

Genome Sequence of an Obligate Intracellular Pathogen of Humans: *Chlamydia trachomatis*

Stephens, R.S., Kalman, S., Lammel, C., Fan, J., Marathe, R., Aravind, L., Mitchell, W., Olinger, L., Tatusov, R., Zhao, Q., Koonin, E. V., Davis, R.W. (1998) *Genome sequence of an obligate intracellular pathogen of humans: Chlamydia trachomatis*. *Science* 282: 754-759. [10.1126/science.282.5389.754](https://doi.org/10.1126/science.282.5389.754).

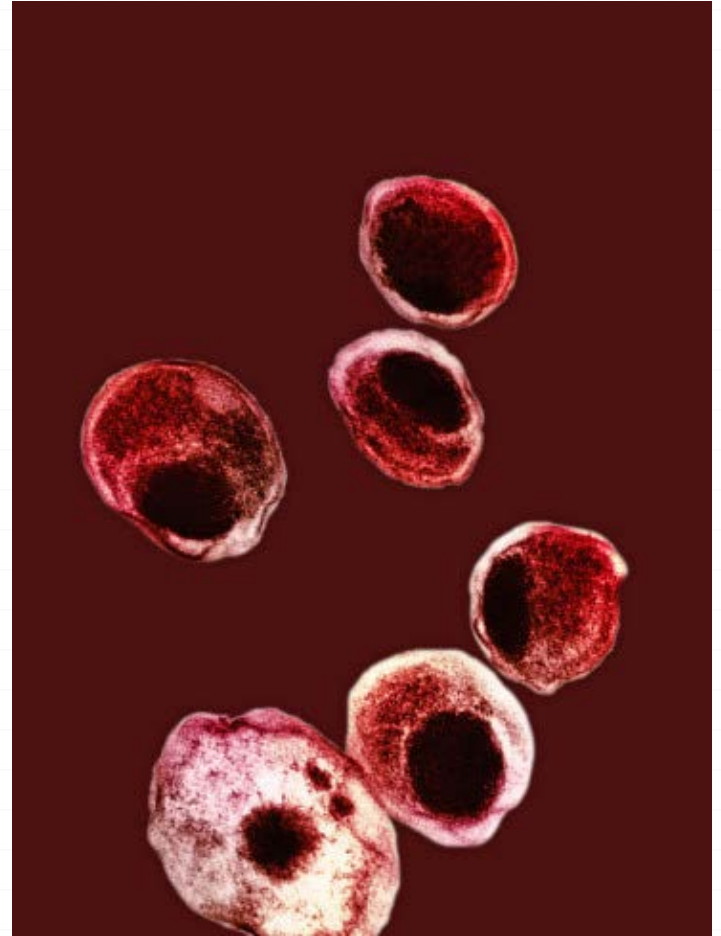
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Loyola Marymount University
November 12, 2013

Outline

- *Chlamydia trachomatis* causes several disease in humans
- *C. trachomatis* strain D/UW-3/CX has a 1,042,519 bp chromosome, 7493 bp plasmid, & 894 protein-coding genes
- Gene expression pathways involved in developmental stage differentiation
- Not all aerobic respiration pathways are complete
- Nutrient uptake across the vacuole is unclear
- Nine paralogous genes were identified encoding Pmp membrane proteins and two proteases
- HKD Superfamily may be crucial in understanding host cell phospholipid modification
- Chlamydial genes originate from horizontal gene transfer

