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► To cite this version:

Cathia Soulié, Laurence Morand-Joubert, Jean-Michel Cottalorda, Charlotte Charpentier, Pantxika Bellecave, et al.. Performance of genotypic algorithms for predicting tropism for HIV-1 CRF01_AE recombinant. *Journal of Clinical Virology*, 2018, 99-100, pp.57-60. 10.1016/j.jcv.2017.12.014. hal-01984179

HAL Id: hal-01984179

<https://hal.science/hal-01984179v1>

Submitted on 10 Sep 2024

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Performance of genotypic algorithms for predicting tropism for HIV-1 CRF01_AE recombinant

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Objectives: There is no consensus about the performances of genotypic rules for predicting HIV-1 non-B subtype tropism. Three genotypic methods were compared for CRF01_AE HIV-1 tropism determination.

Methods: The V3 env region of 207 HIV-1 CRF01_AE and 178 B subtypes from 17 centers in France and 1 center in Switzerland was sequenced. Tropism was determined by Geno2Pheno algorithm with false positive rate (FPR) 5% or 10%, the 11/25 rule or the combined criteria of the 11/25, net charge rule and NXT/S mutations.

Results: Overall, 72.5%, 59.4%, 86.0%, 90.8% of the 207 HIV-1 CRF01_AE were R5-tropic viruses determined by Geno2pheno FPR5%, Geno2pheno FPR10%, the combined criteria and the 11/25 rule, respectively. A concordance of 82.6% was observed between Geno2pheno FPR5% and the combined criteria for CRF01_AE. The results were nearly similar for the comparison between Geno2pheno FPR5% and the 11/25 rule. More mismatches were observed when Geno2pheno was used with the FPR10%. Neither HIV viral load, nor current or nadir CD4 was associated with the discordance rate between the different algorithms.

Conclusion: Geno2pheno predicted more X4-tropic viruses for this set of CRF01_AE sequences than the combined criteria or the 11/25 rule alone. For a conservative approach, Geno2pheno FPR5% seems to be a good compromise to predict CRF01_AE tropism.

Keywords: HIV, tropism, CRF01_AE, Genotypic prediction

Background

The chemokine receptors CCR5 and CXCR4 are the principal coreceptors for entry of HIV-1 into target cells [1,2]. Co-receptor selectivity is determined by genetic sequences within HIV glycoprotein 120 (gp120), particularly in a highly variable and structurally flexible region termed 'V3' which is involved in co-receptor binding [3–5]. The CCR5 antagonists, which inhibit HIV-1 binding on the CCR5-coreceptor, are only active on R5-tropic viruses which implies a tropism determination before their prescription. Then, the determination of tropism is useful in clinical practice.

The simplest genotypic rules such as the 11/25 rule, predict X4 on the basis of the presence of basic residues 11 or 25 of the HIV gp120 V3 loop. The combined criteria of the 11/25, net charge rules and the presence of specific determinants in the gp120 V3 loop were also used to determine HIV tropism [6]. Now, several bioinformatics methods for prediction of HIV coreceptor usage have been proposed, are available as online tools and the most used of them is Geno2pheno [coreceptor] [7]. However, Geno2pheno is based on HIV B subtype V3-loop as viral sequence information input.

The HIV-1 CRF01_AE recombinant is dominant in Asia where its prevalence is 84%, and has contributed towards 4.6% of total HIV-1 infections in terms of worldwide distributions [8,9]. In some European countries, the CRF01_AE was the second major recombinant among HIV non-B subtypes after the CRF02_AG recombinant [10,11]. Several studies underlined the high prevalence of X4-tropism for CRF01_AE recombinant associated with a possible fast disease progression [12–14].

The genotypic determination is now commonly used to determine tropism for HIV-1 B subtype. Because of the increase of HIV non-B subtypes prevalence, the possibility of fast disease progression for the CRF01_AE recombinant and the debate on the performances of genotypic rules or algorithms, it is important to evaluate the performance of different rules or algorithms to determine HIV tropism.

