
This item was submitted to [Loughborough's Research Repository](#) by the author.
Items in Figshare are protected by copyright, with all rights reserved, unless otherwise indicated.

A systems-level study of the transcriptional changes of Dehalococcoides metabolism

PLEASE CITE THE PUBLISHED VERSION

<https://www.grc.org/cellular-systems-biology-conference/2011/>

VERSION

AM (Accepted Manuscript)

LICENCE

CC BY-NC-ND 4.0

REPOSITORY RECORD

Islam, Ahsan, Elizabeth A Edwards, and Radhakrishnan Mahadevan. 2011. "A Systems-level Study of the Transcriptional Changes of Dehalococcoides Metabolism". Loughborough University.
<https://hdl.handle.net/2134/13259099.v1>.

BioZone
Centre for Applied & Environmental Bioengineering Research

Department of Chemical Engineering and Applied Chemistry, University of Toronto, Ontario, Canada



**FACULTY
OF APPLIED
SCIENCE &
ENGINEERING**

The diagram illustrates a groundwater remediation process. At the top, a green area represents the surface with trees. A yellow cylinder labeled "Dehalococcoides containing cylinder" is shown with an arrow pointing down into an "Injection Well". The well is a vertical pipe extending into the "Subsurface" (brown layer) and then into the "Ground water" (blue layer). A downward arrow inside the well indicates the direction of injection. In the groundwater, a red, irregularly shaped "Plume of chlorinated contaminants (PCE, TCE, VC)" is shown. A label "Dehalococcoides" points to a small cluster of black dots within this plume. A white arrow at the bottom points to the right, labeled "Ground water flow direction". The right side of the diagram shows the "Subsurface" and "Ground water" layers meeting at a boundary.

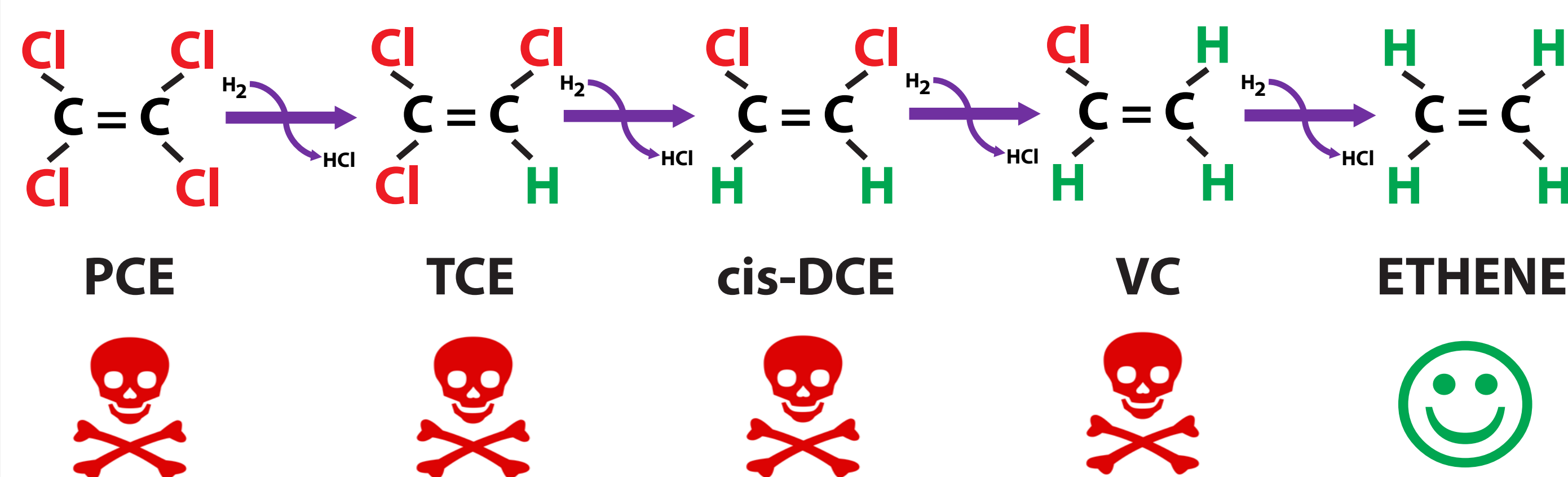


Figure 1 consists of four panels. Panel (a) is a low-magnification transmission electron micrograph (TEM) of a whole spore, showing a dense, granular internal structure and a distinct outer boundary. Panel (b) is a high-magnification TEM of the cell wall, showing a multi-layered structure with arrows pointing to specific layers. Panel (c) is a scanning electron micrograph (SEM) of a spore, showing its oval shape and surface texture. Panel (d) is a TEM of spore fragments, showing the internal structure of the cell wall layers.

