP-Diacylglycerolsynthetase,yeast-specific	Glycerolipid Metabolism	[c] : ctp + h + 0.01 pa_SC <==> 0.01 cdpdag_SC + ppi
R_DASYN_SA	Chro.70059 or Chro.20170	2.7.7.41	CDP-Diacylglycerolsynthetase(Saureus)	Glycerolipid Metabolism	[c] : ctp + h + 0.02 pa_SA <==> 0.02 cdpdag_SA + ppi
R_DASYNm_TC	Chro.70059 or Chro.20170	2.7.7.41	CDP-Diacylglycerolsynthetase,cruzi-specific,mitochondria	Glycerolipid Metabolism	[c] : ctp + h + 0.01 pa_TC <==> 0.01 cdpdag_TC + ppi
R_CDS	Chro.70059 or Chro.20170	2.7.7.41	phosphatidatecytidylyltransferase	Glycerolipid Metabolism	[c] : ctp + h + pa_hs --> cdpdag_hs + ppi
R_ETHAPT_TC	Chro.40314	2.7.8.1	Ethanolaminephosphotransferase,cruzi-specific	Glycerolipid Metabolism	[c] : 0.01 12dgr_TC + cdpea <==> cmp + h + 0.01 pe_TC
R_PEPT_EC	Chro.40314	2.7.8.1	ethanolaminephosphotransferase	Glycerolipid Metabolism	[c] : cmp + h + 0.02 pe_EC <==> 0.02 12dgr_EC + cdpea
R_ETHAPT_SC	Chro.40314	2.7.8.1	Ethanolaminephosphotransferase,yeast-specific	Glycerolipid Metabolism	[c] : 0.01 12dgr_SC + cdpea <==> cmp + h + 0.01 pe_SC
R_PEPT_HP	Chro.40314	2.7.8.1	ethanolaminephosphotransferase	Glycerolipid Metabolism	[c] : cmp + h + pe_HP <==> 12dgr_HP + cdpea
R_PINOS_TC	Chro.80072	2.7.8.11	phosphatidylinositolsynthase,cruzi-specific	Glycerolipid Metabolism	[c] : 0.01 cdpdag_TC + inost --> cmp + h + 0.01 ptd1ino_TC
R_PGPPT	Chro.80072	2.7.8.11	phosphatidyl-CMP:glycerophosphatephosphatidyltransfer	Glycerolipid Metabolism	[c] : cdpdag_hs + glyc3p --> cmp + h + pgp_hs
R_PINOS_SC	Chro.80072	2.7.8.11	phosphatidylinositolsynthase,yeast-specific	Glycerolipid Metabolism	[c] : 0.01 cdpdag_SC + inost --> cmp + h + 0.01 ptd1ino_SC
R_CDIPTr	Chro.80072	2.7.8.11	phosphatidylinositolsynthase(Homosapiens)	Glycerolipid Metabolism	[c] : cdpdag_hs + inost <==> cmp + h + pail_hs
R_CDGGIPT	Chro.80072	2.7.8.11	CDP-digeranyl-sn-glycero-myo-inositol3-phosphatidyltra	Glycerolipid Metabolism	[c] : cdgggp + inost --> cmp + dggpi + h
R_PSSA1_hs	Chro.10133	2.7.8.8	Phosphatidylserinesynthasehomosapiens	Glycerolipid Metabolism	[c] : pchol_hs + ser-L <==> chol + ps_hs
R_PSSA_HP	Chro.10133	2.7.8.8	PhosphatidylserinesynthaseHpspecific	Glycerolipid Metabolism	[c] : cdpdag_HP + ser-L <==> cmp + h + ps_HP
R_CDGGGSAT	Chro.10133	2.7.8.8	CDP-2,3-di-O-geranylgeranyl-sn-glycerosérineO-archaet	Glycerolipid Metabolism	[c] : cdgggp + ser-L --> cmp + dgggps + h
R_PSSA_SA	Chro.10133	2.7.8.8	Phosphatidylserinesyntase(Saureus)	Glycerolipid Metabolism	[c] : 0.02 cdpdag_SA + ser-L <==> cmp + h + 0.02 ps_SA
R_PSSA2_hs	Chro.10133	2.7.8.8	PhosphatidylserinesynthasehomosapiensPhosphatidylserinesynthase,yeast-specific	Glycerolipid Metabolism	[c] : pe_hs + ser-L <==> etha + ps_hs
R_PSERS_SC	Chro.10133	2.7.8.8		Glycerolipid Metabolism	[c] : 0.01 cdpdag_SC + ser-L <==> cmp + h + 0.01 ps_SC
R_PSSA_EC	Chro.10133	2.7.8.8	Phosphatidylserinesyntase(Ecoli)	Glycerolipid Metabolism	[c] : 0.02 cdpdag_EC + ser-L <==> cmp + h + 0.02 ps_EC
R_LPS2	Chro.11000	3.1.1.3	lipase	Glycerolipid Metabolism	[c] : dag_hs + h2o --> Rtotal + h + mag_hs
R_LPS	Chro.11000	3.1.1.3	lipase	Glycerolipid Metabolism	[c] : h2o + tag_hs --> Rtotal3 + dag_hs + h
R_PLA2_2	.	3.1.1.4	phospholipaseA2	Glycerolipid Metabolism	[c] : h2o + pchol_hs --> Rtotal2 + h + lpchol_hs
R_ALKP	Chro.70170	3.1.3.1	alkalinephosphatase	Glycerolipid Metabolism	[c] : dhap + h2o --> dha + pi
R_PIPLCn	Chro.80452 or Chro.20310 or	3.1.4.3	phosphatidylinositolphospholipaseC,nucleus	Glycerolipid Metabolism	[c] : h2o + pail_hs --> dag_hs + h + mi1p-D
R_GPDDA5	Chro.50344 or Chro.40291	3.1.4.46	Glycerophosphodiesterphosphodiesterase(Glycerophosph	Glycerolipid Metabolism	[c] : g3pi + h2o --> glyc3p + h + inost
R_GPDDA4	Chro.50344 or Chro.40291	3.1.4.46	Glycerophosphodiesterphosphodiesterase(Glycerophosph	Glycerolipid Metabolism	[c] : g3pg + h2o --> glyc + glyc3p + h
R_GPDDA3	Chro.50344 or Chro.40291	3.1.4.46	Glycerophosphodiesterphosphodiesterase(Glycerophosph	Glycerolipid Metabolism	[c] : g3ps + h2o --> glyc3p + h + ser-L
R_GPDDA1	Chro.50344 or Chro.40291	3.1.4.46	Glycerophosphodiesterphosphodiesterase(Glycerophosph	Glycerolipid Metabolism	[c] : g3pc + h2o --> chol + glyc3p + h
R_GPDDA2	Chro.50344 or Chro.40291	3.1.4.46	Glycerophosphodiesterphosphodiesterase(Glycerophosph	Glycerolipid Metabolism	[c] : g3pe + h2o --> etha + glyc3p + h
R_PSD_EC	Chro.30247	4.1.1.65	Phosphatidylserinedecarboxylase(Ecoli)	Glycerolipid Metabolism	[c] : h + 0.02 ps_EC --> co2 + 0.02 pe_EC
R_PSD_HP	Chro.30247	4.1.1.65	PhosphatidylserinedecarboxylaseHpspecific	Glycerolipid Metabolism	[c] : h + ps_HP --> co2 + pe_HP
R_PSD_SA	Chro.30247	4.1.1.65	Phosphatidylserinedecarboxylase(Saureus)	Glycerolipid Metabolism	[c] : h + 0.02 ps_SA --> co2 + 0.02 pe_SA
R_G3PCT	.	2.7.7.39	R_glycerol_3_phosphate_cytidylyltransferase	Glycerophospholipid Metabolism	[c] : 1.0 ctp + 1.0 glyc3p + 1.0 h --> 1.0 cdpglyc + 1.0 ppi
R_CDGPT_CT	.	2.7.8.5	R_CDPdiacylglycerolsn_glycerol_3_phosphate_3_phosph	Glycerophospholipid Metabolism	[c] : 1.0 cdpdag_CT + 1.0 glyc3p --> 1.0 cmp + 1.0 h + 1.0 pglyp_CT
R_PGPPH_CT	.	3.1.3.27	R_Phosphatidylglycerophosphate_phosphohydrolase	Glycerophospholipid Metabolism	[c] : 1.0 h2o + 1.0 pglyp_CT --> 1.0 pgly_CT + 1.0 pi
R_PAP_CT	.	3.1.3.4	R_phosphatidic_acid_phosphatase	Glycerophospholipid Metabolism	[c] : 1.0 12dag3p_CT + 1.0 h2o --> 1.0 12dgr_CT + 1.0 pi
R_41R2A1H12BOOX	Chro.21000	1.4.3.4	4-[(1R)-2-Amino-1-hydroxyethyl]-1,2-benzenediol:oxy	Glycine, Serine, and Threonine Metabolism	[c] : h2o + nrpphr + o2 --> 34dhmald + h2o2 + nh4
R_5HOXINOXDA	Chro.21000	1.4.3.4	5-Hydroxytryptamine:oxygenoxidoreductase(deaminati	Glycine, Serine, and Threonine Metabolism	[c] : h2o + o2 + srtn --> 5hoxindact + h2o2 + nh4
R_3HXKYNOXDA	Chro.21000	1.4.3.4	3-Hydroxykynurenamine:oxygenoxidoreductase(deami	Glycine, Serine, and Threonine Metabolism	[c] : 3hxkynam + o2 --> 48dhoxquin + h2o2 + nh4
R_5HXKYNOXDA	Chro.21000	1.4.3.4	5-Hydroxykynurenamine:oxygenoxidoreductase(deami	Glycine, Serine, and Threonine Metabolism	[c] : 5hxkynam + o2 --> 46dhoxquin + h2o2 + nh4
R_41R1H2MAE12BOO	Chro.21000	1.4.3.4	4-[(1R)-1-Hydroxy-2-(methylamino)ethyl]-1,2-benzene	Glycine, Serine, and Threonine Metabolism	[c] : adrnl + h2o + o2 --> 34dhmald + h2o2 + mma
R_TRYPTAOX	Chro.21000	1.4.3.4	Tryptamine:oxygenoxidoreductase(deaminating)(flavin-c	Glycine, Serine, and Threonine Metabolism	[c] : h2o + o2 + trypta --> h2o2 + id3acald + nh4
R_13DAMPPOX	Chro.80360 or Chro.30388	1.4.3.6	1,3-Diaminopropane:oxygenoxidoreductase(deaminatir	Glycine, Serine, and Threonine Metabolism	[c] : 13dampp + h2o + o2 --> bamppald + h2o2 + nh4
R_HISTASE	Chro.80360 or Chro.30388	1.4.3.6	Histaminase	Glycine, Serine, and Threonine Metabolism	[c] : h2o + hista + o2 --> h2o2 + im4act + nh4
R_42A12BOOX	Chro.80360 or Chro.30388	1.4.3.6	4-(2-Aminoethyl)-1,2-benzenediol:oxygenoxidoreducta	Glycine, Serine, and Threonine Metabolism	[c] : dopa + h2o + o2 --> 34dhpac + h2o2 + nh4
R_PTRCOX1	Chro.80360 or Chro.30388	1.4.3.6	Putrescine:oxygenoxidoreductase(deaminating)	Glycine, Serine, and Threonine Metabolism	[c] : h2o + o2 + ptrc --> 4abutn + h2o2 + nh4
R_TYROXDAc	Chro.80360 or Chro.30388	1.4.3.6	Tyramine:oxygenoxidoreductase(deaminating)(flavin-cor	Glycine, Serine, and Threonine Metabolism	[c] : h2o + o2 + tym --> 4hoxpacd + h2o2 + nh4
R_PEAMNO	Chro.80360 or Chro.30388	1.4.3.6	Phenethylamineoxidase	Glycine, Serine, and Threonine Metabolism	[c] : h2o + o2 + peamn --> h2o2 + nh4 + pacald
R_MAOX	Chro.80360 or Chro.30388	1.4.3.6	Methylamineoxidase	Glycine, Serine, and Threonine Metabolism	[c] : h2o + mma + o2 --> fald + h2o2 + nh4
R_NMPTRCOX	Chro.80360 or Chro.30388	1.4.3.6	N-Methylputrescine:oxygenoxidoreductase(deaminating)	Glycine, Serine, and Threonine Metabolism	[c] : nmptrc + o2 --> 1mpyr + h2o2 + nh4
R_HSK	Chro.60426	2.7.1.39	homoserinekinase	Glycine, Serine, and Threonine Metabolism	[c] : atp + hom-L --> adp + h + phom
R_PSP_L	Chro.70469	3.1.3.3	phosphoserinephosphatase(L-serine)	Glycine, Serine, and Threonine Metabolism	[c] : h2o + pser-L --> pi + ser-L
R_PSP_D	Chro.70469	3.1.3.3	phosphoserinephosphatase(D-serine)	Glycine, Serine, and Threonine Metabolism	[c] : h2o + pser-D --> pi + ser-D
R_SERTRS	Chro.80542	6.1.1.11	Seryl-tRNAsynthetase	Glycine, Serine, and Threonine Metabolism	[c] : atp + ser-L + trnaser --> amp + ppi + sertrna
R_GLYTRS	Chro.80123	6.1.1.14	Glycyl-tRNAsynthetase	Glycine, Serine, and Threonine Metabolism	[c] : atp + gly + trnagly --> amp + glytrna + ppi
R_THRTRS	Chro.70201	6.1.1.3	Threonyl-tRNAsynthetase	Glycine, Serine, and Threonine Metabolism	[c] : atp + thr-L + trnathr --> amp + ppi + thrtrna
R_ALCD2x	Chro.80199 or Chro.80198	1.1.1.1	alcoholdehydrogenase(ethanol)	Glycolysis/Gluconeogenesis	[c] : etoh + nad <==> acald + h + nadh
R_GAPD	Chro.60434 or Chro.10337	1.2.1.12	glyceraldehyde-3-phosphatedehydrogenase	Glycolysis/Gluconeogenesis	[c] : g3p + nad + pi <==> 13dpg + h + nadh
R_HEX1	Chro.60435	2.7.1.1	hexokinase	Glycolysis/Gluconeogenesis	[c] : atp + glc-D --> adp + h + g6p
R_PFKg	Chro.20231 or Chro.30172	2.7.1.11	phosphofructokinase,glycosome	Glycolysis/Gluconeogenesis	[c] : atp + f6p --> adp + fdp + h
R_GLUK	.	2.7.1.2	Glucokinase	Glycolysis/Gluconeogenesis	[c] : atp + glc-D --> adp + g6p-B + h
R_PYK	Chro.10234	2.7.1.40	pyruvatekinase	Glycolysis/Gluconeogenesis	[c] : adp + h + pep --> atp + pyr
R_PGKg	Chro.70113	2.7.2.3	phosphoglyceratekinase	Glycolysis/Gluconeogenesis	[c] : 3pg + atp <==> 13dpg + adp
R_ACYP	Chro.70488	3.6.1.7	acylphosphatase	Glycolysis/Gluconeogenesis	[c] : 13dpg + h2o --> 3pg + h + pi
R_PYRDC	Chro.70351	4.1.1.1	pyruvatedecarboxylase	Glycolysis/Gluconeogenesis	[c] : h + pyr --> acald + co2
