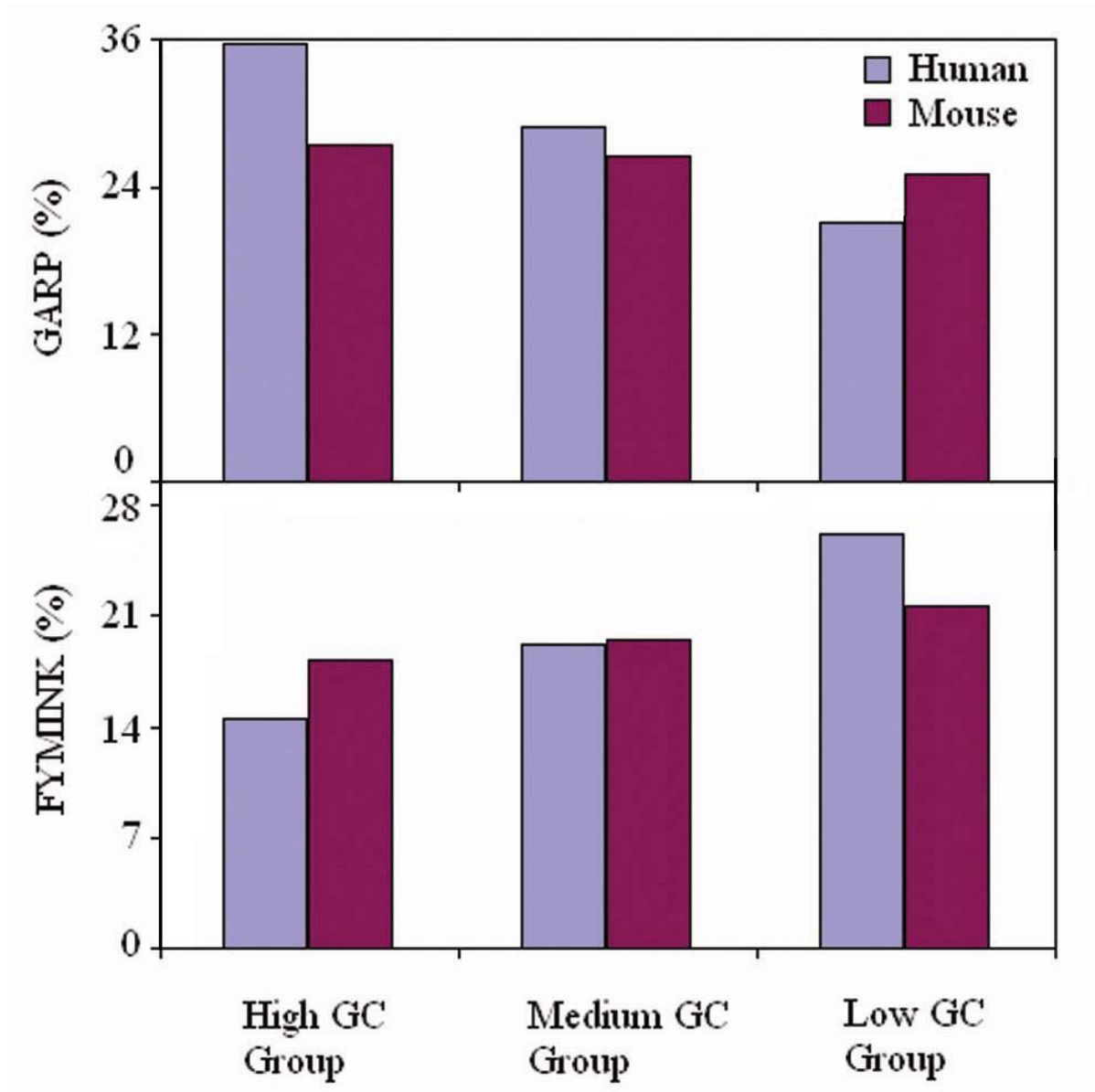