Comparative Genomics

Dehalococcoides Pan-Genome

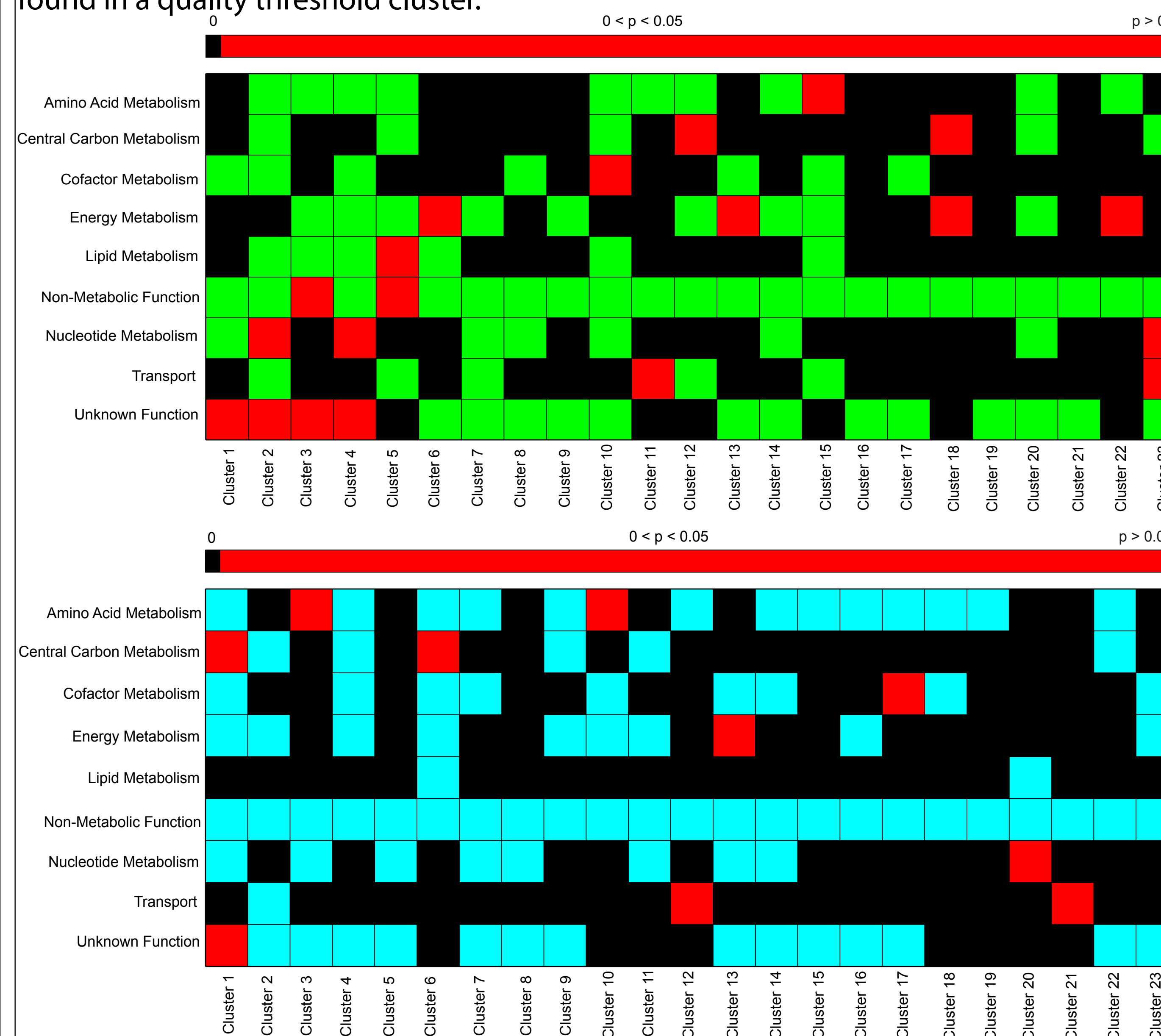
Flux Balance Analysis

***In silico* Pan-Genome-Scale Metabolic Model**

```
graph TD; A[Dehalococcoides Microarray Data] --> B[Remove Duplicate Genes]; B --> C[Mapping Between Dhc Pan-Model and Dhc Array Data]; C --> D[Cluster Array Data Using Quality Threshold Clustering Algorithm]; D --> E[Calculate Hypergeometric Distribution for Genes in All Clusters]; E --> F[Identify Functionally Enriched (p < 0.05) Clusters]; F --> G[Perform Hierarchical Clustering of Functionally Enriched Clusters]; G --> H[Analyze Functionally Enriched Important Clusters]
```

The flowchart illustrates a bioinformatics pipeline for analyzing *Dehalococcoides* microarray data. It begins with the initial data, followed by removing duplicate genes and mapping the data between the Dhc pan-model and the array data. The data is then clustered using a quality threshold algorithm, and a hypergeometric distribution is calculated for all clusters. Functionally enriched clusters (p < 0.05) are identified, and these are further analyzed using hierarchical clustering to identify important clusters.

The top and bottom heat maps show functionally enriched ($p < 0.05$) clusters of strain 195 and strain KB1, respectively. Functional enrichment is determined by calculating the hypergeometric distribution of genes from each model subsystem or functional category found in a quality threshold cluster.



Heatmap visualization showing gene expression data across various conditions. The color scale ranges from 0.0 (blue) to 0.87112516 (red). The y-axis lists genes, and the x-axis lists conditions. Hierarchical clustering is shown on both axes.

Gene List (Y-axis):

- DET1435 (hydrogenase expression protein)
- DET0975 (acetyltransferase, GNAT family)
- DET0372 (phosphatidate cytidyltransferase)
- DET0964 (DNA-specific exonuclease)