R_FBA	Chro.10335	4.1.2.13	fructose-bisphosphatealdolase	Glycolysis/Gluconeogenesis	[c] : fdp <==> dhap + g3p
R_ENO	Chro.50184	4.2.1.11	enolase	Glycolysis/Gluconeogenesis	[c] : 2pg <==> h2o + pep
R_PGI	Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Glycolysis/Gluconeogenesis	[c] : g6p <==> f6p
R_PGM	Chro.10196 or Chro.70471	5.4.2.1	phosphoglyceratemutase	Glycolysis/Gluconeogenesis	[c] : 2pg <==> 3pg
R_PGMT	Chro.20343	5.4.2.2	phosphoglucomutase	Glycolysis/Gluconeogenesis	[c] : g1p <==> g6p
R_ACSm	Chro.10418	6.2.1.1	acetyl-CoAsynthetase	Glycolysis/Gluconeogenesis	[c] : ac + atp + coa --> accoa + amp + ppi
R_RBPC	Chro.20166	4.1.1.39	ribulose-bisphosphatecarboxylase	Glyoxylate and dicarboxylate Metabolism	[c] : co2 + h2o + rb15bp --> 2 3pg + 2 h
R_HISTRS	Chro.80461	6.1.1.21	Histidyl-tRNAsynthetase	Histidine Metabolism	[c] : atp + his-L + trnahis --> amp + histrna + ppi
R_PIN3K_SC	Chro.80217 or Chro.60213	2.7.1.137	1-phosphatidylinositol3-kinase,yeast-specific	Inositol Phosphate Metabolism	[c] : atp + 0.01 ptd1ino_SC --> adp + h + 0.01 ptd3ino_SC
R_PIK3	Chro.80217 or Chro.60213	2.7.1.137	phosphatidylinositol3-kinase	Inositol Phosphate Metabolism	[c] : atp + pail_hs --> adp + h + pail3p_hs
R_PIN4K_SC	Chro.60392 or Chro.80518	2.7.1.67	phosphatidylinositol4-kinase,yeast-specific	Inositol Phosphate Metabolism	[c] : atp + 0.01 ptd1ino_SC --> adp + h + 0.01 ptd4ino_SC
R_PI4P5K_SC	Chro.20207	2.7.1.68	phosphatidylinositol-4-phosphate5-kinase,yeast-specfic	Inositol Phosphate Metabolism	[c] : atp + 0.01 ptd4ino_SC --> adp + h + 0.01 ptd145bp_SC
R_PI4P5K	Chro.20207	2.7.1.68	phosphatidylinositol4-phosphate5-kinase	Inositol Phosphate Metabolism	[c] : atp + pail4p_hs --> adp + h + pail45p_hs
R_MI1345PP	Chro.50026	3.1.3.56	inositol-1,3,4,5-trisphosphate5-phosphatase	Inositol Phosphate Metabolism	[c] : h2o + mi1345p --> mi134p + pi
R_MI145PP	Chro.50026	3.1.3.56	inositol-1,4,5-trisphosphate5-phosphatase	Inositol Phosphate Metabolism	[c] : h2o + mi145p --> mi14p + pi
R_PI45PLC	Chro.40288	3.1.4.11	phosphatidylinositol4,5-bisphosphatephospholipaseC	Inositol Phosphate Metabolism	[c] : h2o + pail45p_hs --> dag_hs + h + mi145p
R_PI45BPP_SC	Chro.40288	3.1.4.11	1-phosphatidylinositol-4,5-bisphosphatephosphodiester	Inositol Phosphate Metabolism	[c] : h2o + 0.01 ptd145bp_SC --> 0.01 12dgr_SC + h + mi145p
R_PIPLC	Chro.80452 or Chro.20310 or	3.1.4.3	phosphatidylinositolphospholipaseC	Inositol Phosphate Metabolism	[c] : h2o + pail_hs --> dag_hs + h + mi1p-D
R_AASAD3	Chro.40330	1.2.1.31	L-aminoadipate-semialdehydedehydrogenase(NADH)	Lysine Biosynthesis	[c] : L2aadp6sa + h2o + nad --> L2aadp + 2 h + nadh
R_AASAD2	Chro.40330	1.2.1.31	L-aminoadipate-semialdehydedehydrogenase(NADH)	Lysine Biosynthesis	[c] : L2aadp + atp + h + nadh --> L2aadp6sa + amp + nad + ppi
R_AASAD1	Chro.40330	1.2.1.31	L-aminoadipate-semialdehydedehydrogenase(NADPH)	Lysine Biosynthesis	[c] : L2aadp + atp + h + nadph --> L2aadp6sa + amp + nadp + ppi

R_LYSTRS	Chro.40267	6.1.1.6	Lysyl-tRNAsynthetase	Lysine Biosynthesis	[c] : atp + lys-L + trnalys --> amp + lystrna + ppi
R_LYSMTF2	Chro.40051	2.1.1.43	histone-lysineN-methyltransferase,nuclear	Lysine Degradation	[c] : Nmelys + amet --> Ndmelys + ahcys
R_LYSMTF3	Chro.40051	2.1.1.43	histone-lysineN-methyltransferase,nuclear	Lysine Degradation	[c] : Ndmelys + amet --> Ntmelys + ahcys
R_LYSMTF1	Chro.40051	2.1.1.43	histone-lysineN-methyltransferase,nuclear	Lysine Degradation	[c] : amet + peplys --> Nmelys + ahcys
R_PRDX	Chro.40093 or Chro.80075 or	1.11.1.7	Peroxidase(multiplesubstrates)	Methane Metabolism	[c] : h2o2 + meoh --> fald + 2 h2o
R_GHMT3	Chro.80302 or Chro.80306	2.1.2.1	glycinehydroxymethyltransferase	Methane Metabolism	[c] : 3htmelys + h --> 4tmeabut + gly
R_GHMT2r	Chro.80302 or Chro.80306	2.1.2.1	glycinehydroxymethyltransferase,reversible	Methane Metabolism	[c] : ser-L + thf <==> gly + h2o + mlthf
R_DNAMT	Chro.50169	2.1.1.37	DNA(cytosine-5-)-methyltransferase,nucleus	Methionine Metabolism	[c] : amet + dna --> ahcys + dna5mtc + h
R_DNAMTSE	Chro.50169	2.1.1.37	DNA(cytosine-5-)-methyltransferase,nucleus	Methionine Metabolism	[c] : dna + seasmet --> dna5mtc + h + seahcys
R_METAT	Chro.70301	2.5.1.6	methionineadenosyltransferase	Methionine Metabolism	[c] : atp + h2o + met-L --> amet + pi + ppi
R_AHC	Chro.30017	3.3.1.1	adenosylhomocysteinase	Methionine Metabolism	[c] : ahcys + h2o <==> adn + hcys-L
R_METTRS	Chro.80398	6.1.1.10	Methionyl-tRNAsynthetase	Methionine Metabolism	[c] : atp + met-L + trnamet --> amp + mettrna + ppi
R_G3POA_CT	.	.	R_glycerol_3_phosphate_O_acyltransferase	Miscellaneous	[c] : 1.0 glyc3p + 0.051 dcacoa + 0.022 trdacoa + 0.023 fa1coa + 0.0092
R_LYSLG_CT	.	.	R_lysylphosphatidylglycerol_synthesis	Miscellaneous	[c] : 1.0 atp + 1.0 lys-L + 1.0 pgly_CT --> 1.0 amp + 1.0 h + 1.0 lysylpgly
R_UGT_CT	.	.	R_UDP_glucosyltransferase_diglucosyl	Miscellaneous	[c] : 1.0 12dgr_CT + 2.0 udpg --> 1.0 d12dg_CT + 2.0 h + 2.0 udp
R_UGT1_CT	.	.	R_UDP_glucosyltransferase_monoglucosyl	Miscellaneous	[c] : 1.0 12dgr_CT + 1.0 udpg --> 1.0 h + 1.0 m12dg_CT + 1.0 udp
R_UGT2_CT	.	.	R_UDP_glucosyltransferase_triglucosyl	Miscellaneous	[c] : 1.0 12dgr_CT + 3.0 udpg --> 3.0 h + 1.0 t12dg_CT + 3.0 udp
R_LIPO1S24_CT	.	.	R_lipoteichoic_acid_synthesis_n24_linked_glucose	Miscellaneous	[c] : 24.0 cdpglyc + 1.0 d12dg_CT + 24.0 udpg --> 24.0 cmp + 48.0 h +
R_LIPO2S24_CT	.	.	R_lipoteichoic_acid_synthesis_n24_linked_N_acety	Miscellaneous	[c] : 24.0 cdpglyc + 1.0 d12dg_CT + 24.0 uacgam --> 24.0 cmp + 48.0 h
R_LIPO3S24_CT	.	.	R_lipoteichoic_acid_synthesis_n24_unliked_D_alan	Miscellaneous	[c] : 24.0 ala-D + 24.0 atp + 24.0 cdpglyc + 1.0 d12dg_CT + 24.0 h2o -->
R_LIPO4S24_CT	.	.	R_lipoteichoic_acid_synthesis_n24_linked_unsubsti	Miscellaneous	[c] : 24.0 cdpglyc + 1.0 d12dg_CT --> 24.0 cmp + 24.0 h + 1.0 lipo4_24
R_TECA1S45	.	.	R_glycerol_teichoic_acid_n45_unlinked_unsubstitut	Miscellaneous	[c] : 45.0 cdpglyc + 1.0 uacgam + 1.0 uacmam --> 45.0 cmp + 1.0 gtca1
R_TECA2S45	.	.	R_glycerol_teichoic_acid_n45_unlinked_D_ala_subs	Miscellaneous	[c] : 45.0 ala-D + 45.0 atp + 45.0 cdpglyc + 45.0 h2o + 1.0 uacgam + 1.0
R_TECA3S45	.	.	R_glycerol_teichoic_acid_n45_unlinked_glucose_su	Miscellaneous	[c] : 45.0 cdpglyc + 1.0 h2o + 1.0 uacgam + 1.0 uacmam + 45.0 udpg -->
R_TECA4S_CT	.	.	R_minor_teichoic_acid_synthesis_n30	Miscellaneous	[c] : 30.0 h2o + 30.0 uacgala + 30.0 udpg --> 60.0 h + 1.0 tcam_CT + 30
R_TEICH45	.	.	R_teichuronic_acid__n45___unlinked__GalNAc_GlcA_re	Miscellaneous	[c] : 45.0 uacgala + 45.0 udpglcur <==> 45.0 h + 1.0 teich_45_CT + 45.0
R_UAGPT3	.	.	R_UDP_N_acetylglucosamine_N_acetylmuramyl__penta	Miscellaneous	[c] : 1.0 uacgam + 1.0 uagmda --> 1.0 h + 1.0 uaagmda + 1.0 udp
R_PPTGS_CT	.	.	R_Peptidoglycan_subunit_synthesis	Miscellaneous	[c] : 1.0 uaagmda --> 1.0 h + 1.0 peptido_CT + 1.0 udcpdp
R_FRTT	.	.	R_farnesyltranstransferase	Miscellaneous	[c] : 1.0 frdp + 1.0 ipdp --> 1.0 ggdp + 1.0 ppi
R_GGTT	.	.	R_geranylgeranyltranstransferase	Miscellaneous	[c] : 1.0 ggdp + 1.0 ipdp --> 1.0 pendp + 1.0 ppi
R_PPTT	.	.	R_trans_pentaprenyltranstransferase	Miscellaneous	[c] : 1.0 ipdp + 1.0 pendp --> 1.0 hexdp + 1.0 ppi
R_HEXTT	.	.	R_trans_hexaprenyltranstransferase	Miscellaneous	[c] : 1.0 hexdp + 1.0 ipdp --> 1.0 hepdp + 1.0 ppi
R_ICHORS	.	.	R_isochorismate_synthase	Miscellaneous	[c] : 1.0 chor <==> 1.0 ichor
R_2S6HCCi	.	.	R_2_succinyl_6_hydroxy_2_4_cyclohexadiene_1_carbox	Miscellaneous	[c] : 1.0 akg + 1.0 h + 1.0 ichor --> 1.0 2shchc + 1.0 co2 + 1.0 pyr
R_SUCBZS	.	.	R_O_succinylbenzoate_CoA_synthase	Miscellaneous	[c] : 1.0 2shchc --> 1.0 h2o + 1.0 sucbz
R_SUCBZL	.	.	R_o_succinylbenzoate_CoA_ligase	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 sucbz --> 1.0 amp + 1.0 ppi + 1.0 sbzcoa
R_NPHS	.	.	R_naphthoate_synthase	Miscellaneous	[c] : 1.0 sbzcoa --> 1.0 coa + 1.0 dhna
R_DHNAOT7	.	.	R_1_4_dihydroxy_2_naphthoate_octaprenyltransferase	Miscellaneous	[c] : 1.0 dhna + 1.0 hepdp + 1.0 nad --> 1.0 2dmmq7 + 1.0 co2 + 1.0 na
R_AMMQT7	.	.	R_S_adenosylmethione2_demthylmenaquinone_methylt	Miscellaneous	[c] : 1.0 2dmmq7 + 1.0 amet + 1.0 nadph --> 1.0 ahcys + 1.0 mql7 + 1.0
R_H2CO3D2	.	.	carboxylicaciddissociation	Miscellaneous	[c] : h + hco3 <==> h2co3
R_IPDPS		1.17.1.2	1-hydroxy-2-methyl-2-(E)-butenyl4-diphosphatereduct	Miscellaneous	[c] : h + h2mb4p + nadh --> h2o + ipdp + nad
R_MECDPDH	.	1.17.4.3	2C-methyl-D-erythritol2,4cyclodiphosphatedehydratase	Miscellaneous	[c] : 2mecdp + h --> h2mb4p + h2o
R_AGPATr_CT	Chro.80165	2.3.1.51	R_1_acylglycerol_3_phosphate_O_acyltransferase	Miscellaneous	[c] : 1.0 1ag3p_CT + 0.051 dcacoa + 0.022 trdacoa + 0.023 fa1coa + 0.0
R_DAGK_CT	Chro.40493	2.7.1.107	R_diacylglycerol_kinase	Miscellaneous	[c] : 1.0 12dgr_CT + 1.0 atp --> 1.0 12dag3p_CT + 1.0 adp + 1.0 h
R_PHCYT_CT	Chro.70332	2.7.7.41	R_phosphatidate_cytidylyltransferase	Miscellaneous	[c] : 1.0 12dag3p_CT + 1.0 ctp + 1.0 h --> 1.0 cdpdag_CT + 1.0 ppi
R_CLPNS2_CT	.	2.7.8.-	R_cardiolipin_synthase	Miscellaneous	[c] : 2.0 pgly_CT --> 1.0 cdlp_CT + 1.0 glyc
R_CDPDSP_CT	Chro.10133	2.7.8.8	R_CDPdiacylglycerol_serine_O_phosphatidyltransferase	Miscellaneous	[c] : 1.0 cdpdag_CT + 1.0 ser-L --> 1.0 cmp + 1.0 h + 1.0 ps_CT
R_PSDC_CT	Chro.30247	4.1.1.65	R_phosphatidylserine_decarboxylase	Miscellaneous	[c] : 1.0 ps_CT --> 1.0 co2 + 1.0 psetha_CT
R_FACOAL100	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C100	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 dca <==> 1.0 amp + 1.0 dcacoa + 1.0 ppi
R_FACOAL130	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C130	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 trdca <==> 1.0 amp + 1.0 trdacoa + 1.0 ppi
R_FACOAL140_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C140	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa1 <==> 1.0 amp + 1.0 fa1coa + 1.0 ppi
