

Supplementary Material: Using Comparative Genomics and Virtual Screening for Antibiotic Drug Discovery

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1 Appendix

Using Comparative Genomics and Virtual Screening for Antibiotic Drug Discovery, 2010

AutoDock	AD	autodock.scripps.edu
AutoDock Tools	ADT	mgltools.scripps.edu/packages/adt
AutoDock Vina	ADV	vina.scripps.edu
Comprehensive Microbial Resource	CMR	cmr.jcvi.org
Database of Essential Genes	DEG	www.essentialgene.org
EBI Bacterial Genomes		www.ebi.ac.uk/2can/genomes/bacteria.html
GenoList	Geno	genodb.pasteur.fr/cgi-bin/WebObjects/GenoList
High-quality Automated and Manual Annotation of Microbial Proteomes	HAMAP	www.expasy.ch/sprot/hamap/index.html
Integr8	Integr8	www.ebi.ac.uk/integr8
Java SE 6	Java	http://java.sun.com/reference/api
Microbial Genome Database	MBGD	mbgd.genome.ad.jp
National Microbial Pathogen Data Resource	NMPDR	www.nmpdr.org/FIG/wiki/view.cgi/Main/EssentialGenes
Natural Products Database	NPD	wiki.compbio.ucsf.edu/wiki
Perl Programming Language	Perl	http://www.perl.org
Profiling of Escherichia coli Chromosome	PEC	www.expasy.ch/sprot/hamap/BACSU.html
Protein Data Bank	PDB	www.pdb.org
SubtiList	Sub	bioweb.pasteur.fr/GenoList/SubtiList
UniProt	UniProt	www.uniprot.org
ZINC	ZINC	zinc.docking.org

Table 11: Web Sites Consulted

NPD vendor	abbreviation	compounds
InterBioScreen	ibs	42,827
Molecular Diversity Preservation Intl.	mdpi	10,653
TimTec	timtec	3,554
AmbInter	ambint	47
Indofine	indofine	1,332
Specs	specs	354
AnalytiCon Discovery	acdisc	19,080

Table 12: Zinc NPD meta-data set, version/date 2008.5, 89425 compounds. This table lists the NPD vendors and number of compounds contributed [NPD website]

Vendor	version	number
Adesis	2007-02-10	960
AF ChemPharm	2010.2	1254
BioBlocks	2009.5	2402
BioSynth	2007	2127
Calbiochem	2008.1	761
CNH Technologies	2009.10	217
Euroasia	2009.10	73
Infarmatik	2010.5	299
SYNCHM OHG	2008.6	2003
Tocris	2005.10	1177
Ubichem	2008.11	1230

Table 13: Micro vendors and number of compounds.

Uniprot	Protein name	Gene name
O05402	Putative peptidoglycan O-acetyltransferase yrhL	yrhL
O05412	Glutamate racemase 2	yrcC
O06485	Putative sugar dehydratase/epimerase yfnG	yfnG
O06486	Probable glucose-1-phosphate cytidylyltransferase	yfnH
O07532	Endopeptidase lytF	lytF
O31751	Undecaprenyl pyrophosphate synthase	uppS
O31753	1-deoxy-D-xylulose 5-phosphate reductoisomerase	dxr
O31771	Uncharacterized membrane protein ymfM	ymfM
O31773	Putative penicillin-binding protein pbpX	pbpX
O31793	Uncharacterized protein ymaG	ymaG
O31822	Probable UTP-glucose-1-phosphate uridylyltransferase yngB	yngB
O31852	D-gamma-glutamyl-meso-diaminopimelic acid endopeptidase cwlS	cwlS
O32032	Penicillin-binding protein 4B	pbpI
O32041	Putative N-acetylmuramoyl-L-alanine amidase yrvJ	yrvJ
O32083	Exo-glucosaminidase lytG	lytG
O32206	Uncharacterized protein yvgJ	yvgJ
O32267	Putative teichuronic acid biosynthesis glycosyltransferase tuaH	tuaH
O32268	Putative teichuronic acid biosynthesis glycosyltransferase tuaG	tuaG
O32269	Teichuronic acid biosynthesis protein tuaF	tuaF
O32270	Teichuronic acid biosynthesis protein tuaE	tuaE
O32271	UDP-glucose 6-dehydrogenase tuaD	tuaD
O32272	Putative teichuronic acid biosynthesis glycosyltransferase tuaC	tuaC
O32273	Teichuronic acid biosynthesis protein tuaB	tuaB
O32274	Putative undecaprenyl-phosphate N-acetylgalactosaminyl 1-phosphate transferase	tuaA
O34413	Putative glycosyltransferase ytcC	yticC
O34669	Cell wall-binding protein yocH	yocH
O34674	Probable cell division protein ytgP	yticP
O34753	Probable undecaprenyl-phosphate N-acetylglucosaminyl 1-phosphate transferase	tagO
O34797	Phosphopantetheine adenylyltransferase	CoaD
O34814	Cell division ATP-binding protein ftsE	ftsE
O34866	Putative carboxypeptidase yodJ	yodJ
O34876	Cell division protein ftsX	ftsX
O34883	Uncharacterized protein ytkC	yticC
O34952	Glycerol phosphate lipoteichoic acid synthase 2	ltaS2
P07373	Stage V sporulation protein E	spoVE
P08750	D-alanyl-D-alanine carboxypeptidase dacA	dacA
P13484	Probable poly(glycerol-phosphate) alpha-glucosyltransferase	tagE
P13485	CDP-glycerol:poly(glycerophosphate) glycerophosphotransferase	tagF
P14192	Bifunctional protein glmU	glmU
P17865	Cell division protein FtsZ	FtsZ
P18159	Phosphoglucomutase	pgcA
P18579	UDP-N-acetylenolpyruvoylglucosamine reductase	murB
P19638	Undecaprenol kinase	dgkA
P19670	UDP-N-acetylglucosamine 1-carboxyvinyltransferase 2	murAB
P24808	N-acetylmuramoyl-L-alanine amidase cwlA	cwlA
P27620	Putative N-acetylmannosaminyltransferase	tagA
P27621	Putative CDP-glycerol:glycerophosphate glycerophosphotransferase	tagB
P27622	Putative major teichoic acid biosynthesis protein C	tagC
P27623	Glycerol-3-phosphate cytidylyltransferase	tagD
P31112	Heptaprenyl diphosphate synthase component 1	hepS
P31114	Heptaprenyl diphosphate synthase component 2	hepT
P32959	Penicillin-binding protein 4*	pbpE
P35150	D-alanyl-D-alanine carboxypeptidase dacB	dacB
P37546	Uncharacterized protein yabE	yabE
P37550	4-diphosphocytidyl-2-C-methyl-D-erythritol kinase	ispE
P37585	UDP-N-acetylglucosamine-N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase	murG
P38050	Penicillin-binding protein 1F	pbpF
P38422	D-alanyl-D-alanine carboxypeptidase dacF	dacF
P39131	UDP-N-acetylglucosamine 2-epimerase	mnaA
P39577	Uncharacterized oxidoreductase dltE	dltE
P39578	Protein dltD	dltD

