

Sauerbrei A, Bohn-Wippert K, Kaspar M, Krumbholz A, Karrasch M, Zell R. 2015. Database on natural polymorphisms and resistance-related non-synonymous mutations in thymidine kinase and DNA polymerase genes of herpes simplex virus types 1 and 2. *J Antimicrob Chemother* *in press*, doi: 10.1093/jac/dkv285, PMID: 26433780

Supplementary Table 1: Natural polymorphisms in TK gene of HSV-1 as aa changes including nt changes, their location, antivirals tested, methods for phenotypic testing and references.

Amino acid change	Nucleotide change	Domain	Antivirals tested	Test methods for phenotype	PMID
C6G	A16G	non-conserved region	Aciclovir (ACV), Foscarnet (FOS)	plaque reduction assay, plating efficiency assay, DNA reduction assay, dye uptake assay, yield reduction assay (enzyme linked virus inhibitory reporter assay - ELVIRA)	19795980 14670581 10882609 11238837 23687576 15456088
H7P	A20C	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
A12P	G34C	non-conserved region	ACV, FOS	plaque reduction assay	20733037
A12T	G34A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
D14V	A41T	non-conserved region	ACV, Brivudin (BVDU), Penciclovir (PCV), Cidofovir (CDV)	modified dye uptake assay including formazan test	20211650
D14Y	G40T	non-conserved region	ACV, BVDU, PCV, CDV, FOS	plaque reduction assay, modified dye uptake assay including formazan test, dye uptake assay	18336925 20211650
Q15L	A44T	non-conserved region	ACV	plaque reduction assay	21778105
A17V	C30T	non-conserved region	ACV	dye uptake assay	10882609
R18C	C52T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
S19P	T55C	non-conserved region	ACV, BVDU, PCV, CDV, FOS	modified dye uptake assay including formazan test	20211650
R20H	G59A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
R20S	C58T/ G59C	non-conserved region	ACV, FOS	plaque reduction assay	20733037
N23S	A68G	non-conserved region	ACV, FOS	plaque reduction assay, DNA reduction assay, dye uptake assay, plating efficiency assay, TK functional assay	19795980 14670581 10882609 23687576
R26H	G77A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
A28V	C83T	non-conserved region	ACV	plaque reduction assay	21778105
L29V	T85G	non-conserved region	ACV, FOS	plaque reduction assay	24075863
R30C	C88T	non-conserved region	ACV, FOS	plaque reduction assay	20733037
R32C	C94T	non-conserved region	ACV, FOS	dye uptake assay	18336925
Q35deletion	deletion (CAA) nt 103-105	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
K36D	A106G/ A108T/C	non-conserved region	ACV, FOS	plaque reduction assay	20733037

K36deletion	deletion (AAA) nt 106-108	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
K36E	A106G	non-conserved region	ACV, FOS	plaque reduction assay, DNA reduction assay, dye uptake assay, plating efficiency assay, yield reduction assay (ELVIRA)	19795980 14670581 10882609 23687576
R41H	G122A	non-conserved region	ACV, FOS	plaque reduction assay, modified dye uptake assay including formazan test with recombinant viruses TK functional assay	14670581 22906425 27426251
L42P	T125C	non-conserved region	ACV, FOS	plaque reduction assay, yield reduction assay (ELVIRA), dye uptake assay, cell growth assay	14670581 10882609 11238837 15456088
Q44H	G132C	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test, DNA reduction assay, TK functional assay	22024514 14670581
Q67R	A200G	non-conserved region	ACV	plaque reduction assay	21778105
L72V	C214T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
R75C	C223T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
D76N	G226A	non-conserved region	ACV, FOS	dye uptake assay	25218782
D77N	G229A	non-conserved region	ACV	dye uptake assay	10882609
I78F	A232T	non-conserved region	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650
R89Q	G266A	non-conserved region	ACV, FOS	plaque reduction assay, yield reduction assay (ELVIRA), dye uptake assay, plating efficiency assay, DNA reduction assay, cell growth assay, TK functional assay	19795980 23582986 14670581 10882609 11238837
A98T	G292A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
I100T	T299C	non-conserved region	ACV, FOS	dye uptake assay	25218782
R106H	G317A	non-conserved region	ACV, BVDU, PCV, FOS	modified dye uptake assay including formazan test with recombinant virus	27426251
E111K	G331A	non-conserved region	ACV, FOS	plaque reduction assay	20733037
A118V	C353T	non-conserved region	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test, modified dye uptake assay including formazan test with recombinant virus	22155911 26055375 27426251
A137T	G409A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
V138F	G412T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
V138I	G412A	non-conserved region	ACV	plaque reduction assay, DNA reduction assay, plating efficiency assay, TK functional assay	19795980 23582986

L139V	C415G	non-conserved region	ACV, BVDU, PCV, FOS	modified dye uptake assay including formazan test with recombinant virus	27426251
A140V	C419T	non-conserved region	ACV, FOS	plaque reduction assay	14670581
H142Y	C424T	non-conserved region	ACV, FOS	dye uptake assay	25218782
E146G	A437G	non-conserved region	ACV, FOS	plaque reduction assay	20733037
H151Y	C451T	non-conserved region	ACV, FOS	dye uptake assay	18336925
A156P	G466C	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
A156V	C467T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
F161L	C481T	non-conserved region	ACV, FOS	plaque reduction assay	14670581
V191A	T572C	non-conserved region	ACV, FOS	plaque reduction assay	20733037
A192V	C575T	non-conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), dye uptake assay, cell growth assay, DNA reduction assay, TK functional assay	19795980 14670581 10882609 11238837 23687576
I214T	T641C	non-conserved region	ACV, FOS	yield reduction assay (ELVIRA)	15456088
D215A	A644C	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
D215H	G643C	non-conserved region	ACV, FOS	dye uptake assay	25218782
D215N	G643A	non-conserved region	ACV	plaque reduction assay	21778105
K219T	A656C	conserved region	ACV, BVDU, PCV, FOS	modified dye uptake assay including formazan test, modified dye uptake assay including formazan test with recombinant virus	22024514 27426251
A233S	G697T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
G240E	G719A	non-conserved region	ACV, FOS	plaque reduction assay, dye uptake assay, plating efficiency assay, DNA reduction assay, cell growth assay, TK functional assay	19795980 23582986 14670581 10882609 11238837
A243S	G727T	non-conserved region	ACV, FOS	plaque reduction assay, dye uptake assay	18336925 20733037
G251C	G751T	non-conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), dye uptake assay, cell growth assay, DNA reduction assay, TK functional assay	19795980 14670581 10882609 11238837 23687576
W259R	T775A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	22024514