R_FACOAL150_anteis	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__anteiso_C150	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa4 <==> 1.0 amp + 1.0 fa4coa + 1.0 ppi
R_FACOAL150_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C150	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa3 <==> 1.0 amp + 1.0 fa3coa + 1.0 ppi
R_FACOAL160_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C160	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa6 <==> 1.0 amp + 1.0 fa6coa + 1.0 ppi
R_FACOAL161_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C161	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa5 <==> 1.0 amp + 1.0 fa5coa + 1.0 ppi
R_FACOAL170_anteis	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__anteiso_C170	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa12 <==> 1.0 amp + 1.0 fa12coa + 1.0 ppi
R_FACOAL170_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C170	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa11 <==> 1.0 amp + 1.0 fa11coa + 1.0 ppi
R_FACOAL171_anteis	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__anteiso_C171	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa10 <==> 1.0 amp + 1.0 fa10coa + 1.0 ppi
R_FACOAL171_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C171	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 fa9 <==> 1.0 amp + 1.0 fa9coa + 1.0 ppi
R_FACOAL180_ISO_	Chro.50052 or Chro.30084	6.2.1.3	R_fatty_acid__CoA_ligase__Iso_C180	Miscellaneous	[c] : 1.0 atp + 1.0 coa + 1.0 ocdcaiso <==> 1.0 amp + 1.0 ppi + 1.0 strc
R_THD2	Chro.80274	1.6.1.1	NAD(P)transhydrogenase	NAD Metabolism	2 h[e] + nadh[c] + nadp[c] --> 2 h[c] + nad[c] + nadph[c]
R_NADTRHD	Chro.10120	1.6.1.2	NADtranshydrogenase	NAD Metabolism	[c] : nad + nadph --> nadh + nadp
R_NADK	Chro.80231	2.7.1.23	NADkinase	NAD Metabolism	[c] : atp + nad --> adp + h + nadp
R_UDPDOLPT_U	Chro.50118	2.4.1.117	UDPglucose:dolichyl-phosphatebeta-D-glucosyltransfera	N-Glycan Biosynthesis	[c] : 0.1 dolp_U + udpg --> 0.1 dolglcp_U + udp
R_UDPDOLPT_L	Chro.50118	2.4.1.117	UDPglucose:dolichyl-phosphatebeta-D-glucosyltransfera	N-Glycan Biosynthesis	[c] : 0.1 dolp_L + udpg --> 0.1 dolglcp_L + udp
R_DOLASNT_Uer	Chro.20179 or Chro.60585	2.4.1.119	Dolichyl-diphosphooligosaccharide:protein-L-asparagine	N-Glycan Biosynthesis	[c] : Asn-X_DASH_Ser_FSLASH_Thr + 0.1 g3m8mpdol_U --> 0.1 doldp_U
R_DOLASNT_Ler	Chro.20179 or Chro.60585	2.4.1.119	Dolichyl-diphosphooligosaccharide:protein-L-asparagine	N-Glycan Biosynthesis	[c] : Asn-X_DASH_Ser_FSLASH_Thr + 0.1 g3m8mpdol_L --> 0.1 doldp_L
R_DOLPMT_L	Chro.50175	2.4.1.83	Dolichyl-phosphateD-mannosyltransferase(liver)	N-Glycan Biosynthesis	[c] : 0.1 dolp_L + gdpmann --> 0.1 dolmanp_L + gdp
R_DOLPMT_U	Chro.50175	2.4.1.83	Dolichyl-phosphateD-mannosyltransferase(uterus)	N-Glycan Biosynthesis	[c] : 0.1 dolp_U + gdpmann --> 0.1 dolmanp_U + gdp
R_DOLPMTcer	Chro.50175	2.4.1.83	Dolichyl-phosphateD-mannosyltransferase	N-Glycan Biosynthesis	dolp[c] + gdpmann[c] --> dolmanp[r] + gdp[c]
R_DOLK	Chro.20170	2.7.1.108	Dolicholkinase	N-Glycan Biosynthesis	[c] : ctp + dolichol --> cdp + dolp + h
R_DOLK_U	Chro.20170	2.7.1.108	Dolicholkinase,human(uterus)	N-Glycan Biosynthesis	[c] : ctp + 0.1 dolichol_U --> cdp + 0.1 dolp_U + h
R_DOLK_L	Chro.20170	2.7.1.108	Dolicholkinase,human(liver)	N-Glycan Biosynthesis	[c] : ctp + 0.1 dolichol_L --> cdp + 0.1 dolp_L + h
R_GLCNACPT_L	Chro.50156	2.7.8.15	UDP-GlcNAc:dolichol-phosphateGlcNAcphosphotransfera	N-Glycan Biosynthesis	[c] : 0.1 dolp_L + uacgam --> 0.1 naglc2p_L + ump
R_GLCNACPT_U	Chro.50156	2.7.8.15	UDP-GlcNAc:dolichol-phosphateGlcNAcphosphotransfera	N-Glycan Biosynthesis	[c] : 0.1 dolp_U + uacgam --> 0.1 naglc2p_U + ump
R_HCO3E	Chro.40064	4.2.1.1	HCO3equilibrationreaction	Nitrogen Metabolism	[c] : co2 + h2o <==> h + hco3
R_H2CO3D	Chro.40064	4.2.1.1	carboxylicaciddissociation	Nitrogen Metabolism	[c] : co2 + h2o <==> h2co3
R_ASNS2	Chro.50501	6.3.1.1	asparaginesynthetase	Nitrogen Metabolism	[c] : asp-L + atp + nh4 --> amp + asn-L + h + ppi
R_GLNS	Chro.60524	6.3.1.2	glutaminesynthetase	Nitrogen Metabolism	[c] : atp + glu-L + nh4 --> adp + gln-L + h + pi
R_ASNS1	Chro.30020	6.3.5.4	asparaginesynthase(glutamine-hydrolysing)	Nitrogen Metabolism	[c] : asp-L + atp + gln-L + h2o --> amp + asn-L + glu-L + h + ppi
R_G1PTT	Chro.80452	2.7.7.24	glucose-1-phosphatethymidylyltransferase	Nucleotide Sugar Metabolism	[c] : dttp + g1p + h --> dtdpglu + ppi
R_TDPGDH	Chro.20206	4.2.1.46	dTDPglucose4,6-dehydratase	Nucleotide Sugar Metabolism	[c] : dtdpglu --> dtdp4d6dg + h2o
R_GALNT	Chro.60231 or Chro.50322 or	2.4.1.41	GalNActransferase,Golgiapparatus	O-Glycan Biosynthesis	[c] : Ser_FSLASH_Thr + udpacgal --> Tn_antigen + h + udp
R_NADH10	Chro.70218	1.6.5.3	NADHdehydrogenase(menaquinone-8&0protons)	Oxidative Phosphorylation	[c] : h + mqn8 + nadh --> mql8 + nad
R_ECHH_1_PERIOD_	Chro.70218	1.6.5.3	EchHydrogenase	Oxidative Phosphorylation	2 fdred[c] + 3 h[c] <==> 2 fdox[c] + h[e] + h2[c]
R_NADH5	Chro.70218	1.6.5.3	NADHdehydrogenase(ubiquinone-8)	Oxidative Phosphorylation	[c] : h + nadh + q8 --> nad + q8h2
R_NADH7	Chro.70218	1.6.5.3	NADHdehydrogenase(menaquinone-8&2protons)	Oxidative Phosphorylation	3 h[c] + mqn8[c] + nadh[c] --> 2 h[e] + mql8[c] + nad[c]
R_NADH6	Chro.70218	1.6.5.3	NADHdehydrogenase(ubiquinone-8&3.5protons)	Oxidative Phosphorylation	4.5 h[c] + nadh[c] + q8[c] --> 3.5 h[e] + nad[c] + q8h2[c]
R_NADH9	Chro.70218	1.6.5.3	NADHdehydrogenase(demethylmenaquinone-8&0proton	Oxidative Phosphorylation	[c] : 2dmmq8 + h + nadh --> 2dmmql8 + nad
R_NADH8	Chro.70218	1.6.5.3	NADHdehydrogenase(demethylmenaquinone-8&2.8proto	Oxidative Phosphorylation	2dmmq8[c] + 3.8 h[c] + nadh[c] --> 2dmmql8[c] + 2.8 h[e] + nad[c]
R_NADH2_DASH_u6o	Chro.70218	1.6.99.3	NADHdehydrogenase,cytosolic/mitochondrial	Oxidative Phosphorylation	h[c] + nadh[c] + q6[c] --> nad[c] + q6h2[c]
R_CYOO_HP	Chro.70168	1.9.3.1	cytochromec553oxidase,Hpylori	Oxidative Phosphorylation	4 focytcc553[c] + 5.98 h[c] + o2[c] --> 4 ficytcc553[c] + 2 h[e] + 1.99 h2
R_PPA_1	Chro.40159	3.6.1.1	inorganicdiphosphatase(oneprotontranslocation)	Oxidative Phosphorylation	h2o[c] + ppi[c] --> h[e] + 2 pi[c]
R_PPA2	Chro.40159	3.6.1.1	inorganictriphosphatase	Oxidative Phosphorylation	[c] : h2o + pppi --> h + pi + ppi
R_PPA	Chro.40159	3.6.1.1	inorganicdiphosphatase	Oxidative Phosphorylation	[c] : h2o + ppi --> h + 2 pi
R_ATPS4r	Chro.60082 and Chro.20424 a	3.6.3.14	ATPsynthase(fourprotonsforoneATP)	Oxidative Phosphorylation	adp[c] + 4 h[e] + pi[c] <==> atp[c] + 3 h[c] + h2o[c]
R_ATPasel	Chro.60082 and Chro.20424 a	3.6.3.14	V-typeATPase,H+transporting,lysosomal	Oxidative Phosphorylation	atp[c] + 3 h[c] + h2o[c] --> adp[c] + 4 h[l] + pi[c]
R_ATPS	Chro.20424 and Chro.70559 a	3.6.3.6	ATPase,cytosolic	Oxidative Phosphorylation	atp[c] + h2o[c] --> adp[c] + h[e] + pi[c]
R_CAATPS	Chro.20424 and Chro.70559 a	3.6.3.6	CaATPase	Oxidative Phosphorylation	atp[c] + 2 ca2[c] + h2o[c] --> adp[c] + 2 ca2[e] + h[e] + pi[c]
R_ATPS1	Chro.20424 and Chro.70559 a	3.6.3.6	H+-exportingATPase	Oxidative Phosphorylation	atp[c] + h[c] + h2o[c] --> adp[c] + 2 h[e] + pi[c]
R_DPCOAK	Chro.20045	2.7.1.24	dephospho-CoAkinase	Pantothenate-Vit B5 and CoA biosynthesis	[c] : atp + dpcoa --> adp + coa + h
R_PNTK	Chro.70552 or Chro.80038	2.7.1.33	pantothenatekinase	Pantothenate-Vit B5 and CoA biosynthesis	[c] : atp + pnto-R --> 4ppan + adp + h
R_PFK_2	Chro.20231	2.7.1.11	Phosphofructokinase	Pentose Phosphate Pathway	[c] : atp + tag6p-D --> adp + h + tagdp-D
R_PFK_3	Chro.20231	2.7.1.11	phosphofructokinase(s7p)	Pentose Phosphate Pathway	[c] : atp + s7p --> adp + h + s17bp
R_PFK	Chro.20231	2.7.1.11	phosphofructokinase	Pentose Phosphate Pathway	[c] : atp + f6p --> adp + fdp + h
R_G6PI2	Chro.20336	5.3.1.9	Glucose-6-phosphateisomerase	Pentose Phosphate Pathway	[c] : g6p-B <==> f6p-B
R_G6PI	Chro.20336	5.3.1.9	Glucose-6-phosphateisomerase	Pentose Phosphate Pathway	[c] : g6p <==> g6p-B
R_SHKK	Chro.30373	2.7.1.71	shikimatekinase	Phenylalanine, Tyrosine and Tryptophan B	[c] : atp + skm --> adp + h + skm5p
R_DHQD	Chro.80609	4.2.1.10	3-dehydroquinatedehydratase	Phenylalanine, Tyrosine and Tryptophan B	[c] : 3dhq <==> 3dhsk + h2o
R_TRPS3	Chro.50503	4.2.1.20	tryptophansynthase(indoleglycerolphosphate)	Phenylalanine, Tyrosine and Tryptophan B	[c] : 3ig3p --> g3p + indole
R_TRPS2	Chro.50503	4.2.1.20	tryptophansynthase(indole)	Phenylalanine, Tyrosine and Tryptophan B	[c] : indole + ser-L --> h2o + trp-L
R_TRPS1	Chro.50503	4.2.1.20	tryptophansynthase(indoleglycerolphosphate)	Phenylalanine, Tyrosine and Tryptophan B	[c] : 3ig3p + ser-L --> g3p + h2o + trp-L
R_TYRTRS	Chro.40444 or Chro.60344	6.1.1.1	tyrosyl-tRNAsynthetase	Phenylalanine, Tyrosine and Tryptophan B	[c] : atp + trnatyr + tyr-L --> amp + ppi + tyrtrna
R_PHETRS	Chro.30378 or Chro.80385	6.1.1.20	Phenylalanyl-tRNAsynthetase	Phenylalanine, Tyrosine and Tryptophan B	[c] : atp + phe-L + trnaphe --> amp + phetrna + ppi
R_UPP3S	.	4.2.1.75	uroporphyrinogen-IIIsynthase	Porphyrin and chlorophyll metabolism	[c] : hmbil --> h2o + uppg3
R_GLUTRS_LPAREN_	Chro.60505 or Chro.80098 or	6.1.1.17	Glutamyl-tRNAsynthetase(Gln)	Porphyrin and chlorophyll metabolism	[c] : atp + glu-L + trnagln --> amp + glutrna_LPAREN_gln_RPAREN_ + pp
R_ACOAD3	Chro.31000 or Chro.41000	1.3.99.3	acyl-CoAdehydrogenase(octanoyl-CoA)	Propanoate Metabolism	[c] : nad + occoa <==> h + nadh + oc2coa
R_ACOAD5	Chro.31000 or Chro.41000	1.3.99.3	acyl-CoAdehydrogenase(dodecanoyl-CoA)	Propanoate Metabolism	[c] : ddcacoa + nad <==> dd2coa + h + nadh
R_ACOAD4	Chro.31000 or Chro.41000	1.3.99.3	acyl-CoAdehydrogenase(decanoyl-CoA)	Propanoate Metabolism	[c] : dcacoa + nad <==> dc2coa + h + nadh