Table 14: 123 *B. subtilis* proteins (part 1)

Uniprot	Protein name	Gene name
P39579	D-alanine-poly(phosphoribitol) ligase subunit 2	dltC
P39580	Protein dltB	dltB
P39581	D-alanine-poly(phosphoribitol) ligase subunit 1	dltA
P39602	Uncharacterized membrane protein ywcD	ywcD
P39604	Uncharacterized membrane protein ywcF	ywcF
P39751	MreB-like protein	mbi
P39763	Protein mreBH	mreBH
P39793	Penicillin-binding protein 1A/1B	ponA
P39844	D-alanyl-D-alanine carboxypeptidase dacC	dacC
P39848	Beta-N-acetylglucosaminidase	lytD
P40750	Penicillin-binding protein 4	pbpD
P40767	Peptidoglycan DL-endopeptidase cwIO	cwIO
P40778	UDP-N-acetylmuramate-L-alanine ligase	murC
P42249	Cell wall hydrolase cwIJ	cwIJ
P42953	Teichoic acid translocation permease protein tagG	tagG
P42954	Teichoic acids export ATP-binding protein TagH	tagH
P42971	Penicillin-binding protein 3	pbpC
P42982	Uncharacterized glycosyltransferase ypjH	ypjH
P46917	Minor teichoic acid biosynthesis protein ggaA	ggaA
P46918	Minor teichoic acid biosynthesis protein ggaB	ggaB
P50740	Isopentenyl-diphosphate delta-isomerase	fni
P50839	Cell cycle protein gpsB	gpsB
P50864	Germination-specific N-acetylmuramoyl-L-alanine amidase	cwlD
P54166	Processive diacylglycerol glucosyltransferase	ugtP
P54383	Geranyltranstransferase	ispA
P54421	Probable endopeptidase lytE	lytE
P54423	Cell wall-associated protease	wprA
P54450	N-acetylmuramoyl-L-alanine amidase cwlH	cwlH
P54473	4-hydroxy-3-methylbut-2-enyl diphosphate reductase	ispH
P54482	4-hydroxy-3-methylbut-2-en-1-yl diphosphate synthase	ispG
P54488	Uncharacterized protein yqgF	yqgF
P54496	Uncharacterized protein yqgS	yqgS
P54523	1-deoxy-D-xylulose-5-phosphate synthase	dxs
P54525	Uncharacterized protein yqiI	yqiI
P54570	ADP-ribose pyrophosphatase	nudF
P70965	UDP-N-acetylglucosamine 1-carboxyvinyltransferase 1	murAA
P70997	Penicillin-binding protein 2D	pbpG
P71062	Uncharacterized sugar transferase epsL	epsL
P94556	Glutamate racemase 1	RacE
P96499	Putative transcriptional regulator yvhJ	yvhJ
P96612	D-alanine-D-alanine ligase	ddl
P96613	UDP-N-acetylmuramoyl-tripeptide-D-alanyl-D-alanine ligase	murF
P96740	Gamma-DL-glutamyl hydrolase	pgdS
Q01465	Rod shape-determining protein mreB	mreB
Q01466	Rod shape-determining protein mreC	mreC
Q01467	Rod shape-determining protein mreD	mreD
Q02112	Membrane-bound protein lytA	lytA
Q02113	Amidase enhancer	lytB
Q02114	N-acetylmuramoyl-L-alanine amidase lytC	lytC
Q02115	Transcriptional regulator lytR	lytR
Q03521	Phospho-N-acetylmuramoyl-pentapeptide-transferase	mraY
Q03522	UDP-N-acetylmuramoylalanine-D-glutamate ligase	murD
Q03523	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate-2,6-diaminopimelate ligase	murE
Q03524	Stage V sporulation protein D	spoVD
Q05852	UTP-glucose-1-phosphate uridylyltransferase	gtaB
Q06320	Sporulation-specific N-acetylmuramoyl-L-alanine amidase	cwlC
Q06755	2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase	ispD
Q06756	2-C-methyl-D-erythritol 2,4-cyclodiphosphate synthase	ispF
Q07833	Wall-associated protein	wapA
Q07868	Penicillin-binding protein 2B	pbpB
Q796K8	Penicillin-binding protein H	pbpH
Q797B3	Glycerol phosphate lipoteichoic acid synthase 1	ltaS1
Q7WY78	Putative transcriptional regulator YwtF	YwtF

Table 15: 123 *B. subtilis* proteins (part 2)

Gram Positive

Abiotrophia defectiva ATCC 49176
Acinetobacter haemolyticus ATCC 19194
Bacillus anthracis
Bacillus cereus (strain ATCC 14579 / DSM 31)
Clostridium botulinum (strain 657 / Type Ba4)
Clostridium difficile (strain 630)
Corynebacterium diphtheriae
Corynebacterium jeikeium (strain K411)
Clostridium perfringens (strain SM101 / Type A)
Clostridium tetani
Corynebacterium tuberculostrictum SK141
Enterococcus faecalis
Enterococcus faecium TX1330
Erysipelothrix rhusiopathiae ATCC 19414
Listeria monocytogenes serotype 4b (strain Clip81459)
Listeria welshimeri serovar 6b (strain ATCC 35897 / DSM 20650 / SLCC5334)
Mycobacterium tuberculosis
Nocardia farcinica
Streptococcus agalactiae 18RS21
Staphylococcus aureus (strain COL)
Streptomyces coelicolor
Staphylococcus epidermidis (strain ATCC 35984 / RP62A)
Streptococcus pneumoniae (strain P1031)
Streptococcus pyogenes serotype M3
Staphylococcus saprophyticus subsp. *saprophyticus* (strain ATCC 15305 / DSM 20229)

Gram Negative

Acinetobacter radioresistens SK82
Brucella abortus (strain S19)
Borrelia burgdorferi (strain ZS7)
Brucella canis (strain ATCC 23365 / NCTC 10854)
Burkholderia mallei
Brucella melitensis biotype 2 (strain ATCC 23457)
Bordetella pertussis
Brucella suis (strain ATCC 23445 / NCTC 10510)
Campylobacter jejuni
Escherichia coli (strain K12)
Francisella tularensis subsp. *tularensis* (strain FSC 198)
Haemophilus influenzae (strain 86-028NP)
Helicobacter pylori (strain HPAG1)
Klebsiella pneumoniae (strain 342)
Leptospira interrogans serogroup *Icterohaemorrhagiae* serovar *copenhageni*
Legionella pneumophila (strain Lens)
Neisseria gonorrhoeae (strain ATCC 700825 / FA 1090)
Neisseria meningitidis serogroup C / serotype 2a (strain ATCC 700532 / FAM18)
Pseudomonas aeruginosa (strain UCBPP-PA14)
Rickettsia rickettsii (strain Iowa)
Salmonella typhimurium (strain D23580)
Salmonella typhi
Treponema pallidum
Vibrio cholerae serotype O1 (strain MJ-1236)
Yersinia pestis (strain D106004)

