

Case of poliomyelitis caused by significantly diverged derivative of the poliovirus type 3 vaccine Sabin strain circulating in the orphanage

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Supplementary material

Table S1. Mutations in the genomes of the Syzran isolates

Genome region	Nucleotide (amino acid) mutation	Genome(s) of Syzran isolates harboring mutation	Genome region	Nucleotide (amino acid) mutation	Genome(s) of Syzran isolates harboring mutation
5'-UTR	G ₁₁₃ →A	all	VP1	C ₂₄₉₃ →U (T ₆ →I)*	all
	C ₁₂₃ →U	C-2		U ₂₅₆₉ →C	P-2
	G ₁₆₂ →A	all but C-3		A ₂₅₉₉ →G	all
	G ₁₈₉ →C	P-2		C ₂₆₁₁ →U	all
	C ₃₄₆ →U	C-2		C ₂₆₃₇ →U (A ₅₄ →V)	all
	G ₃₉₅ →A	all		A ₂₆₃₈ →G	C-2
	U ₄₇₂ →C*	all		U ₂₆₉₃ →A (S ₇₃ →T)	all
	U ₄₈₀ →C	all		A ₂₇₆₂ →G (T ₉₆ →A)	all
	U ₆₀₂ →C	all		U ₂₇₉₀ →C (M ₁₀₅ →T)	all
	G ₆₇₃ →G/A	C-3		G ₂₉₅₉ →A	all
	U ₇₀₈ →C	C-3		G ₂₉₇₄ →A	all
	U ₇₃₈ →C	C-3		A ₃₃₃₈ →G (N ₂₈₈ →D)**	all
	A ₇₇₂ →G	all		G ₃₃₄₄ →A (D ₂₉₀ →N)**	all
VP4	A ₇₇₂ →G	all		U ₃₃₇₆ →C	P-1 and P-2
VP2	A ₉₆₄ →G	C-3	2A	C ₃₅₂₂ →U (T ₄₉ →I)	all
	C ₁₀₃₅ →U (A ₂₉ →V)	P-1 and P-2		G ₃₅₇₉ →A (R ₆₈ →K)	C-2
	C ₁₀₈₄ →U	C-2		G ₃₆₇₆ →U	all
	U ₁₁₂₆ →C	C-3		U ₃₇₁₅ →C	C-2
	C ₁₁₄₁ →U	C-3		U ₃₇₇₈ →C	all but C-3
	A ₁₂₅₂ →G	all	2B	U ₃₈₃₈ →C	all
	G ₁₃₉₀ →A	all		G ₄₀₆₆ →A	all
	A ₁₄₄₀ →U (N ₁₆₄ →I)**	C-1	2C	G ₄₃₄₂ →A	all
	G ₁₄₄₂ →A (A ₁₆₅ →T)**	all		A ₄₄₁₇ →C	all
	U ₁₄₄₆ →C (V ₁₆₆ →A)**	all		A ₄₄₃₃ →G (T ₁₀₇ →A)	all
	G ₁₄₇₇ →A	all		A ₄₆₁₂ →U	C-3
	U ₁₅₄₀ →C	all		G ₄₆₃₀ →A	all
	U ₁₅₄₃ →C	all		U ₄₆₆₃ →C	all
	U ₁₅₉₁ →C	P-1 and P-2		A ₄₇₇₁ →G	P-1 and P-2
	U ₁₅₉₂ →C (L ₂₁₅ →M)	all		C ₄₇₇₄ →U	C-2
	C ₁₅₉₆ →U (A ₂₁₆ →V)	C-3		C ₄₇₈₆ →U	P-2
				U ₄₈₄₉ →C	all
VP3	C ₁₇₉₅ →U	all but C-3		A ₄₈₆₁ →G	all
	G ₁₈₀₇ →A	C-2		G ₄₈₆₈ →A (G ₂₅₂ →S)	all
	U ₁₈₅₅ →C	C-2		A ₄₈₇₂ →G (E ₂₅₃ →G)	all
	C ₁₉₉₈ →U (S ₇₉ →L)**	C-2		C ₄₉₁₇ →U (T ₂₆₈ →M)	all
	U ₂₀₃₄ →C (F ₉₁ →S)*	all but C-3		U ₅₀₃₅ →C	P-1 and P-2
	U ₂₂₉₉ →C	all but C-3			
	U ₂₃₄₀ →A (F ₁₉₃ →Y)	C-3			
	U ₂₄₁₃ →C	all			