R_ACOAD7	Chro.31000 or Chro.41000	1.3.99.3	acyl-CoAdehydrogenase(hexadecanoyl-CoA)	Propanoate Metabolism	[c] : nad + pmtcoa --> h + hdd2coa + nadh
R_ACOAD6	Chro.31000 or Chro.41000	1.3.99.3	acyl-CoAdehydrogenase(tetradecanoyl-CoA)	Propanoate Metabolism	[c] : nad + tdcoa <==> h + nadh + td2coa
R_ACOAD2	Chro.31000 or Chro.41000	1.3.99.3	acyl-CoAdehydrogenase(hexanoyl-CoA)	Propanoate Metabolism	[c] : h + hx2coa + nadh <==> hxcoa + nad

R_ACCOACr	Chro.80425	6.4.1.2	acetyl-CoAcarboxylase,reversiblereaction	Propanoate Metabolism	[c] : accoa + atp + hco3 <==> adp + h + malcoa + pi
R_IMPD	Chro.60012	1.1.1.205	IMPdehydrogenase	Purine Metabolism	[c] : h2o + imp + nad --> h + nadh + xmp
R_RNDR2n	Chro.60090 or Chro.60091	1.17.4.1	ribonucleoside-diphosphatereductase(GDP),nuclear	Purine Metabolism	[c] : gdp + trdrd --> dgdp + h2o + trdox
R_RNDR4n	Chro.60090 or Chro.60091	1.17.4.1	ribonucleoside-diphosphatereductase(UDP),nuclear	Purine Metabolism	[c] : trdrd + udp --> dudp + h2o + trdox
R_ADNK2	Chro.20322	2.7.1.20	adenosinekinase	Purine Metabolism	[c] : adn + gtp --> adp + gmp + h
R_ADNK1	Chro.20322	2.7.1.20	adenosinekinase	Purine Metabolism	[c] : adn + atp --> adp + amp + h
R_ADK2	Chro.50037	2.7.4.3	adenylatekinase(Inorganictriphosphate)	Purine Metabolism	[c] : amp + pppi <==> adp + ppi
R_NDPK10	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:dIDP)	Purine Metabolism	[c] : atp + didp <==> adp + ditp
R_NDPK9	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:IDP)	Purine Metabolism	[c] : atp + idp <==> adp + itp
R_NDPK8	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:dADP)	Purine Metabolism	[c] : atp + dadp <==> adp + datp
R_NDPK7	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:dCDP)	Purine Metabolism	[c] : atp + dcdp <==> adp + dctp
R_NDPK6	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:dUDP)	Purine Metabolism	[c] : atp + dudp <==> adp + dutp
R_NDPK5	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:dGDP)	Purine Metabolism	[c] : atp + dgdp <==> adp + dgtp
R_NDPK4	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:dTDP)	Purine Metabolism	[c] : atp + dtdp <==> adp + dttp
R_NDPK3	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:CDP)	Purine Metabolism	[c] : atp + cdp <==> adp + ctp
R_NDPK2	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:UDP)	Purine Metabolism	[c] : atp + udp <==> adp + utp
R_NDPK1	Chro.40275 or Chro.50237 or	2.7.4.6	nucleoside-diphosphatekinase(ATP:GDP)	Purine Metabolism	[c] : atp + gdp <==> adp + gtp
R_DGK1	Chro.70250	2.7.4.8	deoxyguanylatekinase(dGMP:ATP)	Purine Metabolism	[c] : atp + dgmp <==> adp + dgdp
R_GK1	Chro.70250	2.7.4.8	guanylatekinase(GMP:ATP)	Purine Metabolism	[c] : atp + gmp <==> adp + gdp
R_NTD11	Chro.50026	3.1.3.5	5'-nucleotidase(IMP)	Purine Metabolism	[c] : h2o + imp --> ins + pi
R_NTD10	Chro.50026	3.1.3.5	5'-nucleotidase(XMP)	Purine Metabolism	[c] : h2o + xmp --> pi + xtsn
R_NTD12	Chro.50026	3.1.3.5	5'-nucleotidase(dIMP)	Purine Metabolism	[c] : dimp + h2o --> din + pi
R_NTD9	Chro.50026	3.1.3.5	5'-nucleotidase(GMP)	Purine Metabolism	[c] : gmp + h2o --> gsn + pi
R_NTD8	Chro.50026	3.1.3.5	5'-nucleotidase(dGMP)	Purine Metabolism	[c] : dgmp + h2o --> dgsn + pi
R_NTD1	Chro.50026	3.1.3.5	5'-nucleotidase(dUMP)	Purine Metabolism	[c] : dump + h2o --> duri + pi
R_NTD3	Chro.50026	3.1.3.5	5'-nucleotidase(dCMP)	Purine Metabolism	[c] : dcmp + h2o --> dcyt + pi
R_NTD2	Chro.50026	3.1.3.5	5'-nucleotidase(UMP)	Purine Metabolism	[c] : h2o + ump --> pi + uri
R_NTD5	Chro.50026	3.1.3.5	5'-nucleotidase(dTMP)	Purine Metabolism	[c] : dtmp + h2o --> pi + thymd
R_NTD4	Chro.50026	3.1.3.5	5'-nucleotidase(CMP)	Purine Metabolism	[c] : cmp + h2o --> cytd + pi
R_NTD7	Chro.50026	3.1.3.5	5'-nucleotidase(AMP)	Purine Metabolism	[c] : amp + h2o --> adn + pi
R_NTD6	Chro.50026	3.1.3.5	5'-nucleotidase(dAMP)	Purine Metabolism	[c] : damp + h2o --> dad-2 + pi
R_NT5C	Chro.50026	3.1.3.5	5'-nucleotidase	Purine Metabolism	[c] : h2o + nicrnt --> nicrns + pi
R_PDE1	Chro.30269 or Chro.60462	3.1.4.17	3',5'-cyclic-nucleotidephosphodiesterase	Purine Metabolism	[c] : camp + h2o --> amp + h
R_PDE2	Chro.30269 or Chro.60462	3.1.4.17	3',5'-cyclic-nucleotidephosphodiesterase	Purine Metabolism	[c] : 35cdamp + h2o --> damp + h
R_PDE3	Chro.30269 or Chro.60462	3.1.4.17	3',5'-cyclic-nucleotidephosphodiesterase	Purine Metabolism	[c] : 35cimp + h2o --> h + imp
R_PDE5	Chro.30269 or Chro.60462	3.1.4.17	3',5'-cyclic-nucleotidephosphodiesterase	Purine Metabolism	[c] : 35ccmp + h2o --> cmp + h
R_PDE4	Chro.30269 or Chro.60462	3.1.4.17	3',5'-cyclic-nucleotidephosphodiesterase	Purine Metabolism	[c] : 35cgmp + h2o --> gmp + h
R_AMPDAm	Chro.40214	3.5.4.6	Adenosinemonophosphatedeaminase,mitochondrion	Purine Metabolism	[c] : amp + h + h2o --> imp + nh4
R_AMPDAg	Chro.40214	3.5.4.6	Adenosinemonophosphatedeaminase,glycosome	Purine Metabolism	[c] : amp + h + h2o --> imp + nh4
R_NTPP9	Chro.10434 or Chro.70577	3.6.1.19	Nucleosidetriphosphatepyrophosphorylase(itp)	Purine Metabolism	[c] : h2o + itp --> h + imp + ppi
R_NTPP10	Chro.10434 or Chro.70577	3.6.1.19	Nucleosidetriphosphatepyrophosphorylase(dtp)	Purine Metabolism	[c] : dtp + h2o --> dimp + h + ppi
R_NTPP11	Chro.10434 or Chro.70577	3.6.1.19	Nucleosidetriphosphatepyrophosphorylase(xtp)	Purine Metabolism	[c] : h2o + xtp --> h + ppi + xmp
R_UTPH2e	Chro.60194	3.6.1.5	UTPdiphosphohydrolase	Purine Metabolism	[e] : udp + h2o --> ump + h + pi
R_GTPH2e	Chro.60194	3.6.1.5	GTPdiphosphohydrolase	Purine Metabolism	[e] : gdp + h2o --> gmp + h + pi
R_ATPH2e	Chro.60194	3.6.1.5	ATPdiphosphohydrolase	Purine Metabolism	[e] : adp + h2o --> amp + h + pi
R_UTPH1e	Chro.60194	3.6.1.5	UTPdiphosphohydrolase	Purine Metabolism	[e] : utp + 2 h2o --> ump + 2 h + 2 pi
R_GTPH1e	Chro.60194	3.6.1.5	GTPdiphosphohydrolase	Purine Metabolism	[e] : gtp + 2 h2o --> gmp + 2 h + 2 pi
R_ATPH1e	Chro.60194	3.6.1.5	ATPdiphosphohydrolase	Purine Metabolism	[e] : atp + 2 h2o --> amp + 2 h + 2 pi
R_NDP3ex	Chro.60194	3.6.1.6	nucleoside-diphosphatase(GDP),extracellular	Purine Metabolism	[e] : gdp + h2o --> gmp + h + pi
R_NDP10ex	Chro.60194	3.6.1.6	nucleoside-diphosphatase(IDP),extracellular	Purine Metabolism	[e] : h2o + idp --> h + imp + pi
R_NDP4	Chro.60194	3.6.1.6	nucleoside-diphosphatase(dGDP)	Purine Metabolism	[c] : dgdp + h2o --> dgmp + h + pi
R_NDP6	Chro.60194	3.6.1.6	nucleoside-diphosphatase(dCDP)	Purine Metabolism	[c] : dcdp + h2o --> dcmp + h + pi
R_NDP3	Chro.60194	3.6.1.6	nucleoside-diphosphatase(GDP)	Purine Metabolism	[c] : gdp + h2o --> gmp + h + pi
R_NDP8	Chro.60194	3.6.1.6	nucleoside-diphosphatase(dUDP)	Purine Metabolism	[c] : dudp + h2o --> dump + h + pi
R_NDP8ex	Chro.60194	3.6.1.6	nucleoside-diphosphatase(UTP),extracellular	Purine Metabolism	[e] : h2o + utp --> h + pi + udp
R_NDP3g	Chro.60194	3.6.1.6	nucleoside-diphosphatase(GDP),Golgi	Purine Metabolism	[c] : gdp + h2o --> gmp + h + pi
R_NDP7er	Chro.60194	3.6.1.6	nucleoside-diphosphatase(UDP),endoplasmicreticulum	Purine Metabolism	[c] : h2o + udp --> h + pi + ump
R_NDP7ex	Chro.60194	3.6.1.6	nucleoside-diphosphatase(UDP),extracellular	Purine Metabolism	[e] : h2o + udp --> h + pi + ump
R_NDP7g	Chro.60194	3.6.1.6	nucleoside-diphosphatase(UDP),Golgiapparatus	Purine Metabolism	[c] : h2o + udp --> h + pi + ump
R_ADSL2r	.	4.3.2.2	adenylosuccinatelyase	Purine Metabolism	[c] : 25aics <==> aicar + fum
R_ADSL1r	.	4.3.2.2	adenylsuccinatelyase	Purine Metabolism	[c] : dcamp <==> amp + fum
R_ADSL2	.	4.3.2.2	adenylosuccinatelyase	Purine Metabolism	[c] : 25aics --> aicar + fum
R_ADSL1	.	4.3.2.2	adenylosuccinatelyase	Purine Metabolism	[c] : dcamp --> amp + fum
R_ADNCYC	Chro.50255 or Chro.40352	4.6.1.1	adenylatecyclase	Purine Metabolism	[c] : atp --> camp + ppi
R_GUACYC	Chro.50255 or Chro.30141 or	4.6.1.2	guanylatecyclase	Purine Metabolism	[c] : gtp --> 35cgmp + ppi
R_GMPS	.	6.3.4.1	GMPsynthase	Purine Metabolism	[c] : atp + nh4 + xmp --> amp + gmp + 2 h + ppi
R_RNDR4	Chro.60090 or Chro.60091	1.17.4.1	ribonucleoside-diphosphatereductase(UDP)	Pyrimidine Metabolism	[c] : trdrd + udp --> dudp + h2o + trdox
R_RNDR3	Chro.60090 or Chro.60091	1.17.4.1	ribonucleoside-diphosphatereductase(CDP)	Pyrimidine Metabolism	[c] : cdp + trdrd --> dcdp + h2o + trdox
R_RNDR1	Chro.60090 or Chro.60091	1.17.4.1	ribonucleoside-diphosphatereductase(ADP)	Pyrimidine Metabolism	[c] : adp + trdrd --> dadp + h2o + trdox
R_RNDR2	Chro.60090 or Chro.60091	1.17.4.1	ribonucleoside-diphosphatereductase(GDP)	Pyrimidine Metabolism	[c] : gdp + trdrd --> dgdp + h2o + trdox
R_TRDR	Chro.20464	1.8.1.9	thioredoxinreductase(NADPH)	Pyrimidine Metabolism	[c] : h + nadph + trdox --> nadp + trdrd
R_TRDR2	Chro.20464	1.8.1.9	Thioredoxin(ubiquinone10)reductase(NADPH)	Pyrimidine Metabolism	[c] : h + nadph + q10 --> nadp + q10h2
R_TRDR3	Chro.20464	1.8.1.9	Thioredoxin(ubiquinone10)reductase(NADH)	Pyrimidine Metabolism	[c] : h + nadh + q10 --> nad + q10h2
R_TMDS	Chro.40506 or Chro.30116	2.1.1.45	thymidylatesynthase	Pyrimidine Metabolism	[c] : dump + mlthf --> dhf + dtmp
R_TMDSf	Chro.40506 or Chro.30116	2.1.1.45	thymidylatesynthase(Flavin-dependent)	Pyrimidine Metabolism	[c] : dump + fmnh2 + mlthf --> dtmp + fmn + thf
R_UPPRTr	Chro.10216	2.4.2.9	uracilphosphoribosyltransferase(r)	Pyrimidine Metabolism	[c] : prpp + ura <==> ppi + ump
R_TMDK1	Chro.50398 or Chro.70052	2.7.1.21	thymidinekinase(ATP:thymidine)	Pyrimidine Metabolism	[c] : atp + thymd --> adp + dtmp + h
R_URIK2	Chro.10216 or Chro.20045 or	2.7.1.48	uridinekinase(GTP:Uridine)	Pyrimidine Metabolism	[c] : gtp + uri --> gdp + h + ump
R_URIK1	Chro.10216 or Chro.20045 or	2.7.1.48	uridinekinase(ATP:Uridine)	Pyrimidine Metabolism	[c] : atp + uri --> adp + h + ump
