

## Supplementary Table 2

		99N	99S	00N	00S	01N	01S	02N	02S	03N	03S	04N	04S	05N	05S	06N	06S	07N	07S	08N	08S	09N	09S	10N	10S	11N	11S	12N	12S	13N	13S	14N	14S	15N	15S	
HA	G5V*	0	0	0.828	0.284	0.264	0.152	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	K92T*	0	0	0.828	0.284	0.264	0.152	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	D271N*	0	0	0.824	0.284	0.264	0.152	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	Q33H*	0	0	0.808	0.284	0.092	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	R50G*	0	0	0	0.6	0.58	0.236	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	S199P*	0	0	0	0.6	0.58	0.236	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	P273S*	0	0	0.084	0.6	0.58	0.248	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	S247C*	0	0	0	0.58	0.58	0.236	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	A106V*	0	0	0	0	0.092	0.312	0.94	0.888	0.232	0.02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	N144D*	0	0	0	0	0	0.28	0.928	0.888	0.108	0.02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	S186G*	0	0.072	0	0	0.092	0.312	0.924	0.888	0.232	0.02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	R50G	0	0	0.008	0.096	0.064	0.288	0.052	0.112	0.768	0.904	0.956	1	0.976	0.968	0.5	0.16	0.28	0.056	0.004	0	0	0	0	0.008	0	0	0	0	0	0	0	0	0	0	0
	E83K	0	0	0	0	0	0.048	0.044	0.112	0.768	0.98	1	1	1	0.992	0.96	1	1	0.972	0.82	0.944	1	1	1	1	1	0.992	0.976	0.984	0.996	0.984	0.988	0.976	0.98	0.992	0.996
	A131T	0	0	0	0	0	0	0.024	0.072	0.768	0.98	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.976	0.992	1	1	0.996	0.996	1	0.992	0.996
	S186G	0	0	0	0	0	0	0.032	0.112	0.768	0.98	1	1	1	1	1	1	0.988	1	0.972	1	0.984	1	1	1	1	1	0.976	0.976	0.992	0.992	0.968	0.996	1	1	1
	V202I	0	0	0	0	0	0.048	0.044	0.112	0.768	0.98	1	1	1	1	1	1	1	1	1	1	0.992	1	1	1	1	1	0.976	1	1	0.992	0.996	0.996	0.992	1	1
	W222R	0	0	0	0	0	0.048	0.044	0.112	0.768	0.98	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.976	1	1	1	0.996	0.996	1	1	1
	G225D	0	0	0.008	0.096	0.064	0.288	0.052	0.112	0.768	0.98	1	1	0.96	0.436	0.084	0	0.012	0	0	0	0	0	0	0.008	0	0	0	0	0	0	0	0	0	0	
	L25I	0	0	0	0	0	0	0	0.048	0.744	0.98	1	0.936	0.992	0.952	0.996	1	1	1	0.984	1	1	0.992	0.744	0.992	0.984	1	0.972	0.992	1	1	0.984	0.996	1	0.992	0.996
	H75Q	0	0	0	0	0	0	0	0.048	0.744	0.98	0.988	1	1	1	1	1	1	0.992	1	1	1	0.992	0.964	1	1	1	0.976	1	1	0.992	0.988	0.996	1	1	1
	H155T	0	0	0	0	0	0	0	0.048	0.744	0.98	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.976	1	1	1	0.996	0.996	1	1	1
	Q156H	0	0	0	0	0	0	0	0	0.612	0.98	1	1	1	1	0.968	1	0.988	1	0.992	1	1	1	1	1	1	1	0.976	0.992	1	1	0.996	0.996	1	1	1
	N126D*	0	0	0	0	0	0	0	0	0	0.756	0.624	0.008	0.004	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Y105H*	0	0	0	0	0	0	0	0	0	0.68	0.008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Y159F	0	0	0	0	0	0	0	0	0	0.052	0.184	0.976	0.984	1	1	1	1	1	0.988	1	1	0.992	1	0.992	1	1	0.976	0.992	1	1	0.744	0.26	0.132	0.032	0.032
	S189N	0	0	0	0	0	0	0	0	0	0.104	0.264	0.976	0.984	1	1	1	1	1	1	1	0.96	0.188	0.024	0.008	0	0	0	0	0	0	0	0	0	0	0
	K145N	0	0	0	0	0	0	0	0	0	0	0.004	0.876	0.968	0.62	0.992	1	0.984	1	1	1	0.972	1	1	1	0.976	0.368	0.244	0.36	0.104	0.004	0	0	0	0	
	S227P	0	0	0	0	0	0	0	0	0	0.132	0.2	0.764	0.94	1	1	1	1	1	1	1	1	1	1	1	1	1	0.976	1	1	1	0.996	0.996	1	1	1
	V226I	0	0	0	0	0	0	0	0	0	0	0	0.664	0.904	1	1	1	1	1	1	1	1	1	1	1	1	1	0.976	1	1	1	0.996	0.996	1	1	1
	S193F	0	0	0	0	0	0	0	0	0	0	0	0	0.04	0.564	0.916	1	0.988	1	1	1	1	1	1	0.992	1	1	0.976	1	1	1	0.988	0.988	1	1	1
	D225N	0	0	0	0	0	0	0	0	0	0	0	0	0.04	0.564	0.856	0.84	0.96	1	0.964	0.756	0.86	0.992	1	0.96	0.996	0.992	0.944	0.96	0.988	0.992	0.684	0.208	0.132	0.032	
	G50E*	0	0	0	0	0	0	0	0	0	0	0	0	0.024	0.032	0.492	0.84	0.012	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	G50E	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0	0.62	0.944	0.996	1	1	1	1	0.98	0.996	0.996	0.976	1	1	0.992	0.996	0.996	1	1	