No cell wall

Chlamydia pneumoniae
Chlamydia trachomatis Sweden2
Mycoplasma arthritidis (strain 158L3-1)
Mycoplasma hominis (strain ATCC 23114 / IFO 14850 / NCTC 10111 / PG21)
Mycobacterium leprae
Mycoplasma mycoides subsp. *mycoides* SC
Mycoplasma pneumoniae
Mycoplasma pulmonis
Mycoplasma synoviae (strain 53)
Ureaplasma urealyticum serovar 10 (strain ATCC 33699 / Western)

Table 16: 60 Subject Proteomes

Proteomes	Hits	mean identity	UniProt	GN	3D	other 3D
54	54	55%	P17865	ftsZ	yes	P64170 P0A9A6
51	70	50%	P70965	murAA	no	P0A749
51	70	47%	P19670	murAB	no	P0A749
51	61	46%	O31751	uppS	no	P60472, P60479, O53434
50	54	39%	Q03523	murE	no	P65477, P22188
49	49	46%	O34797	coaD	yes	P0A6I6, P0A530
48	49	46%	P14192	glmU	no	P0ACC7, P96382
48	60	38%	P40778	murC	no	P17952
47	77	34%	P31114	hepT	no	P22939
46	64	51%	Q05852	gtaB	no	P0AEP3
46	66	47%	O31822	yngB	no	P0AEP3, P37744
46	80	39%	P54383	ispA	no	P22939
45	45	36%	P96613	murF	no	P11880
44	57	39%	P96612	ddl	no	Q5HEB7, P95114, P07862
43	46	37%	Q06755	ispD	no	Q46893, Q5F829
42	43	37%	Q03522	murD	no	P14900
41	55	43%	P54523	dxs	no	P77488
39	43	48%	P54482	ispG	no	Q9X7W2
38	38	54%	Q06756	ispF	no	P62617, Q9PM68
38	39	34%	O05412	yrpC	no	Q836J0, P22634
37	133	38%	P54421	lytE	no	P0AFV4
37	139	38%	O31852	cwlS	no	P0AFV4
36	38	46%	O31753	dxr	no	P45568, P64012
36	307	37%	P96740	pgdS	no	P0AFV4, P0AFV4, P0AFV4
35	42	41%	P54570	nudF	no	Q93K97
35	135	39%	O07532	lytF	no	P0AFV4
34	37	44%	P94556	RacE	yes	Q836J0
34	36	39%	P54473	ispH	no	P62623
34	81	35%	P38422	dacF	no	P08506, P0AEB2
33	35	36%	P37585	murG	no	P17443
32	85	36%	P40767	cwlO	no	P0AFV4
32	74	34%	P35150	dacB	no	P0AEB2
30	56	35%	P08750	dacA	no	P08506, P0AEB2
23	27	56%	P39131	mnaA	yes	P27828
22	36	36%	Q06320	cwlC	yes	
22	44	36%	P39581	dltA	yes	Q81G39
20	56	35%	Q7WY78	ywtF	yes	
18	18	46%	P27623	tagD	yes	
18	65	43%	O34669	yocH	no	P0AEZ7
16	16	42%	P50740	fni	yes	
14	25	44%	O34952	ltaS2	yes	
13	14	39%	O06486	yfnH	no	Q8Z5I4
4	4	31%	P39844	dacC	yes	

Table 17: Conservation of *B. subtilis* proteins in 60 Proteomes (where a 3D structure is available).

Proteomes	Hits	mean identity	UniProt	GN	3D	other 3D
25	25	47%	P17865	ftsZ	yes	P0A9A6
25	26	46%	P70965	murAA	no	P0A749
25	25	45%	O31751	uppS	no	P60472
25	26	42%	P19670	murAB	no	P0A749
25	27	36%	Q03523	murE	no	P22188
24	24	42%	O34797	coaD	yes	P0A6I6
23	25	40%	P14192	glmU	no	P0ACC7
23	43	37%	P54383	ispA	no	P22939
23	39	32%	P31114	hepT	no	P22939
23	34	32%	P40778	murC	no	P17952
22	22	56%	Q06756	ispF	no	P62617, Q9PM68
22	28	42%	P54523	dxs	no	P77488
22	22	33%	P96613	murF	no	P11880
21	27	46%	Q05852	gtaB	no	P0AEP3
21	31	43%	O31822	yngB	no	P0AEP3, P37744
21	29	36%	P96612	ddl	no	P07862
21	43	34%	P38422	dacF	no	P08506, P0AEB2
21	22	32%	Q03522	murD	no	P14900
20	20	36%	Q06755	ispD	no	Q46893, Q5F829
19	20	37%	P54473	ispH	no	P62623
19	19	34%	O05412	yrpC	no	P22634
19	40	33%	P35150	dacB	no	P0AEB2
18	18	41%	O31753	dxr	no	P45568
17	95	37%	P96740	pgdS	no	P0AFV4, P0AFV4, P0AFV4
14	42	39%	O07532	lytF	no	P0AFV4
14	40	38%	P54421	lytE	no	P0AFV4
14	40	37%	O31852	cwlS	no	P0AFV4
14	20	32%	P08750	dacA	no	P08506, P0AEB2
14	14	31%	P37585	murG	no	P17443
13	29	36%	P40767	cwlO	no	P0AFV4
12	12	36%	P94556	racE	yes	
12	12	34%	P27623	tagD	yes	
12	16	34%	P54570	nudF	no	Q93K97
9	9	50%	P39131	mnaA	yes	P27828
9	9	39%	Q06320	cwlC	yes	
9	9	38%	O06486	yfnH	no	Q8Z5I4
7	13	32%	P39581	dltA	yes	
4	8	33%	O34669	yocH	no	P0AEZ7
3	3	36%	P50740	fni	yes	
2	2	32%	P39844	dacC	yes	

Table 18: Conservation of *B. subtilis* proteins in 25 Gram Negative Proteomes (where a 3D structure is available).

Proteomes	Hits	mean identity	UniProt	GN	3D	other 3D
25	25	63%	P17865	ftsZ	yes	P64170
25	25	51%	P14192	glmU	no	P96382
25	25	50%	O34797	coaD	yes	P0A530
25	34	48%	O31751	uppS	no	P60479, O53434
24	27	41%	Q03523	murE	no	P65477
23	29	43%	P96612	ddl	no	Q5HEB7, P95114
21	24	47%	P94556	racE	yes	Q836J0
21	58	34%	Q7WY78	ywtF	yes	
19	20	34%	O05412	yrpC	no	Q836J0
16	18	51%	O31753	dxr	no	P64012
16	33	37%	P39581	dltA	yes	Q81G39
15	16	60%	P54482	ispG	no	Q9X7W2
14	18	59%	P39131	mnaA	yes	
14	25	44%	O34952	ltaS2	yes	
14	14	44%	P50740	fni	yes	
12	26	35%	Q06320	cwlC	yes	
7	7	70%	P27623	tagD	yes	
2	2	31%	P39844	dacC	yes	

Table 19: Conservation of *B. subtilis* proteins in 25 Gram Positive Proteomes (where a 3D structure is available).