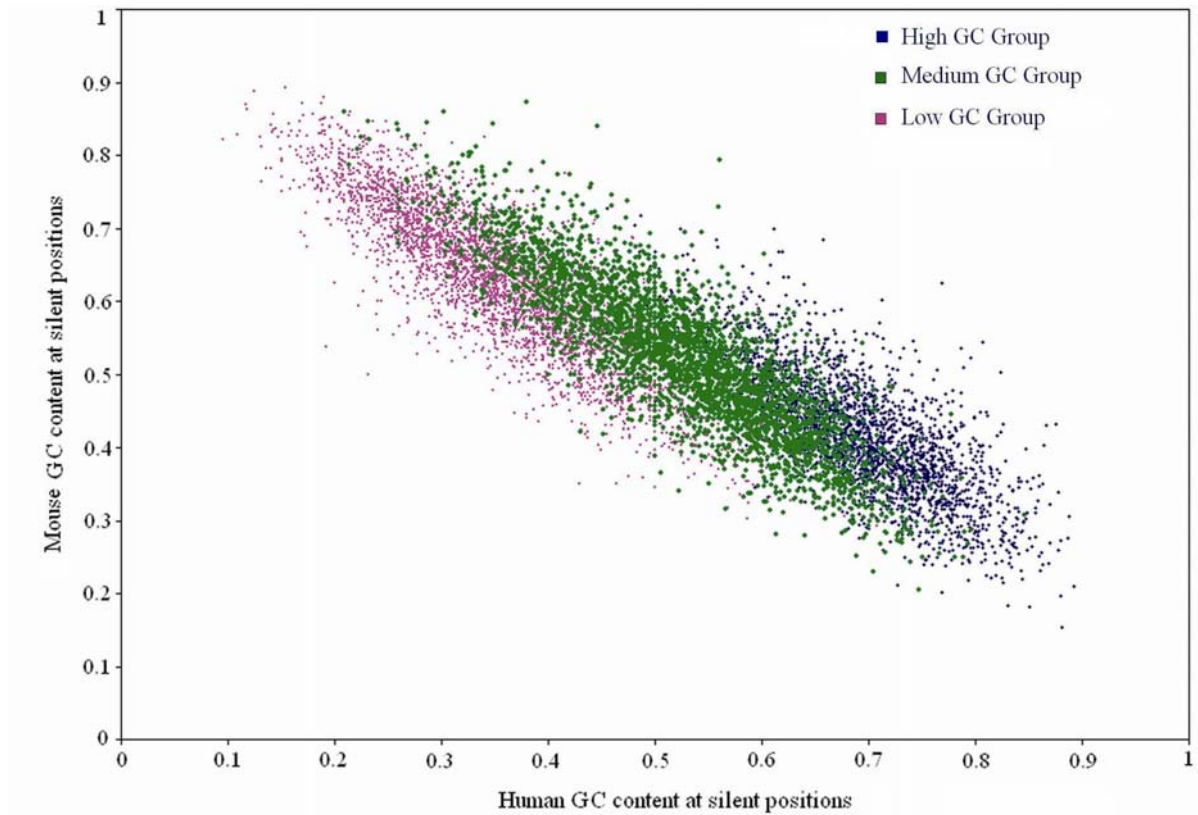