Objectives

The aim of this study was to compare 3 genotypic methods on a set of 207 HIV-1 CRF01_AE recombinants to evaluate the concordance between these measures of HIV-1 tropism.

Study design

This study has enrolled 207 HIV-1 patients infected by CRF01_AE recombinant from 17 centers in France and 1 center in Switzerland. For the comparison of sequences, 178 HIV-1 patients infected by B subtype were studied. The V3 env region was sequenced as previously described and tropism was determined by Geno2pheno algorithm (False Positive Rate, FPR5% or FPR10%, <http://coreceptor.bioinf.mpi-inf.mpg.de/>), the 11/25 rule or the combined criteria of the 11/25, net charge rule and NXT/S [6,15]. Comparisons between groups were performed using Statview Software with the non-parametric Mann-Whitney or chisquared tests.

Results

The CRF01_AE HIV-1 patients had a median plasma HIV-1 viral load of 4.32 log copies/mL (range 1.30-6.79), a median CD4 cell count of 373 cells/mm³ (range 2–1954) and a median of nadir CD4 cell count of 237 cells/mm³ (range 2–993).

A consensus sequence was established with the main amino acid at each of the 35 positions of the V3 loop for B subtypes and CRF01_AE subtypes (Table 1A). At key position 25, R was statistically less frequent for the CRF01_AE recombinant (p = 0.0289) (Table 1B).

Overall, 72.5%, 59.4%, 86.0%, 90.8% of the 207 HIV-1 CRF01_AE were R5-tropic viruses determined by Geno2pheno FPR5%, Geno2pheno FPR10%, the combined criteria and the 11/25 rule, respectively. A concordance of 82.6% (71.0% R5 and 11.6% X4) was observed between Geno2pheno FPR5% and the combined criteria for CRF01_AE (Fig. 1). The results were nearly similar for the comparison between Geno2pheno FPR5% and the 11/25 rule. More mismatches were observed when Geno2pheno was used with the FPR10% (Fig. 1).

Neither HIV viral load, nor current or nadir CD4 was associated with the discordance rate between the different algorithms.

Discussion

The HIV tropism determination was different according to the algorithm used (Geno2pheno FPR5%, Geno2pheno FPR10%, 11/25 rule, and 11/25 rule combined to net charge rule and NXT/S mutation) for this set of CRF01_AE recombinant sequences. The Geno2pheno algorithm predicted more X4-tropic viruses than the two other manual rules. Then, Geno2pheno seems to be more careful concerning the prediction of tropism in regards to the prescription of CCR5 antagonists.

The Geno2pheno algorithm was built on phenotypic-genotypic correlation using HIV-1 B subtype samples [7]. HIV genetic variability between B subtype and CRF01_AE recombinant, especially for the gp120 V3 region, can have consequently an impact on the tropism determination by genotypic algorithms [6,15–17]. Regarding the potential impact of the subtype on the CCR5 inhibitor maraviroc activity, it is important to have cautious rules to determine the HIV tropism to allow adequate prescription of this inhibitor [18–20].

We previously demonstrated that the Geno2pheno FPR5% could be used to predict tropism as well as other genotypic rules for the HIV-1 CRF02_AG recombinant [21]. The present study shows that, for a conservative approach, Geno2pheno FPR5% seemed to be also a good compromise to predict CRF01_AE tropism. The use of this algorithm could facilitate the prediction of HIV tropism in clinical practice.

| gp120 | 296 | 297 | 298 | 299 | 300 | 301 | 302 | 303 | 304 | 305 | 306 | 307 | 308 | 309 | 310 | 311 | 312 | 313 | 314 | 315 | 316 | 317 | 318 | 319 | 320 | 321 | 322 | 323 | 324 | 325 | 326 | 327 | 328 | 329 | 330 |
|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| V3loop | I | 2 | S | 4 | S | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 |
| B | C | T | R | P | N | N | N | T | R | K | S | I | R | I | Q | R | G | P | G | R | A | F | V | T | I | Q | I | G | D | M | R | Q | A | H | C |
| CRF01_AE | C | T | R | P | N | N | T | R | K | S | I | R | I | Q | R | G | P | G | R | A | F | V | T | I | Q | I | G | D | M | R | Q | A | H | C | |
| p | 0.9999 | 0.1169 | 0.9999 | 0.9999 | 0.0001 | 0.1365 | 0.9999 | 0.9498 | 0.5141 | 0.0001 | 0.0001 | 0.0001 | 0.0001 | 0.0002 | 0.0001 | 0.8104 | 0.4378 | 0.0001 | 0.6182 | 0.0011 | 0.0073 | 0.0001 | 0.5882 | 0.0007 | 0.0001 | 0.0422 | 0.9999 | 0.2309 | 0.6388 | 0.6302 | 0.6378 | 0.0002 | 0.3031 | 0.0001 | 0.1608 |