R_CYTK2	.	2.7.4.14	cytidylatekinase(dCMP)	Pyrimidine Metabolism	[c] : atp + dcmp <==> adp + dcdp
R_UMPK5	.	2.7.4.14	UMPkinase(dATP)	Pyrimidine Metabolism	[c] : datp + ump <==> dadp + udp
R_CYTK9	.	2.7.4.14	cytidylatekinase(CMP,dCTP)	Pyrimidine Metabolism	[c] : cmp + dctp <==> cdp + dcdp
R_CYTK8	.	2.7.4.14	cytidylatekinase(CMP,dATP)	Pyrimidine Metabolism	[c] : cmp + datp <==> cdp + dadp
R_CYTK5	.	2.7.4.14	cytidylatekinase(dCMP)	Pyrimidine Metabolism	[c] : ctp + dcmp <==> cdp + dcdp
R_CYTK7	.	2.7.4.14	cytidylatekinase(CMP,UTP)	Pyrimidine Metabolism	[c] : cmp + utp <==> cdp + udp
R_CYTK6	.	2.7.4.14	cytidylatekinase(CMP,CTP)	Pyrimidine Metabolism	[c] : cmp + ctp <==> 2 cdp
R_CYTK1	.	2.7.4.14	cytidylatekinase(CMP)	Pyrimidine Metabolism	[c] : atp + cmp <==> adp + cdp
R_UMPK3	.	2.7.4.14	UMPkinase(UTP)	Pyrimidine Metabolism	[c] : ump + utp <==> 2 udp
R_UMPK2	.	2.7.4.14	UMPkinase(CTP)	Pyrimidine Metabolism	[c] : ctp + ump <==> cdp + udp
R_UMPK7	.	2.7.4.14	UMPkinase(dGTP)	Pyrimidine Metabolism	[c] : dgtp + ump <==> dgdp + udp
R_UMPK6	.	2.7.4.14	UMPkinase(dCTP)	Pyrimidine Metabolism	[c] : dctp + ump <==> dcdp + udp
R_UMPK4	.	2.7.4.14	UMPkinase(GTP)	Pyrimidine Metabolism	[c] : gtp + ump <==> gdp + udp
R_CYTK11	.	2.7.4.14	cytidylatekinase(dCMP,dGTP)	Pyrimidine Metabolism	[c] : dcmp + dgtp <==> dcdp + dgdp
R_CYTK10	.	2.7.4.14	cytidylatekinase(CMP,dGTP)	Pyrimidine Metabolism	[c] : cmp + dgtp <==> cdp + dgdp
R_CYTK13	.	2.7.4.14	cytidylatekinase(dCMP,dATP)	Pyrimidine Metabolism	[c] : datp + dcmp <==> dadp + dcdp
R_CYTK12	.	2.7.4.14	cytidylatekinase(dCMP,dCTP)	Pyrimidine Metabolism	[c] : dcmp + dctp <==> 2 dcdp
R_CYTK14	.	2.7.4.14	cytidylatekinase(dCMP,UTP)	Pyrimidine Metabolism	[c] : dcmp + utp <==> dcdp + udp
R_UMPK	.	2.7.4.14	UMPkinase	Pyrimidine Metabolism	[c] : atp + ump <==> adp + udp
R_DTMPK	Chro.50490	2.7.4.9	dTMPkinase	Pyrimidine Metabolism	[c] : atp + dtmp <==> adp + dtdp
R_DUMPK	Chro.50490	2.7.4.9	dUMPkinase	Pyrimidine Metabolism	[c] : atp + dump <==> adp + dudp
R_DCMPDA	Chro.20294	3.5.4.12	dCMPdeaminase	Pyrimidine Metabolism	[c] : dcmp + h + h2o <==> dump + nh4
R_DCYTD	Chro.20294	3.5.4.14	deoxycytidinedeaminase	Pyrimidine Metabolism	[c] : dcyt + h + h2o --> duri + nh4
R_AP4AH1	.	3.6.1.17	Ap4Ahydrolase,asymmetrically	Pyrimidine Metabolism	[c] : ap4a + h2o --> amp + atp + 2 h
R_DUTPDP	Chro.70577	3.6.1.23	dUTPdiphosphatase	Pyrimidine Metabolism	[c] : dutp + h2o --> dump + h + ppi
R_YUMPS	Chro.20165 or Chro.30435 or	4.2.1.70	yUMPsynthetase	Pyrimidine Metabolism	[c] : r5p + ura <==> h2o + psd5p
R_CBPS	.	6.3.5.5	carbamoyl-phosphatesynthase(glutamine-hydrolysing)	Pyrimidine Metabolism	[c] : 2 atp + gln-L + h2o + hco3 --> 2 adp + cbp + glu-L + 2 h + pi
R_LDH_L	Chro.70063	1.1.1.27	L-lactatedehydrogenase	Pyruvate Metabolism	[c] : lac-L + nad <==> h + nadh + pyr
R_MCLOR	Chro.70063 or Chro.70062	1.1.1.27	3-Mercaptolactate:NAD+oxidoreductase	Pyruvate Metabolism	[c] : mercplac + nad <==> h + mercppyr + nadh
R_2HBO	Chro.70063 or Chro.70062	1.1.1.27	2-Hydroxybutyrate:NAD+oxidoreductase	Pyruvate Metabolism	[c] : 2hb + nad <==> 2obut + h + nadh
R_MDH	Chro.70063 or Chro.70062	1.1.1.37	malatedehydrogenase	Pyruvate Metabolism	[c] : mal-L + nad <==> h + nadh + oaa
R_MDHi2	Chro.70063 or Chro.70062	1.1.1.37	malatedehydrogenase(otherdirection)	Pyruvate Metabolism	[c] : h + nadh + oaa --> mal-L + nad
R_ME1	Chro.50314	1.1.1.38	malicenzyme(NAD)	Pyruvate Metabolism	[c] : mal-L + nad --> co2 + nadh + pyr
R_ME2	Chro.50314	1.1.1.40	malicenzyme(NADP)	Pyruvate Metabolism	[c] : mal-L + nadp --> co2 + nadph + pyr
R_MDH2	Chro.80050	1.1.99.16	Malatedehydrogenase(ubiquinone8asacceptor)	Pyruvate Metabolism	[c] : mal-L + q8 --> oaa + q8h2
R_MDH3	Chro.80050	1.1.99.16	Malatedehydrogenase(menaquinone8asacceptor)	Pyruvate Metabolism	[c] : mal-L + mqn8 --> mql8 + oaa
R_MDH4	Chro.80050	1.1.99.16	Malatedehydrogenase(menaquinone6asacceptor)	Pyruvate Metabolism	[c] : mal-L + mqn6 --> mql6 + oaa
R_ACALD	Chro.80198	1.2.1.10	acetaldehydedehydrogenase(acetylating)	Pyruvate Metabolism	[c] : acald + coa + nad <==> accoa + h + nadh
R_PDH	Chro.40087	1.2.1.51	pyruvatedehydrogenase	Pyruvate Metabolism	[c] : coa + nadp + pyr --> accoa + co2 + nadph
R_ACYP_2	Chro.70488	3.6.1.7	acylphosphatase(2)	Pyruvate Metabolism	[c] : actp + h2o --> ac + h + pi
R_PPC	Chro.50389	4.1.1.31	phosphoenolpyruvatecarboxylase	Pyruvate Metabolism	[c] : co2 + h2o + pep --> h + oaa + pi
R_ACS2	Chro.10418	6.2.1.1	acetyl-CoAsynthase(propionate)	Pyruvate Metabolism	[c] : atp + coa + ppa --> amp + ppcoa + ppi
R_ACS	Chro.10418	6.2.1.1	acetyl-CoAsynthetase	Pyruvate Metabolism	[c] : ac + atp + coa --> accoa + amp + ppi

R_RDH3a	Chro.40258	1.1.1.105	retinoldehydrogenase(11-cis,NADPH)	Retinol-Vit A Metabolism	[c] : nadp + retinol-cis_DASH_11 <==> h + nadph + retinal-11_DASH_cis
R_RDH1a	Chro.40258	1.1.1.105	retinoldehydrogenase(all-trans,NADPH)	Retinol-Vit A Metabolism	[c] : nadp + retinol <==> h + nadph + retinal
R_RDH2a	Chro.40258	1.1.1.105	retinoldehydrogenase(9-cis,NADPH)	Retinol-Vit A Metabolism	[c] : nadp + retinol-9_DASH_cis <==> h + nadph + retinal-cis_DASH_9
R_RDH1	Chro.40258	1.1.1.105	retinoldehydrogenase(all-trans)	Retinol-Vit A Metabolism	[c] : nad + retinol <==> h + nadh + retinal
R_RDH3	Chro.40258	1.1.1.105	retinoldehydrogenase(11-cis,NADH)	Retinol-Vit A Metabolism	[c] : nad + retinol-cis_DASH_11 <==> h + nadh + retinal-11_DASH_cis
R_RDH2	Chro.40258	1.1.1.105	retinoldehydrogenase(9-cis,NADH)	Retinol-Vit A Metabolism	[c] : nad + retinol-9_DASH_cis <==> h + nadh + retinal-cis_DASH_9
R_RDH4	Chro.40258	1.1.1.105	retinoldehydrogenase(13-cis,NADH)	Retinol-Vit A Metabolism	[c] : nad + retinol-cis_DASH_13 <==> h + nadh + retinal-cis_DASH_13
R_RBFSb	Chro.80106	2.5.1.9	riboflavinsynthase	Riboflavin Metabolism-Vit B2	[c] : 2 dmlz --> 4r5au + ribflv
R_RBFSa	Chro.80106	2.5.1.9	riboflavinsynthase	Riboflavin Metabolism-Vit B3	[c] : 4r5au + db4p --> dmlz + 2 h2o + pi
R_ACP1_LPAREN_FM	Chro.20071 or Chro.80016 or	3.1.3.2	acidphosphatase(FMN)	Riboflavin Metabolism-Vit B4	[c] : fmn + h2o --> pi + ribflv
R_SULR	Chro.40087	1.8.2.2	sulfitereductase(NADPH2)	Selenoamino acid metabolism	[c] : 3 h2o + h2s + 3 nadp <==> 5 h + 3 nadph + so3
R_SEAHCYSHYD	Chro.30017	3.3.1.1	Se-Adenosylselenohomocysteinehydrolase	Selenoamino acid metabolism	[c] : h2o + seahcys --> adn + selhcys
R_SIAASE	.	3.2.1.18	sialidase	Sphingoglycolipid Metabolism	[c] : 2 h2o + s2l2n2m2mn --> 2 acnam + l2n2m2mn
R_UDPGDr	Chro.80111	1.1.1.22	UDPglucose6-dehydrogenase	Starch and Sucrose Metabolism	[c] : h2o + 2 nad + udpg <==> 3 h + 2 nadh + udpglcur
R_GLCP	Chro.60284	2.4.1.1	glycogenphosphorylase	Starch and Sucrose Metabolism	[c] : glycogen + pi --> g1p
R_GLPASE2	Chro.60284	2.4.1.1	glycogenphosphorylase(amyls->glc-D)	Starch and Sucrose Metabolism	[c] : glygn3 + 7 h2o --> Tyr-ggn + 7 glc-D
R_GLPASE1	Chro.60284	2.4.1.1	glycogenphosphorylase(glygn2->dxtrn)	Starch and Sucrose Metabolism	[c] : glygn2 + 3 pi --> dxtrn + 3 g1p
R_TRE6PS	Chro.80565	2.4.1.15	alpha,alpha-trehalose-phosphatesynthase(UDP-forming)	Starch and Sucrose Metabolism	[c] : g6p + udpg --> h + tre6p + udp
R_GBEZ	Chro.60381	2.4.1.18	1,4-alpha-glucanbranchingenzyme	Starch and Sucrose Metabolism	[c] : 14glun --> glycogen + h2o
R_GLBRAN	Chro.60381	2.4.1.18	1,4-alpha-glucanbranchingenzyme(glygn1->glygn2)	Starch and Sucrose Metabolism	[c] : glygn1 --> glygn2
R_AMALT1	Chro.60114	2.4.1.25	Amylomaltase(maltotriose)	Starch and Sucrose Metabolism	[c] : malt + malttr --> glc-D + maltttr
R_AMALT2	Chro.60114	2.4.1.25	Amylomaltase(maltotetraose)	Starch and Sucrose Metabolism	[c] : malt + maltttr --> glc-D + maltpt
R_AMALT3	Chro.60114	2.4.1.25	Amylomaltase(maltopentaose)	Starch and Sucrose Metabolism	[c] : malt + maltpt --> glc-D + malthx
R_AMALT4	Chro.60114	2.4.1.25	Amylomaltase(maltohexaose)	Starch and Sucrose Metabolism	[c] : malt + malthx --> glc-D + malthp
R_AMY2e	Chro.80574 or Chro.50082 or	3.2.1.1	alpha-amylase,extracellular(glygn2->glygn4)	Starch and Sucrose Metabolism	[e] : glygn2 + 8 h2o --> 8 glc-D + glygn4
R_AMY1e	Chro.80574 or Chro.50082 or	3.2.1.1	alpha-amylase,extracellular(strch1->strch2)	Starch and Sucrose Metabolism	[e] : 8 h2o + strch1 --> 8 glc-D + strch2
R_GLCGSD	Chro.80574 or Chro.70613 or	3.2.1.3	glucan1,4-alpha-glucosidase	Starch and Sucrose Metabolism	[c] : glycogen + h2o --> glc-D
R_GLDBRAN	Chro.60114	3.2.1.33	glycogendebranchingenzyme	Starch and Sucrose Metabolism	[c] : dxtrn + h2o --> glc-D + glygn3
R_PGI3	Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Starch and Sucrose Metabolism	[c] : g6p-A <==> f6p
R_PGI2	Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Starch and Sucrose Metabolism	[c] : g6p-A <==> g6p-B
R_PGI1	Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Starch and Sucrose Metabolism	[c] : g6p-B <==> f6p
R_DXPRIi	.	1.1.1.267	1-deoxy-D-xylulosereductoisomerase	Sterol Biosynthesis	[c] : dxyl5p + h + nadph --> 2me4p + nadp
R_IPDDI	.	5.3.3.2	isopentenyl-diphosphateD-isomerase	Sterol Biosynthesis	[c] : ipdp <==> dmpp
R_DMATT	Chro.40285	2.5.1.1	dimethylallyltranstransferase	Terpenoid Biosynthesis	[c] : dmpp + ipdp --> grdp + ppi
R_GRTT	Chro.40285	2.5.1.10	geranyltranstransferase	Terpenoid Biosynthesis	[c] : grdp + ipdp --> frdp + ppi
R_SQLS	Chro.10227	2.5.1.21	Squalenesynthase	Terpenoid Biosynthesis	[c] : 2 frdp + h + nadph --> nadp + 2 ppi + sql
R_H2Ot	.	.	H2Otransportviadiffusion	Transport, Extracellular	h2o[e] <==> h2o[c]
R_CYSt2r	.			Transport, Extracellular	cys-L[e] + h[e] <==> cys-L[c] + h[c]
R_METt2r				Transport, Extracellular	h[e] + met-L[e] <==> h[c] + met-L[c]
R_GLNt2r				Transport, Extracellular	gln-L[e] + h[e] <==> gln-L[c] + h[c]
R_ILEt2r				Transport, Extracellular	h[e] + ile-L[e] <==> h[c] + ile-L[c]
