J AIDS Clin Res 2016, 7:9(Suppl)
http://dx.doi.org/10.4172/2155-6113.C1.015

Using transcriptome sequencing technology to screen key genes related to HIV-1 unsusceptibility from HEPS subjects in China

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Understanding of unsusceptibility mechanisms of HIV-1 highly exposed and persistently seronegative (HEPS) individuals may provide new treatment strategies or vaccine targets. Although a mutation known as CCR5Δ32 in the CCR5 gene can protect certain individuals against HIV infection, the CCR5Δ32 genotype is rarely found in Chinese population, suggesting Chinese HEPS persons have other unsusceptibility mechanisms. We used transcriptome sequencing technology to screen key genes related to HIV-1 unsusceptibility from HEPS subjects in China. HEPS subjects were strictly selected according to the HEPS standards. Age, gender and ethnic-matched healthy individuals were enrolled as control. Peripheral blood mononuclear cells (PBMCs) were isolated from peripheral blood samples and total cellular mRNA was then extracted for high-throughput transcriptome sequencing (Hi-Seq 2000). Totally, there were 1906 differentially expressed genes between one HEPS sample (GH01) and one control sample (C01), with 1139 up-regulated genes and 767 down-regulated genes in sample GH01. Among them, 15 genes have been reported to be associated with HIV-1 unsusceptibility and 30 genes have been reported to be related to HIV-1 infection/replication, however, no reports show their relationship to HIV-1 unsusceptibility. GO function enrichment and KEGG pathway analyses show seven significantly differential pathways (Q value<0.05) between two samples. Among them, two pathways, including natural killer cell mediated cytotoxicity pathway and antigen processing and presentation pathway, have been reported to be closely associated with HIV-1 infection. The above data lay a solid foundation for the future research on specific mechanisms responsible for HIV-1 unsusceptibility in HEPS subjects in China.

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Bayesian Cox proportional hazards model and insights from the censored quantile regression model for pediatric and adolescent HIV/AIDS patients on antiretroviral treatment

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Survival analysis techniques are often used in biostatistics, epidemiological and clinical research to model time until event data. Many of these techniques have recently been further enhanced through the advent of modern computational advancements. The purpose of this study is to fit a Bayesian proportional hazards model and a censored quantile regression model to pediatric data and then compare the results in terms of the rich of inferences on the effect of the different prognostic risk factors on ART patient survival times. A retrospective cohort study design was conducted for children who initiated anti-retroviral treatment (ART) between 01 January 2006 and 31 December 2010. The sampling frame constituted 1605 pediatric patients and from these a final sample of 813 children was selected from those who initiated ART between 01 January 2006 and 31 December 2010. Imputation was performed for all variables that had missing cases so that a full dataset will be used for the analysis. The results from a Bayesian proportional hazards model indicate that not being an infant had a positive effect on survival time. Patients initiating treatment in clinical stage-II instead of stage-IV had a significant positive effect on survival time. The results from the censored quantile regression model are more revealing, highlighting that initiating in clinical stage-II had a significant positive effect on survival time during the early periods of initiation compared to initiating in clinical stage-IV. The effect reduces towards the 80th quantile, that is, towards the end of the follow-up period. Initiating treatment in clinical stages-I and III was not significantly different from initiating in clinical stage-IV. The results also reveals that patient gender has a significant effect during the early periods of starting ART but not significant at any other point during treatment. These insights are only possible from using censored quantile regression models in modeling time to event data. The conclusion from this study is that more insights are obtained from using censored quantile regression models as compared to the proportional hazards models framework. However, noting that the censored quantile regression models do not give hazard ratios, it is our belief that if these models are applied together, then we can get both the important insights into the dynamics of the prognostic risk factor effects as well as the hazard ratios associated with them.

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