***Chlamydia trachomatis* causes several disease in humans**

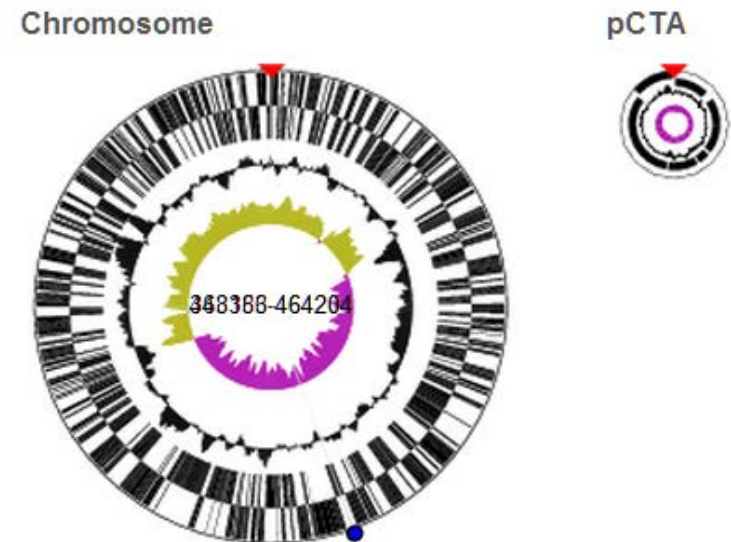
- Trachoma
 - Primary cause of preventable blindness
- Genital tract infections
 - Most common
- Pelvic inflammatory disease, ectopic pregnancy, chronic pelvic pain, epididymitis, infant pneumonia
- May increase risk of HIV infection



http://www.allposters.com/-sp/The-Bacteria-Chlamydia-Trachomatis-Posters_i9006245_.htm

***C. trachomatis* strain D/UW-3/CX has a 1,042,519 bp chromosome and a 7493 bp plasmid**

- o EBs isolated from host cells by sonication on ice
- o Remove extracellular DNA and purify with Renografin
- o Hydrodynamic shearing
- o Sequencing reactions with dye-labeled primers
- o Assemble sequences with Phrap and Phred software



http://bacteria.ensembl.org/chlamydia_trachomatis_a_har_13/Location/Genome

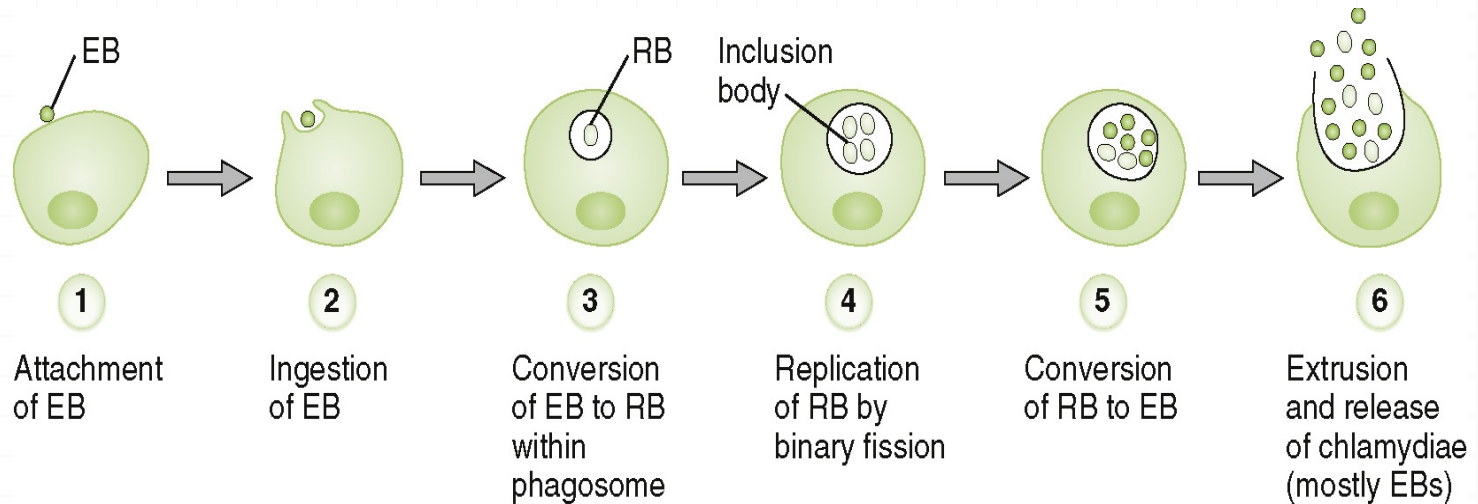
Legend:

