

Supplementary Figure 1. Phylogenetic analysis of GT4 NS3 sequences

Black lettering: Patient sequences from the Elbasvir/Grazoprevir Phase 2/3 development program; Red lettering: North American sequences from external databases; Green lettering: Selected sequences used for Lab evaluation; OT: Other GT4 sequences from external databases



Supplementary Figure 2. Phylogenetic analysis of GT4 NS5A sequences

Black lettering: Patient sequences from the Elbasvir/Grazoprevir Phase 2/3 development program; Red lettering: North American sequences from external databases; Green lettering: Selected sequences used for Lab evaluation; OT: Other GT4 sequences from external databases



Supplementary Figure 3. An alignment of NS5A subtype sequences

			1	50
GU814265	NS5A (4a)	(1)	AESWLVWVWDVWVCTVLSDFKTWLNKAKLLPLMPGI	PFLSCQRGYKGEWRGD
DQ418784	NS5A (4a)	(1)	ADSWLVWVWDVWVCTVLSDFKTWLNKAKLLPLMPGV	PFLSCQRGYRGEWRGE
FJ025854	NS5A (4b)	(1)	DTSWLREIWDVWVCTVLSDFKTWLNKAKLLPAMPGL	PFLSCQRGYKGEWRGD
FJ025855	NS5A (4b)	(1)	DTNWLREIWDVWVCTVLSDFKSWLNKAKLMPSMPGI	PFLSCQKGYKGVWRGD
FJ462435	NS5A (4b)	(1)	DSSWFREIWDVWVCTVLTDFKNWLNKAKLLPSMPGV	PFISCQRGYKGVWRGD
DQ418786	NS5A (4d)	(1)	DSSWFREIWDVWVCTVLTDFKNWLNKAKLLPSMPGV	PFISCQRGYKGVWRGD
EU392172	NS5A (4d)	(1)	DRSWLWEIWDVWVCTVLSDFKTWLNKAKLLPRMPGV	PFISCQRGYRGVWRGD
EF589161	NS5A (4f)	(1)	DSSWLWEIWDVWVCTVLSDFKTWLNKAKLLQMPGV	PFISCQKGYKGEWRGD
JX227963	NS5A (4g)	(1)	DSSWLREIWDVWVCTVLTDFKTWLNKAKLLPRMPGL	PFLSCQKGFKEWRGD
JX227971	NS5A (4g)	(1)	DSSWLREIWDVWVCTVLSDFKTWLNKAKLLPLMPGL	PFLSCQKGYRGEWRGD
FJ462433	NS5A (4m)	(1)	DRSWLWEVWDVWVCTVLSDFKTWLNKAKLLPSMPGI	PFLSCQRGYKGEWRGD
JX227972	NS5A (4m)	(1)	DRSWLWEVWDVWVCTVLSDFKTWLNKAKLLPSMPGI	PFISCQKGYKGEWRGD
JX227977	NS5A (4o)	(1)	TLDFWFEIWDVWVCTVLSDFKTWLNKAKLMPTMPGI	PFLSCQKGFKEWRGD
FJ462434	NS5A (4q)	(1)	CTSWLRDIWDVWVCTVLSDFKTWLNKAKLLPRMPGI	PFLSCQKGYRGEWRGE
			51	100
GU814265	NS5A (4a)	(51)	GVMHTT	CPCGADLAGHIKNGSMRITGPKTCSNTWHGTFPINAYTTGPGVP
DQ418784	NS5A (4a)	(51)	GIMHTK	CPCGAELAGHIKNGSMRITGPKTCSNTWHGTFPINAYTTGPGVP
FJ025854	NS5A (4b)	(51)	GVMHTK	CPCGADIAGHIKNGSMRIVGPRTCNTWHGTFPINATTTGSGVP
FJ025855	NS5A (4b)	(51)	CVMHTT	CPCGAELAGHIKNGSMRIVGPKTCSNTWHGTFPINASTTGAGVP
FJ462435	NS5A (4b)	(51)	GVMHTR	CPCGAELAGHIKNGSMRIVGPKTCSNTWHGTFPINTHTTGPVP
