

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* 71:6-16, doi: 10.1093/jac/dkv285, PMID: 26433780

Supplementary Table 6: Natural polymorphisms in DNA pol of HSV-2 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	References
A9T	G25A	non-conserved region (pre NH ₂ -terminal domain)	Aciclovir (ACV), Foscarnet (FOS)	plaque reduction assay	14670581
G12R	G34C	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
P15S	C43T	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	14670581
P15R	C43T	non-conserved region (pre NH ₂ -terminal domain)	ACV, Brivudin (BVDU), FOS, Penciclovir (PCV), Cidofovir (CDV)	modified dye uptake assay including formazan test	20211650
R18P	G53C	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
Q34H	G102T/C	non-conserved region (pre NH ₂ -terminal domain)	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650
A36G	C107G	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
P37L	C110T	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	20733037
C40W	C120G	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	modified dye uptake assay including formazan test	22024514
R41H	G122A	non-conserved region (pre NH ₂ -terminal domain)	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650

Q43R	C127A/ A128G	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	20733037
H49Y	C145T	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	20733037
T53A	A157G	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
L60P	T179C	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	20733037
Q64R	A191G	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
R101W	C301T	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
L128S	C381A/ T382G	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
E139K	G415A	non-conserved region (pre NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	14670581
T144P	A430C	non-conserved region (NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
I153T	T458C	non-conserved region (NH ₂ -terminal domain)	ACV, FOS	plaque reduction assay	24075863
T202M	C605T	non-conserved region (NH ₂ -terminal domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
R203Q	G608A	non-conserved region (NH ₂ -terminal domain)	ACV, FOS	modified dye uptake assay including formazan test	22024514

L229M	C685A	non-conserved region (NH2-terminal domain)	ACV, FOS	plaque reduction assay	24075863
A232T	G694A	non-conserved region (NH2-terminal domain)	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650
A251V	C752T	non-conserved region (NH2-terminal domain)	ACV, FOS	plaque reduction assay	24075863
N286Y	A856T	non-conserved region (NH2-terminal domain)	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	20211650
I291V	A871G	non-conserved region (NH2-terminal domain)	ACV, FOS	plaque reduction assay	24075863
A300T	G898A	non-conserved region (NH2-terminal domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
G324E	G971A	non-conserved region (NH2-terminal domain)	ACV, FOS	plaque reduction assay	20733037
F336L	T1006C	non-conserved region (NH2-terminal domain)	ACV, FOS	plaque reduction assay	24075863
T347M	C1040T	non-conserved region (NH2-terminal domain)	ACV, FOS	plaque reduction assay	24075863
Q507H	G1521C/T	non-conserved region (3'-5'-exonuclease domain)	ACV, FOS	plaque reduction assay	20733037
A547V	C1640T	conserved region d-region C (3'-5'-exonuclease domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
R628C	C1882T	non-conserved region	ACV, FOS	plaque reduction assay	26338148

G646S	G1936T	non-conserved region	ACV, FOS	plaque reduction assay	24075863
D671N	G2011A	non-conserved region	ACV, FOS	plaque reduction assay	20733037
D676G	C2028G	non-conserved region	ACV, FOS	plaque reduction assay	20733037
D676N	G2026A	non-conserved region	ACV, FOS	plaque reduction assay	20733037
deletion (DD) aa 676-677	deletion (GACGAC) nt 2026-2031	non-conserved region	ACV, FOS	plaque reduction assay	20733037
deletion (DED) aa 677-679	deletion (GACGAG GAC) nt 2029-2037	non-conserved region	ACV, FOS	plaque reduction assay	20733037
E678G	A2033G	non-conserved region	ACV, PCV, FOS	plaque reduction assay	20733037 26338148
G680R	G2039A	non-conserved region	ACV, FOS	plaque reduction assay	20733037
G680D	G2039A	non-conserved region	ACV, FOS	plaque reduction assay	24075863
deletion (GD) aa 681-682	deletion (GACGAG) nt 2041-2046	non-conserved region	ACV, FOS	plaque reduction assay	20733037
E682G	A2045G	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26338148
E682K	A2045G	non-conserved region	ACV, FOS	plaque reduction assay	20733037