Proteomes	Hits	mean identity	UniProt	GN	3D	other 3D
1	1	100%	P39844	dacC	yes	
1	1	100%	P50740	fni	yes	
1	1	100%	P17865	ftsZ	yes	
1	1	100%	P39131	mnaA	yes	
1	1	100%	O34797	CoaD	yes	
1	1	100%	P27623	tagD	yes	
1	2	66%	O05412	yrpC	no	P94556
1	2	66%	P94556	racE	yes	
1	3	59%	P96499	yvhJ	no	Q7WY78
1	3	59%	Q02115	lytR	no	Q7WY78
1	3	58%	Q7WY78	ywtF	yes	
1	4	62%	P54496	yqgS	no	O34952
1	4	61%	O34952	ltaS2	yes	
1	4	60%	Q797B3	ltaS1	no	O34952
1	4	60%	O32206	yvgJ	no	O34952
1	4	53%	Q06320	cwlC	yes	
1	5	52%	P54525	yqiI	no	Q06320
1	5	48%	O32041	yrvJ	no	Q06320
1	7	46%	P54423	wprA	no	P04189
1	8	46%	Q02114	lytC	no	Q06320
1	8	43%	O32268	tuaG	no	P39621
1	11	37%	P39581	dltA	yes	Q08787
1	27	43%	P54421	lytE	no	O05495
1	31	44%	O07532	lytF	no	O05495 O34816

Table 20: Redundancy of 123 *B. subtilis* proteins in the *B. subtilis* Proteome (where a 3D structure is available). Using BLAST with an E-value of 0.1 and filtered with a sequence identity threshold of $\geq 30\%$.

UniProt	GN	proteomes with no hits
17865	ftsZ	Ureaplasma urealyticum serovar 10 (strain ATCC 33699 / Western) Chlamydia pneumoniae Chlamydia trachomatis Sweden2 Mycoplasma pneumoniae
O34797	coaD	Ureaplasma urealyticum serovar 10 (strain ATCC 33699 / Western) Mycoplasma synoviae (strain 53) Mycoplasma arthritidis (strain 158L3-1) Chlamydia pneumoniae Mycoplasma hominis (strain ATCC 23114 / IFO 14850 / NCTC 10111 / PG21) Rickettsia rickettsii (strain Iowa) Mycoplasma pulmonis Chlamydia trachomatis Sweden2 Mycoplasma pneumoniae

Table 21: FtsZ and CoaD versus 60 proteomes: missing proteomes. Using BLAST with an E-value of 0.0001 and filtered with a sequence identity threshold of $\geq 30\%$.

UniProt	GN	proteomes with no hits
P17865	ftsZ	
O34797	coaD	
Q7WY78	ywtF	Clostridium tetani Clostridium botulinum (strain 657 / Type Ba4) Abiotrophia defectiva ATCC 49176 Acinetobacter haemolyticus ATCC 19194
P94556	racE	Streptomyces coelicolor Erysipelothrix rhusiopathiae ATCC 19414 Nocardia farcinica Abiotrophia defectiva ATCC 49176

Table 22: FtsZ, CoaD, YwtF, RacE versus 25 Gram Positive Proteomes: missing proteomes. Using BLAST with an E-value of 0.0001 and filtered with a sequence identity threshold of $\geq 30\%$.

receptor	$mean_a$	$mean_b$	min_a	min_b	max_a	max_b
FtsZ	-7.96	-6.48	-12.10	-10.70	-3.00	-2.80
CoaD	-6.72	-5.77	-10.20	-9.70	-2.70	-2.40
YwtF	-6.21	-5.20	-9.10	-8.50	-2.40	-2.20
RacE	-5.02	-4.29	-7.70	-7.70	-1.90	-1.70

Table 23: Docking Scores for NPD ligands (a) versus Micro Vendor ligands (b).

Table 24: Scores and properties of **best** NPD ligands docked with FtsZ.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-12.1	ZINC04236084	504.543	0.92	-3.58	-23.14	1	10	108	0	2
-11.9	ZINC12879888	482.904	1.64	0.55	-67.28	7	10	169	1	4
-11.6	ZINC08764269	445.471	4.68	2.98	-26.54	1	7	98	0	3
-11.6	ZINC12878248	491.524	3.14	5.45	-61.79	5	10	152	1	6
-11.5	ZINC04236042	447.882	1.79	-3.04	-16.81	1	8	95	0	2
-11.5	ZINC04270603	484.536	3.94	-1.93	-56.66	2	9	97	1	6
-11.5	ZINC08789396	511.942	3.36	-3.84	-65.1	5	10	152	1	6
-11.5	ZINC04259821	449.447	1.84	4.34	-62.57	2	11	130	1	6
-11.5	ZINC04259824	463.474	2.26	4.05	-52.66	3	11	122	1	6
-11.5	ZINC12883374	477.544	3.94	10.27	-61.65	4	7	99	1	3
-11.5	ZINC12897545	443.455	4.61	12.96	-22.84	1	7	103	0	3
-11.5	ZINC12902067	493.543	3.44	7.38	-65.63	5	8	119	1	3
-11.6	Averages	474.69	2.96	2.97	-48.56	3.08	9.00	120.33	0.67	4.17

Table 25: Scores and properties of **worst** NPD ligands docked with FtsZ.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-3.6	ZINC00167189	115.201	2.81	-0.3	-1.84	0	1	12	0	2
-3.6	ZINC01845901	129.228	3.55	-0.66	-1.54	0	1	12	0	4
-3.6	ZINC01846032	115.201	2.73	-0.49	-1.59	0	1	12	0	2
-3.6	ZINC03844512	135.599	-2.34	0.43	-27.96	0	2	16	1	0
-3.6	ZINC04701625	87.122	1.32	-0.2	-1.63	0	2	29	0	1
-3.6	ZINC04712486	88.106	0.12	2.19	-5.32	0	2	18	0	2
-3.6	ZINC01594581	165.03	1.4	1.24	-2.92	0	1	17	0	1
-3.6	ZINC04701702	82.106	0.54	1.55	-5.8	1	2	28	0	0
-3.5	ZINC03852275	212.43	2.37	0.65	-4.32	0	0	0	0	4
-3.5	ZINC03882605	115.201	2.81	-0.3	-1.86	0	1	12	0	2
-3.4	ZINC01698890	82.102	0.4	3.15	-7.14	0	1	17	0	0
-3.4	ZINC13410577	88.106	0.12	0.8	-3.3	0	2	18	0	2
-3.3	ZINC01841344	101.174	2.28	-0.55	-1.9	0	1	12	0	1
-3.0	ZINC01846561	134.25	1.6	0.33	-10.94	0	0	0	0	0
-3.0	ZINC01736852	186.222	2.61	23.16	-24.77	0	0	0	0	1

