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OH1 from Orf virus: a new tyrosine phosphatase Distinct structural features & triple substrate specificity

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Urf virus -ORFV- is the causative agent of contagious ecthyma. It belongs to the Parapoxvirus genus of the Poxviridae family

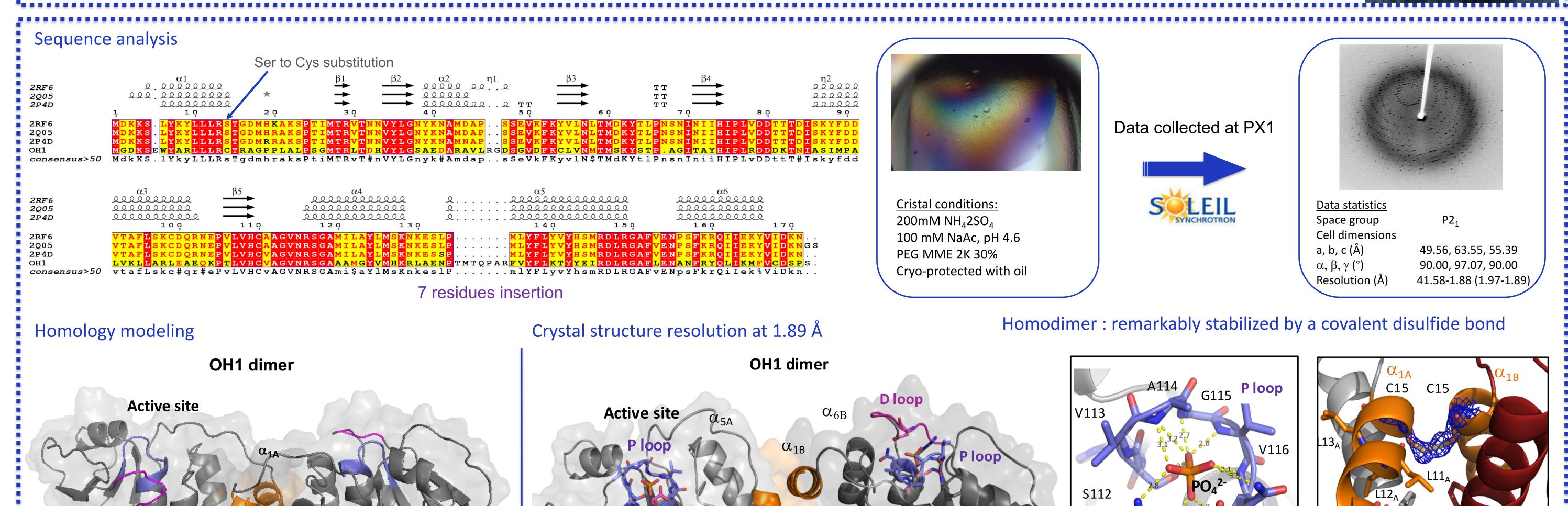
(poxviruses) and infects a wide range of animals. It has been responsible for widespread pandemics, such as Variola virus in humans¹. The DNA genome of poxviruses contains at least 90 conserved genes essential for viral replication and specific additional genes involved in pathogenesis and interaction with the host².

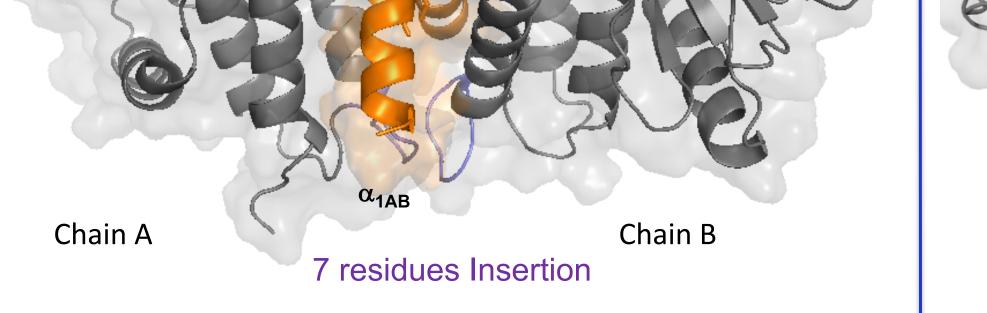
ORFV elicits a short-lived immune response in the host, contributing to multiple reinfections in animals³. This feature is further enhanced by the presence of viral genes that modulate the host immune response. Among these regulators, ORFV encodes for a tyrosine phosphatase -named OH1- that is widely conserved in poxviruses. OH1has possibly a role in the inhibition of the host JAK-STAT signaling pathway⁴, analogous to the role of the homologous protein VH1 in Vaccinia virus⁵⁻⁶.