DQ418786	NS5A (4d)	(51)	GVMHTR	CPCGAELAGHIKNGSMRIVGPKTCSNTWHGTFPINTHTTGPVP
EU392172	NS5A (4d)	(51)	GVMHTT	CPCGAELAGHVKNGSMRIVGPKTCSNTWHGTFPINAYTTGPSVP
EF589161	NS5A (4f)	(51)	GVMHTI	CPCGAELAGHIKNGSMRIVGPRTCNTWHGTFPINAYTTGPGVP
JX227963	NS5A (4g)	(51)	GVMHTT	CPCGAQIAGHIKNGSMRIVGPKTCSNTWHGTFPINAYTTGPGVP
JX227971	NS5A (4g)	(51)	GVMHTV	CPCGASIAGHIKNGSMRIVGPKTCSNTWHGTFPINARTTGPGVP
FJ462433	NS5A (4m)	(51)	GVVHTK	CPCGARLAGHIKNGSMRIVGPRTCNTWQGTFFPINAYTTGPGVP
JX227972	NS5A (4m)	(51)	GVVHTK	CPCGARLAGHIKNGSMRIVGPKTCSNTWQGTFFPINAYTTGPGVP
JX227977	NS5A (4o)	(51)	GVMHTI	CPCGANLAGHIKNGSMRIVGPKTCSNTWHGTFPINAYTTGPGVP
FJ462434	NS5A (4q)	(51)	GVMHTT	CPCGAELAGHIKNGSMRIVGPKTCSNTWHGTFPINAYTTGPGVP
			101	150
GU814265	NS5A (4a)	(101)	IPAPNYKFALWRVSAEDYVEVRRVGD	FHYVTGVTQDNIKPCQVPAPEFF
DQ418784	NS5A (4a)	(101)	VPAPNYKFALWRVSAEEYVEVRRVGD	FHYVTGVTQDNIKPCQVPAPEFF
FJ025854	NS5A (4b)	(101)	VPAPNYKFALWRVSAEEYVEVRRVGD	FHYITGMTQDNIKPCQVPAPEFF
FJ025855	NS5A (4b)	(101)	IPAPNYKFALWRVSAEEYVEIRRVGE	FHYVTGMTQDNIKPCQVPAPEFF
FJ462435	NS5A (4b)	(101)	IPAPNYKFALWRVSAEDYVEVRRVGD	FHYITGVTQDNIKPCQVPAPEFF
DQ418786	NS5A (4d)	(101)	IPAPNYKFALWRVSAEDYVEVRRVGD	FHYITGVTQDNIKPCQVPAPEFF
EU392172	NS5A (4d)	(101)	IPAPNYKFALWRVSAEEYVEVRRVGE	FHYITGVTQDNIKPCQVPAPEFF
EF589161	NS5A (4f)	(101)	IPAPNYTFALWRVSAEEYVQVRKVG	DFHYVTGVTQDKIKPCQVPAPEFF
JX227963	NS5A (4g)	(101)	VPAPNYKFALWRVSAEEYVEVRRVGD	YHYVVGVTQDNIKPCQVPAPEFF
JX227971	NS5A (4g)	(101)	VPAPNYKFALWRVSAEEYVEVRRVGD	YHYVVGVTQDNIKPCQVPAPEFF
FJ462433	NS5A (4m)	(101)	IPAPNYKFALWRVSAEEYVEVRRVGD	FHYITGVTQDSIKPCQVPSPEFF
JX227972	NS5A (4m)	(101)	IPAPNYKFALWRVSAEEYVEVRRVGD	FHYITGVTQDTIKPCQVPSPEFF
JX227977	NS5A (4o)	(101)	IPAPNYEFALWRVSAEEYVEVRRVGE	FHYVTGMTQDNIKPCQVPAPEFF
FJ462434	NS5A (4q)	(101)	IPAPNYKFALWRVSAEEYVEVRRVGD	FHYITGVTQDNIKPCQVPAPEFF
			151	200
GU814265	NS5A (4a)	(151)	TEVDGIRLHRHAPKCKPLLRDEV	SFSVGLNSFVVGSQLPCEPEPDVAULT
DQ418784	NS5A (4a)	(151)	TEVDGIRLHRHAPKCKPLLRDEV	TFSVGLNSFVVGSQLPCEPEPDVAULT
FJ025854	NS5A (4b)	(151)	TEVDGVRHLHRYAPDCKPLLRDEV	SFSVGLNTFVVGSQLPCEPEPDVHULT
FJ025855	NS5A (4b)	(151)	TEVDGVRHLHRYAPPCKPLLRDEV	QFTVGLNTFVVGSQLPCEPEPDVQVLT
FJ462435	NS5A (4b)	(151)	TEVDGVRHLHRYAPPCKPLLRDEV	SFSVGLNNSFVVGSQLPCEPEPDVSVLT