*Adaptive mutations

**Mutations in the antigenic sites

Genome region	Nucleotide (amino acid) mutation	Genome(s) of Syzran isolates harboring mutation	Genome region	Nucleotide (amino acid) mutation	Genome(s) of Syzran isolates harboring mutation
3A	C ₅₁₁₆ →U	C-3	3D	G ₆₀₈₆ →A (V ₃₇ →I)	all
	A ₅₁₁₉ →G	P-1 and P-2		A ₆₁₀₉ →G	all
	G ₅₁₄₆ →U (R ₁₅ →S)	all		U ₆₁₅₇ →C	all but C-3
	A ₅₁₅₈ →G	P-1 and P-2		U ₆₂₄₄ →C	all
	C ₅₃₅₇ →U (H ₈₆ →Y)	C-3		C ₆₂₆₆ →C/U	C-3
3B	A ₅₃₆₅ →G	C-2		G ₆₃₀₄ →C	all
	C ₅₃₈₆ →U	all		C ₆₃₃₇ →U	C-2
	U ₅₃₉₈ →C	all		U ₆₃₆₄ →U/C	C-3
	G ₅₄₂₅ →A	all		A ₆₄₉₀ →G	all
3C	C ₅₅₂₄ →U	all		U ₆₅₅₀ →C	all
	A ₅₅₆₇ →G (I ₄₇ →V)	all		U ₆₅₆₂ →C	all
	C ₅₅₉₇ →U	C-2		C ₆₅₈₉ →U	all
	C ₅₆₀₂ →A (D ₅₈ →E)	all but C-3		C ₆₅₉₂ →U	C-2
	C ₅₆₇₇ →U	all		A ₆₆₅₈ →G	C-2
	U ₅₈₃₂ →C (I ₁₃₅ →T)	all		A ₆₆₆₄ →A/G	C-3
	C ₅₈₅₄ →U	all		C ₆₇₆₉ →U	all

*Adaptive mutations

**Mutations in the antigenic sites

Table S2. Mutations* in the genomes of Syzran isolates found in other vaccine-related polioviruses type 3.

Genome region	Nucleotide (amino acid) mutation	Genome(s) of Syzran isolates harboring mutation	Known or assumed biological relevance of mutation	Previous report (s) of same mutation in Sabin-3-derived viruses
5'-UTR	G ₁₆₂ →A	all but C-3	Stabilization of domain II structure	1, 2
	G ₃₉₅ →A	all	Stabilization of domain IV structure	1-4
	U ₄₈₀ →C	all	Stabilization of domain V structure	1, 2
	U ₆₀₂ →C	all	–	1, 5
	U ₇₃₈ →C	C-3	–	1
VP4	A ₇₇₂ →G	all	–	4
VP2	A ₉₆₄ →G	C-3	–	2
	C ₁₀₃₅ →U (A ₂₉ →V)	P-1, P-2	–	6
	G ₁₃₉₀ →A	all	–	2
	G ₁₄₄₂ →A (A ₁₆₅ →T)	all	Region of antigenic site 2	1, 7**, 8
	U ₁₄₄₆ →C (V ₁₆₆ →A)	all	Antigenic site 2	1, 7
VP3	U ₁₅₉₂ →C (L ₂₁₅ →M)	all	–	1
	C ₁₇₉₅ →U	all but C-3	–	1
	C ₁₉₉₈ →U (S ₇₉ →L)	C-2	Antigenic site 4	9
	U ₂₂₉₉ →C	all but C-3	–	1, 2
VP1	U ₂₄₁₃ →C	all	–	5
	C ₂₆₃₇ →U (A ₅₄ →V)	all	–	1, 2, 4, 5, 9, 10
	U ₂₇₉₀ →C (M ₁₀₅ →T)	all	Interaction with poliovirus receptor	1, 2, 3, 5, 7, 9, 10
	A ₃₃₃₈ →G (N ₂₈₈ →D)	all	Antigenic site 3	1, 2, 9
2A	G ₃₃₄₄ →A (D ₂₉₀ →N)	all	Antigenic site 3	1
	G ₃₆₇₆ →U	all	–	1
2C	U ₃₇₇₈ →C	all but C-3	–	2
	A ₄₄₃₃ →G (T ₁₀₇ →A)	all	–	1
3C	C ₄₉₁₇ →U (T ₂₆₈ →M)	all	–	4, 9
	U ₅₈₃₂ →C (I ₁₃₅ →T)	all	Stabilization of ciRNA structure	1, 11

*Without three known adaptive mutations observed in most variants of Sabin-3.