Supplementary Figure 1: Total percentage occurrence of Gly, Ala, Arg and Pro (encoded by G/C-rich codons) and that of Phe, Tyr, Met, Ile, Asn and Lys (encoded by A/U-rich codons) in high GC, medium GC and low GC groups of human (violet bars) and mouse (pink bars) orthologous proteins.



Supplementary Figure 2: Scatter plot of GC content of silent substitution positions of human and their corresponding mouse orthologous genes for high GC (blue), medium GC (green) and low GC (pink) groups. Human and mouse orthologous sequences, both having greater than 50 synonymous codons and gap free alignment regions with greater than 100 residues were considered here. For each orthologous pair, GC-content was calculated only for the silent substitution sites, i.e., the sites where synonymous substitutions had occurred between identical residues of the mouse and human orthologs.



Supplementary Table 1a: Number of replacements between each residue pairs of mouse-human orthologs for high GC group

		Human																			
		Gly	Ala	Arg	Pro	Phe	Tyr	Met	Ile	Asn	Lys	Ser	Thr	Cys	Trp	Val	Leu	Glu	Asp	His	Gln
Mouse	Gly	108023	1803	1031	140	16	11	56	39	268	121	2516	231	216	85	481	94	898	847	94	173
	Ala	1944	114592	206	1852	66	12	241	266	118	103	2447	4020	56	17	3144	385	718	449	69	132
	Arg	1222	241	94532	484	24	60	87	41	127	2518	806	262	371	317	99	541	244	79	1343	2448
	Pro	137	1779	556	97186	48	23	45	41	42	63	2097	806	36	20	168	1634	94	50	330	804
	Phe	26	95	53	108	61030	791	24	188	14	2	356	46	158	24	249	1757	8	7	80	18
	Tyr	31	30	127	48	700	44400	6	17	80	12	188	26	318	16	14	77	22	69	917	74
	Met	67	386	115	68	33	6	29276	611	13	130	77	764	5	11	1601	1753	86	15	6	55
	Ile	98	565	57	83	229	20	757	56297	73	32	265	1045	12	1	4572	1500	28	15	20	18
	Asn	572	240	225	52	14	71	16	53	45150	457	2878	569	44	3	46	33	211	1367	553	133
	Lys	260	186	3412	78	3	7	131	30	407	70500	237	413	4	33	88	70	1257	137	103	1244
	Ser	3749	4160	953	3603	334	143	87	187	2145	171	107933	2926	552	79	346	734	208	403	282	219
	Thr	422	6873	262	1227	69	17	851	749	514	415	2831	70689	44	8	949	342	213	157	69	110
	Cys	284	84	454	61	130	254	8	12	25	5	593	38	38249	96	48	86	6	21	145	40
	Trp	99	17	366	27	16	12	11	3	0	9	72	9	82	22224	20	135	15	2	10	115
	Val	672	4484	93	268	208	20	1318	3756	37	50	346	878	46	19	94462	2515	297	112	27	73
	Leu	123	492	707	2060	1387	71	1211	1012	30	54	728	322	88	144	2321	172576	92	28	300	712
	Glu	1170	1014	284	94	7	12	47	19	149	785	153	155	8	15	365	61	101420	3237	67	1267
	Asp	1167	703	84	61	9	41	14	23	1088	112	381	144	18	6	130	27	3799	71227	219	125
	His	136	67	1899	457	44	611	12	22	427	64	245	76	143	17	23	259	85	232	38676	1405
	Gln	208	167	3389	975	17	46	44	11	90	845	167	111	63	151	68	807	1477	99	1382	68409

The value in each cell (i, j) indicates the number of times the amino acid residue for the ith row in mouse orthologous proteins replaced by the amino acid residue for the jth column in the human protein for high GC group.

Supplementary Table 1b: Number of replacements between each residue pairs of mouse-human orthologs for medium GC group

		Human																			
		Gly	Ala	Arg	Pro	Phe	Tyr	Met	Ile	Asn	Lys	Ser	Thr	Cys	Trp	Val	Leu	Glu	Asp	His	Gln
Mouse	Gly	109247	1572	1062	122	26	28	59	72	394	235	2560	253	242	90	673	118	1337	1064	80	164
	Ala	1715	107394	209	1688	112	30	281	455	196	177	2972	4753	66	10	3561	433	769	488	56	140
	Arg	1178	176	89218	447	30	81	127	71	243	4017	934	376	395	322	104	479	356	78	1276	2372
	Pro	112	1570	438	97714	98	33	68	80	55	92	3113	1114	48	28	195	1691	105	52	462	1033
	Phe	28	94	33	129	64953	888	39	326	24	15	512	76	172	29	319	2079	18	14	99	23
	Tyr	31	30	96	54	749	48308	10	21	130	16	230	37	380	25	27	97	18	96	982	83
	Met	57	312	149	56	54	8	33868	1105	27	173	103	879	10	12	1642	1648	80	11	13	67
	Ile	95	536	94	97	343	27	1016	70057	153	86	340	1406	23	2	4982	1676	48	42	25	27
	Asn	467	203	233	70	17	147	28	135	55218	823	3213	770	42	4	59	47	269	1585	606	128
	Lys	283	169	3701	89	9	17	201	84	825	90225	329	527	11	33	114	109	1514	176	110	1341
	Ser	2782	3507	848	3804	523	244	134	330	3626	371	121625	3652	735	95	410	1041	230	502	320	247
	Thr	348	5566	351	1150	82	33	1024	1486	875	631	3113	79120	44	8	1134	337	220	169	64	124
	Cys	272	82	369	78	177	418	9	18	55	15	804	51	37847	90	42	129	13	22	174	45
	Trp	100	17	262	16	21	19	16	8	3	17	86	14	97	21791	30	165	19	3	12	112
	Val	610	3759	114	253	387	26	1671	5839	66	109	378	1066	50	23	97764	2663	365	139	28	87
	Leu	98	451	519	1999	2062	115	1483	1820	51	81	991	420	109	185	2527	171268	109	46	343	781
	Glu	1383	850	317	100	10	16	88	36	251	1336	201	210	13	25	401	111	112810	3833	85	1463
	Asp	1209	661	80	67	15	112	17	48	1566	203	483	182	29	4	192	33	4443	79104	262	133
	His	116	53	1350	415	61	880	14	30	618	135	304	80	187	22	31	313	124	323	40412	1611
	Gln	205	116	2676	902	20	94	46	21	177	1292	203	108	45	135	85	828	1601	161	1522	75314