DQ418786	NS5A (4d)	(151)	TEVDGVRHLHRYAPPCKPLLRDEV	SFSVGLNNSFVVGSQLPCEPEPDVSVLT
EU392172	NS5A (4d)	(151)	TEVDGVRHLHRYAPPCKPLLRDEV	SFTVGLNNSFVVGSQLPCEPEPDVAVVT

EF589161	NS5A	(4f)	(151)	TEVDGVR IHRHAPCKPLLTDEVTF SVGLNSFVVGSQLPCEPEPDVAVLT
JX227963	NS5A	(4g)	(151)	TEVDG VNLHRYAPPCKPLLRDEVTF SVGLNTFVVGSQLPCEPEPDVAVLT
JX227971	NS5A	(4g)	(151)	TEVDG VRLHRYAPPCKPLLRDEVTF SVGLNTFVVGSQLPCEPEPDVAVLT
FJ462433	NS5A	(4m)	(151)	TEVDG VRIHRHAPDCKPLLRDEVTF TVGLNTFVVGSQLPCEPEPDVAVLT
JX227972	NS5A	(4m)	(151)	TEVDG VRIHRHAPDCKPLLRDEVTF TVGLNSFVVGSQLPCEPEPDVAVLT
JX227977	NS5A	(4o)	(151)	TEVDG VRLHRHAPKCKPLLRREEVTF SVGLNSFVVGSQLPCEPEPDVVVT
FJ462434	NS5A	(4q)	(151)	TEVDG VRLHRHAPCKPLLRDEVAFTVGLNSFVVGSQLPCEPEPDVAVLT
			201	250
GU814265	NS5A	(4a)	(201)	SMLTDPSH ITAESARRRLARGSRPSLASSASQLSAPSLKATCTAPHDSP
DQ418784	NS5A	(4a)	(201)	SMLTDPSH ITAETASRRRLARGSPPSLASSASQLSAPSLKATCTARHGSP
FJ025854	NS5A	(4b)	(201)	SMLTDPSH LTAETARRRLARGSPPSLASSASQLSAPSLKATCTAHHDSP
FJ025855	NS5A	(4b)	(201)	SMLTDPSH ITAEAAARRRLARGSPPEASSASQLSAPSLKATCTTNHHSP
FJ462435	NS5A	(4b)	(201)	SMLTDPSH VTAEQAARRLGRGSPPSLASSASQLSAPSLKATCTAHHDSP
DQ418786	NS5A	(4d)	(201)	SMLTDPSH VTAEQAARRLGRGSPPSLASSASQLSAPSLKATCTAHHDSP
EU392172	NS5A	(4d)	(201)	SMLTDPSH ITAEAAARRRLARGSPPSLASSASQLSAPSLKATCTDHKDSP
EF589161	NS5A	(4f)	(201)	SMLTDPSH ITAEAAARRRLARGSPPSLASSASQLSAPSLKATCTAHHSSP
JX227963	NS5A	(4g)	(201)	SMLTDPSH ITAESARRRLARGSPPSLASSASQLSAPSLKATCTTNHHSP
JX227971	NS5A	(4g)	(201)	SMLTDPSH ITAESARRRLARGSPPSLASSASQLSAPSLKATCTAHHDSP
FJ462433	NS5A	(4m)	(201)	SMLTDPSHMTAETARRRLARGSPPSLASSASQLSAPSLKATCPADH DSP
JX227972	NS5A	(4m)	(201)	SMLTDPSH ITAETARRRLARGSPPSLASSASQLSAPSLKATCPADH DSP
JX227977	NS5A	(4o)	(201)	SMLTDPSH VTAEAAARRRLARGSPPSLASSASQLSAPSLKATCAAHD -TP
FJ462434	NS5A	(4q)	(201)	SMXTDPSH ITAEAAARRRLARGSPPSLASSASQLSAPSLKATCTQH DSP
			251	300
GU814265	NS5A	(4a)	(251)	GTDLLEANLLW----GSTA TRVETDEKVIILDSFESCVAEPNDDREVSVA
DQ418784	NS5A	(4a)	(251)	GTDLLEANLLW----GSAATR VETDERVIILDSFEP CVAESDDKKEVSVA
FJ025854	NS5A	(4b)	(251)	DADLLEANLLWRQEMG SNI TRVESENKVVVLD SFEP LVAEP-DDVEI STA
FJ025855	NS5A	(4b)	(251)	DADLLEANLLWRQEMG GN I TRVESENKVVVLD SFEP LVAEX-DSGEV SV P
FJ462435	NS5A	(4b)	(251)	DADLLEANLLWRQEMG GD I TRVESKNKVVILDSF DPLVAEE-EDGEI SV P