VH1 was structurally characterized in both Vaccinia and Variola virus⁷⁻⁸ and was shown as the first dual specificity phosphatase DUSP⁹. Vaccinia VH1 structure reveals a typical DUSP fold and a homodimeric quaternary organization with an extensive domain swapping of the N-terminal α -helices stabilized by non-covalent interactions.

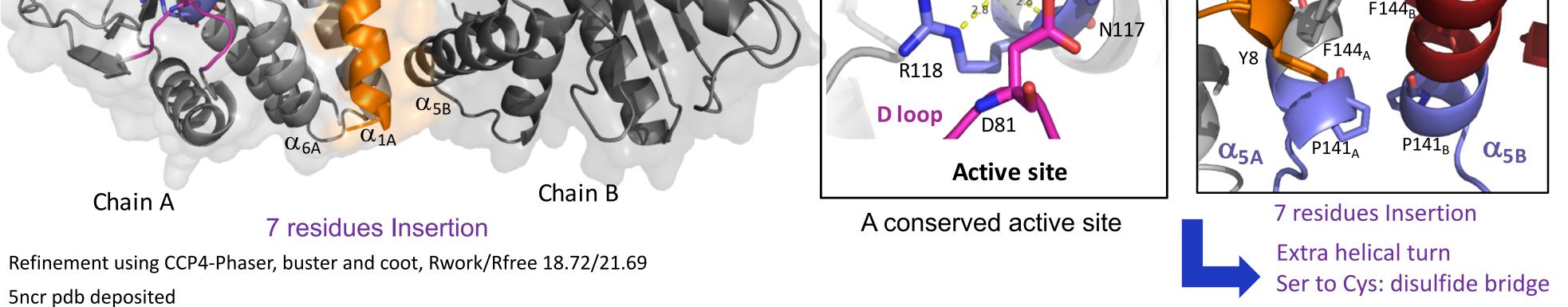


This dimerization is proposed to be a structural and mechanistic feature to regulate & recognate its putative substrate STAT1¹⁰. Sequence analysis and homology modeling of OH1, using VH1 as 3D template, revealed both a 7 residues gap insertion and a critical Ser to Cys substitution that could impede the quaternary dimeric organization. We investigate in vitro and in silico OH1 as a virulence factor phosphatase.



