学位論文抄録
Abstract of Thesis

Circulating pre-treatment and acquired HIV drug resistance Mutations in Dar es Salaam, Tanzania

（タンザニアで流行する薬剤耐性 HIV-1 変異に関する研究）

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Background and Purpose:

We investigated the prevalence and patterns of pre-treatment and acquired HIV-drug resistance mutations (DRM) in Tanzania as "treat all" strategy, virological monitoring and progressive increase in usage of tenofovir are being implemented in HIV treatment program.

Methods:

Viral RNAs were isolated from plasma of 60 antiretroviral therapy (ART)-naïve and 166 treated but viremic (>400 copies/ml) HIV-1-infected adults attending care and treatment clinic at Muhimbili national hospital, Dar es Salaam, Tanzania, between June and October 2017. Viral genes encoding protease and reverse transcriptase and integrase were PCR amplified and directly sequenced.

Results:

Viral genotyping of successfully amplified samples revealed pre-treatment DRM in 14/47 (29.8%) of ART-naïve subjects. Of these, 7/47 (14.9%) harboured mutations that confer high-level resistance to at least one drug of the default first-line regimen. In treated but viremic subjects, DRM were found in 100/111 (90%), where, DRM against NNRTI, NRTI and PI were observed in 95/100 (95%), 92/100 (92%) and 13/100 (13%), respectively. Tenofovir-resistance mutations K65R, K70G/E or ≥3 thymidine analogue resistance mutations including M41L and L210W were found in 18/36 (50%) of subjects on tenofovir containing regimen at failure. Four patients harboured multiple DRM, which can confer resistance to all available ART regimens in Tanzania. In contrast we did not detect any major integrase resistance mutation, accessory resistance mutations ware present in 8/158 (5.1%) of all integrase sequences.

Conclusions:

Taken together, pre-treatment and acquired DRM were highly prevalent which represented a major risk for the efficacy of ART program in Tanzania. Availability of newer generation of antiretroviral drugs with higher genetic barrier to resistance and robust treatment monitoring is warranted for effective and sustainable HIV treatment.