Conflicts of interest statement None to declare.

Funding

None declared.

Acknowledgment

This study was supported by the ANRS (Agence Nationale de Recherche sur le Sida et les hépatites virales).

ANRS AC11 Resistance Study Group: Aix en Provence (Dr E Lagier); Amiens (Dr C. Roussel); Angers (Dr H. Le Guillou); Avicenne (Dr C. Alloui); Besançon (Dr D. Bettinger); Bicêtre (Dr C. Pallier); Bordeaux (Pr H. Fleury, Dr S. Reigadas, Dr P. Bellecave, Dr P. Recordon-Pinson); Brest (Pr C. Payan, Dr S. Vallet); Caen (Pr A. Vabret); Clermont-Ferrand (Dr C. Henquell, Dr A. Mirand); Créteil (Dr M. Bouvier-Alias); Dijon (Dr A. de Rougemont); Fort de France (Dr G. Dos Santos); Grenoble (Pr P. Morand, Dr A. Signori-Schmuck); Lille (Dr L. Bocket); Limoges (Pr S. Rogez); Lyon (Dr P. Andre, Dr J.C. Tardy, Dr M.A. Trabaud); Marseille (Dr C. Tamalet); Metz-Thionville (Dr C. Delamare); Montpellier (Dr B. Montes); Nancy (Pr E. Schvoerer); Nantes (Pr V. Ferre, Dr E. AndréGarnier); Nice (Dr J. Cottalorda); Orléans (Dr J. Guinard, Dr A. Guiguon); Paris-Bichat Claude Bernard (Dr D. Descamps, Dr C. Charpentier, Dr B. Visseaux, Dr G. Peytavin); Paris-Cochin (Dr A. Krivine); Paris-HEGP (Dr A. Si-Mohamed); Paris-Necker (Dr V. Avettand-Fenoel); Paris-Pitié-Salpêtrière (Dr A.G. Marcelin, Pr V. Calvez, Dr C. Soulié, Dr M. Wirden); Paris Saint-Antoine (Dr L. MorandJoubert, Dr S. Lambert-Niclot,); Paris-Saint Louis (Dr C. Delaugerre, Dr M.L. Chaix); Paris-Tenon (Dr C. Amiel, Dr V. Schneider); Poitiers (Dr G. Giraudeau); Reims (Dr V. Brodard); Rennes (Dr A. Maillard); Rouen (Pr J.C. Plantier); Saint Denis (Dr C. Chaplain); Saint Etienne (Dr T. Bourlet); Strasbourg (Pr S. Fafi-Kremer, Pr F. Stoll-Keller, Dr M.P Schmitt, Dr H. Barth); Suisse (Dr S. Yerly); Toulon (Dr C. Poggi); Toulouse (Pr J. Izopet, Dr S. Raymond); Tours (Pr F. Barin, Dr A. Chaillon); Versailles (Dr S. Marque-Juillet); Paul Brousse (Pr A.M. Roque-Afonso, Dr C Pallier); INSERM UMR-S1136 (Dr P. Flandre, M. Grudé, Dr L. Assoumou, Dr D. Costagliola).