**In this article only amino acid substitutions were listed.

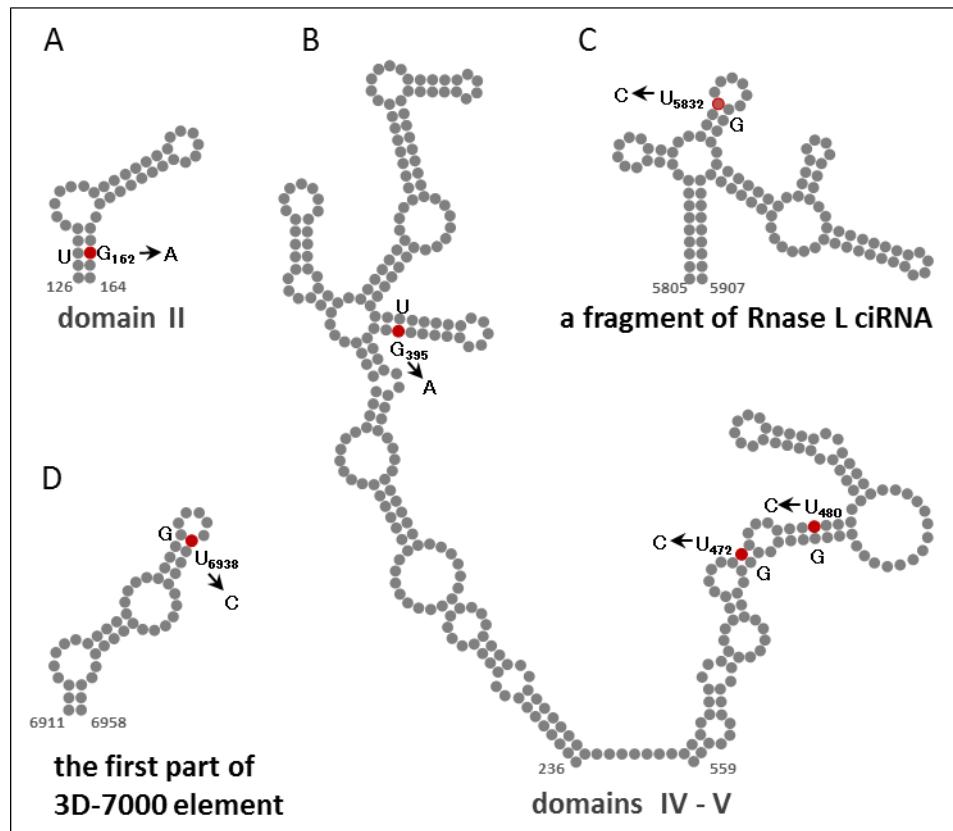


Figure S1. Nucleotide substitutions in the phylogenetically conserved RNA structural elements of the genomes of the poliovirus isolates, in comparison with the Sabin-3 strain. The positions of changed nucleotides are marked in red, and corresponding mutations are indicated; the nucleotides involved in the resulting base-pairing are also shown. A. Domain II of 5'UTR. B. Domains IV-V of 5'UTR [12]. C. A fragment of Rnase L competitive inhibitor element of viral RNA (ciRNA) [13]. D. The first conservative structural element of 3D-7000 [14].