DQ418786	NS5A	(4d)	(251)	DADLLEANLLWRQEMG GD I TRVESKNKVVILDSF DPLVAEE-EDGEI SV P
EU392172	NS5A	(4d)	(251)	GVDLLEANLLW----GANATR VESDKVLIILDSFEP LVAET-DDREV SV P
EF589161	NS5A	(4f)	(251)	GQDLLEANLLW----GTSATR VELGDKVMVLD SFEP LVAE--EDKEV SV E
JX227963	NS5A	(4g)	(251)	DADLLEANLLWRQEMG SNI TRVESESKVVILDSF DPLVAET-DDREV SV A
JX227971	NS5A	(4g)	(251)	DADLLEANLLWRQEMG NN I TRVESENKVVILDSF EP LVAET-DDKEV SV A
FJ462433	NS5A	(4m)	(251)	GADLLEANLLW----GAGATR VETDSKVVVLD SFEP LRAET-DDREI SV A
JX227972	NS5A	(4m)	(251)	GTDLLEANLLW----GASATR VETDAKVVVLD SFEP LRAEP-DDREI SV A
JX227977	NS5A	(4o)	(250)	GSDLLEANLLW----GSNVTR IESETKVVTLDSF EP IVAES-DDREV SV A
FJ462434	NS5A	(4q)	(251)	GTDLLEANLLW----GAGVTR IESEDKVMVLD SFEP ITAEQ-EDREV SV A
			301	350
GU814265	NS5A	(4a)	(297)	AEILRP-TKKFPPALPIWARPDYNPPLTETWKQ QDYKPPTVHGCALPPGK
DQ418784	NS5A	(4a)	(297)	AEILRP-TKKFPPALPIWARPDYNPPLTETWKQ RDYCPPTVYGCALPPSK
FJ025854	NS5A	(4b)	(300)	AEVMRR-VKKFPPALPIWARPDYNPPLLEPWKQ PDYIPPVVHGCALPPNK
FJ025855	NS5A	(4b)	(300)	AEILRR-SKRFPPKLPPIWARPDYNPPLIEPWKQ PDYTPPVVHGCALPPSK
FJ462435	NS5A	(4b)	(300)	AEILRR-TKRFPPAIPVWARPDYNPPLLETWKR PDYIPPVVHGCALPPSK
DQ418786	NS5A	(4d)	(300)	AEILRR-TKRFPPAIPVWARPDYNPPLLETWKR PDYIPPVVHGCALPPSK
EU392172	NS5A	(4d)	(296)	AEILRT-SKKFPRAMP IWAQPAYNPPLIETWKQ PDYEP PVVHGCALPPDK
EF589161	NS5A	(4f)	(295)	AEILRPGK KKFPPAIPWARPDYNPPLVESWKQ PDYEP PVVHGCALPPSN
JX227963	NS5A	(4g)	(300)	AEALRK-TKKFPQAI PVWARPDYNPPLIETWKK PDYDPPAVHGCALPPGG
JX227971	NS5A	(4g)	(300)	AEILRK-TRKFPRAMPVWARPDYNPPLLEKWK EPDYDPPVHGCALPAGG
FJ462433	NS5A	(4m)	(296)	AEVLC P-SKRFPPALPIWARPDYNPPLVEAWKR PDYDPPVHGCALPSSR
JX227972	NS5A	(4m)	(296)	AEVLRP-SKRFPPALPIWARPDYNPPLVEPWKQ PDYDPPVHGCALPSSK
JX227977	NS5A	(4o)	(295)	AEILRT-SKKFPAAIPVWARPEYNPPLVDTWKR PDYQPPVHGCALPSSK
FJ462434	NS5A	(4q)	(296)	AEILRPSR KKFPPAIPVWARADYNPPLVEVWKQ PGYDPPVHGCALPPSG
			351	400
GU814265	NS5A	(4a)	(346)	QPPVPPRR-KRTVQLTESV VSTALAE LAAKTFGQSEPS SDRD TDLTTPT
DQ418784	NS5A	(4a)	(346)	QPPVPPRR-KRTVQLTESV ASALAE LAAKTFGQPELGS DSGADLTTPT
FJ025854	NS5A	(4b)	(349)	PAPVPPRR-KRVVALSESNVSSALAM LAAKTFGQPD-DADSGTGLTSPT
FJ025855	NS5A	(4b)	(349)	PTPVPPRR-KRAIVLTESNVSSALADLA AKVLSQPDADVDSGTGLTLPS

FJ462435	NS5A	(4b)	(349)	PTPVPPSRR-KRMVALTESNVSEALAE LAIKSFGQPAADADSGTGFTSPT