■ Gene Density ▲ GC content ▬ GC skew ▲ Origin

894 protein-coding genes were found and functional assignments made for 604 of them

- PEPDATA, FRAMES – translate genome
- BLASTP – find ORFs
- BLASTP-(-mp4-option), CLUSTALW – find start codons
- PSI-BLAST – find homologous protein sequences
- EMOTIF – find sequence motifs
- COGNITOR – find Clusters of Orthologous Groups

C. trachomatis genome codes for σ factors that initiate developmental stage changes



<https://www.inkling.com/read/rapid-review-microbiology-and-immunology-rosenthal-tan-3rd/chapter-17/chlamydiae-and-zoonotic>

o σ Factors- σ^{28} and σ^{54}

o σ Factor regulatory system:

o RsbW-like single domain histidine kinase, two RsbV orthologs, and a RsbU-like protein phosphatase

The DNA Repair, Transcription, and Translation Systems in *C. trachomatis* Are Similar To Those in Other Organisms

- Two predicted helicases Swi/Snf2 family of helicases involved in DNA repair
- Mechanistic similarities in Chlamydiae and eukaryotic chromatin dynamics
 - SET AND SWIB domains
- Translational Machinery
 - Aminoacyl-transfer RNA (tRNA), two identical ribosomal RNA operons, complete set of ribosomal proteins, translation factors, RNA modification enzymes

***C. Trachomatis* Genome Reveals Complete Glycolytic Pathways**

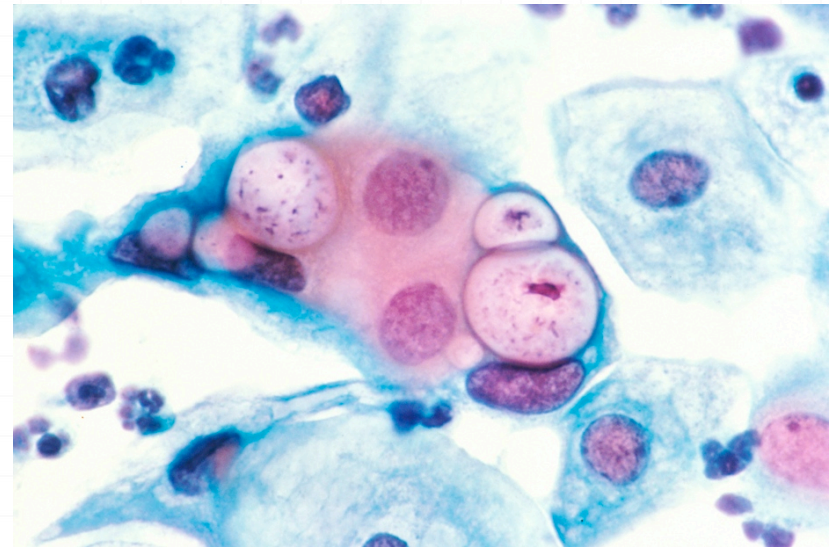
- Central carbon source is likely glutamate
 - Glucose and 2-oxoglutarate play supplementary roles depending on the chlamydial development stage.
- Contains complete glycogen synthesis and degradation system
 - Supports hypothesis of a central role for glucose or glucose derivatives as primary carbon source for some developmental stages.
- Contain an intact glycolytic pathway
 - Exception is fructose-1,6-diphosphate aldolase not being identified.

The TCA Cycle Is Incomplete In Contrast to the Fatty Acid and Phospholipid Synthesis Pathways

- The tricarboxylic acid (TCA) cycle found to be incomplete because certain genes could not be identified.
 - However, the cycle could be fed by an uptake of glutamine or by uptake of 2-oxoglutarate.
- Contains extensive number of genes for enzymes of fatty acid and phospholipid biosynthesis.
 - Suggests that chlamydiae synthesize fatty acids, phosphatidylethanolamine, and phosphatidylglycerol de novo.

