

**Figure S4**

LS-24_I	7	NAAFRS.S.K.....N.N	EAYFFINDKYVLLD.Y.AP..GS.SA..D....	KV.
LS-24_II	65	DCSFDT...E.....N.N	EAFIFYENFCALID.Y.AP..HKK..D....	KI.
LS-24_III	121	DAAYRS.T.R.....G.K	EVYLFKGDQYARID.Y.G..S.....N....	SM.
LS-24_IV	175	DAAFAS.H.K.....T.N	EVYFFKDDHYARVK.V.TP...GGK...L....	A.I
1GEN_I	476	DGLAQI.....R.....G..	EIFFFKDRFVLR.TVTP.....R..D.....	K.PM
1GEN_II	521	DAVYEA...Q.....EE.	KAVFFAGNEYWIYS...A.....S.....	TL.
1GEN_III	569	DAAFNWS.....K.....NK.	KTYIFAGDKFWRVNE...VK....K.....	KM.
1GEN_IV	618	DAVVD.LQ..G.....GG.	HSYFFKGGAYLKLLEN...Q....S.LK...S.V	
3BA0_I	290	AVVT.V..G.....N..	KIFFFKDRFFWL.K.V...SE...R..P.....	KTS
3BA0_II	333	EAAYEI..EA.....RN	QVFLFKDDKYWLIS..N.....L.....	RP.
3BA0_III	381	DAAVFN..P.R.....FY.	RTYFFVDNQYWRVDE...RR....Q.....	MM.
3BA0_IV	430	DAVFYS..K.....N..	KYYFFQGSNQFEYD.F..L...L.Q.....	R.I
1PEX_I	285	DAITSL.....R.....G..	ETMIFKDRFFVRLH...PQ...Q..V.....	DA
1PEX_II	329	DAAYEH...PS.....HD.	LIFIFRGRKFWALN..G.....Y.....	DI.
1PEX_III	378	SAAVHF..E.D.....TG	KTLLFSGNQVWRVYD.D..TN...H.....	IM.
1PEX_IV	427	DAVYEK...N.....G..	YIYFFNGPIQFEYS.I..W...S..N....	R.I
1SU3_I	285	DAITTI.....R.....G..	EVMFFKDRFYMR.....T.....	
1SU3_II	329	EAAYEF...AD.....RD.	EVRFFKGNKYWAVQG...Q.....NV.	
1SU3_III	378	DAALSE..EN.....TG	KTYFFVANKYWRVYD.E..YK...R.....	SM.
1SU3_IV	427	DAVFMK...D.....G..	FFYFFHGTQRYKFD.P..K...T..K....	R.I
1QHU_I	34	DATFLD.D.N.....G..	TMLFFKDEFVWKS...H.....RGI	
1QHU_II	75	DAAFRH...G.....H..T	SVYLIKGDKVWVYT...S.....	
1QHU_III	121	DAAVEC...HRGECQ.....DE.	GILFFQGNRKWFVLDL...T...T..G....	T.K
1QHU_IV	166	TSALRW...LG.....RYY	CFQGNQFLRN.P.V...SG...EV.	
1HNX_IV	378	..ALCM...E..KPLGNSCSTSG.P.	NLYLIHGPNLYCYR.HV...D...K.LNAA...	
1HXX_I	236	SAMVS.DN..H.....G.	ATYVFSGSHYWRLD.....	
1HXX_II	281	DAAFSW...E.....D..	KLYLIQDTKVYVFLT...KG...GY...TL.	
1HXX_III	333	DAAFVC...PG.....S..S	RLHIMAGRLLWVLDL.L..K...SG...AQATW	
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LS-24_I		L..Y.....GP.TPVRDG..F....	KSLN..QT...IFG.S..YG.I.....	64
LS-24_II		I..L.....G.P.KKIADV..F....	PFEE..GT..VFE...SG.I.....	120
LS-24_III		V..N..A.....E.I.KSISSG...Y....	PCFR..NT...IFE...SG.A.....	174
LS-24_IV		M.....DG.V.REIVDY..W....	PSLK..DI...V...P...L.....	227
1GEN_I		.....G.PLL..VATF...W...PE...L.....	PE...K.I.....	520
1GEN_II		E...R.....GY.P.KPLTSL.....G...L..P.....	PD.VQ.RV.....	568
1GEN_III		D...P.....GF.P.KLIAD.A.W..N..A..I.....	P.....DNL.....	617
1GEN_IV		.....KF..GSIKS.D.W...LG.....C.....		660
3BA0_I		.....VN..LISS.L.W...PTL.....PS...G..I.....		332
3BA0_II		E...P.....NY.P.KSI.HS...F...G...F.P.....	N.FVKK.I.....	380
3BA0_III		D...P.....GY.P.KLITKN...F...Q..GI.....G.....	PK.I.....	429
3BA0_IV		T..K.....TLKS.N..SW.F.G.....C.....		470
1PEX_I		.....EL..FLTKSE.....W...PEL.....P.....	NR.I.....	328
1PEX_II		L..E.....GY.P.KKI.SE...L..G...LP.....L.P.....	K.EVK.KI.....	376
1PEX_III		D...K.....DY.P.RLIEED...F...P...GI.....G.D.....	K.V.....	426
1PEX_IV		V..R.....VMPANSILWC.....		466
1SU3_I		N.P..FYPE...V.E.L.NFISVF...W...P...QL.....P.....	NG.L.....	328
1SU3_II		L..H.....GY.P.KDIYSSE...G...FP.....RTVK.HI.....		377
1SU3_III		D...P.....GY.P.KMIAHDF...P...GI.....G.....	HK.V.....	426
1SU3_IV		L..T.....LQKA.N..SW.F.N...C.....		466
1QHU_I		.....R..EL.ISER...W...KN...F...IG...P.V.....		74
1QHU_II		.....P.KSLQDE...F...P...GI.....P.....	FPL.....	113
1QHU_III		..K.....E..RS.WP.....A.V.....G...N.C.....		165
1QHU_IV		...P.P.....GY.P.LDVRD...Y.....		204
1HXX_IV		.....KNLP.Q.P.QRVSRL...L.....G.....		434
1HXX_I		TNR.D.G...W.H.S.WPIAHQ...W...PQG..P.....S.....	T.V.....	280
1HXX_II		V...N.....GYP..KRLEKEL...G...S..P.PVI.....SLE.AV.....		332
1HXX_III		...T.....EL..PW.....P.....H...EK.V.DG...		377

**Figure S4.** Structure-based multiple sequence alignment of repeat sequences.

Structure-based multiple sequence alignment of hemopexin domains from MMPs, mammalian serum hemopexin and LS-24. The sequences have been designated by the PDB codes and by Roman numerals based on the location of blade with respect to the N-terminal of the fold. The sequence alignment presents the discernible insertions in the sequences of hemopexin folds. The linker regions in the case of LS-24 are longer and comprises of three short  $\alpha$ -helices of one turn, in comparison to shorter linker with a single  $\alpha$ -helix in other hemopexin domains of the mammalian origin. Sequences highlighted with yellow and turquoise, demarcate  $\beta$ -sheet and  $\alpha$ -helix respectively.