ANRS clinical centers: Aix en Provence (Dr T. Allegre); Amiens (Pr J.L. Schmit); Angers (Dr J. M. Chennebault); Avicenne (Pr O. Bouchaud); Besançon (Pr N. Magy-Bertrand); Bicêtre (Pr J.F Delfraissy); Bordeaux (Pr M. Dupon, Pr P. Morlat, Pr D. Neau); Brest (Pr S. Ansart, Dr S. Jaffuel); Caen (Pr R. Verdon); Clermont-Ferrand (Dr C. Jacomet); Créteil (Pr Y. Lévy, Dr S. Dominguez); Dijon (Pr P. Chavanet; Pr L. Piroth); Fort de France (Dr A. Cabié); Grenoble (Dr P. Leclercq); LilleTourcoing (Dr F. Ajana, Dr A. Cheret); Limoges (Pr P. Weinbreck); Lyon (Dr L. Cotte); Marseille (Dr I. Poizot-Martin, Dr I. Ravaut); MetzThionville (Dr B. Christian, Dr F. Truchetet, Dr M. Grandidier); Montpellier (Pr. J. Reynes); Nancy (Pr T. May, Dr F. Goehringer); Nantes (Pr F. Raffi); Nice (Pr P. Dellamonica); Orléans (Dr T. Prazuck, Dr L. Hocqueloux); Paris-Bichat Claude Bernard (Pr P. Yéni, Dr R. Landman, Pr Yazdanpanah); Paris-Cochin (Dr O. Launay); Paris-HEGP (Prof. L. Weiss); Paris-Necker (Dr J.P. Viard); Paris-Pitié-Salpêtrière (Pr C. Katlama, Dr A. Simon); Paris-Saint Antoine (Pr P.M. Girard, Pr J.L. Meynard); Paris-Saint Louis (Pr J.M. Molina); Paris Tenon (Pr G. Pialoux); Pointe-à-Pitre (Pr B. Hoen, Dr M.T. Goeger-Sow, Dr I. Lamaury, Dr G. Beaucaire); Reims (Pr R. Jausaud, Dr C. Rouger); Rennes (Pr C. Michelet); Rouen (Dr F. Borsa-Lebas, Pr F. Caron); Saint Denis (Dr M.A. Khuong); Saint Etienne (Pr. F. Lucht); Strasbourg (Dr D. Rey); Suisse (Dr A Calmy); Toulon; Toulouse (Pr B. Marchou); Tours (Dr G. Gras), Versailles (Dr A. Greder-Belan); Villejuif (Pr D. Vittecoq, Dr E. Teicher).

REFERENCES

- [1] E. Poveda, V. Briz, M. Quiñones-Mateu, V. Soriano, HIV tropism: diagnostic tools and implications for disease progression and treatment with entry inhibitors, *AIDS Lond. Engl.* 20 (2006) 1359–1367, <http://dx.doi.org/10.1097/01.aids.0000233569.74769.69>.

[0000233569.74769.69](http://dx.doi.org/10.1097/01.aids.0000233569.74769.69).

- [2] E.A. Berger, P.M. Murphy, J.M. Farber, Chemokine receptors as HIV-1 coreceptors: roles in viral entry, tropism, and disease, *Annu. Rev. Immunol.* 17 (1999) 657–700, <http://dx.doi.org/10.1146/annurev.immunol.17.1.657>.