Table 26: Scores and properties of **best** NPD ligands docked with CoaD.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-10.2	ZINC03846570	406.398	2.54	-7.67	-25.96	3	9	114	0	2
-10.2	ZINC11990702	508.746	7.71	3.82	-6.33	0	2	26	0	3
-9.9	ZINC08299195	499.639	3.2	-1.62	-56.27	3	8	98	1	6
-9.8	ZINC00626233	403.394	2.44	-2.54	-25.59	3	8	113	0	3
-9.8	ZINC02161153	425.509	1.55	-5.74	-47.06	5	8	126	1	4
-9.8	ZINC08790850	508.554	3.7	-2.43	-29.33	3	8	98	1	2
-9.7	ZINC04084160	399.494	3.53	-0.01	-9.54	1	5	56	0	2
-9.7	ZINC04265432	473.553	6.12	-2.55	-18.11	0	4	47	0	2
-9.6	ZINC04024540	392.502	6.76	-0.38	-9.28	0	3	32	0	2
-9.6	ZINC04046363	393.379	1.84	-1.8	-43.44	3	9	128	1	2
-9.6	ZINC04222852	475.501	3.45	-4.64	-24.51	3	9	114	0	6
-9.6	ZINC04265785	462.508	7.54	0.19	-32.07	2	4	65	0	0
-9.6	ZINC02726701	453.539	2.86	-2.59	-57.76	3	8	123	0	4
-9.6	ZINC08789670	463.47	0.34	-5.25	-66.98	5	10	144	1	4
-9.6	ZINC09033658	494.527	3.3	-2.46	-31.8	3	8	98	1	2
-9.6	ZINC11990701	508.746	7.71	3.06	-7.71	0	2	26	0	3
-9.6	ZINC02126798	447.515	3.92	6.75	-53.24	5	8	117	1	3
-9.6	ZINC12885345	491.524	1.23	4	-54.31	5	10	145	1	5

Table 27: Scores and properties of **worst** NPD ligands docked with CoaD.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-3.4	ZINC03843380	206.33	-5.3	5.4	-84.48	0	4	18	2	5
-3.4	ZINC00032315	204.366	3.36	1.96	-5.82	0	0	0	0	0
-3.4	ZINC04712488	78.074	0.4	3.86	-8.96	0	2	47	0	0
-3.4	ZINC01698890	82.102	0.4	3.15	-7.14	0	1	17	0	0
-3.4	ZINC02168303	132.213	0.76	1.52	-6.37	0	2	25	0	0
-3.4	ZINC00895439	154.256	-0.33	-5.66	-4.87	2	2	40	0	3
-3.4	ZINC01763921	165.239	1.04	1.64	-6.62	0	3	46	0	3
-3.4	ZINC03852211	154.256	-0.33	-5.4	-4.94	2	2	40	0	3
-3.3	ZINC01845901	129.228	3.55	-0.66	-1.54	0	1	12	0	4
-3.3	ZINC04701625	87.122	1.32	-0.2	-1.63	0	2	29	0	1
-3.2	ZINC03844512	135.599	-2.34	0.43	-27.96	0	2	16	1	0
-3.2	ZINC03882605	115.201	2.81	-0.3	-1.86	0	1	12	0	2
-3.1	ZINC00167189	115.201	2.81	-0.3	-1.84	0	1	12	0	2
-3.0	ZINC01841344	101.174	2.28	-0.55	-1.9	0	1	12	0	1
-2.9	ZINC01736852	186.222	2.61	23.16	-24.77	0	0	0	0	1
-2.8	ZINC03852275	212.43	2.37	0.65	-4.32	0	0	0	0	4
-2.8	ZINC04712486	88.106	0.12	2.19	-5.32	0	2	18	0	2
-2.8	ZINC13410577	88.106	0.12	0.8	-3.3	0	2	18	0	2
-2.7	ZINC01846561	134.25	1.6	0.33	-10.94	0	0	0	0	0

Table 28: Scores and properties of **best** NPD ligands docked with YwtF.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-9.1	ZINC08791231	478.552	4.49	-0.83	-18.27	2	7	85	0	4
-9.0	ZINC04235629	369.464	5.15	-0.3	-15.64	2	3	49	0	1
-9.0	ZINC04817561	522.645	6.76	-0.49	-13.4	0	6	66	0	2
-9.0	ZINC08790760	511.989	4.55	-2.74	-46.7	4	7	98	1	3
-9.0	ZINC12878012	497.962	4.19	9.69	-45.86	4	7	99	1	3
-9.0	ZINC12883374	477.544	3.94	10.27	-61.65	4	7	99	1	3
-8.9	ZINC08789997	497.962	4.17	-3.04	-61.56	4	7	98	1	3
-8.9	ZINC08790433	482.515	4.2	-0.41	-18.2	2	7	85	0	4
-8.9	ZINC08790759	511.989	4.55	-2.64	-61.09	4	7	98	1	3
-8.9	ZINC12885214	497.962	4.15	10.09	-68.52	4	7	99	1	3
-8.9	ZINC12902067	493.543	3.44	7.38	-65.63	5	8	119	1	3
-8.8	ZINC08297842	456.449	2.11	-3.22	-21.16	2	8	90	0	2
-8.8	ZINC02161108	472.609	4.88	11.07	-35.98	3	6	83	1	3
-8.8	ZINC12894751	433.532	3.77	8.9	-27.73	2	7	84	1	0
-8.8	ZINC12902062	493.543	3.44	6.95	-46.08	5	8	119	1	3

Table 29: Scores and properties of **worst** NPD ligands docked with YwtF.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-3.0	ZINC01532620	103.121	-1.1	-2.48	-66.33	3	3	67	0	3
-3.0	ZINC01788405	117.172	-3.9	0.53	-33.37	2	3	43	1	2
-3.0	ZINC01845901	129.228	3.55	-0.66	-1.54	0	1	12	0	4
-3.0	ZINC01846032	115.201	2.73	-0.49	-1.59	0	1	12	0	2
-3.0	ZINC03844512	135.599	-2.34	0.43	-27.96	0	2	16	1	0
-3.0	ZINC04701625	87.122	1.32	-0.2	-1.63	0	2	29	0	1
-3.0	ZINC04712488	78.074	0.4	3.86	-8.96	0	2	47	0	0
-3.0	ZINC01594581	165.03	1.4	1.24	-2.92	0	1	17	0	1
-3.0	ZINC04701702	82.106	0.54	1.55	-5.8	1	2	28	0	0
-2.9	ZINC00167189	115.201	2.81	-0.3	-1.84	0	1	12	0	2
-2.9	ZINC03843381	206.33	-5.3	5.95	-89.67	0	4	18	2	5
-2.9	ZINC03843383	206.33	-5.3	5.5	-89.86	0	4	18	2	5
-2.9	ZINC03882605	115.201	2.81	-0.3	-1.86	0	1	12	0	2
-2.9	ZINC01728496	146.24	1.05	2.91	-7.23	0	2	36	0	2
-2.9	ZINC01763921	165.239	1.04	1.64	-6.62	0	3	46	0	3
-2.7	ZINC03852275	212.43	2.37	0.65	-4.32	0	0	0	0	4
-2.6	ZINC01841344	101.174	2.28	-0.55	-1.9	0	1	12	0	1
-2.6	ZINC01846561	134.25	1.6	0.33	-10.94	0	0	0	0	0
-2.6	ZINC13410577	88.106	0.12	0.8	-3.3	0	2	18	0	2
-2.5	ZINC04712486	88.106	0.12	2.19	-5.32	0	2	18	0	2
-2.4	ZINC01736852	186.222	2.61	23.16	-24.77	0	0	0	0	1