- DET0365 (2-methyl-D-erythritol 2,4-cyclophosphate dehydratase)
- DET0417 (L-glutamine transport via ABC system)
- DET0591 (hypothetical protein)
- DET0509 (glucose-6-phosphate isomerase)
- DET0185 (formate dehydrogenase accessory protein)
- DET0776 (methyltransferase GldB)
- DET0473 (ribosomal protein S10)
- DET0838 (phosphoribosylglycinamide synthetase)
- DET0839 (phosphoribosylaminoimidazole carboxylase)
- DET0518 (8-methylthiothiobase-1-phosphate isomerase)
- DET0435 (phosphoribosylpyrophosphate synthetase)
- DET1218 (phosphoserine phosphatase (L-serine))
- DET1224 (cob(I)lam adenosyltransferase)
- DET0418 (L-glutamine transport via ABC system)
- DET1145 (hypothetical protein)
- DET0371 (1-deoxy-D-xylulose-5-phosphate reductoisomerase)
- DET0552 (DNA primase)
- DET0592 (hypothetical protein)
- DET0395 (glycoprotease family protein)
- DET0742 (ribose-phosphate isomerase)
- DET0374 (ribosome recycling factor)

Condition List (X-axis):

- Transition # 1
- Late Stationary # 2
- Late Stationary # 1
- Late Stationary # 3
- ANAS Supernatant # 2
- ANAS Supernatant # 3
- ANAS Supernatant # 1
- Early Stationary # 3
- Early Stationary # 2
- Early Stationary # 1
- Lowell Conc # 3
- Lowell Conc # 2
- Lowell Conc # 1
- HighBIC Conc # 3
- HighBIC Conc # 2
- HighBIC Conc # 1
- Early Exponential # 3
- Early Exponential # 2
- Early Exponential # 1
- Late Exponential # 3
- Late Exponential # 2
- Late Exponential # 1
- Transition # 3
- Transition # 2
- Regular195 # 2
- Regular195 # 1
- Regular195 # 3

This dendrogram shows the hierarchical clustering of a quality threshold cluster of strain 195 genes. The cluster is functionally enriched with genes from nucleotide metabolism and unknown proteins as determined by hypergeometric distribution analysis of the quality threshold clusters. Annotations are color coded according to the model subsystems as depicted in *Dehalococcoides* metabolic network.