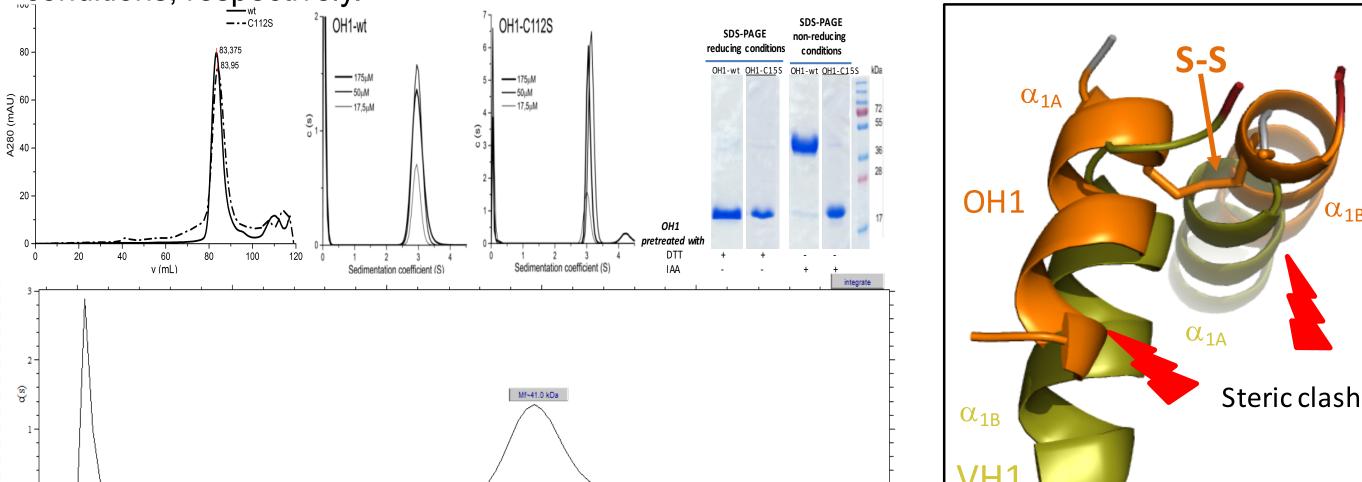


Chains A and B modeled with modeler mod9.13 with Vaccinia VH1 as template. Reconstruction of the homodimer using PyMOL –align. Check with Coot.



Covalent dimerization: disulfide bridge incompatible with domain swapping of $\alpha 1$

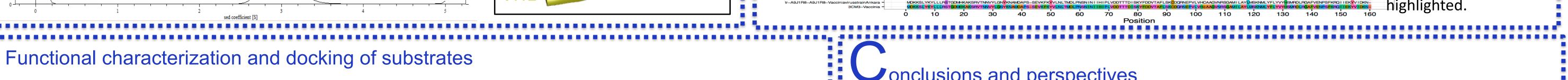
To confirm that Cys 15 is involved in the covalent dimerization of OH1 in solution, an OH1-C15S mutant was produced and purified, and its covalent dimer formation capacity was evaluated. OH1-wt and OH1-C15S proteins were pretreated with a reducing (DTT) or an alkylating (IAA) agent of Cys, and the results were evaluated by SDS-PAGE under reducing and non-reducing conditions, respectively.



Phylogenetic studies: how parapoxvirus associates Ser 15 to Cys substitution with other aa changes.

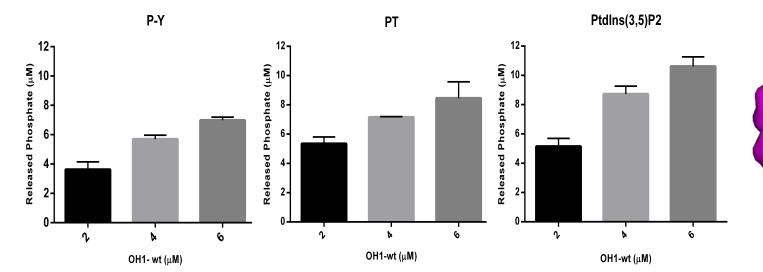
CH1 could represent Parapoxvirus genus phosphatases, since Cys15 is only conserved within this group, and is absent in all members of the Orthopoxvirus genus, such as Vaccinia/Variola VH1, and several other members of the Poxviridae family.