Table 30: Scores and properties of **best** NPD ligands docked with RacE.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-7.7	ZINC03844349	407.43	0.3	-12.97	-149.76	8	9	146	2	3
-7.7	ZINC04015296	493.478	5.35	-0.41	-30.73	0	7	90	0	1
-7.7	ZINC04692014	464.379	0.35	-13.03	-21.58	8	12	210	0	3
-7.6	ZINC04349223	480.378	-0.62	-14.93	-20.03	9	13	230	0	4
-7.6	ZINC04349341	464.379	-0.36	-14.93	-21.97	8	12	210	0	4
-7.6	ZINC04349550	464.379	0.35	-13.78	-23.04	8	12	210	0	3
-7.6	ZINC08790691	477.497	2.18	-5.6	-40.78	5	10	144	1	4
-7.6	ZINC08876663	463.517	3.52	-2	-49.4	4	7	98	1	3
-7.6	ZINC12876895	449.443	1.3	3.15	-47.68	5	10	145	1	3
-7.6	ZINC12881872	497.915	2.41	2.84	-43.76	5	10	145	1	4
-7.5	ZINC03947432	448.38	0.19	-12.35	-20.07	7	11	190	0	4
-7.5	ZINC04349745	432.381	0.52	-12.5	-20.82	7	10	181	0	3
-7.5	ZINC02130311	462.526	2.61	-6.23	-46.17	5	8	123	1	3
-7.5	ZINC08627133	490.507	3.4	-8.82	-21.1	4	9	114	0	6
-7.5	ZINC08681631	480.378	-0.62	-15.55	-18.6	9	13	230	0	4
-7.5	ZINC08789670	463.47	0.34	-5.25	-66.98	5	10	144	1	4
-7.5	ZINC08876671	464.498	1.08	-7.03	-57.49	5	9	132	1	4
-7.5	ZINC08876675	464.498	1.08	-6.26	-57.36	5	9	132	1	4
-7.5	ZINC12882459	476.553	3.11	4.76	-46.33	5	8	124	1	3
-7.5	ZINC12883470	497.915	2.41	2.59	-37.28	5	10	145	1	4
-7.5	ZINC13409398	420.812	3.06	3.35	-19.89	3	8	121	0	1
-7.5	ZINC13409402	465.263	3.19	3.45	-19.66	3	8	121	0	1
-7.5	ZINC13424725	464.379	-0.36	-9.4	-17.73	8	12	211	0	4
-7.5	ZINC13424741	464.379	-0.33	-9.62	-20.16	8	12	211	0	4

Table 31: Scores and properties of **worst** NPD ligands docked with RacE.

Score	ZINC ID	MWT	LogP	Desolv apolar	Desolv polar	HBD	HBA	tPSA	charge	rb
-2.3	ZINC00167189	115.201	2.81	-0.3	-1.84	0	1	12	0	2
-2.3	ZINC03844512	135.599	-2.34	0.43	-27.96	0	2	16	1	0
-2.3	ZINC03852275	212.43	2.37	0.65	-4.32	0	0	0	0	4
-2.3	ZINC03882605	115.201	2.81	-0.3	-1.86	0	1	12	0	2
-2.3	ZINC04701625	87.122	1.32	-0.2	-1.63	0	2	29	0	1
-2.3	ZINC01594581	165.03	1.4	1.24	-2.92	0	1	17	0	1
-2.2	ZINC01846032	115.201	2.73	-0.49	-1.59	0	1	12	0	2
-2.2	ZINC01698890	82.102	0.4	3.15	-7.14	0	1	17	0	0
-2.1	ZINC01841344	101.174	2.28	-0.55	-1.9	0	1	12	0	1
-2.1	ZINC01736852	186.222	2.61	23.16	-24.77	0	0	0	0	1
-2.1	ZINC13410577	88.106	0.12	0.8	-3.3	0	2	18	0	2
-2.0	ZINC01846561	134.25	1.6	0.33	-10.94	0	0	0	0	0
-1.9	ZINC04712486	88.106	0.12	2.19	-5.32	0	2	18	0	2

Table 32: Compounds similar to ZINC4236084 (FtsZ top scoring ligand). Source: <http://zinc.docking.org>.

#	ZINC code	MWT	LogP	HBD	HBA	tPSA	charge	rb
1	ZINC04236084	504.543	0.92	1	10	108	0	2
2	ZINC03839244	504.543	0.93	2	10	117	0	3
3	ZINC03839444	352.346	1.03	2	7	88	0	1
4	ZINC03840439	518.57	1.21	2	10	117	0	3
5	ZINC03841297	461.518	2.82	2	8	96	0	3
6	ZINC03841756	498.539	2.10	1	9	91	0	3
7	ZINC04222703	463.514	0.96	3	9	104	1	2
8	ZINC04235839	352.37	0.84	3	7	84	1	1
9	ZINC04235846	449.507	2.73	1	8	88	0	3
10	ZINC04235859	419.437	1.63	1	8	88	0	2
11	ZINC04235870	422.397	-0.51	3	10	131	0	2
12	ZINC04235877	447.535	3.21	1	7	78	0	3
13	ZINC04235880	461.518	3.05	1	8	88	0	2
14	ZINC04235909	455.47	2.00	1	8	88	0	2
15	ZINC04235947	423.449	0.54	3	9	104	1	3
16	ZINC04235964	449.531	1.13	3	8	95	1	3
17	ZINC04235966	463.514	0.96	3	9	104	1	2
18	ZINC04235977	409.398	0.13	2	9	108	0	2
19	ZINC04236001	476.533	3.54	2	9	100	0	2
20	ZINC04236010	352.37	0.84	3	7	84	1	1
21	ZINC04236013	436.468	2.52	2	9	100	0	3
22	ZINC04236018	433.508	2.71	1	7	78	0	3
23	ZINC04236020	447.491	2.54	1	8	88	0	2
24	ZINC04236032	485.496	2.06	1	9	97	0	3
25	ZINC04236051	409.422	-0.44	4	9	115	1	2
26	ZINC04236056	435.504	1.10	3	8	95	1	3
27	ZINC04236057	449.487	0.93	3	9	104	1	2
28	ZINC04236069	436.468	2.31	2	9	100	0	2
29	ZINC04236081	393.399	0.80	1	8	88	0	1