A265T	G793A	non-conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, TK functional assay	14670581 23687576
V267L	G799T	non-conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), DNA reduction assay, dye uptake assay, cell growth assay, TK functional assay	19795980 14670581 10882609 11238837 23687576
P268L	C803T	non-conserved region	ACV, FOS	dye uptake assay	25218782
P268M	C802A/C803T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
P268T	C802A	non-conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), dye uptake assay, DNA reduction assay, cell growth assay, TK functional assay	19795980 14670581 10882609 11238837 23687576
G271D	G812A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
A272T	G814A	non-conserved region	ACV, FOS	dye uptake assay	18336925
E273K	G817A	non-conserved region	ACV, FOS	plaque reduction assay	20733037
E273Q	G817C	non-conserved region	ACV, FOS	plaque reduction assay	20733037
P274T	C820A	non-conserved region	ACV, FOS	dye uptake assay	18336925
Q275P	A824C	non-conserved region	ACV, FOS	plaque reduction assay, modified dye uptake assay including formazan test	22024514 21778105
S276G	A826G	non-conserved region	ACV, FOS	plaque reduction assay	14670581
S276R	C828A	non-conserved region	ACV, BVDU, PCV, FOS	modified dye uptake assay including formazan test, modified dye uptake assay including formazan test with recombinant virus	22024514 27426251
N277K	C831A/G	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
N277S	A830G	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
R281Q	G842A	non-conserved region	ACV, FOS	plaque reduction assay, dye uptake assay, plating efficiency assay, DNA reduction assay	19795980 14670581 10882609
D286E	C858A	conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), dye uptake assay, cell growth assay, TK functional assay	19795980 14670581 10882609 11238837 6293376
R293W	C877T	non-conserved region	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650
A294V	C881T	non-conserved region	ACV, FOS	dye uptake assay	18336925
P295T	C883A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	22024514

L298R	T893G	non-conserved region	ACV, BVDU, PCV, FOS	modified dye uptake assay including formazan test with recombinant virus	27426251
P299S	G895A/ C896G	non-conserved region	ACV, FOS	dye uptake assay	25218782
G302S	C958A	non-conserved region	ACV, FOS	plaque reduction assay	14670581
D303N	G907A	non-conserved region	ACV, FOS	plaque reduction assay	24075863
A309V	C926T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
A316V	C947T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
H323Y	C967T	non-conserved region	ACV, FOS	plaque reduction assay	20733037
L327M	C980A	non-conserved region	ACV, FOS	dye uptake assay	18336925
D328E	T984G/A	non-conserved region	ACV, FOS	dye uptake assay	18336925
S332L	T994C/ C995T	non-conserved region	ACV	DNA reduction assay, plating efficiency assay	19795980
S332P	T994C	non-conserved region	ACV, FOS	dye uptake assay	18336925
A334T	G1000A	non-conserved region	ACV, FOS	plaque reduction assay	20733037
G335D	G1004A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
L341R	C1021A/ T1022C	non-conserved region	ACV, FOS	dye uptake assay	25218782
S345P	T1033C	non-conserved region	ACV, BVDU, PCV, FOS	modified dye uptake assay including formazan test, modified dye uptake assay including formazan test with recombinant virus, DNA reduction assay, TK functional assay	22024514 23582986 23026414 27426251
G346W	G1036T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
V348I	G1042A	non-conserved region	ACV, BVDU, PCV, FOS	plaque reduction assay, modified dye uptake assay including formazan test with recombinant virus, plating efficiency assay, yield reduction assay (ELVIRA), DNA reduction assay, TK functional assay	19795980 14670581 22906425 15456088 27426251
T350I	C1049T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
T350S	A1048T	non-conserved region	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650
V352I	G1054A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
S357C	C1070G	non-conserved region	ACV, FOS	plaque reduction assay	20733037
I358V	A1072G	non-conserved region	ACV, FOS	plaque reduction assay	24075863
D363N	G1087A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375

L364P	T1091C	non-conserved region	ACV	dye uptake assay, TK functional assay	10882609 16970995
M367T	T1100C	non-conserved region	ACV	dye uptake assay	10882609
G373E	G1118A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26055375
E374A	A1124C	non-conserved region	ACV	dye uptake assay	10882609
A375P	A1123C	non-conserved region	ACV	plaque reduction assay	24075863
N376H	A1126C	non-conserved region	ACV, FOS	plaque reduction assay, plating efficiency assay, yield reduction assay (ELVIRA), dye uptake assay, cell growth assay, TK functional assay	19795980 14670581 10882609 11238837 23687576
N376P	A1126C/ A1123C	non-conserved region	ACV, FOS	plaque reduction assay, cell growth assay	20733037 11238837
N376T	A1127C	non-conserved region	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650