K140I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0	0.62	0.944	0.988	1	0.948	0.988	1	0.98	0.976	0.992	0.932	0.948	1	0.984	0.996	0.996	1	1
Q261R	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0	0.58	0.912	0.984	0.964	0.984	0.94	0.848	0.96	0.988	0.972	0.976	1	1	1	0.964	0.98	0.904	0.884
K173Q	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.044	0.524	0.816	0.948	1	1	0.992	1	1	0.956	1	1	1	0.996	0.996	1	1
E62K*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.052	0.7	0.576	0.052	0.044	0.004	0	0	0	0	0	0	0	0
K158N*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.052	0.7	0.576	0.052	0.044	0.004	0	0	0	0	0	0	0	0
N189K*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.04	0.7	0.576	0.052	0.044	0.004	0	0	0	0	0	0	0	0
N144K*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.04	0.696	0.576	0.052	0.044	0.004	0	0	0	0	0	0	0	0
V213A*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0.564	0.128	0.016	0.032	0	0	0	0	0	0	0	0	0
P194L*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0.56	0.128	0.016	0.032	0	0	0	0	0	0	0	0	0
K158N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.112	0.4	0.94	0.956	0.996	0.976	1	1	1	0.944	0.996	1	1
N189K	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.112	0.4	0.94	0.956	0.996	0.976	1	1	1	0.996	0.996	1	1
T212A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.112	0.356	0.86	0.596	0.936	0.832	0.784	0.964	1	0.996	0.996	1	1
N45S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.112	0.4	0.852	0.8	0.876	0.732	0.504	0.104	0.016	0	0.008	0	0
D53N*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.132	0.352	0.668	0.356	0.236	0.348	0.096	0.004	0	0	0	0
I230V*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.092	0.352	0.668	0.356	0.236	0.328	0.096	0.004	0	0	0	0
Y94H*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.044	0.352	0.664	0.356	0.236	0.348	0.096	0.004	0	0	0	0
E280A*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.144	0.344	0.62	0.356	0.236	0.348	0.096	0.004	0	0	0	0
N312S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.012	0.204	0.48	0.152	0.64	0.672	0.6	0.884	0.98	0.988	0.988	1	1
V223I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.016	0.632	0.732	0.632	0.896	0.996	0.996	0.996	1	1	
A198S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.02	0.624	0.672	0.608	0.884	0.988	0.988	0.988	0.988	0.992	
N145S*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.004	0.572	0.556	0.292	0.012	0.012	0	0.008	0	0	
S45N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0.02	0.164	0.348	0.884	0.984	0.996	0.98	1	1	
T48I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.02	0.164	0.348	0.884	0.984	0.996	0.988	1	1	
N278K	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.008	0.028	0.164	0.348	0.884	0.996	0.936	0.996	1	1	
S157L	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.02	0.164	0.316	0.872	0.936	0.84	0.864	0.872	0.988	
N145S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.004	0.12	0.836	0.984	0.94	0.972	1	0.992	
Q33R	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.02	0.156	0.336	0.808	0.932	0.888	0.976	1	1	
N53D*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.004	0.096	0.52	0.72	0.596	0.448	0.176	0.012	
T128A*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.004	0.02	0.344	0.7	0.604	0.44	0.184	0.02	
R142G*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.004	0.02	0.344	0.7	0.624	0.448	0.184	0.02	
N225D	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.18	0.512	0.816	0.98
Q311H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.176	0.512	0.816	0.98
L3I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.176	0.488	0.816	0.98
N144S	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.176	0.492	0.816	0.98
F159Y	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.112	0.42	0.816	0.98
K160T	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.164	0.42	0.772	0.928