

OHD1 PROJECT: TARGETS COLLECTION

Organism : Leishmania other species

Proposed targets with UniProtKB info and feasibility evaluation (protein production and purification and protein crystallization)

1. Pteridine reductase 1(PTR1)
2. DHFR (Dihydrofolate reductase)
3. Trypanothione reductase (TR)
4. trypanothione synthetase
5. nitroreductase
6. sterol 14-alpha demethylase (CYP51) from Leishmania infantum
7. MetAP1 methionine aminopeptidase 1
8. LmCPB2 refers to a specific cysteine protease found in the parasite Leishmania mexicana
9. LdcCA (carbonic anhydrase)
10. Tryparedoxin peroxidase (cTXNPx)
11. Cell Division Cycle (cdc)-2-Related Kinase 12 (CRK12) Receptor ((Cdc2-related kinase 12)) of Leishmania donovani
12. Leishmania zinc-dependent metalloprotease GP63
13. Leishmania donovani dipeptidylcarboxypeptidase
14. Leishmania Malic enzyme
15. glyceraldehyde 3-phosphate dehydrogenase
16. citrate synthase enzyme (LdCS)
17. cytochrome bc1
18. oxidosqualene cyclase
19. L. donovani Topoisomerase IB (predicted)
20. cysteinyl proteases (predicted) and LdCALP (Leishmania donovani calpain-like protein) (predicted)
21. Prolyl-tRNA synthetase (predicted)
22. Arginase (ARG) (predicted)
23. Nicotinamidase (predicted)

	Target	Organism	Status in UniProtKB	Protein production feasibility	Notes	Feasibility in structural study	Notes
1	Pteridine reductase 1 (PTR1)	Leishmania major (Q01782)	Evidence at protein level	Feasible, low risk	In house production protocol (effective and reliable in <i>E. coli</i> cells)	Feasible, low risk	In house crystallization protocol (optimized by HT crystallization trials @ Diamond)
		Leishmania donovani (Q6QDB5)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		Leishmania tarentolae (P42556)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology	Feasible, low/moderate risk	NO report in literature; protocols available on enzymes of other species with good sequence homology (see last page); HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
2	DHFR (Dihydrofolate reductase)	Leishmania major (P07382)	Evidence at protein level	Feasible, low risk	In house production protocol (effective and reliable in <i>E. coli</i> cells)	Feasible, low/moderate risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology	Feasible, low risk	NO report in literature; protocols available on enzymes of other species with high sequence homology (see next page); HT methods @ UniSI/Diamond	moderate risk	NO report in literature (HT methods @ Diamond)
3	Trypanothione reductase (TR)	Leishmania infantum (A4HSF7)	Evidence at protein level	Feasible, low risk	Protocol in literature by Ilari (optimized by HT methods @ UniSI/Diamond)	Feasible	Protocol in literature by Ilari (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)

4	Trypanothione synthetase	Leishmania major (Q711P7)	Evidence at protein level	Feasible, low risk	Protocol in literature by Ilari (optimized by HT methods @ UniSI/Diamond)	Feasible, low risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology/ predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
5	nitroreductase	All Leishmania species	Inferred from homology	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
6	sterol 14-alpha demethylase (CYP51)	Leishmania infantum (A4HV18, A2TEF2)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible	Report in literature (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
7	MetAP1 methionine aminopeptidase 1	All Leishmania species	Inferred from homology	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
8	LmCPB2 cysteine protease	Leishmania mexicana (Q95ZD6)	Inferred from homology	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
9	LdcCA (carbonic anhydrase)	Leishmania donovani (18 sequences)	Inferred from homology/ predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	Low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ Diamond)
		All Leishmania species	Inferred from homology/ predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	Low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ Diamond)
10	Tryparedoxin peroxidase (cTXNPx)	Leishmania major (E9ADX4, Q4QF76)	Evidence at protein level	Feasible, low risk	Protocol in literature by Ilari (optimized by HT methods @ UniSI/Diamond)	Feasible, low risk	Protocol in literature by Ilari (optimized by HT crystallization trials @ Diamond)