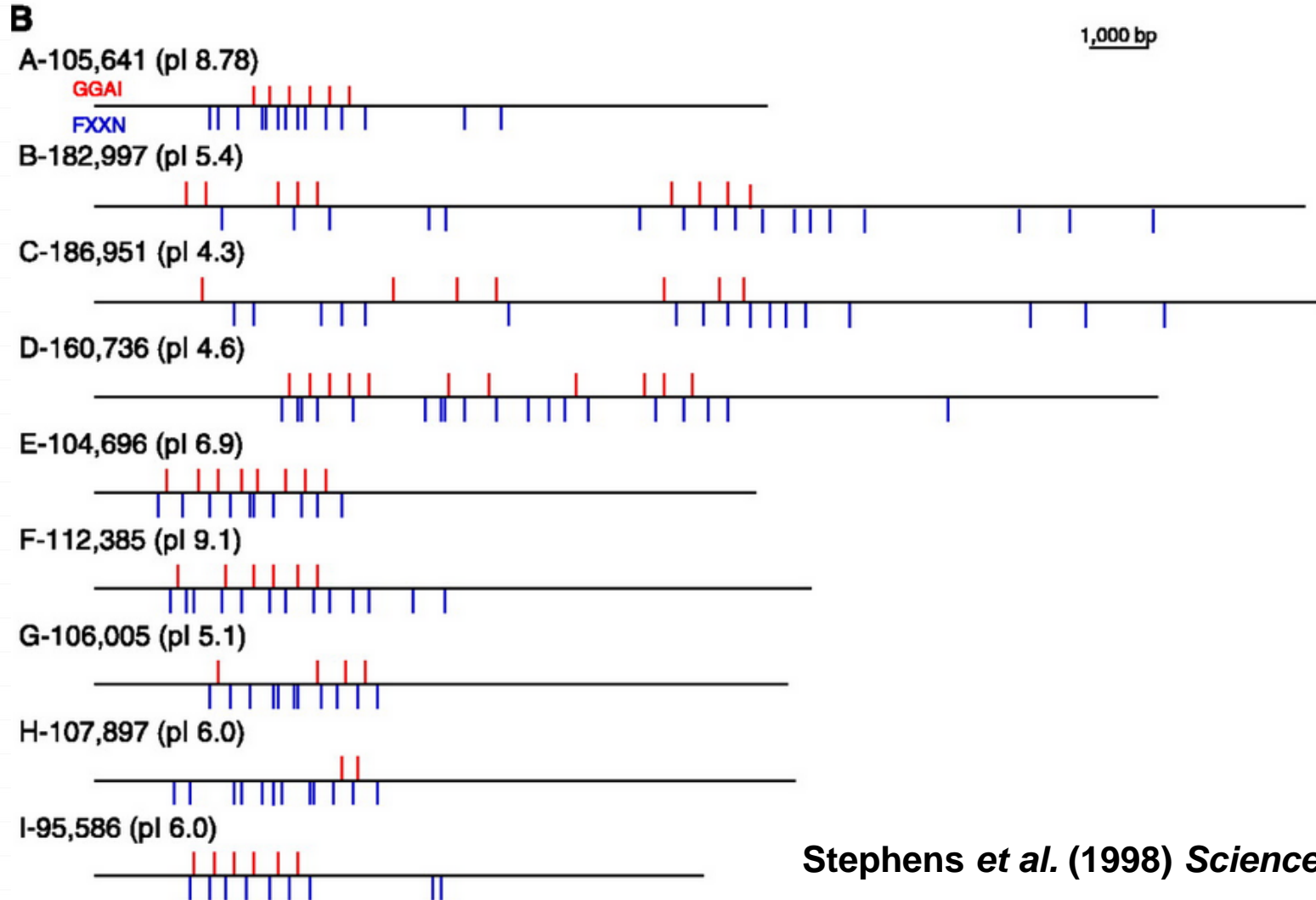
Nutrient Uptake Across the Vacuole is Unclear

- Chlamydia invade eukaryotic cells
 - Grow within an intracellular vacuole, called an inclusion (does not fuse with lysosomes).
- Intracellular vacuolar inclusion is apparently not permeable to small compounds.
 - Process by which chlamydiae obtain required nutrients is unknown.
- Transport operon identified in genome encodes certain proteins associated with vacuole.
 - Examples: TolB, TolQ, and ExbD-like proteins.