R_LEUt2r				Transport, Extracellular	h[e] + leu-L[e] <==> h[c] + leu-L[c]
R_SULabc				Transport, Extracellular	atp[c] + h2o[c] + so4[e] --> adp[c] + h[c] + pi[c] + so4[c]
R_PROt2r				Transport, Extracellular	h[e] + pro-L[e] <==> h[c] + pro-L[c]
R_ARGt2r				Transport, Extracellular	arg-L[e] + h[e] <==> arg-L[c] + h[c]
R_ASPt2r				Transport, Extracellular	asp-L[e] + h[e] <==> asp-L[c] + h[c]
R_ALAt2				Transport, Extracellular	ala-L[e] + h[e] --> ala-L[c] + h[c]
R_HISt2r				Transport, Extracellular	h[e] + his-L[e] <==> h[c] + his-L[c]
R_LYSt2r				Transport, Extracellular	h[e] + lys-L[e] <==> h[c] + lys-L[c]
R_SERt2r				Transport, Extracellular	h[e] + ser-L[e] <==> h[c] + ser-L[c]
R_THRt2				Transport, Extracellular	h[e] + thr-L[e] --> h[c] + thr-L[c]
R_TRPt2r				Transport, Extracellular	h[e] + trp-L[e] <==> h[c] + trp-L[c]
R_TYRt2r				Transport, Extracellular	h[e] + tyr-L[e] <==> h[c] + tyr-L[c]
R_VALt2r				Transport, Extracellular	h[e] + val-L[e] <==> h[c] + val-L[c]
R_PIt2				Transport, Extracellular	h[e] + pi[e] <==> h[c] + pi[c]
R_CMPtrans				Transport, Extracellular	cmp[e] + h[e] --> cmp[c] + h[c]
R_AMPtrans				Transport, Extracellular	amp[e] + h[e] --> amp[c] + h[c]
R_GMPtrans				Transport, Extracellular	gmp[e] + h[e] --> gmp[c] + h[c]
R_GLCt1r				Transport, Extracellular	glc-D[e] <==> glc-D[c]
R_CO2t				Transport, Extracellular	co2[e] <==> co2[c]
R_NH4t				Transport, Extracellular	nh4[e] <==> nh4[c]
R_PHEt2r				Transport, Extracellular	h[e] + phe-L[e] <==> h[c] + phe-L[c]
R_TRPTRS	Chro.70176	6.1.1.2	Tryptophanyl-tRNAsynthetase	Tryptophan metabolism	[c] : atp + trnatrp + trp-L --> amp + ppi + trptrna
R_ALCD2m	Chro.80199 or Chro.80198	1.1.1.1	alcoholdehydrogenase(ethanol),mitochondrial	Tyrosine metabolism	[c] : etoh + nad <==> acald + h + nadh
R_DOPABMO	.	1.14.17.1	dopaminebeta-monooxygenase	Tyrosine metabolism	[c] : ascb-L + dopa + o2 --> dhdascb + h2o + nrpphr
R_G5SD2	Chro.70551	1.2.1.41	glutamate-5-semialdehydedehydrogenase	Urea Cycle and Metabolism of Amino Grou	[c] : glu5p + h + nadh --> glu5sa + nad + pi
R_G5SD	Chro.70551	1.2.1.41	glutamate-5-semialdehydedehydrogenase	Urea Cycle and Metabolism of Amino Grou	[c] : glu5p + h + nadph --> glu5sa + nadp + pi
R_GLU5K	Chro.70551 or Chro.20246	2.7.2.11	glutamate5-kinase	Urea Cycle and Metabolism of Amino Grou	[c] : atp + glu-L --> adp + glu5p
R_OIVD2	.	1.2.4.4	R_2_oxoisovalerate_dehydrogenase__acylating_3_meth	Valine, Leucine, and Isoleucine Biosynthes	[c] : 1.0 3mob + 1.0 coa + 1.0 nad --> 1.0 co2 + 1.0 ibcoa + 1.0 nadh
R_OIVD3	.	1.2.4.4	R_2_oxoisovalerate_dehydrogenase__acylating_3_meth	Valine, Leucine, and Isoleucine Biosynthes	[c] : 1.0 3mop + 1.0 coa + 1.0 nad --> 1.0 2mbcoa + 1.0 co2 + 1.0 nadh
R_LEUTRS	Chro.50330 or Chro.50331	6.1.1.4	Leucyl-tRNAsynthetase	Valine, Leucine, and Isoleucine Biosynthes	[c] : atp + leu-L + trnaleu --> amp + leutrna + ppi
R_ILETRS	Chro.30434	6.1.1.5	Isoleucyl-tRNAsynthetase	Valine, Leucine, and Isoleucine Biosynthes	[c] : atp + ile-L + trnaile --> amp + iletrna + ppi
R_VALTRS	Chro.80361	6.1.1.9	Valyl-tRNAsynthetase	Valine, Leucine, and Isoleucine Biosynthes	[c] : atp + trnaval + val-L --> amp + ppi + valtrna

Appendix B: Gap Analysis Results

REACTION IDs	ENZYME NAME	PATHWAY	EC NUMBER	REACTION ADDED THROUGH GAP ANALYSIS
While integrating proteomic data, following highlighted reaction that were inserted through Gap Analysis algorithm were later found to be existing in oocyst stage of parasite hence not included in the figure 8, gap analysis reaction classification				
R_BIOMASS	biomass	Biomass	.	[c] : 0.257980584 ala-L + 0.176597196 arg-L + 0.218152121 asn-L + 0.230278549 asp-L + 0.04
R_UAG4E	R_UDP_N_acetylglucosamine_4_epimerase	Aminosugar Metabolism	5.1.3.7	[c] : 1.0 uacgam --> 1.0 uacgala
R_DXPRIi	1-deoxy-D-xylulosereductoisomerase	Biosyhthesis of Steroids	1.1.1.267	[c] : dxyl5p + h + nadph --> 2me4p + nadp
R_MECDPS	2-C-methyl-D-erythritol2,4-cyclodiphosphatesynthase	Biosyhthesis of Steroids	4.6.1.12	[c] : 2p4c2me --> 2mecdp + cmp
R_IPDDI	isopentenyl-diphosphateD-isomerase	Biosyhthesis of Steroids	5.3.3.2	[c] : ipdp <==> dmpp
R_DXPS	1-deoxy-D-xylulose5-phosphatesynthase	Biosynthesis of Steroids	2.2.1.7	[c] : g3p + h + pyr --> co2 + dxyl5p
R_CDPMEK	4-(cytidine5'-diphospho)-2-C-methyl-D-erythritolkinase	Biosynthesis of Steroids	2.7.1.148	[c] : 4c2me + atp --> 2p4c2me + adp + h
R_MEPCT	2-C-methyl-D-erythritol4-phosphatecytidylyltransferase	Biosynthesis of Steroids	2.7.7.60	[c] : 2me4p + ctp + h --> 4c2me + ppi
R_KAS2	R_b_ketoacyl_synthetase__n_C140	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 accoa + 17.0 h + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + 5.0 h2o + 12.0 nadp
R_KAS8	R_b_ketoacyl_synthetase__palmitate__n_C160	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 accoa + 20.0 h + 7.0 malcoa + 14.0 nadph --> 7.0 co2 + 8.0 coa + 6.0 h2o + 1.0 hdca +
R_KAS13	R_b_ketoacyl_synthetase__n_C180	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 accoa + 23.0 h + 8.0 malcoa + 16.0 nadph --> 8.0 co2 + 9.0 coa + 7.0 h2o + 16.0 nadp
R_KAS141	R_b_ketoacyl_synthetase__n_C141	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 accoa + 16.0 h + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa + 5.0 h2o + 11.0 nadp
R_KAS7	R_b_ketoacyl_synthetase__n_C161	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 accoa + 19.0 h + 7.0 malcoa + 13.0 nadph --> 7.0 co2 + 8.0 coa + 6.0 h2o + 1.0 hdcea
R_KAS17	R_b_ketoacyl_synthetase__n_C181	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 accoa + 22.0 h + 8.0 malcoa + 15.0 nadph --> 8.0 co2 + 9.0 coa + 7.0 h2o + 15.0 nadp
R_KAS100iso	R_b_ketoacyl_synthetase__branched(iso)_C100	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 8.0 h + 1.0 ibcoa + 3.0 malcoa + 6.0 nadph --> 3.0 co2 + 4.0 coa + 1.0 dca + 2.0 h2o + 6.0
R_KAS130iso	R_b_ketoacyl_synthetase__branched(iso)_C130	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 11.0 h + 1.0 ivcoa + 4.0 malcoa + 8.0 nadph --> 4.0 co2 + 5.0 coa + 1.0 trdca + 3.0 h2o +
R_KAS1	R_b_ketoacyl_synthetase__Iso_C140_	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 14.0 h + 1.0 ibcoa + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 coa + 1.0 fa1 + 4.0 h2o +
R_KAS3	R_b_ketoacyl_synthetase__Iso_C150	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 14.0 h + 1.0 ivcoa + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 coa + 1.0 fa3 + 4.0 h2o +
R_KAS6	R_b_ketoacyl_synthetase__Iso_C160	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 17.0 h + 1.0 ibcoa + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + 1.0 fa6 + 5.0 h2o +
R_KAS11	R_b_ketoacyl_synthetase__Iso_C170	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 17.0 h + 1.0 ivcoa + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + 1.0 fa11 + 5.0 h2o +
R_KAS180iso	R_b_ketoacyl_synthetase__Iso_C180	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 20.0 h + 1.0 ibcoa + 7.0 malcoa + 14.0 nadph --> 7.0 co2 + 8.0 coa + 1.0 ocdcaiso + 6.0 h2
R_KAS5	R_b_ketoacyl_synthetase__Iso_C161	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 16.0 h + 1.0 ibcoa + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa + 1.0 fa5 + 5.0 h2o +
R_KAS9	R_b_ketoacyl_synthetase__Iso_C171	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 16.0 h + 1.0 ivcoa + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa + 1.0 fa9 + 5.0 h2o +
R_KAS4	R_b_ketoacyl_synthetase__Anteiso_C150	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 2mbcoa + 14.0 h + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 coa + 1.0 fa4 + 4.0 h2o
R_KAS12	R_b_ketoacyl_synthetase__Anteiso_C170	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 2mbcoa + 17.0 h + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + 1.0 fa12 + 5.0 h2o
R_KAS10	R_b_ketoacyl_synthetase__branched(iso)_C171	Fatty Acid_Biosynthesis	2.3.1.41	[c] : 1.0 2mbcoa + 16.0 h + 6.0 malcoa + 11.0 nadph --> 6.0 co2 + 7.0 coa + 1.0 fa10 + 5.0 h2o
R_MAN1PT2r	mannose-1-phosphateguanylyltransferase(GDP)reversible	Fructose and Mannose Metabolism	2.7.7.22	[c] : gdp + h + man1p <==> gdpmann + pi
R_PLA2_2	phospholipaseA2	Glycerophospholipid Metabolism	3.1.1.4	[c] : h2o + pchol_hs --> Rtotal2 + h + lpchol_hs
R_G3PCT	R_glycerol_3_phosphate_cytidylyltransferase	Glycerophospholipid Metabolism	2.7.7.39	[c] : 1.0 ctp + 1.0 glyc3p + 1.0 h --> 1.0 cdpglyc + 1.0 ppi
R_CDGPT_CT	R_CDPdiacylglycerolsn_glycerol_3_phosphate_3_phosphatidylt	Glycerophospholipid Metabolism	2.7.8.5	[c] : 1.0 cdpdag_CT + 1.0 glyc3p --> 1.0 cmp + 1.0 h + 1.0 pglyp_CT
R_PGPPH_CT	R_Phosphatidylglycerophosphate_phosphohydrolase	Glycerophospholipid Metabolism	3.1.3.27	[c] : 1.0 h2o + 1.0 pglyp_CT --> 1.0 pgly_CT + 1.0 pi
R_PAP_CT	R_phosphatidic_acid_phosphatase	Glycerophospholipid Metabolism	3.1.3.4	[c] : 1.0 12dag3p_CT + 1.0 h2o --> 1.0 12dgr_CT + 1.0 pi
R_GLUK	Glucokinase	Glycolysis/Gluconeogenesis	2.7.1.2	[c] : atp + glc-D --> adp + g6p-B + h
R_G3POA_CT	R_glycerol_3_phosphate_O_acyltransferase	Miscellaneous	.	[c] : 1.0 glyc3p + 0.051 dcacoa + 0.022 trdacoa + 0.023 fa1coa + 0.0092 tdcoa + 0.022 ttdcecoa
R_LYSLG_CT	R_lysylphosphatidylglycerol_synthesis	Miscellaneous	.	[c] : 1.0 atp + 1.0 lys-L + 1.0 pgly_CT --> 1.0 amp + 1.0 h + 1.0 lysylpgly_CT + 1.0 ppi
R_UGT_CT	R_UDP_glucosyltransferase__diglucosyl	Miscellaneous	.	[c] : 1.0 12dgr_CT + 2.0 udpg --> 1.0 d12dg_CT + 2.0 h + 2.0 udp
R_UGT1_CT	R_UDP_glucosyltransferase__monoglucosyl	Miscellaneous	.	[c] : 1.0 12dgr_CT + 1.0 udpg --> 1.0 h + 1.0 m12dg_CT + 1.0 udp
R_UGT2_CT	R_UDP_glucosyltransferase__triglucosyl	Miscellaneous	.	[c] : 1.0 12dgr_CT + 3.0 udpg --> 3.0 h + 1.0 t12dg_CT + 3.0 udp