0.0 -0.38709477 0.943013

TCEM # 1
TCM # 9
MeOH # 3
MeOH # 4
MeOH # 6
MeOH # 8
MeOH # 1
MeOH # 2
MeOH # 5
TCM # 9
TCM # 2
TCM # 7
Starved (4 d) # 3
TCM # 4
Starved (4 d) # 2
Starved (4 d) # 1
Starved (4 d) # 4
TCM # 6
TCM # 8
VCH # 2
VCH # 3
TCM # 3
TCM # 1
Starved (1 year)
MeOH # 10
MeOH # 9
MeOH # 7
VCH # 10
VCH # 10
Starved (4 d) # 3
DCEM

0.92767456
0.9629823
1.0
-0.18526828
-0.40736596
1.0

KB1_0853 (adenylosuccinate lyase)
KB1_0852 (phosphoribosylaminimidazole carboxylase)
KB1_1165 (niflavin synthase)
KB1_1166 (carnitine-5-phosphoribosylaminimidazole reductase)
KB1_0747 (phosphoglycerate mutase)
KB1_0685 (ribose-5-phosphate isomerase)
KB1_0733 (pyruvate ferredoxin oxidoreductase)
KB1_0718 (pyroglutamate synthase)
KB1_1218 (trigger factor)
KB1_1127 (glutamate synthase)
KB1_1129 (imidazole-glycyl-3-phosphate synthase)
KB1_0730 (pyroglutamate synthase)
KB1_1011 (hypothetical protein)
KB1_1030 (30S ribosomal protein S18)
KB1_0734 (NADH dehydrogenase (ubiquinone))
KB1_1026 (nucleic acid binding protein)
KB1_0520 (50S ribosomal protein L4)
KB1_0522 (50S ribosomal protein L2)
KB1_1028 (pyrrolo-quinoline quinone)
KB1_0547 (50S ribosomal protein L17)

This dendrogram shows the hierarchical clustering of a quality threshold cluster of strain KB1 genes. The cluster is functionally enriched with genes from central carbon metabolism and unknown proteins as determined by hypergeometric distribution analysis of the quality threshold clusters. Annotations are color coded according to the model subsystems as depicted in *Dehalococcoides* metabolic network.

1. Strain 195 seems to transport L-glutamine from the medium as L-glutamine transporters are upregulated during early exponential growth phase and in the autoclaved mixed culture (ANAS) supernatant experiments.

2. All genes in cluster 2 of strain 195 are upregulated with addition of autoclaved mixed culture (ANAS) supernatant.

3. Metabolism of riboflavin - a biomass precursor - plays important role in strain KB1 metabolism.

4. Genes involved in ribose metabolism including riboflavin synthesis, purine metabolism, and pentose phosphate pathway in both strains are co-regulated.

1. Islam, M. A. et al. 2010. PLoS Comput Biol 2010 Aug 19; 6(8): e1000887.
2. Johnson, D. R. et al. 2009. FEMS Microbiol Lett. 294(2): 198-206.
3. Johnson, D. R. et al. 2008. Appl Environ Microbiol. 74(9): 2864-2872.
4. Alison S. Waller. 2009. PhD Thesis, University of Toronto.
5. Heyer, L. J. et al. 1999. Genome Research. 9: 1106-1115.

1. Genome Canada and Ontario Genomics Institute.
2. Ontario Graduate Scholarship.
3. SERDP, University of Toronto, Natural Sciences and Engineering Research Council (NSERC), Canada

Reaction	Gene
----------	------

Reaction	Gene
----------	------

10

Amino Acid Metabolis

Central Carbon Metabo

Energy Metabolism

Lipid Metabolism

Lipid Metabolism

Nucleotide Metabolism

Transport

Exchange

Exchange

This cytoscape network represents the pan-genome-scale reconstructed metabolic network of *Dehalococcoides*. Genes are represented by circles and reactions are represented by round rectangles. Both genes and reactions are categorized according to the model subsystems and represented by different colors. Edges in the network are depicting gene-protein-reaction associations. Genes and reactions involved in energy metabolism such as, reductive dehalogenases, ferredoxin hydrogenases, and NADH dehydrogenases are clustered together as represented by orange color.