National Library of Medicine (2010)

FXXN and GGAI tetrameric motifs found in each of the nine genes



Stephens *et al.* (1998) *Science* 282.

HKD Superfamily may be crucial in understanding host cell phospholipid modification

PLD1.2_Hs_2627323	459	Y	L	W	A	H	H	E	K	L	V	I	I	D	Q	S	V	A	F	V	G	G	I	D	L	A	Y	G	R	486
PLD1.1_Hs_2627323	891	E	L	I	Y	V	H	S	K	L	L	A	I	D	D	N	T	V	I	I	G	S	A	N	I	N	D	R	S	918
Y190_Hp_2313277	162	I	K	K	R	M	H	N	K	L	F	I	V	D	N	F	A	V	I	I	G	G	R	N	I	G	D	N	Y	189
VK04.1_VACCV_335358	108	Y	S	R	V	N	H	A	K	Y	M	V	T	D	-	K	T	A	Y	I	G	T	S	N	W	T	G	N	Y	137
VK04.2_VACCV_335358	320	L	G	G	V	L	H	T	K	F	W	I	S	D	N	T	H	I	Y	L	G	S	A	N	M	D	W	R	S	346
PSS.1_Ec_147389	134	A	L	G	V	L	H	F	K	G	F	I	I	D	D	S	V	L	Y	S	G	A	S	L	N	D	V	Y	L	170
PSS.2_Ec_147389	353	D	D	N	T	Y	H	L	K	G	M	W	V	D	D	K	W	M	L	I	T	G	N	N	L	N	P	R	A	380
CT154.1_Ct	136	G	R	T	L	Q	H	K	K	T	M	L	A	D	F	Q	T	V	V	T	G	S	A	N	Y	T	D	L	S	163
CT154.2_Ct	282	T	E	G	V	L	H	T	K	I	C	C	I	D	N	K	T	L	I	F	G	S	A	N	W	S	G	A	G	309
CT155.1_Ct	119	G	C	S	L	L	H	R	K	T	L	L	I	D	N	N	I	V	V	T	G	T	A	N	Y	T	E	A	S	146
CT155.2_Ct	211	C	E	G	I	L	H	T	K	V	C	C	I	D	S	S	T	L	I	I	G	S	V	N	W	S	R	G	G	238
CT157.1_Ct	195	P	Q	I	C	L	H	K	K	T	T	L	I	D	N	Q	L	T	I	I	G	T	A	N	Y	T	K	S	S	222
CT157.2_Ct	341	P	Q	I	C	L	H	K	K	T	T	L	I	D	N	Q	L	T	I	I	G	T	A	N	Y	T	K	S	S	368
CT158.1_Ct	10	N	Q	A	R	L	H	C	K	N	I	V	V	D	G	S	L	V	I	T	G	S	A	N	F	S	D	A	A	37
CT158.2_Ct	157	E	N	A	L	L	H	C	K	V	G	L	I	D	T	N	L	L	I	T	G	S	A	N	W	T	V	R	G	184
CT084.1_Ct	126	H	R	K	L	M	H	Q	K	T	M	A	I	D	G	E	L	A	W	I	G	S	A	N	F	T	L	A	S	153
CT084.2_Ct	272	T	P	Y	Q	L	H	H	K	F	G	I	F	D	K	K	T	L	I	T	G	S	V	N	W	S	E	N	G	299
CT284.1_Ct	137	N	V	T	E	S	H	T	K	L	S	I	V	D	G	K	Y	I	F	I	G	G	S	N	L	E	D	L	Q	164
CT284.2_Ct	386	A	N	T	Q	L	H	K	K	C	M	L	V	D	D	H	I	L	V	I	G	S	Y	N	F	G	K	K	S	413
Consensus (80%)		H	.	K	.	.	h	.	D	.	.	.	h	h	.	G	s	.	s	h	s	.	.	.	