References

1. Laassri M.; Zagorodnyaya T.; Chumakov K. Vaccine Derived Poliovirus RNA Sequences (Unpublished).
2. Rakoto-Andrianarivelo M.; Gumede N.; Jegouic S.; Balanant J.; Andriamamonjy S.N.; Rabemanantsoa S.; Birmingham M.; Randriamanalina B.; Nkolomoni L.; Venter M.; Schoub B.D.; Delpéroux F.; Reynes J.M. Reemergence of recombinant vaccine-derived poliovirus outbreak in Madagascar. *J Infect Dis.* **2008**, *197*, 1427-1435, doi: 10.1086/587694.
3. Blomqvist S.; Savolainen-Kopra C.; Paananen A.; El Bassioni L.; El Maamoon Nasr E.M.; Firstova L.; Zamiatina N.; Kutateladze T.; Roivainen M. Recurrent isolation of poliovirus 3 strains with chimeric capsid protein Vp1 suggests a re-combination hot-spot site in Vp1. *Virus Res.* **2010**, *151*, 246–251, doi: 10.1016/j.virusres.2010.05.006.
4. Shahmahmoodi S.; Parvaneh N.; Burns C.; Asghar H.; Mamishi S.; Tabatabaei H.; Chen Q.; Teimourian S.; Gooya M.M.; Esteghamati A.R.; Mousavi T.; Yousefi M.; Farrokhi K.; Mashlool M.; Kew O.; Nategh R. Isolation of a type 3 vaccine-derived poliovirus (VDPV) from an Iranian child with X-linked agammaglobulinemia. *Virus Res.* **2008**, *137*, 168-172, doi: 10.1016/j.virusres.2008.07.006.
5. Savolainen-Kopra C.; Samoilovich E.; Kahelin H.; Hiekka A.K.; Hovi T.; Roivainen M. Comparison of poliovirus recombinants: accumulation of point mutations provides further advantages. *J Gen Virol.* **2009**, *90*, 1859-1868, doi: 10.1099/vir.0.010942-0.
6. Cassemiro K.M.S.M.; Burlandy F.M.; da Silva EE. Rare natural type 3/type 2 intertypic capsid recombinant vaccine-related poliovirus isolated from a case of acute flaccid paralysis in Brazil, 2015. *J Gen Virol.* **2016**, *97*, 1545-1550, doi: 10.1099/jgv.0.000484.
7. Yakovenko M.L.; Cherkasova E.A.; Rezapkin G.V.; Ivanova O.E.; Ivanov A.P.; Eremeeva T.P.; Baykova O.Y.; Chumakov K.M.; Agol V.I. Antigenic evolution of vaccine-derived polioviruses: changes in individual epitopes and relative stability of the overall immunological properties. *J Virol.* **2006**, *80*, 2641–2653, doi:10.1128/JVI.80.6.2641-2653.2006.
8. Blomqvist S.; Bruu A.L.; Stenvik M.; Hovi T. Characterization of a recombinant type 3/type 2 poliovirus isolated from a healthy vaccinee and containing a chimeric capsid protein VP1. *J Gen Virol.* **2003**, *84*, 573-580, doi: 10.1099/vir.0.18708-0.
9. World Health Organization (WHO). Report of the second meeting of the technical consultation group for global eradication of poliomyelitis. WHO/EPI/GEN/98/04. Geneva, Switzerland, 1998. Available online: http://apps.who.int/iris/bitstream/10665/63994/1/WHO_EPI_GEN_98.04.pdf])
10. Cherkasova E.; Laassri M.; Chizhikov V.; Korotkova E.; Dragunsky E.; Agol V.I.; Chumakov K. Microarray analysis of evolution of RNA viruses: evidence of circulation of virulent highly divergent vaccine-derived polioviruses. *Proc Natl Acad Sci USA.* **2003**, *100*, 9398-9403, doi: 10.1073/pnas.1633511100.
11. Famulare M.; Chang S.; Iber J.; Zhao K.; Adeniji J.A.; Bukbuk D.; Baba M.; Behrend M.; Burns C.C.; Oberste M.S. Sabin vaccine reversion in the field: a comprehensive analysis of Sabin-like poliovirus isolates in Nigeria. *J Virol.* **2015**, *90*, 317-331, doi: 10.1128/JVI.01532-15.
12. Pilipenko E.V.; Blinov V.M.; Romanova L.I.; Sinyakov A.N.; Maslova S.V. Agol V.I. Conserved structural domains in the 5'-untranslated region of picornaviral genomes: an analysis of the segment controlling translation and neurovirulence. *Virology.* **1989**, *168*, 201–209, doi:10.1016/0042-6822(89)90259-6.
13. Han J.Q.; Townsend H.L.; Jha B.K.; Paranjape J.M.; Silverman R.H.; Barton D.J. A phylogenetically conserved RNA structure in the poliovirus open reading frame inhibits the antiviral endoribonuclease RNase L. *J Virol.* **2007**, *81*, 5561–5572, doi:10.1128/JVI.01857-06.
14. Burrill C.P.; Westesson O.; Schulte M.B.; Strings V.R.; Segal M.; Andino R.J. Global RNA structure analysis of poliovirus identifies a conserved RNA structure involved in viral replication and infectivity. *Virology.* **2013**, *87*, 11670-11683, doi: 10.1128/JVI.01560-13.