deletion (ED) aa 682-683	deletion (GAGGAC) nt 2044-2049	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26338148
deletion (DGDE) aa 683-686	deletion (GACGGGGAC GAG) nt 2047-2058	non-conserved region	ACV, FOS	plaque reduction assay	20733037
insertion (DGDE) aa 683-686	insertion (GACGGGGAC GAG) nt 2047-2058	non-conserved region	ACV, FOS	plaque reduction assay	20733037
insertion (GD) aa 686-687	insertion (GGCGAC) nt 2056-2061	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26338148
D708N	G2100A	conserved region II (palm domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
D716N	G2146A	conserved region II (palm domain)	ACV, BVDU, FOS, PCV, CDV	modified dye uptake assay including formazan test	14670581
E746K	G2236A	non-conserved region (palm domain)	ACV, FOS	plaque reduction assay	22155911
Q799R	G2396A	non-conserved region (fingers domain)	ACV, FOS	plaque reduction assay	20733037
T801P	A2401C	non-conserved region (fingers domain)	ACV, BVDU, FOS, PCV, CDV	plaque reduction assay, modified dye uptake assay including formazan test	14670581 20211650
E803K	G2407A	non-conserved region (fingers domain)	ACV, FOS	plaque reduction assay	24075863
A869D	C2606A	non-conserved region (palm domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
A879V	C2636T	non-conserved region (palm domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148

P880H	C2639A	non-conserved region (palm domain)	ACV, BVDU, PCV, FOS, CDV	modified dye uptake assay including formazan test	20211650
T903M	C2708T	non-conserved region (palm domain)	ACV, FOS	plaque reduction assay	20733037
A904G	C2711G	non-conserved region (palm domain)	ACV, FOS	plaque reduction assay	14670581
A905E	C2714A	non-conserved region (palm domain)	ACV, FOS	plaque reduction assay	14670581
M910I	G2730A/C/T	non-conserved region (palm domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
K913M	A2738T	non-conserved region (palm domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
T987S	C2960G	non-conserved region (thumb domain)	ACV, FOS	modified dye uptake assay including formazan test	22024514
L995F	A2985C/T	non-conserved region (thumb domain)	ACV, BVDU, PCV, FOS, CDV	modified dye uptake assay including formazan test	20211650
A1000T	G2998A	non-conserved region (thumb domain)	ACV, FOS	plaque reduction assay	20733037
R1025H	G3074A	non-conserved region (thumb domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
I1026S	T3077G	non-conserved region (thumb domain)	ACV, BVDU, PCV, FOS, CDV	modified dye uptake assay including formazan test	20211650
A1083T	G3247A	non-conserved region (thumb domain)	ACV, FOS	plaque reduction assay	20733037

deletion (PGDEPA) aa 1106-1111	deletion (CCAGGGGAC GAGCCCGCC) nt 3316-3333	non-conserved region (thumb domain)	ACV, FOS	plaque reduction assay	20733037
insertion (APGDEPA) aa 1112-1119	insertion (GCCCCAGGG GACGAGCCC GCC) nt 3334-3354	non-conserved region (thumb domain)	ACV, FOS	modified dye uptake assay including formazan test	26338148
A1114V	C3341T	non-conserved region (thumb domain)	ACV, FOS	plaque reduction assay	20733037
E1149G	A3446G	non-conserved region (thumb domain)	ACV, FOS	plaque reduction assay	20733037
A1156T	G3466A	non-conserved region (thumb domain)	ACV, FOS	plaque reduction assay	24075863
A1209V	C3626T	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26338148
A1223V	C3668T	non-conserved region	ACV, FOS	plaque reduction assay	20733037
R1230Q	G3689A	non-conserved region	ACV, FOS	modified dye uptake assay including formazan test	26338148