

**Figure S1**

**A**

	A	C	D	F	G	H	I	K	L	M	N	P	Q	R	S	T	V	Total	
Observed frequency	A	4.3	4.0	0.0	0.0	8.0	0.7	1.8	0.5	2.3	0.0	10.7	1.0	0.0	1.0	15.8	26.7	9.5	86.3
	C	3.2	0.3	0.0	0.0	2.2	0.0	4.5	0.5	4.3	0.3	35.3	0.5	0.0	0.0	5.0	4.0	7.5	67.6
	G	3.0	1.3	1.0	0.0	8.0	0.0	0.8	1.0	0.0	11.3	1.7	0.0	0.0	8.8	16.2	2.8	56.0	
	U	5.5	0.3	0.0	1.0	6.8	0.3	2.8	0.0	8.3	2.7	41.7	13.8	1.0	0.0	12.3	7.2	13.2	117.0
	Total	16.0	6.0	1.0	1.0	25.0	1.0	10.0	2.0	15.0	3.0	99.0	17.0	1.0	1.0	42.0	54.0	33.0	327

  

	A	C	D	F	G	H	I	K	L	M	N	P	Q	R	S	T	V	Total	
Expected frequency	A	4.2	1.6	0.3	0.3	6.6	0.3	2.6	0.5	4.0	0.8	26.1	4.5	0.3	0.3	11.1	14.3	8.7	86.3
	C	3.3	1.2	0.2	0.2	5.2	0.2	2.1	0.4	3.1	0.6	20.5	3.5	0.2	0.2	8.7	11.2	6.8	67.6
	G	2.7	1.0	0.2	0.2	4.3	0.2	1.7	0.3	2.6	0.5	16.9	2.9	0.2	0.2	7.2	9.2	5.6	56.0
	U	5.7	2.1	0.4	0.4	8.9	0.4	3.6	0.7	5.4	1.1	35.4	6.1	0.4	0.4	15.0	19.3	11.8	117.0
	Total	16.0	6.0	1.0	1.0	25.0	1.0	10.0	2.0	15.0	3.0	99.0	17.0	1.0	1.0	42.0	54.0	33.0	327

$P$ -value(Aln4, residue 4) =  $5.7 \times 10^{-7}$

**B**