The value in each cell (i, j) indicates the number of times the amino acid residue for the ith row in mouse orthologous proteins replaced by the amino acid residue for the jth column in the human protein for medium GC group.

Supplementary Table 1c: Number of replacements between each residue pairs of mouse-human orthologs for low GC group

		Human																			
		Gly	Ala	Arg	Pro	Phe	Tyr	Met	Ile	Asn	Lys	Ser	Thr	Cys	Trp	Val	Leu	Glu	Asp	His	Gln
Mouse	Gly	116738	1465	953	92	42	42	80	175	646	311	2411	313	293	61	894	126	1901	1462	100	155
	Ala	1658	114211	162	1674	113	37	338	885	343	307	3975	6393	73	9	4193	499	1058	669	73	173
	Arg	972	167	96369	303	37	116	211	178	395	6603	955	486	292	178	127	433	389	105	1230	1912
	Pro	101	1354	311	103845	137	73	63	164	129	142	4178	1470	61	15	225	1742	123	66	563	1282
	Phe	20	70	28	102	78174	1186	41	449	35	20	659	66	213	25	371	2330	13	10	88	23
	Tyr	28	28	84	30	949	59346	8	37	211	26	305	35	571	33	31	128	34	127	1040	95
	Met	50	248	146	45	60	11	42450	1900	58	272	129	1028	5	6	1624	1477	61	25	13	50
	Ile	84	531	119	100	471	33	1288	95635	325	198	401	1733	18	8	6335	2035	62	63	46	26
	Asn	366	174	209	49	29	245	47	278	78601	1524	3733	975	56	1	84	60	347	2030	715	163
	Lys	254	156	4059	71	13	28	258	198	1467	132079	341	718	12	13	134	99	1907	234	105	1436
	Ser	2102	3195	808	3304	869	452	155	613	6508	547	149355	4498	892	50	485	1561	283	705	370	222
	Thr	286	5117	427	972	88	50	1166	2612	1630	1150	3563	96024	62	9	1190	391	282	204	84	138
	Cys	222	75	262	79	356	774	10	36	103	16	1167	62	41061	103	32	122	8	52	224	64
	Trp	63	3	184	14	37	24	16	9	7	20	76	5	103	23298	22	178	19	4	16	94
	Val	496	3264	122	205	577	41	1995	9402	117	175	466	1309	61	18	111615	3023	384	226	37	75
	Leu	81	363	353	1519	2990	140	1764	3003	88	141	1353	428	110	153	2685	193480	104	29	366	641
	Glu	1478	807	277	85	17	34	102	95	387	2056	212	236	14	16	489	113	144658	5014	115	1679
	Asp	1081	541	62	50	20	159	26	90	2520	262	506	189	36	5	254	50	5952	100062	329	144
	His	81	45	872	362	96	1348	15	48	1258	184	373	92	239	17	32	325	108	421	46930	1931
	Gln	144	119	1758	760	27	114	48	46	221	1970	202	131	49	85	77	695	1765	144	1765	90319

The value in each cell (i, j) indicates the number of times the amino acid residue for the ith row in mouse orthologous proteins replaced by the amino acid residue for the jth column in the human protein for low GC group.