- [3] [R.A. Fouchier, M. Groenink, N.A. Kootstra, M. Tersmette, H.G. Huisman, F. Miedema, H. Schuitemaker, Phenotype-associated sequence variation in the third variable domain of the human immunodeficiency virus type 1 gp120 molecule, J.Virol. 66 \(1992\) 3183–3187.](#)
- [4] [M.A. Jensen, A.B. van't Wout, Predicting HIV-1 coreceptor usage with sequence analysis, AIDS Rev. 5 \(2003\) 104–112.](#)
- [5] [D.R. Briggs, D.L. Tuttle, J.W. Sleasman, M.M. Goodenow, Envelope V3 amino acid sequence predicts HIV-1 phenotype \(co-receptor usage and tropism for macrophages\), AIDS Lond. Engl. 14 \(2000\) 2937–2939.](#)
- [6] S. Raymond, P. Delobel, S. Rogez, S. Encinas, P. Bruel, C. Pasquier, K. SandresSauné, B. Marchou, P. Massip, J. Izopet, Genotypic prediction of HIV-1 CRF01-AE tropism, J. Clin. Microbiol. 51 (2013) 564–570, <http://dx.doi.org/10.1128/JCM.02328-12>.
- [7] T. Lengauer, O. Sander, S. Sierra, A. Thielen, R. Kaiser, Bioinformatics prediction of HIV coreceptor usage, Nat. Biotechnol. 25 (2007) 1407–1410, <http://dx.doi.org/10.1038/nbt1371>.
- [8] K.A. Lau, J.J.L. Wong, Current trends of HIV recombination worldwide, Infect. Dis. Rep. 5 (2013) e4, <http://dx.doi.org/10.4081/idr.2013.s1.e4>.
- [9] J. Hemelaar, E. Gouws, P.D. Ghys, S. Osmanov, Global and regional distribution of HIV-1 genetic subtypes and recombinants in 2004, AIDS Lond. Engl. 20 (2006) W13–23, <http://dx.doi.org/10.1097/01.aids.0000247564.73009.bc>.
- [10] V. von Wyl, R.D. Kouyos, S. Yerly, J. Böni, C. Shah, P. Bürgisser, T. Klimkait, R. Weber, B. Hirschel, M. Cavassini, C. Staehelin, M. Battegay, P.L. Vernazza, E. Bernasconi, B. Ledergerber, S. Bonhoeffer, H.F. Günthard, Swiss HIV Cohort Study, The role of migration and domestic transmission in the spread of HIV-1 nonB subtypes in Switzerland, J. Infect. Dis. 204 (2011) 1095–1103, <http://dx.doi.org/10.1093/infdis/jir491>.
- [11] [Marcelin Anne-Geneviève, M. Santoro, C. Charpentier, A. Storto, D. Di Carlo, W. Gennari, C.F. Perno, V. Calvez, D. Descamps, F. Ceccherini-Silberstein, Epidemiological Study of Doravirine Associated Resistance Mutations in HIV-1-infected Treatment-Naïve Patients from Two Large Databases in France and Italy, \(2017\) in: Roma, Italy.](#)
- [12] Y. Li, Y. Han, J. Xie, L. Gu, W. Li, H. Wang, W. Lv, X. Song, Y. Li, J.-P. Routy, T. Ishida, A. Iwamoto, T. Li, CACT0810 group, CRF01_AE subtype is associated with X4 tropism and fast HIV progression in Chinese patients infected through sexual transmission, AIDS Lond. Engl. 28 (2014) 521–530, <http://dx.doi.org/10.1097/QAD.000000000000125>.
- [13] X. Li, Y. Xue, L. Zhou, Y. Lin, X. Yu, X. Wang, X. Zhen, W. Zhang, Z. Ning, Q. Yue, J. Fu, F. Shen, J. Gai, Y. Xu, J. Mao, X. Gao, X. Shen, L. Kang, G. Vanham, H. Cheng, Y. Wang, M. Zhuang, X. Zhuang, Q. Pan, P. Zhong, Evidence that HIV-1 CRF01_AE is associated with low CD4 + T cell count and CXCR4 co-receptor usage in recently infected young men who have sex with men (MSM) in Shanghai, China, PLoS One 9 (2014) e89462, <http://dx.doi.org/10.1371/journal.pone.0089462>.
- [14] S.W.-C. To, J.H.-K. Chen, K.-H. Wong, K.C.-W. Chan, Z. Chen, W.-C. Yam, Determination of the high prevalence of dual/mixed- or X4-tropism among HIV type 1 CRF01_AE in Hong Kong by genotyping and phenotyping methods, AIDS Res. Hum. Retroviruses 29 (2013) 1123–1128, <http://dx.doi.org/10.1089/aid.2013.0067>.

