

**TABLE S4****Genes in the top 2.5% of individual-domain nonsynonymous  $F_{ST}$  differentiation.**

Gene ID	Gene Name	Domain	Nonsyn $F_{ST}$
FBgn0033093	CG3270	DAO	0.38458
FBgn0038260	CG14855	MFS_1	0.384254
FBgn0033697	Cyp6t3	p450	0.384211
FBgn0034295	CG10911	DUF725	0.360936
FBgn0051380	CG31380	APH	0.342056
FBgn0003510	Sry-alpha	Serendipity_A	0.33336
FBgn0045476	Gr64e	7tm_7	0.329101
FBgn0051205	CG31205	Trypsin	0.319649
FBgn0032602	CG13278	ASC	0.298351
FBgn0034513	CG13423	Peptidase_C1_2	0.296861
FBgn0085213	CG34184	DM4_12	0.290632
FBgn0260466	Indy-2	Na_sulph_symp	0.287405
FBgn0030946	CG6659	Dpy19	0.284422
FBgn0030752	CG9947	CDC50	0.282683
FBgn0038850	CG17279	JHBP	0.280486
FBgn0028852	CG15262	NOT2_3_5	0.278706
FBgn0020377	Sr-CII	MAM	0.27817
FBgn0031305	Iris	DUF3610	0.27248
FBgn0033443	CG1698	SNF	0.268159
FBgn0051099	CG31099	DUF227	0.265062
FBgn0021764	sdk	fn3	0.263057
FBgn0032066	CG9463	Glyco_hydro_38C	0.258052
FBgn0038005	Cyp313a5	p450	0.257784
FBgn0003486	spo	p450	0.2534
FBgn0038465	Irc	An_peroxidase	0.247982
FBgn0054005	CG34005	DUF725	0.242942
FBgn0038541	TyrRII	7tm_1	0.239625
FBgn0054049	CG34049	CAP	0.237954
FBgn0045487	Gr36a	7tm_7	0.236246

We calculated the mean nonsynonymous  $F_{ST}$  of each PFam domain in each gene and took the most-differentiated domain as that gene's representative domain. We list the top 2.5% of individual-domain differentiated genes.