

Ulandelwano lobude phambi konyango lwe-HIV-1 yokusetyenziswa kwifilogenitikhi ukubonakaliswa ukubuya kwentsholongwane kwakhona

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I-Abstract

Nangona i-antiretroviral yonyango (i-ART) iphumelele ekuthomalaiseni ukukhula kwentsholongwane ebantwini abaphila ne-HIV (i-PLWH), intsholongwane iyaqhubela ethuben ichaphezela iiseli kwaye zingaphinda zivele xa unyang luphazamisekile. Ngaphambili siye saqaphela, kwabasetyhini evela kwi-CAPRISA 002 Iqela losulelo oluqatha, Kwazulu-Natal, uninzi lweentshongolwane ezikwaziyo ukuphinda zenziwe kusuka amaqhingga enziwe kweli dama lifihliweyo elinxulumene kakhulu nokujikeleza kwentsholongwane kwigazi phakathi kunya kaowandulela ukuqualiswa kwe-ART. Ngelixa iintsholongwane eziphinda-phindiweyo kune nezibangelwayo zisuka kwidami elinye kwaye zidibana, aziloluhlu lunye. Besijonge ukufumanisa ukuba intsholongwane ephinda-phindiweyo yafakwa nini kwidami elifihlakeleyo kabantu basetyhini abalithoba ukusuka kwiqela elifanayo elifumana ukuphindaphindwa kwentsholongwane (Bangaphantsi kwama-1000 e-RNA iikopi/ml) ubuncinane kunya omnye emva kokuqualiswa kwe-ART, kusetyenziswa iindlela ze-filogenetikhi. Iingingqi ezintathu zofuzo, ezimbini kwi-env kune nenye kwi-nef zandiswa kwaye zalandelelana zavela kwi-RNA yentsholongwane ethathwe kwiplasma ngokuphakathi emva kweenyanga ezintandathu rhoqo ukusuka kusulelo oluqatha ukuya ekualisweni kwe-ART, kwaye nangexesa lokuphinda kuqhagamshelwane, kusetyenziswa i-Illumina MiSeq ene-Primer ID (i-PID). Unxulmano lwentsholongwane ebuyelayo kwiintsholongwane zangaphambi kwe-ART kwamiselwa, usebenzisa ubuninzi obunokwenzeka njengemithi ene-patristic, i-clade kune neendlela zokubeka usebenzisa umbhobho wokuthandana wesiko (<https://primer-id.org/ogy>). Zontathu ezinginqi zofuzo zikhuliswe ngempumelelo kwaye zilandelelaniswe kwabasetyhini abalithoba. Ngokuphakathi, I-354 ye-PID yokulandelelana kwemvumelwano (uluhlu lwe-18-4760) ngexesa ngalinye kwiningqi yaphambi kwe-ART kune ne-293 ye-PID yokuvumelana lwentsholongwane yokubotshwa kakhona (uluhlu lwe-3-2383) ekubotsheni kwakhona lwenziwe kumthathi-nxaxheba ngamnye. Ukungaondakali kakuhle kwimithi yefilogenetikhi kunokuba sisiphumo sokusuleka ngeendlela ezinini kune nemigca eyahluka-hlukaneyo echongiwe njengomceli mngeni kwindlela yethu yokwenza. Ukumisela eyona ndlela/iindlela zokuvelisa imithi kusetyenziswa ulungelewaniso lobude olulolona lufanelekileyo kwaye ukujongana nokungacaci ukuba kosulelo oluninzi kune nemigca eyahlukanisiweyo okanye edibeneyo idala ubaluleko.

Imvelaphi

- Idama elifihlakeleyo le-HIV-1 lihlala lingoyena mqobo kunya kabantu abaphila ne-HIV (PLWH), ngaphandle konyango olusebenzayo lwe-antiretroviral (ART).
- Upahazamiseko locinezelo lwe-ART, lukholisa ukukhokelela kwintsholongwane ekhawulezayo ukubuya kwidama elifihlakeleyo.
- Iintsholongwane ezibuya ngexesa lokudityanisa kwakhona zimele iqhezu kuphela lalo vimba ufhakeleyo.
- Ngapha koko, iintsholongwane zivuselelw kwi-vitro zisebenzisa iindlela ezinje ngovavanyo bobungakanani bokukhula kwentsholongwane (qVOA) kune nezo zivila ngexesa lokubuyela kwakhona okanye ukuphazamiseka konyango ziyadibana, kodwa zohlkile i-1,2.
- Uphononongo lwangaphambili lubonise ukuba uninzi lwedama njengoko lilinganiswe ne-proviral okanye ukukhula kolandelelwano lwentsholongwane eyasekwa kufutshane nexesa lokuqualiswa kwe-ART 3,4,5. Sijonge ukuvavanya ukuba oku kufunyanisiweyo kuyahambelana na neentsholongwane ezibuyelayo.