R_LIPO1S24_CT	R_lipoteichoic_acid_synthesis__n24__linked__glucose_substit	Miscellaneous	.	[c] : 24.0 cdpglyc + 1.0 d12dg_CT + 24.0 udpg --> 24.0 cmp + 48.0 h + 1.0 lipo1_24_CT + 24.0
R_LIPO2S24_CT	R_lipoteichoic_acid_synthesis__n24__linked__N_acetylglucos	Miscellaneous	.	[c] : 24.0 cdpglyc + 1.0 d12dg_CT + 24.0 uacgam --> 24.0 cmp + 48.0 h + 1.0 lipo2_24_CT + 24
R_LIPO3S24_CT	R_lipoteichoic_acid_synthesis__n24__unliked__D_alanine_su	Miscellaneous	.	[c] : 24.0 ala-D + 24.0 atp + 24.0 cdpglyc + 1.0 d12dg_CT + 24.0 h2o --> 24.0 amp + 24.0 cmp
R_LIPO4S24_CT	R_lipoteichoic_acid_synthesis__n24__linked__unsubstituted	Miscellaneous	.	[c] : 24.0 cdpglyc + 1.0 d12dg_CT --> 24.0 cmp + 24.0 h + 1.0 lipo4_24_CT
R_TECA1S45	R_glycerol_teichoic_acid__n45__unlinked__unsubstituted	Miscellaneous	.	[c] : 45.0 cdpglyc + 1.0 uacgam + 1.0 uacmam --> 45.0 cmp + 1.0 gtca1_45_CT + 46.0 h + 1.0
R_TECA2S45	R_glycerol_teichoic_acid__n45__unlinked__D_ala_substituted	Miscellaneous	.	[c] : 45.0 ala-D + 45.0 atp + 45.0 cdpglyc + 45.0 h2o + 1.0 uacgam + 1.0 uacmam --> 45.0 amp
R_TECA3S45	R_glycerol_teichoic_acid__n45__unlinked__glucose_substitut	Miscellaneous	.	[c] : 45.0 cdpglyc + 1.0 h2o + 1.0 uacgam + 1.0 uacmam + 45.0 udpg --> 45.0 cmp + 1.0 gtca3
R_TECA4S_CT	R_minor_teichoic_acid_synthesis__n30	Miscellaneous	.	[c] : 30.0 h2o + 30.0 uacgala + 30.0 udpg --> 60.0 h + 1.0 tcam_CT + 30.0 udp + 30.0 ump
R_TEICH45	R_teichuronic_acid__n45__unlinked__GalNAc_GlcA_repeated	Miscellaneous	.	[c] : 45.0 uacgala + 45.0 udpglcur <==> 45.0 h + 1.0 teich_45_CT + 45.0 udp + 45.0 ump
R_UAGPT3	R_UDP_N_acetylglucosamine_N_acetylmuramyl__pentapeptide	Miscellaneous	.	[c] : 1.0 uacgam + 1.0 uagmda --> 1.0 h + 1.0 uaagmda + 1.0 udp
R_PPTGS_CT	R_Peptidoglycan_subunit_synthesis	Miscellaneous	.	[c] : 1.0 uaagmda --> 1.0 h + 1.0 peptido_CT + 1.0 udcpdp
R_FRTT	R_farnesyltranstransferase	Miscellaneous	.	[c] : 1.0 frdp + 1.0 ipdp --> 1.0 ggdp + 1.0 ppi
R_GGTT	R_geranylgeranyltranstransferase	Miscellaneous	.	[c] : 1.0 ggdp + 1.0 ipdp --> 1.0 pendp + 1.0 ppi
R_PPTT	R_trans_pentaprenyltranstransferase	Miscellaneous	.	[c] : 1.0 ipdp + 1.0 pendp --> 1.0 hexdp + 1.0 ppi
R_HEXTT	R_trans_hexaprenyltranstransferase	Miscellaneous	.	[c] : 1.0 hexdp + 1.0 ipdp --> 1.0 hepdp + 1.0 ppi
R_ICHORS	R_isochorismate_synthase	Miscellaneous	.	[c] : 1.0 chor <==> 1.0 ichor
R_2S6HCCi	R_2_succinyl_6_hydroxy_2_4_cyclohexadiene_1_carboxylate_	Miscellaneous	.	[c] : 1.0 akg + 1.0 h + 1.0 ichor --> 1.0 2shchc + 1.0 co2 + 1.0 pyr
R_SUCBZS	R_O_succinylbenzoate_CoA_synthase	Miscellaneous	.	[c] : 1.0 2shchc --> 1.0 h2o + 1.0 sucbz
R_SUCBZL	R_o_succinylbenzoate_CoA_ligase	Miscellaneous	.	[c] : 1.0 atp + 1.0 coa + 1.0 sucbz --> 1.0 amp + 1.0 ppi + 1.0 sbzcoa
R_NPHS	R_naphthoate_synthase	Miscellaneous	.	[c] : 1.0 sbzcoa --> 1.0 coa + 1.0 dhna
R_DHNAOT7	R_1_4_dihydroxy_2_naphthoate_octaprenyltransferase	Miscellaneous	.	[c] : 1.0 dhna + 1.0 hepdp + 1.0 nad --> 1.0 2dmmq7 + 1.0 co2 + 1.0 nadh + 1.0 ppi
R_AMMQT7	R_S_adenosylmethione2_demthylmenaquinone_methyltransfer	Miscellaneous	.	[c] : 1.0 2dmmq7 + 1.0 amet + 1.0 nadph --> 1.0 ahcys + 1.0 mql7 + 1.0 nadp
R_H2CO3D2	carboxylicacidddissociation	Miscellaneous	.	[c] : h + hco3 <==> h2co3
R_MECDPDH	2C-methyl-D-erythritol2,4cyclodiphosphatedehydratase	Miscellaneous	1.17.4.3	[c] : 2mecdp + h --> h2mb4p + h2o
R_CLPNS2_CT	R_cardiolipin_synthase	Miscellaneous	2.7.8.-	[c] : 2.0 pgly_CT --> 1.0 cdlp_CT + 1.0 glyc
R_UPP3S	uroporphyrinogen-IIIsynthase	Porphyrin and chlorophyll metabolism	4.2.1.75	[c] : hmbil --> h2o + uppg3
R_ADSL2r	adenylosuccinatelyase	Purine Metabolism	4.3.2.2	[c] : 25aics <==> aicar + fum
R_ADSL1r	adenylsuccinatelyase	Purine Metabolism	4.3.2.2	[c] : dcamp <==> amp + fum
R_ADSL2	adenylosuccinatelyase	Purine Metabolism	4.3.2.2	[c] : 25aics --> aicar + fum
R_ADSL1	adenylosuccinatelyase	Purine Metabolism	4.3.2.2	[c] : dcamp --> amp + fum
R_GMPS	GMPsynthase	Purine Metabolism	6.3.4.1	[c] : atp + nh4 + xmp --> amp + gmp + 2 h + ppi
R_CYTK2	cytidylatekinase(dCMP)	Pyrimidine Metabolism	2.7.4.14	[c] : atp + dcmp <==> adp + dcdp
R_UMPK5	UMPkinase(dATP)	Pyrimidine Metabolism	2.7.4.14	[c] : datp + ump <==> dadp + udp
R_CYTK9	cytidylatekinase(CMP,dCTP)	Pyrimidine Metabolism	2.7.4.14	[c] : cmp + dctp <==> cdp + dcdp
R_CYTK8	cytidylatekinase(CMP,dATP)	Pyrimidine Metabolism	2.7.4.14	[c] : cmp + datp <==> cdp + dadp
R_CYTK5	cytidylatekinase(dCMP)	Pyrimidine Metabolism	2.7.4.14	[c] : ctp + dcmp <==> cdp + dcdp
R_CYTK7	cytidylatekinase(CMP,UTP)	Pyrimidine Metabolism	2.7.4.14	[c] : cmp + utp <==> cdp + udp
R_CYTK6	cytidylatekinase(CMP,CTP)	Pyrimidine Metabolism	2.7.4.14	[c] : cmp + ctp <==> 2 cdp
R_CYTK1	cytidylatekinase(CMP)	Pyrimidine Metabolism	2.7.4.14	[c] : atp + cmp <==> adp + cdp
R_UMPK3	UMPkinase(UTP)	Pyrimidine Metabolism	2.7.4.14	[c] : ump + utp <==> 2 udp
R_UMPK2	UMPkinase(CTP)	Pyrimidine Metabolism	2.7.4.14	[c] : ctp + ump <==> cdp + udp
R_UMPK7	UMPkinase(dGTP)	Pyrimidine Metabolism	2.7.4.14	[c] : dgtp + ump <==> dgdp + udp
R_UMPK6	UMPkinase(dCTP)	Pyrimidine Metabolism	2.7.4.14	[c] : dctp + ump <==> dcdp + udp
R_UMPK4	UMPkinase(GTP)	Pyrimidine Metabolism	2.7.4.14	[c] : gtp + ump <==> gdp + udp
R_CYTK11	cytidylatekinase(dCMP,dGTP)	Pyrimidine Metabolism	2.7.4.14	[c] : dcmp + dgtp <==> dcdp + dgdp
R_CYTK10	cytidylatekinase(CMP,dGTP)	Pyrimidine Metabolism	2.7.4.14	[c] : cmp + dgtp <==> cdp + dgdp
R_CYTK13	cytidylatekinase(dCMP,dATP)	Pyrimidine Metabolism	2.7.4.14	[c] : datp + dcmp <==> dadp + dcdp
R_CYTK12	cytidylatekinase(dCMP,dCTP)	Pyrimidine Metabolism	2.7.4.14	[c] : dcmp + dctp <==> 2 dcdp
R_CYTK14	cytidylatekinase(dCMP,UTP)	Pyrimidine Metabolism	2.7.4.14	[c] : dcmp + utp <==> dcdp + udp
R_UMPK	UMPkinase	Pyrimidine Metabolism	2.7.4.14	[c] : atp + ump <==> adp + udp
R_AP4AH1	Ap4Ahydrolase,asymmetrically	Pyrimidine Metabolism	3.6.1.17	[c] : ap4a + h2o --> amp + atp + 2 h
R_CBPS	carbamoyl-phosphatesynthase(glutamine-hydrolysing)	Pyrimidine Metabolism	6.3.5.5	[c] : 2 atp + gln-L + h2o + hco3 --> 2 adp + cbp + glu-L + 2 h + pi
R_SIAASE	sialidase	Sphingoglycolipid Metabolism	3.2.1.18	[c] : 2 h2o + s2l2n2m2mn --> 2 acnam + l2n2m2mn
R_H2Ot	H2Otransportviadiffusion	Transport, Extracellular	.	h2o[e] <==> h2o[c]
R_CYSt2r		Transport, Extracellular		cys-L[e] + h[e] <==> cys-L[c] + h[c]
R_DOPABMO	dopaminebeta-monooxygenase	Tyrosine metabolism	1.14.17.1	[c] : ascb-L + dopa + o2 --> dhdascb + h2o + nrpphr
R_OIVD2	R_2_oxoisovalerate_dehydrogenase__acylating_3_methyl_2_o	Valine, Leucine, and Isoleucine Biosyn	1.2.4.4	[c] : 1.0 3mob + 1.0 coa + 1.0 nad --> 1.0 co2 + 1.0 ibcoa + 1.0 nadh
R_OIVD3	R_2_oxoisovalerate_dehydrogenase__acylating_3_methyl_2_o	Valine, Leucine, and Isoleucine Biosyn	1.2.4.4	[c] : 1.0 3mop + 1.0 coa + 1.0 nad --> 1.0 2mbcoa + 1.0 co2 + 1.0 nadh

Appendix C: Predicted Essential Reactions in the Model

REACTION IDs	ENZYME NAME	PATHWAY	EC NUMBER	GENE IDs	REACTION
R_biomass_target	Biomass Rxn	Biomass Objective	.		[c] : 0.257980584 ala-L + 0.176597196 arg-L + 0.218152121 asn-L + 0.230278549 asp-L + 0.0
R_G3POA_CT	R_glycerol_3_phosphate_O_acyltransfer	.	.		[c] : glyc3p + 0.051 dcacoa + 0.022 trdacoa + 0.023 fa1coa + 0.0092 tdcoa + 0.022 ttdcecoa +
R_LYSLG_CT	R_lysylphosphatidylglycerol_synthesis	.	.		[c] : atp + lys-L + pgly_CT --> amp + h + lysylpgly_CT + ppi
R_UGT_CT	R_UDP_glucosyltransferase__diglucosyl	.	.		[c] : 12dgr_CT + 2.0 udpg --> d12dg_CT + 2.0 h + 2.0 udp
R_UGT1_CT	R_UDP_glucosyltransferase__monoglucc	.	.		[c] : 12dgr_CT + udpg --> h + m12dg_CT + udp
R_UGT2_CT	R_UDP_glucosyltransferase__triglucosyl	.	.		[c] : 12dgr_CT + 3.0 udpg --> 3.0 h + t12dg_CT + 3.0 udp
R_AGPATr_CT	R_1_acylglycerol_3_phosphate_O_acylt	.	2.3.1.51	Chro.80165	[c] : 1ag3p_CT + 0.051 dcacoa + 0.022 trdacoa + 0.023 fa1coa + 0.0092 tdcoa + 0.022 ttdcecc
R_PHCYT_CT	R_phosphatidate_cytidylyltransferase	.	2.7.7.41	Chro.70059 o	[c] : 12dag3p_CT + ctp + h --> cdpdag_CT + ppi
R_CLPNS2_CT	R_cardiolipin_synthase	.	2.7.8.-		[c] : 2.0 pgly_CT --> cdlp_CT + glyc
R_CDPDSP_CT	R_CDPdiacylglycerol_serine_O_phosphat	.	2.7.8.8	Chro.70250	[c] : cdpdag_CT + ser-L --> cmp + h + ps_CT
R_PSDC_CT	R_phosphatidylserine_decarboxylase	.	4.1.1.65	Chro.30247	[c] : ps_CT --> co2 + psetha_CT
R_P5CD	_1-pyrroline-5-carboxylatedehydrogenas	Arginine and Proline Metabolism	1.5.1.12	Chro.60426 o	[c] : 1pyr5c + 2 h2o + nad --> glu-L + h + nadh
R_PRO1x	prolineoxidase(L-proline,NAD)	Arginine and Proline Metabolism	1.5.1.2	Chro.60426	[c] : nad + pro-L --> 1pyr5c + 2 h + nadh
R_KAS12	R_b_ketoacyl_synthetase__Anteiso_C17	Fatty Acid Biosynthsis	2.3.1.41		[c] : 2mbcoa + 17.0 h + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + fa12 + 5.0 h2o + 12
R_KAS100iso	R_b_ketoacyl_synthetase__branched(iso	Fatty Acid Biosynthsis	2.3.1.41		[c] : 8.0 h + ibcoa + 3.0 malcoa + 6.0 nadph --> 3.0 co2 + 4.0 coa + dca + 2.0 h2o + 6.0 nadp
R_KAS130iso	R_b_ketoacyl_synthetase__branched(iso	Fatty Acid Biosynthsis	2.3.1.41		[c] : 11.0 h + ivcoa + 4.0 malcoa + 8.0 nadph --> 4.0 co2 + 5.0 coa + trdca + 3.0 h2o + 8.0 na
R_KAS1	R_b_ketoacyl_synthetase__Iso_C140	Fatty Acid Biosynthsis	2.3.1.41		[c] : 14.0 h + ibcoa + 5.0 malcoa + 10.0 nadph --> 5.0 co2 + 6.0 coa + fa1 + 4.0 h2o + 10.0 n
R_KAS6	R_b_ketoacyl_synthetase__Iso_C160	Fatty Acid Biosynthsis	2.3.1.41		[c] : 17.0 h + ibcoa + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + fa6 + 5.0 h2o + 12.0 n
R_KAS180iso	R_b_ketoacyl_synthetase__Iso_C180_	Fatty Acid Biosynthsis	2.3.1.41		[c] : 20.0 h + ibcoa + 7.0 malcoa + 14.0 nadph --> 7.0 co2 + 8.0 coa + ocdcaiso + 6.0 h2o + 1
R_KAS7	R_b_ketoacyl_synthetase__n_C161	Fatty Acid Biosynthsis	2.3.1.41		[c] : accoa + 19.0 h + 7.0 malcoa + 13.0 nadph --> 7.0 co2 + 8.0 coa + 6.0 h2o + hdcea + 13.