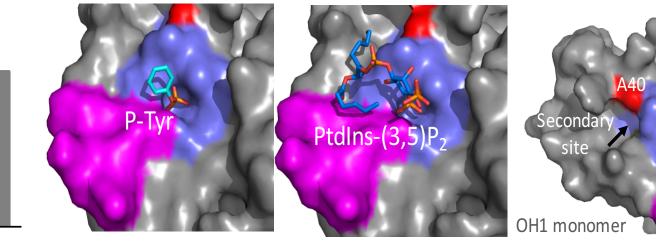
| j | • | | Multiple se | equence |
|----------|--|--|---|-------------|
| | tr-Q6TVD1-Bovine-papular-stomatitis-virus - | EAKNDWYAKLLLRCTRAGAP I YLRLTEYVYLGSAEDARAVVMASGVDFKCVVNMTTAAP-ES I AVYH I PLRDDNVTS I EGV I PPLVKLLERLEAEKKPTLVHCVAG I NRSGAAAMAY IMHRWFVFFLKTYYELRDSRGAFLENNNFRYQL I KWFVTGA | Maicipic 30 | guence |
| _ | tr-D3IZ73-Pseudocowpox-virus - tr-D3IZK4-Pseudocowpox-virus - | GININGSWARLLENGTRAGTPLTFRLTEHVYLGSAEDARSVLRESGUDFACLUNUTING IP-SGLTATHTPLODDETNITATIMFALVALLENGEAERAPTLVHCVAGTINGSAQAVWAYVMHKRFVYFLKTYYETRULARGELENANFRMQLTNNWFVCSSS GINISBWARLLENGTRAGTPLTFRLTEHVYLGSAEDARSVLRESGUDFACLUNUTINSTP-SGLTAYHTPLDDDETNITATIMFALVALLENGEAERAPTLVHCVAGTINGSAAVWAYVMHKRFVYFLKTYYETRULAGFLENANFRMQLTNWFVCSSS | | |
| | tr-Q6TVR3-Orf-virus-SA2000 - | | | |
| _ | tr-A0A0A7MA86-Parapoxvirus-red-deer | DDKNDWYARLLLRCTCGGTPV/MRLTEYVYLGNAEDARRVVRETGVPFCCVVN/ITTSTP-SGITAYHIPLRDDDVTDISAIMPPLVKLLERLEAERRPTLVHCVAGINRSGAAMMAY IMHRRFVYFLKTYFELRDLRGAFLENONFRLQLIKLEVV | alignment | of 64 |
| | tr-Q6TW43-orf-virus - | GDKSEWYARLLLRCTRAGPPLALRLTDHVYLGSAEDARAVLRDSGVDFKCLVNVITMSTP-AG I TAYH I PLRDDDTTN I AS IMPALVKLLARLEAEQKPTLVHCVAGVNRSGAAAMGYVM-IKRFVYFLKTYYE I RDLRGAFLENANFRYQL I MVPVCDSPS | unginnent | |
| | tr-W5U9D4-Orf-virus - | GDKSEWYÄRLLIRGTRÄGPPLÄLRLTDHVYLGSAEDARAVLRDSGVDFKCLVNMTMSTP-AGITÄYHIPLRDDDTTNITSIMPÄLVKLLÄRLEAEKKPTLVHCVAGVNRSGAAAVGYVMHKRFVYFLKTYYEIRDLRGAFLENANFRYOLIKMFVCDSPS | U | |
| | tr-Q070F0-Nile-crocodilepox-virus - | GGKSNLYRDL I LMSTD-TRAAFLQVTKN I YLGGYDNVSSGEF-RRHGFAY I LNLSYRAEGVKV I SLNVEDSPRQN I SQYFKRFNALLDHGEKSDKK I LVHCVAGVNRSGAAVLSYL I SKKL I YFLF I YHLLKRKRGAFVENAAFREQ I VSYYVA | - I I I | |
| | tr-Q6VZG4-Canarypox-virus - | | phosphatases | |
| | sp-Q9J592-fowlpox-virus - | MDEKQLYKHI I TKSTN-TCVKFTK I TDYVYLGNYRNV I ELPN-KTFFKY I VNVSMLLKRTD I TVLHFPLEDNDTVS I SKH I DAVTYVLKKCESLK I PVLVHCMAG I NRSSAMIMGYLME I RV I YFLY I YHELKY I RGAF I ENKSFLNQ I I DKY I | phosphalases | |
| | tr-Q70H20-Fowlpox-virus - | MDERQLYRHITTRSTN-TCVRFTRTTDYVYLGNYHNVTELPNRTFFRYTVNVSMLLRHIDTTVLHFPLEDNDTVSTSRHIDAVTYVLRRCESLRTPVLVHCMAGINHSSAMIMGYLMETHVTYFLYTYHELRSTRGAFTENRSFLNQTTDRYT | | |
| | tr-A0A068EF29-Penguinpox-virus - | MDEKQLYKHI I TK <mark>S</mark> TN-TCVKFTK I TDYVYLGNYKNVTELPNKTFFKY I VNVSMLLKRTD I TVLHFPLEDNDTVS I SKHI DAVTDVLKKCESLK I PVLVHCMAG I NRSSAMIMSYLME I RVI YFLY I YHELKS I RGAF I ENKSFLKQ I I DKY I | | |
