

Table S2. Distribution of LBD types and domain models in the total LBD dataset.

Domain superfamily	LBD type	Domain model	No. of LBDs	% of each domain model
4HB_MCP	Single 4HB	4HB_MCP_1	12754	17.597
		TarH	2840	3.918
		CHASE3	1133	1.563
	Double 4HB	HBM	906	1.250
	<i>Subtotal:</i>		<i>17633</i>	<i>24.328</i>
Cache-like	Double Cache	dCache_1	11216	15.475
		Cache_3-Cache_2	1381	1.905
		dCache_3	598	0.825
		dCache_2	560	0.773
		Ykul_C	5	0.007
	Single Cache	sCache_2	4049	5.586
		sCache_3_3	779	1.075
		sCache_3_2	179	0.247
		Diacid_rec	90	0.124
		CHASE4	35	0.048
		CHASE8	23	0.032
		<i>Subtotal:</i>	<i>18915</i>	<i>26.097</i>
		Unknown	Unknown	UNKNOWN
PAS	PAS	PAS_3	6704	9.249
		PAS_9	2096	2.892
		PAS_4	1459	2.013
		PAS_8	430	0.593
		PAS	316	0.436
		PAS_7	19	0.026
		PAS_10	3	0.004
		PAS_6	1	0.001
		<i>Subtotal:</i>	<i>11028</i>	<i>15.215</i>
		GAF	GAF	GAF
GAF_2	232			0.320
GAF_3	1			0.001
<i>Subtotal:</i>	<i>1019</i>			<i>1.406</i>
Protoglobin	Protoglobin	Protoglobin	1682	2.321
		Globin	20	0.028
		Bac_globin	6	0.008
		<i>Subtotal:</i>	<i>1708</i>	<i>2.357</i>
PBP	Periplasmic Binding Proteins	Phosphonate-bd	74	0.102
		SBP_bac_5	64	0.088
		SBP_bac_3	60	0.083
		Peripla_BP_4	50	0.069
		SBP_bac_8	36	0.050
		OpuAC	13	0.018
		Peripla_BP_5	9	0.012
		DctP	8	0.011
		SBP_bac_1	5	0.007
		Peripla_BP_3	4	0.006
		NMT1_2	4	0.006
		Peripla_BP_6	3	0.004
		NMT1	2	0.003
		<i>Subtotal:</i>	<i>332</i>	<i>0.458</i>
HNOX-like	Heme and NO binding	HNOB	235	0.324
4Fe-4S	Iron-sulfur cluster binding	FeS	78	0.108
		Fer4_10	54	0.075
		Fer4	46	0.063
		Fer4_7	14	0.019
		Fer4_9	11	0.015
		Fer4_6	3	0.004
		Fer4_20	3	0.004
		<i>Subtotal:</i>	<i>209</i>	<i>0.288</i>
		GPCR-A	GPCR-like	7TMR-DISM_7TM
NADP-Rossman	NAD binding	GFO_IDH_MocA	15	0.021
		Semialdehyde_dh	4	0.006
		<i>Subtotal:</i>	<i>19</i>	<i>0.026</i>
Gx-transp	Transporter	5TM-5TMR_LYT	26	0.036
Beta-propeller	Extracellular binding	Reg_prop	38	0.052
GBD	Galactose binding	7TMR-DISMED2	10	0.014
		CBM_4_9	2	0.003
		<i>Subtotal:</i>	<i>12</i>	<i>0.017</i>
TPR	Protein-Protein interactions	TPR_19	6	0.008