DQ418786	NS5A	(4d)	(349)	PTPVPPSRR-KRMVALTESNVSEALAE LAIKSFGQPAADADSGTGFTSPT
EU392172	NS5A	(4d)	(345)	PTPVPPRR-KRAVALSESNISAALASLADKTFGQPVVSSDSGAAISTPT
EF589161	NS5A	(4f)	(345)	QPPVPPRRRKKTVVLSESTVSDALADLAAKSFGRPESEPD SGAGFTTPT
JX227963	NS5A	(4g)	(349)	LPVPPRR-KRTVVLTESSVSGALAE LAKKTFSPSTQD TDSGAGLTSPT
JX227971	NS5A	(4g)	(349)	LPVPPRR-KRAVVLTESNVSEALAE LATKSFSSSTQD TDSGAALTSPT
FJ462433	NS5A	(4m)	(345)	PTPVPPRR-KRAVVLSESVISSALADLAAKSFSGAESDSGAGLTSPT
JX227972	NS5A	(4m)	(345)	TTPVPPRR-KRAVVLSESVISSALADLAAKSFSGQSGVESDSGAGLSSPT
JX227977	NS5A	(4o)	(344)	PAPVPPRR-KRTVVLDESTVSNVLAGLAEKTFGRPEPDFDSE GASITTT
FJ462434	NS5A	(4q)	(346)	TTPVPPRR-KRTVVLTESKVAEALSDLAAKTFSESSHD SGAGLTTSS
			401	450
GU814265	NS5A	(4a)	(395)	ETTDSGPIVDDASDDGSYSSMPLEGE PGDPDLTSDSWSTVS --- GSED
DQ418784	NS5A	(4a)	(395)	ETTHSGPILADDASDNGSYSSMPLEGE PGDPDLTSDSWSTVS --- GSED
FJ025854	NS5A	(4b)	(397)	ETTNPDP SIADDRSDDGSFSSMPLEGE PGDPDLTSDSWSTVS --- GSDD
FJ025855	NS5A	(4b)	(398)	ETSTPDPPIADDRSDDGSFSSMPLEGE PGDPDLTSDSWSTVS --- GSED
FJ462435	NS5A	(4b)	(398)	DTSTPDSPADDDKSDDGSFSSMPLEGE PGDPDLTSDSWSTVS --- GSED
DQ418786	NS5A	(4d)	(398)	DTSTPDSPADDDKSDDGSFSSMPLEGE PGDPDLTSDSWSTVS --- GSED
EU392172	NS5A	(4d)	(394)	ETSEPDPIIADDKSDESYSMPLEGE PGDPDLTSDSWSTVS --- GSED
EF589161	NS5A	(4f)	(395)	GTSDSGPIVDDASDDGSYSSMPLEGE PGDPDLTSDSWSTVS --- GSED
JX227963	NS5A	(4g)	(398)	ETSEPDPEADSQDDGSYSSMPLEGE PGDPDLTSDSWSTVS --- GSED
JX227971	NS5A	(4g)	(398)	DTSKPDSSEADDQDDGSYSSMPLEGE PGDPDLTSDSWSTVS --- SSED
FJ462433	NS5A	(4m)	(394)	EPSEPDPIVDDRSDDESYSMPLEGE PGDPDLGSDSWSTVS --- GSED
JX227972	NS5A	(4m)	(394)	EPSEPDPIVDDRSDDESYSMPLEGE PGDPDLGSDSWSTVS --- GSED
JX227977	NS5A	(4o)	(393)	ETPDGPIVDDQDDGSYSSMPLEGE PGDPDLTSDSWSTVS --- ESED
FJ462434	NS5A	(4q)	(395)	ETSRPDPPIVDDASDDGSYSSMPLEGE PGDPDLTSDSWSTVSSSQGTED
			451	
GU814265	NS5A	(4a)	(442)	VVCC
DQ418784	NS5A	(4a)	(442)	VVCC
FJ025854	NS5A	(4b)	(444)	VVCC
FJ025855	NS5A	(4b)	(445)	VVCC
FJ462435	NS5A	(4b)	(445)	VVCC
DQ418786	NS5A	(4d)	(445)	VVCC
EU392172	NS5A	(4d)	(441)	VVCC
EF589161	NS5A	(4f)	(442)	VVCC
JX227963	NS5A	(4g)	(445)	V---
JX227971	NS5A	(4g)	(445)	V---
FJ462433	NS5A	(4m)	(441)	VVCC
JX227972	NS5A	(4m)	(441)	VVCC
JX227977	NS5A	(4o)	(440)	VVCC
FJ462434	NS5A	(4q)	(445)	V---