		Leishmania braziliensis (A4HCL7)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		Leishmania infantum (A0A6L0XFC6)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
11	Cell Division Cycle (cdc)-2-Related Kinase 12 (CRK12) Receptor (Cdc2-related kinase 12)	Leishmania donovani (A0A3S7WQK2, A0A6J8F7A4)	Inferred from homology	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond) 881-aa protein	moderate risk	NO report in literature (HT methods @ Diamond); 881-aa protein
		Leishmania infantum (A0A6LOWJ69), Leishmania braziliensis (A0A3P3YZE8)	Inferred from homology	Feasible, moderate/high risk	NO report in literature (HT methods @ UniSI/Diamond); big protein (881 aa)	Moderate/high risk	NO report in literature (HT methods @ Diamond); big protein (881 aa)
12	zinc-dependent metalloprotease GP63 (Leishmanolysin)	Leishmania major (P08148)	Evidence at protein level	Feasible, high risk	Protocol in literature for protein production in Leishmania (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All other Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
13	Leishmania donovani dipeptidylcarboxypeptidase (oligopeptidase A)	Leishmania donovani (Q4KXL2)	Inferred from homology	moderate/high risk	NO report in literature (HT methods @ UniSI/Diamond); big protein (678 aa)	Moderate/high risk	NO report in literature (HT methods @ Diamond); big protein (678 aa)
		All other Leishmania species	Inferred from homology	moderate/high risk	NO report in literature (HT methods @ UniSI/Diamond); big protein (678 aa)	Moderate/high risk	NO report in literature (HT methods @ Diamond); big protein (678 aa)

14	Malic enzyme	All Leishmania species	Inferred from homology/predicted	moderate/high risk	NO report in literature (HT methods @ UniSI/Diamond); big protein (>500 aa)	Moderate/high risk	NO report in literature (HT methods @ Diamond); big protein (>500 aa)
15	glyceraldehyde 3-phosphate dehydrogenase	Leishmania donovani (A2CIL3)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
	glyceraldehyde 3-phosphate dehydrogenase, glycolsomal	Leishmania Mexicana (Q27890)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
	glyceraldehyde 3-phosphate dehydrogenase	All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
16	citrate synthase	Leishmania donovani (E9BDQ0)	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
		All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
17	cytochrome bc1	All Leishmania species	Evidence at transcript level /inferred from homology	high risk	NO report in literature (HT methods @ UniSI/Diamond); membrane protein complex	high risk	NO report in literature (HT methods @ Diamond); membrane protein complex
18	oxidosqualene cyclase (Squalene synthase)	All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
19	Topoisomerase I	Leishmania infantum (Q9GPZ9)	Evidence at protein level	Feasible, low/moderate risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)

	DNA topoisomerase type IB small subunit	Leishmania donovani (Q8WQM6)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
20	cysteinyI proteases and Leishmania donovani calpain-like protein	Class of proteins					
21	Prolyl-tRNA synthetase	Leishmania major (Q4QDS0)	Evidence at protein level	Feasible, low/moderate risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond); big protein (731 aa)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond); big protein (731 aa)
		All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond); big protein (>700 aa)	moderate risk	NO report in literature (HT methods @ Diamond); big protein (>700 aa)
22	Arginase	Leishmania mexicana (Q6TUJ5)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)
23	Nicotinamidase	Leishmania infantum (A4HRG8)	Evidence at protein level	Feasible, low risk	Protocol in literature (optimized by HT methods @ UniSI/Diamond)	Feasible, low/medium risk	Protocol in literature (optimized by HT crystallization trials @ Diamond)
		All Leishmania species	Inferred from homology/predicted	Feasible, low/moderate risk	NO report in literature (protocols available on enzymes of other species, HT methods @ UniSI/Diamond)	moderate risk	NO report in literature (HT methods @ Diamond)

	Target	Number of entries in UniProtKB	Number of species in UniProtKB	Sequence identity
1	Pteridine reductase 1 (PTR1)	26	21	93-71%
2	DHFR (Dihydrofolate reductase)	26	21	98-82%
3	Trypanothione reductase (TR)	38	21	70-98%
4	Trypanothione synthetase	51	21	74-98%
5	nitroreductase	34	21	63-98%
6	sterol 14-alpha demethylase (CYP51)	5	4	97-98%
7	MetAP1 methionine aminopeptidase 1	22	21	50-98%
8	CPB2 cysteine protease	1	1	
9	carbonic anhydrase	76	21	Different predicted isoforms
10	Tryparedoxin peroxidase (cTXNPx)	35	21	2 main families of proteins
11	Cell Division Cycle (cdc)-2-Related Kinase 12 (CRK12) Receptor	4	3	77-95%
12	zinc-dependent metalloprotease GP63 (Leishmanolysin)	54	21	52-94%
13	Leishmania donovani dipeptidylcarboxypeptidase (oligopeptidase A)	27	21	55-98%
14	Leishmania Malic enzyme	61	21	54-98%
15	glyceraldehyde 3-phosphate dehydrogenase	37	21	53-98%
16	citrate synthase	33	21	49-97%
17	cytochrome bc1	Membrane protein complex		
18	oxidosqualene cyclase (Squalene synthase)	22	21	74-97%
19	Topoisomerase I	>50	21	2 main families of proteins
20	cysteinyI proteases and Leishmania donovani calpain-like protein	Class of proteins		
21	Prolyl-tRNA synthetase	29	21	81-98%
22	Arginase	28	21	74-98%
23	Nicotinamidase	21	21	68-98%