		ANAPC3	1	0.001
		<i>Subtotal:</i>	<i>7</i>	<i>0.010</i>
Cupin	Nucleotide binding	cNMP_binding	7	0.010
HHH	Helix-turn-Helix	HHH_5	2	0.003
E-set	Sugar binding	Y_Y_Y	10	0.014
Phosphatase	Cyanide binding	Rhodanese	10	0.014
P-loop-NTPase	Nucleotide binding	ABC_tran	1	0.001
		ABC_sub_bind	1	0.001
		<i>Subtotal:</i>	<i>2</i>	<i>0.003</i>
No assigned superfamily	Zinc binding	CZB	1629	2.248
	PilJ	PilJ	1095	1.511
	Nitrate and nitrite binding	NIT	923	1.273
	Oxygen binding	Hemerythrin	276	0.381
		PocR	166	0.229
	c-di-GMPbinding	PilZ	270	0.373
	Amino acid binding	FIST_C	220	0.304
		FIST	219	0.302
	Domain of unknown function	DUF3365	213	0.294
	Hydrogen binding	Fe_hyd_lg_C	124	0.171
	Adenosyl group binding	CBS	65	0.090
	Ammonium transporter	Ammonium_transp	64	0.088
	Integral membrane sensor	MHYT	36	0.050
	Ligand binding	PrpR_N	18	0.025
	Putative LBD	He_PIG	8	0.011
	Putative LBD	Response_reg	7	0.010
	Putative LBD	Htr2	7	0.010
	Domain of unknown function	DUF4077	5	0.007
	Putative LBD	AhpC-TSA	5	0.007
	Putative LBD	Pro_CA	4	0.006
	Integral membrane domain	MASE3	4	0.006
	Putative LBD	DapB_N	4	0.006
	Putative LBD	Pyr_redox_2	3	0.004
	Putative LBD	NADH_4Fe-4S	3	0.004
	Putative LBD	H_kinase_N	3	0.004
	Domain of unknown function	DUF2222	3	0.004
	Putative LBD	TPR_16	2	0.003
	Putative LBD	T7SS_ESX_EspC	2	0.003
	Phosphate/sugar binding	PTS_EIIC	2	0.003
	Putative LBD	MASE4	2	0.003
	Putative LBD	GGDEF	2	0.003
	Domain of unknown function	DUF948	2	0.003
	Putative LBD	B12-binding	2	0.003
	Putative LBD	AIP3	2	0.003
	Putative LBD	YkyA	1	0.001
	Putative LBD	Vps53_N	1	0.001
	Putative LBD	VPS28	1	0.001
	Putative LBD	Usher	1	0.001
	Putative LBD	UPF0184	1	0.001
	Putative LBD	Ufd2P_core	1	0.001
	Putative LBD	Transgly	1	0.001
	Putative LBD	Tox-URI2	1	0.001
	Putative LBD	TnpV	1	0.001
	Putative LBD	THF_DHG_CYH_C	1	0.001
	Putative LBD	THF_DHG_CYH	1	0.001
	Putative LBD	SURF1	1	0.001
	Putative LBD	SpoIIAA-like	1	0.001
	Putative LBD	SOR_SNZ	1	0.001
	Putative LBD	Sensor_TM1	1	0.001
	Putative LBD	SDH_alpha	1	0.001
	Putative LBD	Porin_4	1	0.001
	Putative LBD	PhoU	1	0.001
	Putative LBD	Pentapeptide_4	1	0.001
	Putative LBD	Pentapeptide	1	0.001
	Putative LBD	PapC_N	1	0.001
	Putative LBD	OMS28_porin	1	0.001
	Putative LBD	NAD_binding_3	1	0.001
	Putative LBD	Mut7-C	1	0.001
	Putative LBD	MerR_1	1	0.001
	Putative LBD	LXG	1	0.001
	Putative LBD	Lipoprotein_7	1	0.001
	Putative LBD	Ion_trans_2	1	0.001
	Putative LBD	ING	1	0.001
	Putative LBD	IGPD	1	0.001
	Putative LBD	IclR	1	0.001
	Putative LBD	HTH_ParB	1	0.001
	Putative LBD	Glyco_hydro_2_N	1	0.001
	Putative LBD	Glyco_hydro_106	1	0.001
	Putative LBD	FRB_dom	1	0.001
	Putative LBD	FHIPEP	1	0.001
	Putative LBD	Fe-ADH	1	0.001
	Putative LBD	F420_oxidored	1	0.001
	Putative LBD	Exonuc_VII_L	1	0.001

Putative LBD	EMC3_TMCO1	1	0.001
Putative LBD	EF-hand_11	1	0.001
Putative LBD	EAL	1	0.001
Domain of unknown function	DUF442	1	0.001
Domain of unknown function	DUF4118	1	0.001
Domain of unknown function	DUF3235	1	0.001
Domain of unknown function	DUF1640	1	0.001
Putative LBD	DNA_pol_A_exo1	1	0.001
Putative LBD	CHASE	1	0.001
Putative LBD	Cas_DxTHG	1	0.001
Putative LBD	bZIP_2	1	0.001
Putative LBD	BLUF	1	0.001
Putative LBD	Band_7	1	0.001
Putative LBD	Bac_rhodopsin	1	0.001
Putative LBD	Asparaginase	1	0.001
Putative LBD	Alanine_zipper	1	0.001
Quorum sensing	AI-2E_transport	1	0.001
Putative LBD	5_3_exonuc_N	1	0.001
Putative LBD	5_3_exonuc	1	0.001
Putative LBD	2CSK_N	1	0.001
	<i>Subtotal:</i>	<i>5449</i>	<i>7.52</i>
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	TOTAL:	72480	100