Analysis of longitudinal *nef* sequence variation throughout HIV-2 infection

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Background: Human Immunodeficiency Virus type 1 (HIV-1) and type 2 (HIV-2) may case a severe immunodeficiency in humans (AIDS). However HIV-2 is more frequently associated with lower levels of transmission and disease progression, compared with HIV-1 infections. The role of *nef* gene *in vivo* during the development of AIDS has been clearly demonstrated in simian immunodeficiency virus infected *Rhesus* macaques model, but the determinants which play a role in the pathogenesis of HIV are relatively poorly understood. However, even less is known about the role of *nef* in HIV-2 infections.

Methods: In this study, it was analyzed the variation of 48 *nef* gene sequences, obtained from samples taken between 1994 and 2009, corresponding to 17 HIV-2-infected individuals with different clinical stages of infection. The sequences obtained by Nested PCR were classified by phylogenetic analysis and the functional protein motifs, described as important in CD4 and MHC-I downregulation and in viral infectivity were also analyzed.

Results: In all individuals were identified *nef* sequences from group A of HIV-2, which encoded possible functional and complete protein. There was a greater conservation of residues in the Nef sequences of individuals in the symptomatic stage (63%), comparatively to individuals in the asymptomatic stage (19%). While some functional motifs (MGxxxS1, DDDD93, RR137 and DD205) and also residues (G128, I141 and L142) remained conserved, others (YSRF39, LRAR21, PxxP101, EE185) revealed changes during the follow-up period. The PxxP motif exhibited wide inter-individual variation *in vivo* from an HIV-1-like tetra-proline motif (PxxP)3 to disruption of the minimal core PxxPLR motif. The disruption was observed in 11 sequences exclusively from asymptomatic individuals ($p = 0.021$). The sequence motif variation towards tetra-proline configuration was observed in 2 symptomatic individuals during time of infection. The results also revealed the existence of a negative selective pressure, as well as codons under positive pressure in the sequences.

Conclusion: In this HIV-2-infected individuals studied, it was observed a need for a greater degree of Nef protein conservation in a symptomatic phase. Sequences altered and potentially critical for the Nef function *in vivo*, in earlier stages of infection, may contribute at some level to a different pattern in viral pathogenesis and disease progression.

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Prediction of R5, X4 HIV-1 coreceptor usage based on physicochemical properties of envelope V3- loop using artificial neural network

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Background: HIV-1 cell entry commonly uses, in addition to CD4, one of the chemokine receptors CCR5 or CXCR4 as coreceptor. Human immunodeficiency virus type 1 (HIV-1) isolates can be classified phenotypically according to the primary coreceptor used to enter the cells. Third variable region (V3- loop) of the gp120 subunit of the HIV-1 envelope protein has been identified as a major determinant of coreceptor usage. Knowledge of coreceptor usage is critical for monitoring disease progression and for supporting therapy with the novel drug class of coreceptor antagonists. Predictive methods for inferring coreceptor usage based on the third V3- loop region can provide us with these monitoring facilities while avoiding expensive phenotypic assays. In this study we applied an artificially neural network on physiochemical data, derived from V3- loop sequence to predict coreceptor usage of viral isolate.

Methods: At first authors has collected two reliable set of data that define the biochemical and structural conditions of co receptor usage of virus. In the next step we have developed an ANN models to predict virus coreceptor usage and compare the results of ANN models with MLR model. In the ANN model, two levels of 1 and 2 are used as output vector or goal, respectively for R4 and R5 and the physiochemical aspects are input variables, also it was in MLR model.

Results: The process of training and testing of this new model is done using a set of collected data. ANN model with $R2 = 0.99$ and $RMSE = 15.18$ in training stage and $R2 = 0.91$ and $RMSE = 187.8$ in testing stage is superior in predicting the coreceptor usage. Several statistical and graphical criterions are used to check the accuracy of the model.

Conclusion: The coreceptor usage values predicted by the ANN model satisfactorily compared with the measured data. The predicted values were also compared with those predicted using linear regression model. The presented methodology in this modeling is a new approach in estimating coreceptor usage and can be combined with other models and empirical methods of coreceptor usage determination.

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HIV: Therpeutics

55.001

Clinical and immunologic response of HIV patients on different ART regimens at Gondar University Hospital (GUH)

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Background: As HIV treatment program expands in resource poor countries, antiretroviral drug selection is