| | tr-A0A068EG98-Pigeonpox-virus - | MDEKQLYKHI I TKSTN-TCVKFTK I TDYVYLGNYKNVTELPNKTFFKY I VNVSMLLKRTD I TVLHFPLEDNDTVS I SKHI DAVTDVLKKCESLK I PVLVHCMAG I NRSSAMIMSYLME I RV I YFLYVYHELKS I RGAF I ENKSFLKQ I I DKY I | sequences fr | om tha |
| _ | tr-Q98249-Molluscum-contagiosum-virus-subtype-1 - | MDKKQLYRRLILKSTSVMTKDELRITEYVYLGSYNNAMALES-SGVPFRYVLMMSMVLPGSSATIVHIPIPDNDQVHIAKYFDGVAAFLERCEKSHTPVLVHCIAGVNRSGAMIMAYLLHTRVIYFLGIKDIRGAFLENASFKRQLVDHYL | sequences in | oni uie |
| | tr-U3UBD0-Squirrelpox-virus - | | | |
| | tr-Q77PC3-Rabbit-fibroma-virus - | MOKKSLYENVLLKSTGALPKAR I RVTDYVYLGNYNDAKAVPT-SGYGFKY I LNLTTE I KNSSVT I I HVPLVDDEYTDL TKYFDYTTTELSNCEDKHYPVLVHCMAGVIRSGAI I MAYLMSRKRWFLY I Y SI REGRGAFLENPSFRRD I EKY I I NET- | | |
| | tr-Q85315-Rabbit-fibroma-virus - tr-Q8V3M6-Swinepox-virus - | MDKKSLYENVLLKSTGALPKAR I RVTDYVYLGNYNDAKAVPT-SGVGFKY I LNLTTE I KNSSVT I I HMPL VDDEYTDL TKYFDYTTFLSNCEDKHYPVL VHOMAGVNRSGA I IMAYLMSRKFMYFL Y I YHS I REORGAFLENPSFRQ I I EKY I I NET- MDRKSLYENVLLKSTGSLTKAKARVTEYVYLGNYNDA I NI CS-SE I PFKY I LNLTTELKNSS I NI I HMPL I DDEHTDLHKYFDYVTSLLEKCOKNEHA I LVHC I AGVNRSGAM I MAYLMHRRF I YFLYVYHLWREKRGAF I ENPSFRKQ I I DKY I I NEST | | ~ ~ ~ ~ ~ ~ |
| | tr-Q9IGU7-Tanapox-virus - | MORKICITEW LIKSTGLINKAKARY DISTALLING SCIENT FILLING FRANCISCUM INTERVISION IN THE STOCK STATE INTO STATE S | Parapoxvirus | genus |
| | tr-Q9DHP1-Yaba-like-disease-virus | MORKET YENVELKSTELEPKAKARVTDYVYLGNYNALSTIRE-YGTORKT LINETTE ET USSYNTTHWELDINETTDE TIKHEFYYTHYESKOKHNYTPVELYHCTASVINBOADAWIIMAYLMTKRFINFELYYYSWAEGRAAFEENYSFRATTEN YTN | | 901103 |
| | tr-H6TA62-Cotia-virus - | MORKSLYEW/LLKSTGYLEKAKAR/TE/VYLLGN/NDA/IN/E/SOV/FR/JUNLTPE/VNSP/N/IH/LPL/IN/E/CIA/SOV/FR/JUNLTPE/VNS/FR/JUNLTPE/VNSF/R/JUNLTPE/VNSP/R/JUNLTPE/VNSP/R/JUNLTPE/VNSF/R/JUNLTPE | | - |
| | tr-A0A097IVT2-Cotia-virus - | | | |
| | tr-Q91T23-Lumpy-skin-disease-virus - | MOKKSLYENVLLKSTGSLPKAKARVTDYVYLGNYDDA INA I S-SNVNFKY I LNLTTEFNDSR IN I I HVPL I DOEKTNLNDHFDYVTNFLSK DEEHYPVLVHCVAGVNRSGAM IMAY LMSKRF I YFLY I Y SVAEKRGAF I ENPSFRKQL I DKY I I NELK | (top 6 seg | uences). |
| | tr-A0A075CH78-Goatpox-virus - | MDKKSLYENVLLKSTGSLPKAKARVTDYVYLGNYDDA I NA I S-SNVNFKY I LNLTTEFNDSR I N I I HMPL I DDEKTNLNDHFDYVTKFLSKCDEEHYPVLVHCVAGVNRSGAMIMAYLMSKRF I YFLY I YHSVREKRGAF I ENPSFRKQL I DKY I I NE | $\mu \nu \mu \nu \sigma$ | uchccsj. |
| | tr-Q6TUU3-Yaba-monkey-tumor-virus - | | ` | • |
| | tr-B2CWH6-Myxoma-virus - | | | r |
| | sp-Q85297-Myxoma-virus - | MDKKSLYENVLLKSTGALPKARVRVTDYVYLGNYNDAKAAPT-SGIGFKYILNLTTEIKNSSITIIHMPLVDDEYTDLTKYFDYATTFLSNCEDKHYPVLVHCMAGVNRSGAIIMAYLMSRKFMYFLYIYHSIREORGAFLENPSFRRQIIEKYIINEHK | The position | on of |