Ukubaluleka

- Uhlalutyo lwemvelaphi yethutyana yentsholongwane ebuyayo luya kubonelela ngengqiqo engcono yeqhezu lendawo yokugcina amanzi ekwaziyo ukuvela kwakhona ngexesa lophazamiseko lonyango.
- Ukuqondwa okuphculweyo kwe-HIV-1 yeendlela yedami inokwazisa izicwangciso-qhinga zokuthintela ukuyilwa kune nokuzingisa kwayo.

Imibilelo

Abathathi nxaxheba bonke abavela kwa-CAPRISA 002 Iqela losulelo olungamandla



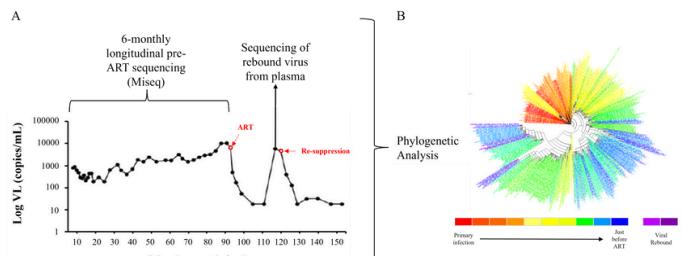
Iindlela zokusebenza

Abathathi-nxaxheba kuphando

- Usulelo olungapheliyo lwe-PLWH olusuka kwiqela le-CAPRISA002 abaccinezelwe ngokwentsholongwane kangangesithuba sonyaka omnye, balandelwa kukubuya kwentsholongwane egazini bachongwa.

Ulandelwano lwe-ART yangaphambili kune nentsholongwane ebuyayo

- Ulandelwano olunzulu lwe-Illumina MiSeq kune nesazisi se-Primer yasetyenziselwa ukuvela ulandelwano kwi-RNA yentsholongwane evela kwi-plasma, isampulwa rhoqo kwiinyanga ezi-6 zonyango lwangaphambili kwenziwa njalo nakule ibuyayo (Figa 1A).



Ifiga yoku-1: Amaggabantsintshi e-pre-ART kune nendlela yokulandelelana kwentsholongwane ebuyayo

- Ixesha lokungena kwentsholongwane yentsholongwane ebuyayo kwidami lenziwe kusetyenziswa kwemithi enokwenzenka kakhuluene-patristic, i-clade kunye nokubekwa iindlela usebenzisa okuqhelekileyo ukuthandana umbhobho (<https://primer-id.org/ogy>) (Figure 1B)
- Imimandla emithathu ye-genomic (i-V1V2, i-V4V5 kunye ne-nef, HXB2: 8678-9156) zandiswe kwimpendulo ebanzi esufunyaniswe kwi-plasma RNA (figa yesi-2). Imimandla yofuzo yakhethwa ngokusekelwe kumsebenzi wangaphambili obonisa ukuba bavelise uphawu olunamandle lwesti-5 i-filogenethiki.
- Ngaphantsi kwe-18 ulandeletlano lwemvumelwano ngenqaku lexesha ngalinye laphambi kwe-ART yathathwa njengomsebenzi ongaphumelelanga.
- Ulandelelwano olukrwada luyafundwa lwaqhutywa ngokusetyenziswa kombobho oqhelekileyo obhalwe ngeelwimi zenkubo lwe-Python kunye ne-R (https://github.com/HIVDiversity/NGS_processing_pipeline; DOI: 10.5281/zenodo.3372202).
- Ukuhluzwa komgangatho, ukudityaniswa kokufundwa kwesiphelo esigqithelayo kunye nokusebenza kwe-Primer ID kwenziwa kusetyenziswa inkqubo ye-MotifBinner2.R (<https://github.com/HIVDiversity/MotifBinner2>; DOI: 541 10.5281/zenodo.3372204).