A majority of Chlamydial genes are a result of horizontal gene transfer.

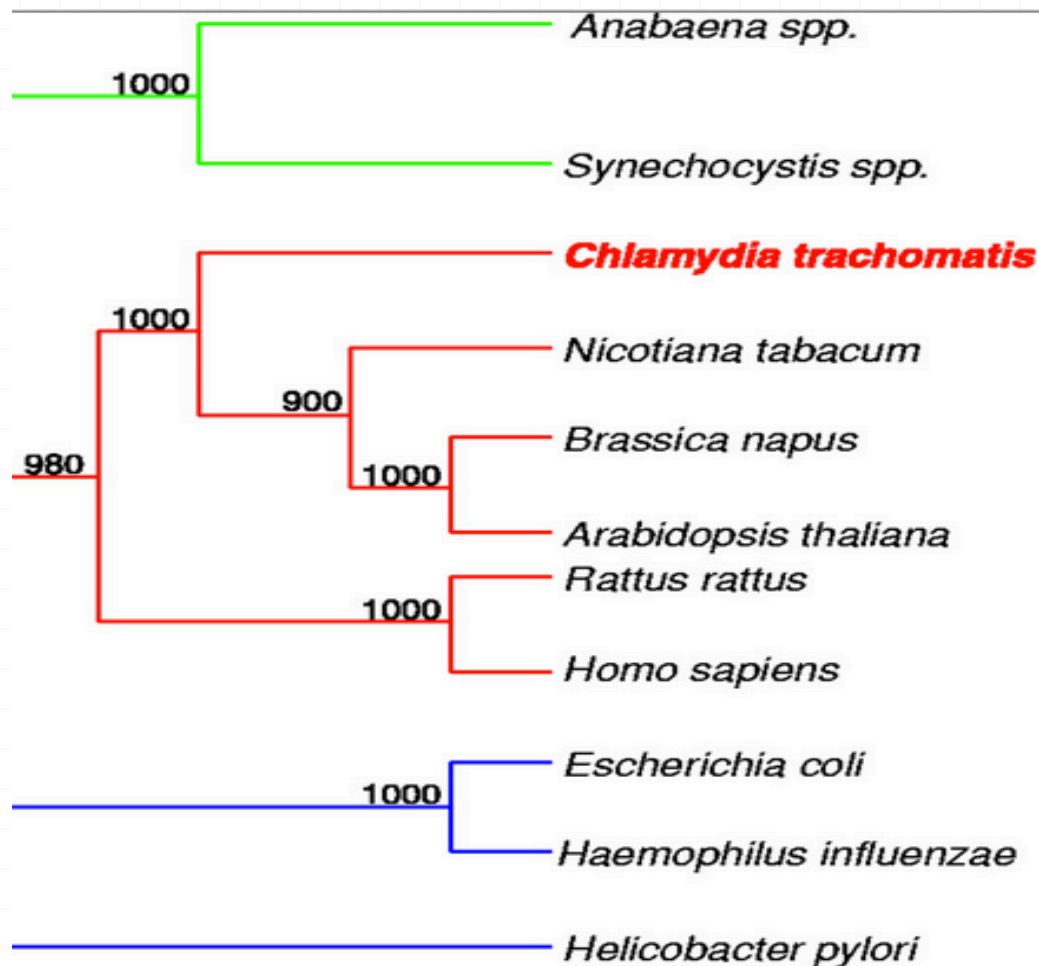
Table 1

Horizontally transferred genes in *Chlamydia trachomatis*.