- [15] P. Recordon-Pinson, C. Soulié, P. Flandre, D. Descamps, M. Lazrek, C. Charpentier, B. Montes, M.-A. Trabaud, J. Cottalorda, V. Schneider, L. Morand-Joubert, C. Tamalet, D. Desbois, M. Macé, V. Ferré, A. Vabret, A. Ruffault, C. Pallier, S. Raymond, J. Izopet, J. Reynes, A.-G. Marcelin, B. Masquelier, ANRS AC11 Resistance Study Group, Evaluation of the genotypic prediction of HIV-1 coreceptor use versus a phenotypic assay and correlation with the virological response to maraviroc: the ANRS GenoTropism study, *Antimicrob. Agents Chemother.* 54 (2010) 3335–3340, <http://dx.doi.org/10.1128/AAC.00148-10>.
- [16] E. Seclén, C. Garrido, M. del, M. González, J. González-Lahoz, C. de Mendoza, V. Soriano, E. Poveda, High sensitivity of specific genotypic tools for detection of X4 variants in antiretroviral-experienced patients suitable to be treated with CCR5 antagonists, *J. Antimicrob. Chemother.* 65 (2010) 1486–1492, <http://dx.doi.org/10.1093/jac/dkq137>.
- [17] E. Delgado, A. Fernández-García, Y. Vega, T. Cuevas, M. Pinilla, V. García, M. Sánchez, M. González, A.M. Sánchez, M.M. Thomson, L. Pérez-Álvarez, Evaluation of genotypic tropism prediction tests compared with in vitro co-receptor usage in HIV-1 primary isolates of diverse subtypes, *J. Antimicrob. Chemother.* 67 (2012) 25–31, <http://dx.doi.org/10.1093/jac/dkr438>.
- [18] R.M. Gulick, J. Lalezari, J. Goodrich, N. Clumeck, E. DeJesus, A. Horban, J. Nadler, B. Clotet, A. Karlsson, M. Wohlfeiler, J.B. Montana, M. McHale, J. Sullivan, C. Ridgway, S. Felstead, M.W. Dunne, E. van der Ryst, H. Mayer, MOTIVATE Study Teams, Maraviroc for previously treated patients with R5 HIV-1 infection, *N. Engl. J. Med.* 359 (2008) 1429–1441, <http://dx.doi.org/10.1056/NEJMoa0803152>.
- [19] D.A. Cooper, J. Heera, J. Goodrich, M. Tawadrous, M. Saag, E. DeJesus, N. Clumeck, S. Walmsley, N. Ting, E. Coakley, J.D. Reeves, G. Reyes-Teran, M. Westby, E. Van Der Ryst, P. Ive, L. Mohapi, H. Mingrone, A. Horban, F. Hackman, J. Sullivan, H. Mayer, Maraviroc versus efavirenz, both in combination with zidovudine-lamivudine, for the treatment of antiretroviral-naïve subjects with CCR5-tropic HIV-1 infection, *J. Infect. Dis.* 201 (2010) 803–813, <http://dx.doi.org/10.1086/650697>.
- [20] G. Fätkenheuer, M. Nelson, A. Lazzarin, I. Konourina, A.I.M. Hoepelman, H. Lampiris, B. Hirschel, P. Tebas, F. Raffi, B. Trottier, N. Bellos, M. Saag, D.A. Cooper, M. Westby, M. Tawadrous, J.F. Sullivan, C. Ridgway, M.W. Dunne, S. Felstead, H. Mayer, E. van der Ryst, MOTIVATE 1 and MOTIVATE 2 Study Teams, Subgroup analyses of maraviroc in previously treated R5 HIV-1 infection, *N. Engl. J. Med.* 359 (2008) 1442–1455, <http://dx.doi.org/10.1056/NEJMoa0803154>.
- [21] C. Soulié, D.B. Fofana, N. Boukli, S. Sayon, S. Lambert-Niclot, M. Wirden, A. Simon, C. Katlama, V. Calvez, P.M. Girard, A.G. Marcelin, L. Morand-Joubert, Performance of genotypic algorithms for predicting tropism of HIV-1CRF02_AG subtype, *J. Clin. Virol. Off. Publ. Pan Am. Soc. Clin. Virol.* 76 (2016) 51–54, <http://dx.doi.org/10.1016/j.jcv.2016.01.010>.

Amino acid consensus sequences of V3 loop-gp120 HIV B subtype and CRF01_AE recombinants.