| | tr-Q77GL6-Lumpy-skin-disease-virus - | MDKKSLYENVLLKSTGSLPKAKARVTDYVYLGNYDDA I NA I S-SNVNFKY I LNLTTEFNDSR I N I I HMPL I DDEKTNLNDHFDYVTNFLSKODEEHYPVLVHCVAGVNRSGAMIMAYLMSKRF I YFLY I YHSWREKRGAF I ENPSFRKQL I DKY I I NE | | |
| _ | tr-Q77GC9-Lumpy-skin-disease-virus - | MDKKSLYENVLLKSTGSLPKAKARVTDYVYLGNYDDA I NA I S-SNVNFKY I LNLTTEFNDSR I N I I HMPL I DDEKTNLNDHFDYVTNFLSKODEEHYPVLVHCVAGVNRSGAMIMAYLMSKRF I YFLY I YHSVREKRGAF I ENPSFRKQL I DKY I I NE | | ••••••• |
| | tr-Q91MT8-Lumpy-skin-diseaseVIRUS - | MDKKSLYENVLLKSTGSLPKAKARVTDYVYLGNYDDA I NA I S-SNVNFKY I LNLTTEFNDSR I N I I HMPL I DDEKTNLNDHFDYVTNFLSKODEEHYPVLVHCVAGVNRSGAMIMAYLMSKRF I YFLY I YHSWREKRGAF I ENPSFRKQL I DKY I I NE- | | _ |
| _ | tr-Q9WH06-Sheeppox-virus - | MDKKSLYENVLLKSTGSLPKAKARVTDYVYLGNYDDA I NA I S-SNVKFKY I LNLTTEFNDSR I N I I HMPL I DDEKTNLNDHFDYVTNFLSKODEEHYPVLVHCVAGVNRSGAMIMAYLMSKRF I YFLY I YHSVREKRGAF I ENPSFRKQL I DKY I I NE | | raduar |
| | tr-T2AU07-Myxoma-virus - | MDKKSLYENVLLKSTGALPKARVRVTDYVYLGNYNDAKAAPT-SDIGFKYILNLTTEIKNSSITIIHMPLVDDEYTDLTKYFDYATTFLSNQDDKHYPVLVHQMAGVNRSGAIIMAYLMSRKFMYFLYIYHSIREQRGAFLENPSFRRQIIEKYIINET- | conserved | residues |
| | tr-Q08FA1-Deerpox-virus - | | | |
| | tr-Q08FS1-Deerpox-virus - | MOKKSLYENVLLKSTGSLPKAKARVTNYVYLGNYNDALNAPY-SDIQFKYILNLTTELKNSHINIIHMPLIDDEQTDLSKHFDYVTDFLSKOAQQYPVLVHCVAGVNRSGAMIMAYLMTKRFIYFLYIY SMREQRGAFLENPSFRKQIIEKYIINER- | | |
| | tr-G3EIF7-Yoka-poxvirus - | MOKKSLVKYLLLR TGDMCKAKSRVTKNVVMCNYKNMEAPC-SIVDFKY I UNLTWEFCDSNINI I HI PLI DDMSTDI SKYFDYVTDFLTK DDERNEPVLVHCVAGVINSSGMI LAYMMSRNMVYFLVYY TLADLRGAFVENSSFRROI I ERY I I NYL- | · · · · · · · | |
| | sp-P80994-Raccoon-poxvirus - tr-Q0NJL8-Variola-virus - | MDKKSLYKYLLLRSTGDIHRAKSRVTNNVYLGNYKNAMEAPS-SEVKFKYILNLTMDFTNSNINIIHVPMVDDTSTDISIYFDDITAFLSKOOGRNEPVLVHCAAGVNRSGAMILAYLMSKMMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- MDKKSLYKYLLLRSTGDMRRAKSRVTNNVYLGNYKNAINAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKOOGRNEPVLVHCVAGVNRSGAMILAYLMSKMMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- | specific | to |
| | sp-P33064-Variola-virus - | MORKSLYKYLLINSTGUMMANASHVIIMAVILANS-SEVKERIVLINDLINDLINDLINDLINDLINDLINDLINDLINDLIND | Specific | ιO |
| | tr-Q0N562-Variola-virus - | MORKSLYKYLLINSTGUMPRAKSRYTINVYLGNYKNAWARS-SEVKERTYLINDLINDLINDLINDLINDLINDLINDLINDLINDLIND | | |
| | tr-Q0NLW9-Variola-virus - | | • | |