Chlamydial gene	Support for horizontal transfer
Topoisomerase I, COOH-terminal domain (CT643), and stand-alone SWIB protein (CT460)	The α -helical SWIB domain detected only in eukaryotic chromatin-associated proteins.
SET domain protein (CT737)	SET domain found only in numerous eukaryotic chromatin-associated proteins.
Methionyl-tRNA synthetase (Met-RS) (CT032)	Chlamydial Met-RS groups with eukaryotic ones in phylogenetic analysis. A C2C2 "little finger" domain is conserved in <i>Chlamydia</i> , Archaea, and eukaryotes, to the exclusion of the other bacteria. An accessory, COOH-terminal RNA-binding domain is present in bacterial Met-RS, but not in <i>Chlamydia</i> , Archaea, or eukaryotes.
Pyrophosphate-dependent phosphofructokinase 1 and 2 (CT205, CT207)	Much greater similarity to eukaryotic than to bacterial orthologs, with the exception of the spirochetes.
Glucose-1-phosphate adenylyltransferase (CT489)	Supported by phylogenetic analysis (39); likely chloroplast origin in plants.
Glycogen phosphorylase (CT248)	Supported by phylogenetic analysis (39).
UDP-glucose pyrophosphorylase (CT715)	No easily detectable bacterial homologs.
Adenine nucleotide translocases 1 and 2 (CT495, CT065)	ATP/ADP translocases of this family are detectable only in <i>Rickettsia</i> and in plants.

Stephens *et al.* (1998) *Science* 282.

Tracing the phylogeny of enoyl-acyl carrier protein reductase



MOD for Chlamydia trachomatis Strain A/HAR-13 Is EnsemblBacteria

Chlamydia trachomatis A/HAR-13

Chlamydia trachomatis A/HAR-13

Chlamydia trachomatis A/HAR-13


Provider [European Nucleotide Archive](#) | Taxonomy ID [315277](#)


CTA_0498

Go

e.g. [rplE](#) or [Chromosome:592980-593522](#) or [synthetase](#)

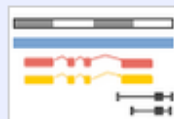
Genome assembly: [GCA_000012125.1](#)

 More information and statistics

 Download DNA sequence (FASTA)




View karyotype





Example region

Gene annotation

What can I find? Protein-coding and non-coding genes, splice variants, cDNA and protein sequences, non-coding RNAs.

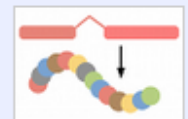
 More about this genebuild

 Download genes, cDNAs, ncRNA, proteins (FASTA)

 Update your old Ensembl IDs




Example gene



Example transcript

Comparative genomics

What can I find? Gene families based on HAMAP and PANTHER classification.

 More about comparative analysis



Gene families

Variation

This species currently has no variation database. However you can process your own variants using the Variant Effect Predictor.

 Variant Effect Predictor



The EnsemblBacteria Database is an Electronically Curated, Meta Database

- o Data is free to use by anyone for any purpose
- o Funded by
 - o European Molecular Biology Laboratory
 - o United Kingdom Biotechnology and Biosciences Research Council
 - o The Bill and Melinda Gates Foundation
 - o The Wellcome Trust

Concluding Remarks

- *C. trachomatis* strain D/UW-3/CX has a 1,042,519 bp chromosome and a 7493 bp plasmid
- Gene expression pathways involved in developmental stage differentiation
- Not all aerobic respiration pathways are complete
- Nutrient uptake across the vacuole is unclear
- HKD Superfamily may be crucial in understanding host cell phospholipid modification
- Many of the chlamydial genes are a result of horizontal gene transfer with bacterial ancestors and eukaryotic hosts

References

- Stephens, R.S., Kalman, S., Lammel, C., Fan, J., Marathe, R., Aravind, L., Mitchell, W., Olinger, L., Tatusov, R., Zhao, Q., Koonin, E. V., Davis, R.W. (1998) Genome sequence of an obligate intracellular pathogen of humans: *Chlamydia trachomatis*. *Science* **282**: 754-759. 10.1126/science.282.5389.754.
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<<http://www.sciencemag.org/site/feature/data/982604.xhtml>>.
Accessed 8 November 2013.