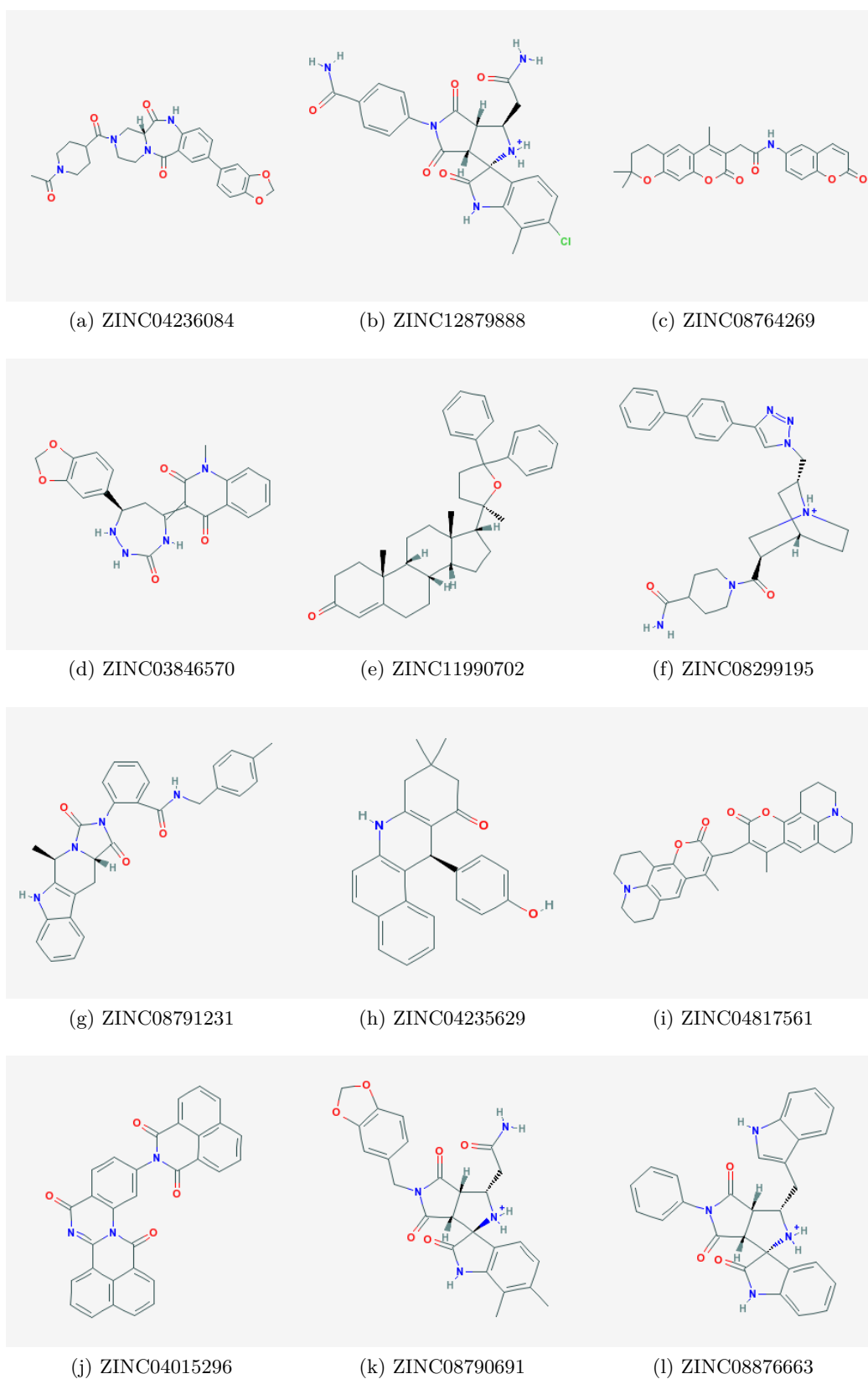


Figure 13: Top scoring ligands for FtsZ (a,b,c) CoaD (d,e,f) YwtF (g,h,i) RacE (j,k,l). Images: <http://pubchem.ncbi.nlm.nih.gov>.

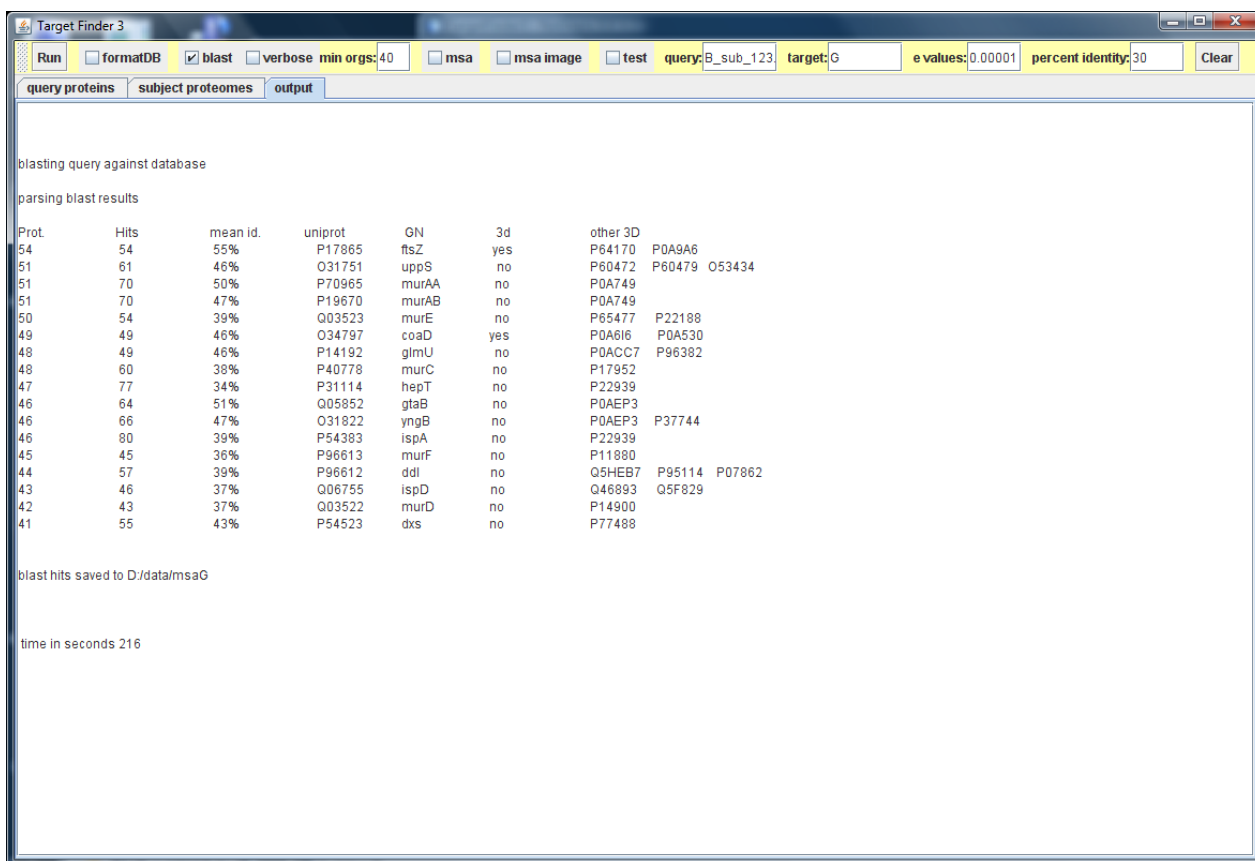


Figure 14: Target Finder: uses BLAST for pairwise sequence alignment and MUSCLE for multiple sequence alignment.