| | tr-Q0NCN7-Variola-virus-isolate-Human-South-Africa - | MDKKSLYKYLLLRSTGDMRAKSRVTNNVYLGNYKNAWNAPS-SEVKFKYVLNLTMDLPNSN IN I IHI PLVDOTTTD I SKYFDDVTAFLSK DORNEPVLVHCVAGVNRSGAM I LAY LMSKNMLYFLYYY HSWRDLRGAFVENPSFKRQ I I EKYV I DKN- | naranovvirus | that |
| | tr-Q0NG54-Variola-virus - | MDKKSLYKYLLLRSTGDWRRAKSRVTNNVYLGNYKNAWNAPS-SEVKFKYVLNLTMDLPNSNINIIH PLVDDTTTDISKYFDDVTAFLSKCCQRNEPVLVHCVAGVNRSGAMILAYLMS-KMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- | parapoxvirus | ιιαι |
| | tr-Q76Q11-Variola-minor-virus - | MDKKSLYKYLLLRSTGDMRRAKSRVTNNVYLGNYKNAWNAPS-SEVKFKYVLNLTMDLPNSNINIIH PLVDDTTTDISKYFDDVTAFLSKCORNEPVLVHCVAGVNRSGAMILAYLMSKNMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- | | |
| | tr-Q8V2S5-Camelpox-virus - | | | |
| | tr-Q775U6-Camelpox-virus-strain-CMS - | MDKKSLYKYLLLRSTGDMYRAKSRVTNNVYLGNYKNAWDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKCOQRNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- | strongly corre | Viatod to |
| _ | tr-Q8JLD2-Ectromelia-virus - | | | Idleu lu |
| | tr-Q5IXT4-Monkeypox-virus - | | | |
| | tr-Q8QMW6-Cowpox-virus - | MDKKSLYKYLLLRSTGDMHRAKSRVTNNVYLGNYKNAWDAPS-SEVKFKYVLNLTMDFPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKQDQRNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVYHSWRDLRGAFVENPSFKRQIIEKYVIDKN- | | _ |
| | tr-I0AZF8-Ectromelia-virus - | MDKKSLYKYLLLRSTGDMHRAKSRVTNNVYLGNYKNAWDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKODQQNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVYHSWRDLRGAFVENPSFKRQIIEKYVIDKN- | | |
| | tr-Q8V4Z3-Monkeypox-virus-Zaire - | MDKKSLYKYLLLRSTGDMHRAKSRVTNNVYLGNYKNAMDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKODGRNEPVLVHCVAGVNRSGAMILAYLMSKNMLYFLYVYHSWRDLRGAFVENPSFKRQIIEKYVIDKN- | the N-termi | nal Ser |
| - | tr-G0XX41-Cowpox-virus - | | | |
| | tr-M9WG49-Vaccinia-virus - | MOKKSLVKYLLLRSTGDWRRAKSRVTNNVVLGNYKNAWDARS-SEVKEKYVLNLTMDLPNSNINI I HI PLVDDTTTDI SKYFDDVTAFLSKDORNEPVLVHCAAGVIRSGAMI LAYLWSKNMLYFLYVY SWRDLRGAFVENPSFKROI I EKYVIDKI- | | |
| _ | tr-Q80DY2-Cowpox-virus - | MDKKSLYKYLLLRSTGDMHRAKSRVTNNVYLGNYKNAMDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKODQRNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- MDKKSLYKYLLLRSTGDMHRAKSRVTNNVYLGNYKNAMDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKODQRNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- | | C |
| | tr-Q0NPB0-Taterapox-virus - sp-P20495-Vaccinia-virusstrain-Copenhagen - | MDKKSLYKYLLLFSTGDMHKAKSHVTINNVYLGNYKNAWDAPS-SEVKFKTYLNLTINDLPNSNINTTHTPLVDDTTD1SKYFDDVTAFLSKEDXPNEPVLVHCAAGVNRSGAMTLAYLMSKMMLYFLYYTSWHDLRGAPVENPSFKRQTTEKYTTXN | 15 to | |