R_KAS8	R_b_ketoacyl_synthetase__palmitate	Fatty Acid Biosynthsis	2.3.1.41		[c] : accoa + 20.0 h + 7.0 malcoa + 14.0 nadph --> 7.0 co2 + 8.0 coa + 6.0 h2o + hdca + 14.0
R_KAS2	R_b_ketoacyl_synthetase__n_C140	Fatty Acid Biosynthsis	2.3.1.41		[c] : accoa + 17.0 h + 6.0 malcoa + 12.0 nadph --> 6.0 co2 + 7.0 coa + 5.0 h2o + 12.0 nadp +
R_FACOAL170_anteiso	R_fatty_acid__CoA_ligase__anteiso_C17	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + fa12 <==> amp + fa12coa + ppi
R_FACOAL100	R_fatty_acid__CoA_ligase__Iso_C100	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + dca <==> amp + dcacoa + ppi
R_FACOAL130	R_fatty_acid__CoA_ligase__Iso_C130	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + trdca <==> amp + trdacoa + ppi
R_FACOAL140_ISO	R_fatty_acid__CoA_ligase__Iso_C140	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + fa1 <==> amp + fa1coa + ppi
R_FACOAL160_ISO	R_fatty_acid__CoA_ligase__Iso_C160	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + fa6 <==> amp + fa6coa + ppi
R_FACOAL180_ISO	R_fatty_acid__CoA_ligase__Iso_C180	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + ocdcaiso <==> amp + ppi + strcoaiso
R_FACOAL161	fatty-acid--CoAligase(hexadecenoate)	Fatty Acid Biosynthsis	6.2.1.3	Chro.50052 o	[c] : atp + coa + hdcea <==> amp + hdcoa + ppi
R_GLNS	glutaminesynthetase	Glutamate metabolism	6.3.1.2	Chro.60524	[c] : atp + glu-L + nh4 --> adp + gln-L + h + pi
R_G3PD1ir	glycerol-3-phosphatedehydrogenase(NA	Glycerolipid Metabolism	1.1.1.8	Chro.20028	[c] : dhap + h + nadh --> glyc3p + nad
R_CDGPT_CT	R_CDPdiacylglycerolsn_glycerol_3_phos	Glycerophospholipid Metabolism	2.7.8.5		[c] : cdpdag_CT + glyc3p --> cmp + h + pglyp_CT
R_PGPPH_CT	R_Phosphatidylglycerophosphate_phosp	Glycerophospholipid Metabolism	3.1.3.27		[c] : h2o + pglyp_CT --> pgly_CT + pi
R_PAP_CT	R_phosphatidic_acid_phosphatase	Glycerophospholipid Metabolism	3.1.3.4		[c] : 12dag3p_CT + h2o --> 12dgr_CT + pi
R_GAPD	glyceraldehyde-3-phosphatedehydrogen	Glycolysis/Gluconeogenesis	1.2.1.12	Chro.60434 o	[c] : g3p + nad + pi <==> 13dpg + h + nadh
R_PYK	pyruvatekinase	Glycolysis/Gluconeogenesis	2.7.1.40	Chro.10234	[c] : adp + h + pep --> atp + pyr
R_FBA	fructose-bisphosphatealdolase	Glycolysis/Gluconeogenesis	4.1.2.13	Chro.10335	[c] : fdp <==> dhap + g3p
R_ENO	enolase	Glycolysis/Gluconeogenesis	4.2.1.11	Chro.50184	[c] : 2pg <==> h2o + pep
R_PGM	phosphoglyceratemutase	Glycolysis/Gluconeogenesis	5.4.2.1	Chro.10196 o	[c] : 2pg <==> 3pg
R_NADK	NADkinase	NAD Metabolism	2.7.1.23	Chro.80231	[c] : atp + nad --> adp + h + nadp
R_RNDR4	ribonucleoside-diphosphatereductase(UD	Purine Metabolism	1.17.4.1	Chro.60090 o	[c] : trdrd + udp --> dudp + h2o + trdox
R_ADNK2	adenosinekinase	Purine Metabolism	2.7.1.20	Chro.20322	[c] : adn + gtp --> adp + gmp + h
R_NDPK4	nucleoside-diphosphatekinase(ATP:dTDP	Purine Metabolism	2.7.4.6	Chro.40275 o	[c] : atp + dtdp <==> adp + dttp
R_GK1	guanylatekinase(GMP:ATP)	Purine Metabolism	2.7.4.8	Chro.70250	[c] : atp + gmp <==> adp + gdp
R_NTD7	5'-nucleotidase(AMP)	Purine Metabolism	3.1.3.5	Chro.50026	[c] : amp + h2o --> adn + pi
R_NTD5	5'-nucleotidase(dTMP)	Purine Metabolism	3.1.3.5	Chro.50026	[c] : dtmp + h2o --> pi + thymd
R_RNDR2	ribonucleoside-diphosphatereductase(GD	Pyrimidine Metabolism	1.17.4.1	Chro.60090 o	[c] : gdp + trdrd --> dgdp + h2o + trdox
R_RNDR1	ribonucleoside-diphosphatereductase(AD	Pyrimidine Metabolism	1.17.4.1	Chro.60090 o	[c] : adp + trdrd --> dadp + h2o + trdox
R_RNDR3	ribonucleoside-diphosphatereductase(CD	Pyrimidine Metabolism	1.17.4.1	Chro.60090 o	[c] : cdp + trdrd --> dcdp + h2o + trdox
R_TRDR	thioredoxinreductase(NADPH)	Pyrimidine Metabolism	1.8.1.9	Chro.20464	[c] : h + nadph + trdox --> nadp + trdrd
R_DTMPK	dTMPkinase	Pyrimidine Metabolism	2.7.4.9	Chro.50490	[c] : atp + dtmp <==> adp + dtdp
R_DCMPDA	dCMPdeaminase	Pyrimidine Metabolism	3.5.4.12	Chro.20294	[c] : dcmp + h + h2o <==> dump + nh4

Appendix D: Optimization result of oocyst and sporozoite stage data with nodel *i*NV213

Gene IDs	EC Numbers	Enzyme	Pathway	Reaction
Reaction present in oocyst stage only				
Chro.40493	2.7.1.107	R_diacylglycerol_kinase	.	[c] : 12dgr_CT + atp --> 12dag3p_CT + adp + h
Chro.60435	2.7.1.1	hexokinase	Glycolysis/Gluconeogenesis	[c] : atp + glc-D --> adp + h + g6p
Chro.40330	1.2.1.31	L-aminoadipate-semialdehydedehydrogenase(NADPH)	Lysine Biosynthesis	[c] : L2aadp + atp + h + nadph --> L2aadp6sa + amp + nadp + ppi
Chro.40330	1.2.1.31	L-aminoadipate-semialdehydedehydrogenase(NADH)	Lysine Biosynthesis	[c] : L2aadp6sa + h2o + nad --> L2aadp + 2 h + nadh
Chro.40159	3.6.1.1	inorganicdiphosphatase	Oxidative Phosphorylation	[c] : h2o + ppi --> h + 2 pi
Chro.50026	3.1.3.5	5'-nucleotidase(UMP)	Purine Metabolism	[c] : h2o + ump --> pi + uri
Chro.50026	3.1.3.5	5'-nucleotidase(AMP)	Purine Metabolism	[c] : amp + h2o --> adn + pi
Chro.20322	2.7.1.20	adenosinekinase	Purine Metabolism	[c] : adn + atp --> adp + amp + h
Chro.50398 o	2.7.1.21	thymidinekinase(ATP:thymidine)	Pyrimidine Metabolism	[c] : atp + thymd --> adp + dtmp + h
Chro.10216 o	2.7.1.48	uridinekinase(ATP:Uridine)	Pyrimidine Metabolism	[c] : atp + uri --> adp + h + ump
Chro.10216 o	2.7.1.48	uridinekinase(GTP:Uridine)	Pyrimidine Metabolism	[c] : gtp + uri --> gdp + h + ump
Chro.50389	4.1.1.31	phosphoenolpyruvatecarboxylase	Pyruvate Metabolism	[c] : co2 + h2o + pep --> h + oaa + pi
Chro.50314	1.1.1.38	malicenzyme(NAD)	Pyruvate Metabolism	[c] : mal-L + nad --> co2 + nadh + pyr
Chro.50314	1.1.1.40	malicenzyme(NADP)	Pyruvate Metabolism	[c] : mal-L + nadp --> co2 + nadph + pyr
Reactions presnt in sporozoite stage only				
	.	Glucokinase	Glycolysis/Gluconeogenesis	[c] : atp + glc-D --> adp + g6p-B + h
Chro.60194	3.6.1.6	nucleoside-diphosphatase(GDP)	Nucleotide Salvage Pathway	[c] : gdp + h2o --> gmp + h + pi
Chro.20336	5.3.1.9	Glucose-6-phosphateisomerase	Pentose Phosphate Pathway	[c] : g6p <==> g6p-B
Chro.60194	3.6.1.6	nucleoside-diphosphatase(dCDP)	Purine Metabolism	[c] : dcdp + h2o --> dcmp + h + pi
Chro.60194	3.6.1.6	nucleoside-diphosphatase(dUDP)	Purine Metabolism	[c] : dudp + h2o --> dump + h + pi
Chro.60194	3.6.1.6	nucleoside-diphosphatase(UDP)	Purine Metabolism	[c] : h2o + udp --> h + pi + ump
	2.7.4.14	cytidylatekinase(dCMP)	Pyrimidine Metabolism	[c] : ctp + dcmp <==> cdp + dcdp
Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Starch and Sucrose Metabolism	[c] : g6p-A <==> g6p-B
Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Starch and Sucrose Metabolism	[c] : g6p-A <==> f6p
Chro.20336	5.3.1.9	glucose-6-phosphateisomerase	Starch and Sucrose Metabolism	[c] : g6p-B <==> f6p
Reactions commonly present in both the stages				
	.	phosphoglyceratekinase	Carbon Fixation	[c] : 3pg + atp <==> 13dpg + adp
	.	triose-phosphateisomerase	Fructose and Mannose Metabolism	[c] : dhap <==> g3p
	.	phosphoglyceratekinase	Glycolysis/Gluconeogenesis	[c] : 3pg + atp <==> 13dpg + adp
	.	pyruvatedecarboxylase	Glycolysis/Gluconeogenesis	[c] : h + pyr --> acald + co2
	.	enolase	Glycolysis/Gluconeogenesis	[c] : 2pg <==> h2o + pep
	.	phosphoglyceratemutase	Glycolysis/Gluconeogenesis	[c] : 2pg <==> 3pg
	.	glucose-6-phosphateisomerase	Glycolysis/Gluconeogenesis	[c] : g6p <==> f6p
	.	glyceraldehyde-3-phosphatedehydrogenase	Glycolysis/Gluconeogenesis	[c] : g3p + nad + pi <==> 13dpg + h + nadh
	.	pyruvatekinase	Glycolysis/Gluconeogenesis	[c] : adp + h + pep --> atp + pyr
	.	alcoholdehydrogenase(ethanol)	Glycolysis/Gluconeogenesis	[c] : etoh + nad <==> acald + h + nadh
	.	fructose-bisphosphatealdolase	Glycolysis/Gluconeogenesis	[c] : fdp <==> dhap + g3p
	.	phosphofructokinase,glycosome	Glycolysis/Gluconeogenesis	[c] : atp + f6p --> adp + fdp + h
	.	adenylosuccinatelyase	IMP Biosynthesis	[c] : 25aics --> aicar + fum
	.	adenylosuccinatelyase	Nucleotides	[c] : dcamp --> amp + fum
	.	phosphofructokinase	Pentose Phosphate Pathway	[c] : atp + f6p --> adp + fdp + h
	.	adenylosuccinatelyase	Purine Metabolism	[c] : 25aics <==> aicar + fum
	.	nucleoside-diphosphatekinase(ATP:dADP)	Purine Metabolism	[c] : atp + dadp <==> adp + datp
	.	nucleoside-diphosphatekinase(ATP:dCDP)	Purine Metabolism	[c] : atp + dcdp <==> adp + dctp
	.	nucleoside-diphosphatekinase(ATP:dGDP)	Purine Metabolism	[c] : atp + dgdp <==> adp + dgtp
	.	nucleoside-diphosphatekinase(ATP:CDP)	Purine Metabolism	[c] : atp + cdp <==> adp + ctp
	.	nucleoside-diphosphatekinase(ATP:UDP)	Purine Metabolism	[c] : atp + udp <==> adp + utp
	.	adenylsuccinatelyase	Purine Metabolism	[c] : dcamp <==> amp + fum
	.	nucleoside-diphosphatekinase(ATP:GDP)	Purine Metabolism	[c] : atp + gdp <==> adp + gtp
	.	guanylatekinase(GMP:ATP)	Purine Metabolism	[c] : atp + gmp <==> adp + gdp
	.	UMPkinase(CTP)	Pyrimidine Metabolism	[c] : ctp + ump <==> cdp + udp
	.	UMPkinase(dGTP)	Pyrimidine Metabolism	[c] : dgtp + ump <==> dgdp + udp
	.	UMPkinase	Pyrimidine Metabolism	[c] : atp + ump <==> adp + udp
	.	UMPkinase(dCTP)	Pyrimidine Metabolism	[c] : dctp + ump <==> dcdp + udp
	.	cytidylatekinase(dCMP)	Pyrimidine Metabolism	[c] : atp + dcmp <==> adp + dcdp
	.	cytidylatekinase(CMP,dCTP)	Pyrimidine Metabolism	[c] : cmp + dctp <==> cdp + dcdp
	.	cytidylatekinase(CMP,dATP)	Pyrimidine Metabolism	[c] : cmp + datp <==> cdp + dadp
	.	cytidylatekinase(CMP,UTP)	Pyrimidine Metabolism	[c] : cmp + utp <==> cdp + udp
	.	cytidylatekinase(CMP,CTP)	Pyrimidine Metabolism	[c] : cmp + ctp <==> 2 cdp
	.	cytidylatekinase(CMP)	Pyrimidine Metabolism	[c] : atp + cmp <==> adp + cdp
	.	UMPkinase(UTP)	Pyrimidine Metabolism	[c] : ump + utp <==> 2 udp
	.	UMPkinase(dATP)	Pyrimidine Metabolism	[c] : datp + ump <==> dadp + udp
	.	UMPkinase(GTP)	Pyrimidine Metabolism	[c] : gtp + ump <==> gdp + udp
	.	cytidylatekinase(dCMP,dGTP)	Pyrimidine Metabolism	[c] : dcmp + dgtp <==> dcdp + dgdp
	.	cytidylatekinase(CMP,dGTP)	Pyrimidine Metabolism	[c] : cmp + dgtp <==> cdp + dgdp
	.	cytidylatekinase(dCMP,dATP)	Pyrimidine Metabolism	[c] : datp + dcmp <==> dadp + dcdp
	.	cytidylatekinase(dCMP,dCTP)	Pyrimidine Metabolism	[c] : dcmp + dctp <==> 2 dcdp
	.	cytidylatekinase(dCMP,UTP)	Pyrimidine Metabolism	[c] : dcmp + utp <==> dcdp + udp
	.	malatedehydrogenase(otherdirection)	Pyruvate Metabolism	[c] : h + nadh + oaa --> mal-L + nad
	.	L-lactatedehydrogenase	Pyruvate Metabolism	[c] : lac-L + nad <==> h + nadh + pyr
	.	malatedehydrogenase	Pyruvate Metabolism	[c] : mal-L + nad <==> h + nadh + oaa
	.	H2Otransportviadiffusion	Transport, Extracellular	h2o[e] <==> h2o[c]
	.	alcoholdehydrogenase(ethanol),mitochondrial	Tyrosine metabolism	[c] : etoh + nad <==> acald + h + nadh
	.			glc-D[e] <==> glc-D[c]

VITA

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