Erratum to: Phenotypic and genetic characterization of varicella-zoster virus mutants resistant to acyclovir, brivudine and/or foscarnet

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The authors would like to correct the errors in the original publication of the article. The errors include details under the sub-headings “Sequence evolution of selected VZV genes in resistant Mutants”, Discussion, and in Figs. 3 and 4 and Table 3. The corrected sentences, figures and table are given below for your reading.

As the amino acid substitutions Asn479Ile and Arg601Met were observed in the viral DNA polymerase (vDNA pol) and not in the viral thymidine kinase (vTK), the following sentences were modified accordingly.

The corrected paragraph under the sub-heading “Sequence evolution of selected VZV genes in resistant mutants” should read:

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After adaptation, a selection of genes (Table 1) of all resistant isolates and corresponding parental virus controls was amplified and sequenced. In 7 of 9 of the resistant strains, nucleotide exchanges were found in at least one analyzed ORF (Table 3). Exclusively, only the MR-PFA mutant showed nucleotide exchanges although the IC50 values of all resistant MR isolates increased beyond the tenfold of cutoff values. Nucleotide exchanges were mainly found in the viral thymidine kinase gene (vTK, ORF 36, Fig. 4) as well as in the viral DNA polymerase gene (vDNApol, ORF 28, Fig. 3). Sequence analysis of our resistant isolates revealed several mutations in the vTK gene resulting in aa substitutions. One aa exchange was found in ACV-resistant isolate PP, namely at positions 256 (Thr → Met), whereas BVdU-resistant isolates PP-BVdU and 06-BVdU contained exchanges at positions 62 (Ile → Phe) and 85 (Leu → Pro). In addition, strain 06-BVdU contained a premature stop codon at codon position 296 (Table 3). Interestingly, MR-PFA displayed an aa exchange at codon position 92 (Leu → Met) within the vTK gene although PFA does not depend on vTK phosphorylation and pharmacologically affects the vDNA pol. Mutations within the vDNA pol (ORF 28) of our isolates led to aa exchanges at positions 684 (Aln → Val) and 804 (Ile → Thr) in isolate PP-PFA, in isolate 06-PFA at positions 662 (Lys → Glu) and 773(Ala → Val), and in isolate MR-PFA at position 680 (Val → Ala) (Table 3). 06-ACV presented exchanges at positions 479 (Asn → Ile) and 601 (Arg → Met) as well as PP-ACV, which showed one exchange at position 1180 (Met → Thr). Additionally, isolate PP-BVdU also showed nucleotide exchanges in the important viral transactivator IE 62 gene (ORF 62) and in the viral glycoprotein gI gene (ORF 67). The sequences of the PP-BVdU IE 62 and gI genes were compared to other sequences listed in NCBI by using the BLAST algorithm

Table 3 Non-silent mutations found in resistant isolates and corresponding amino acid substitutions

Resistant isolates IC ₅₀	ORF	Protein	Nucleotide position and substitution	Amino acid position and substitution
ACV				
PP/753.5 μ M	28	vDNA pol	T 3539 C	Met 1180 Thr
	36	vTK	C 767 T	Thr 256 Met
06/4289 μ M	28	vDNA pol	A 1436 T	Asn 479 Ile
	28	vDNApol	G 1802 T	Arg 601 Met
MR/1610.5 μ M			None	None
BVdU				
PP/3180 μ M	36	vTK	A 184 T	Ile 62 Phe
	62	IE 62	A 3071 G	Gln 1024 Arg
	67	gI	G 101 A	Ser 34 Asn
06/963 μ M	36	vTK	T 254 C	Leu 85 Pro
	36	vTK	T 887 G	Leu 296 Stop
MR/719 μ M			None	None
PFA				
PP/811 μ M	28	vDNA pol	C 2051 T	Ala 684 Val
	28	vDNA pol	T 2411 C	Ile 804 Thr
06/1321 μ M	28	vDNA pol	A 1984 G	Lys 662 Glu
	28	vDNA pol	C 2318 T	Ala 773 Val
MR/1326 μ M	28	vDNA pol	T 2039 C	Val 680 Ala
	36	vTK	C 274 A	Leu 92 Met

Fig. 3 Amino acid substitutions found within the vDNA pol encoded by ORF28. Black boxes indicate highly conserved regions. Mutations found in our resistant isolates are indicated in red

[12–20]. None of our detected base exchanges (A 3071 G, G 101 A, Table 3) were issued in this database.

The corrected sentences under Discussion are given below. The second sentence should read as:

Even though only one aa substitution found at position 62 (Ile → Phe) in isolate PP-BVdU is located within the active domain of the ATP-binding site of the vTK, the post-adaptational IC₅₀ of the resistant isolates 06-BVdU,

Fig. 4 Amino acid substitutions within the viral thymidine kinase (vTK). Filled boxes indicate stop codons, and empty boxes indicate aa substitutions. Blue boxes represent functional domains of the protein. Mutations found in our resistant isolates are indicated in red

PP-ACV/BVdU and MR-PFA exhibited a distinct rise beyond the tenfold proving resistance toward ACV.

In second paragraph, the fourth sentence should read as:

These findings suggest a complete loss of the functional activity of the vTK, although all other aa substitutions are located peripheral to the active ATP-binding site.

In fifth paragraph, the fourth sentence should read as:

All of our clinical isolates resistant to PFA presented aa substitutions, five in total, whereas three nt substitutions within the vDNA pol gene resulting in aa exchanges were found in ACV-resistant isolates PP-ACV and 06-ACV. Interestingly, 5 of 8 of these substitutions appeared within regions II and III.

The authors would like to apologize for any inconvenience this may have caused to the readers of the journal.