| | tr-Q77TK5-Vaccinia-virus-strain-Copennagen - | MORKSLYKYLLENSTGUMHKAKSHVTINNYLGUNYKNAWDARS-SEVKEKTVLINLINDLENSINITITITITISKYDDVTAELSKOCKINEPVLINLCAASVINISSAMILLAYLMSKIMLYFLYYTSVINDLENAAFVERISENKITTISKYTUNVYLGUNYKNAWDARS-SEVKEKTVLINLINDLENSINITITITITISKYTUNDYTTIDISKYFDDVTAELSKOCKINEPVLINLCAASVINISSAMILLAYLMSKIMLYFLYYTSVINDLENAAFVERISENKITTISKYTUNDYTGUN | | CyJ |
| | tr-Q//TK5-vaccinia-virus-strain-Tian-Tan- tr-Q1M1M0-Vaccinia-virus - | MORKSLYKYLLENSTGUMHRAKSRYTINNYLGUNYKNAWDARS-SEVKERTYLINLINDLENSINTITITITIEKTYUDVITALSKUDDINEPYLVHCAAGVINBSGAWILLAYLMSKMULYFLYYTSMHDLENARYVENTSENRUTTEKTYUDKN- MORKSLYKYLLENSTGUMHRAKSRYTINNYLGUNYKNAWDARS-SEVKERTYLVNLTNDLENSINTITITITISKTPODYTAFLSKUDDINEPYLVHCAAGVINBSGAWILLAYLMSKMULYFLYYTSMHDLENARYVENTSENRUTTEKTYUDKN- | | |
| _ | tr-Q6RZK3-Rabbitpox-virus - | | — I . I. | • |
| | sp-P07239-Vaccinia-virusstrain-Western-Reserve - | MOKKSLYKYLLLRSTGDWHKAKSRVTNVYLGNYKNAWDAPS-SEVKFKYVLNLTNDLPNSNINI I HI PLVDDTTTD I SKYFDDVTAFLSKCDORNEPVLVHCAAGVVRSGAM I LAYLMSKNMLYFLYYH SVADLRGAFVENPSFKRQ I LEKYV I DKN- | substitution | ic |
| | tr-Q76RC6-Vaccinia-virus - | MDKKSLYKYLLLRSTGDMHKAKSRVTNNVYLGNYKNAWDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKCDORNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVY-SWADLRGAFVENPSFKRQIIEKYVIDKN- | σανστιτατιστ | 12 |
| | tr-B9U1I4-B9U1I4Vaccinia-virus - | MDKKSLYKYLLLRSTGDMHKAKSRVTNNVYLGNYKNAWDAPS-SEVKFKYVLNLTMDLPNSNINIIHIPLVDDTTTDISKYFDDVTAFLSKCOQRNEPVLVHCAAGVNRSGAMILAYLMSKNMLYFLYVYHSVRDLRGAFVENPSFKRQIIEKYVIDKN- | | |
| | tr-Q0GNY5-Q0GNY5-HorsepoxVirus - | | . | |
| | | | | |



OH1 is a dual specificity phosphatase.

OH1 unexpectedly reveals its ability to dephosphorylate phosphatidylinositol 3,5 biphosphate.





Docking analysis, using ADT, of several phosphatidylinositol phosphates confirm that they can be accommodated in the active site of OH1. This new activity could be relevant in phosphoinositide recycling during virion maturation.

onclusions and perspectives

OH1 displays structural features compared to viral VH1 phosphatases.

Orf virus OH1 phosphatase is a covalent dimer involving the N-terminal Cys15.

OH1 possibly depicts the structure of Parapoxvirus genus phosphatases.

OH1 is a dual specificity phosphatase that presents activity towards PInsP in vitro.

By analogy with VH1, the homodimer could recognate & regulate its host STAT1.

Pull-down experiments of OH1 with STAT1, and protein-protein docking of OH1 complexed to STAT1 are in progress.

SCIENCE & IMPACI





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