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Abstract of Doctoral Dissertation

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Applicant's name: Md Ishtiaq Rashid

Identification and characterization of high risk HTLV-1 carriers for HAM development utilizing machine learning-based approach

(機械学習アプローチを用いた HAM 発症高リスク HTLV-1 キャリアの同定と特徴解析)

HTLV-1-associated myelopathy (HAM) develops in a part of HTLV-1-infected individuals while most of the individuals remain asymptomatic. This complicates the identification of HTLV-1 carriers at elevated risk. In this study, we integrated HTLV-1 proviral load and antibody titers against Tax, Env, Gag p15, p19, and p24 proteins in a machine learning (ML) framework to identify and characterize high risk individuals likely to develop HAM. We stratified asymptomatic carrier samples employing an anomaly detection model. We further developed and validated classifier models capable of distinguishing three clinical subgroups, carrier, ATL, and HAM for assessing the anomaly carrier samples as unseen test data. With most anomaly carrier samples (~76.47%) predicted as HAM, further statistical and interpretative analysis revealed the 'HAM-like' characteristics of the anomaly carrier samples indicating elevated risk. Additionally, significant heterogeneity in immune response was observed among other asymptomatic carriers. As an exploratory, hypothesis-generating study, our findings are preliminary and aim to propose potential biomarkers and computational strategies that warrant validation in future longitudinal investigations. Our machine learning-based approach offers a novel and insightful tool for identifying and evaluating high risk characteristics for HAM, providing a holistic view of the complex immune dynamics of asymptomatic carriers of HTLV-1.