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|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Gp120 | 296 | 297 | 298 | 299 | 300 | 301 | 302 | 303 | 304 | 305 | 306 | 307 | 308 | 309 | 310 | 311 | 312 | 313 | 314 | 315 | 316 | 317 | 318 | 319 | 320 | 321 | 322 | 323 | 324 | 325 | 326 | 327 | 328 | 329 | 330 |
| V3loop | T | Z | S | I | S | G | T | S | S | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 |
| HXB2 | G | T | R | P | N | N | T | R | K | S | I | R | I | Q | R | Q | P | G | R | A | F | V | T | I | G | I | Q | D | M | R | Q | A | H | G | |
| B | C | T | S | F | N | N | T | R | Q | S | I | R | I | G | P | G | R | A | F | V | A | V | G | D | I | I | D | D | I | R | Q | A | H | G | |
| CRF01_AE | C | T | S | F | N | N | T | R | T | D | I | R | I | G | P | G | Q | V | F | V | R | T | G | D | I | I | D | D | I | R | K | A | V | C | |
| p | 0.9999 | 0.1189 | 0.9999 | 0.9999 | 0.0001 | 0.1865 | 0.9999 | 0.0496 | 0.5141 | 0.0001 | 0.0001 | 0.0001 | 0.0001 | 0.0002 | 0.0001 | 0.8104 | 0.4338 | 0.0001 | 0.0162 | 0.0611 | 0.0073 | 0.0001 | 0.5802 | 0.0007 | 0.0001 | 0.0422 | 0.9999 | 0.2269 | 0.0288 | 0.6302 | 0.6378 | 0.0002 | 0.0031 | 0.0001 | 0.1600 |

Table 1B

Distribution of amino acid at position 11 and 25 of V3 loop-gp120. In bold, the major amino acid.

| | | B subtype | CRF01_AE recombinant |
|------|-----|-----------|----------------------|
| 11 S | A | 0.5 | |
| | D | 1.5 | |
| | G | 29.0 | 13.2 |
| | H | | 0.5 |
| | K | | 1.0 |
| | L | 0.5 | |
| | N | 0.5 | 1.0 |
| | P | | 0.5 |
| | R | 7.5 | 8.5 |
| | S | 59.5 | 75.4 |
| 25 I | T | 0.5 | 0.5 |
| | Y | 0.5 | |
| | A | 5.7 | 6.4 |
| | D | 33.0 | 56.1 |
| | E | 22.2 | 17.0 |
| | G | 5.7 | 8.5 |
| | H | 1.4 | 0.9 |
| | I | 7.1 | 2.6 |
| | K | 2.4 | 1.3 |
| | N | 3.8 | 3.4 |
| Q | 9.4 | 1.7 | |
| R | 6.1 | 0.4 | |
| S | 2.8 | 0.9 | |
| T | 0.5 | 0.4 | |
| V | | 0.4 | |

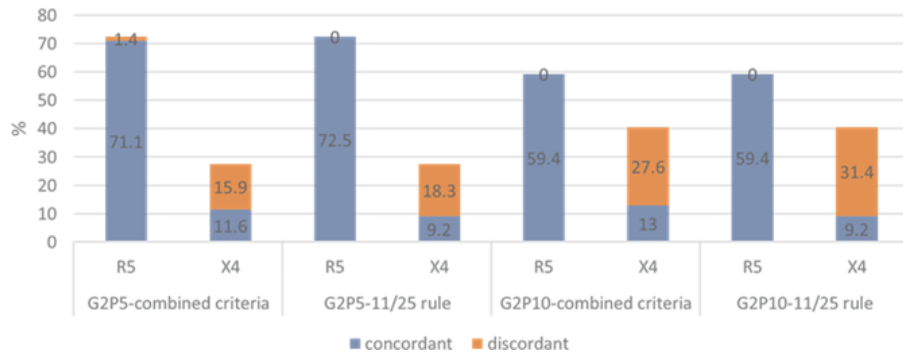


Fig. 1. Representation of tropism prediction by different algorithm for CRF01_AE recombinant.