Evaluation of the risk of HTLV-1-associated diseases by analyzing the host immune responses and proviral load

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Background:
Host immune responses to HTLV-1 differ among the status of HTLV-1-associated diseases. To identify the high-risk groups for ATL or HAM/TSP, we focus on humoral immunity against HTLV-1 and proviral load (PVL).
Methods:
Humoral immunity against HTLV-1 proteins, such as Tax, Env, Gag p15, p19 and p24, was evaluated by the Luciferase Immunoprecipitation System (LIPS) assay using plasma or serum obtained from 287 carriers including 24 carriers developed ATL (CDA), 25 ATL cases, and 56 HAM cases.
Results:
HAM/TSP patients had high antibody responses to all antigens evaluated. ATL patients had low antibody responses to them except for Gag p19 and p24.-Next, partial least square (PLS) analysis was performed to identify high-risk cases using antibody data and PVL. HAM and ATL samples were well clustered in a two-dimensional plane, respectively. We observed a clinically reasonable result that CDA samples were located around the boundary between ATL and carrier. Based on this result, carrier samples that are close or overlap with the ATL cluster might be high-risk for developing ATL. We searched for somatic mutations by target sequencing in seven high-risk cases and one carrier who had high antibody responses and was close to HAM/TSP in PLS. Three of high-risk cases had driver mutation of ATL, while there was no mutation in the carrier without the signature of high-risk. Importantly, the clonality of infected cells in subjects which had driver mutations were polyclonal pattern.
Conclusion:
We evaluated the risk of HTLV-1-associated diseases using the antibodies to several HTLV-1 proteins and PVL. We identified the high-risk carriers by multivariate analysis. Target sequencing detected mutations of the driver genes in the carriers who were considered as high-risk for ATL, suggesting usefulness of our strategy.

Disclosure of Interest Statement:

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