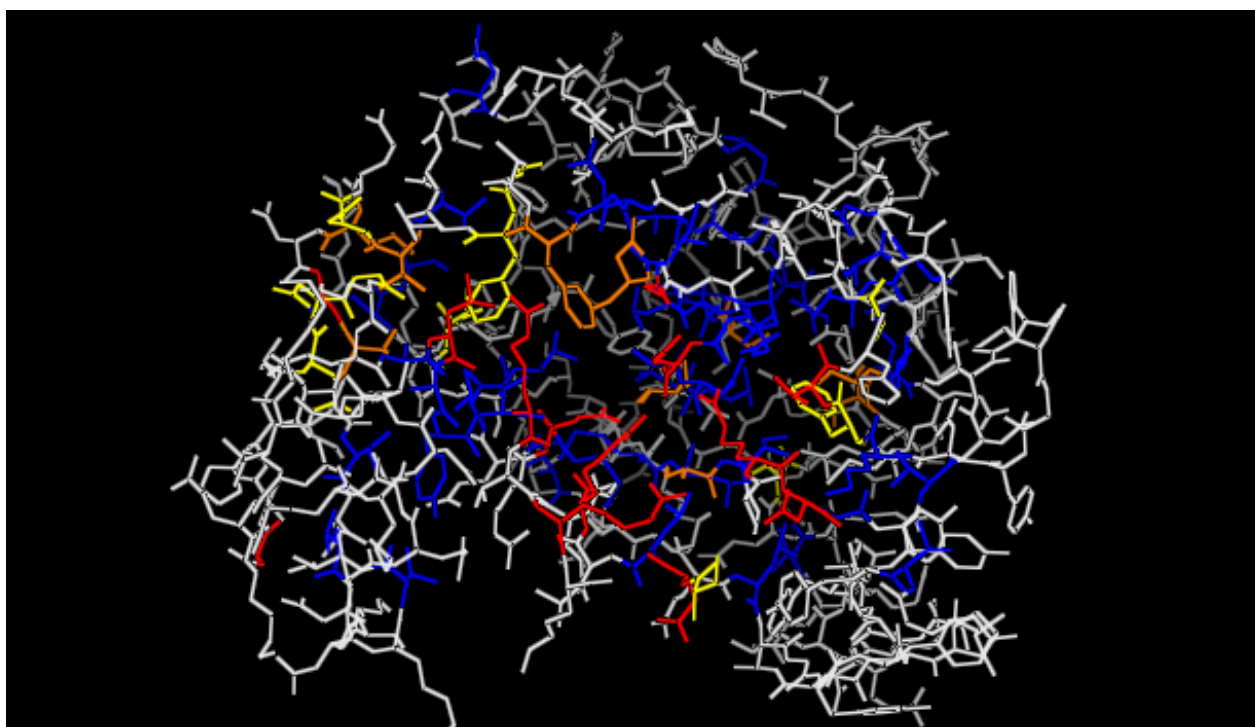


Figure 15: YwtF rendered as lines and colored by conservation score: gray {0.5}, blue {6,7}, yellow {8}, orange {9}, red {10,11}. Red indicates the most highly conserved residues.

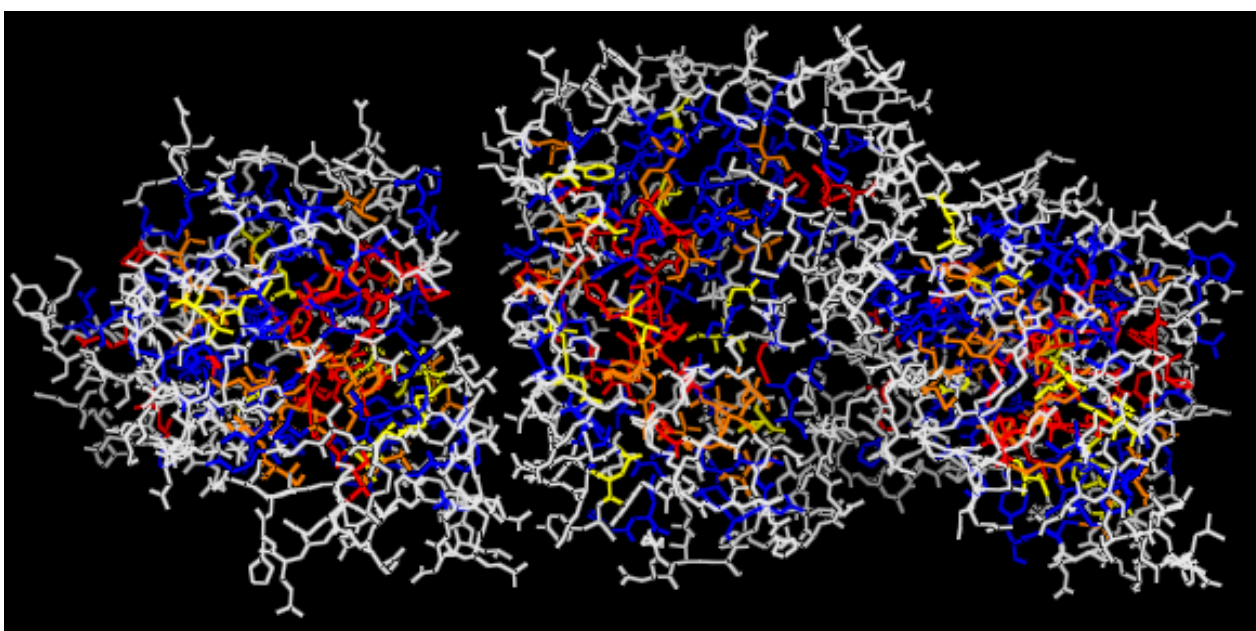


Figure 16: RacE rendered as lines and colored by conservation score: gray {0..5}, blue {6,7}, yellow {8}, orange {9}, red {10,11}. Red indicates highly conserved residues – most of these are internal and not apparent when this molecule is rendered as surface.