243

Machine Learning-Driven Analysis of Epigenetic Signatures in Primary Immunodeficiency Disorders: Investigating Histone Modification Dynamics

Dr. Rohit Rajput[1], Dr DK Khatri[1]
[1]F H Medical College & Hospital, Agra, India

Objective:
This study aims to investigate the role of histone modifications in the pathophysiology of Primary Immunodeficiency Disorders (PIDs), an emerging yet underexplored area of epigenetic research. The primary goal is to identify epigenetic biomarkers associated with disease onset and severity, using machine learning techniques to uncover regulatory patterns that may inform diagnosis and therapeutic strategies.

Background:
PIDs are a diverse group of inherited immune disorders often linked to monogenic mutations. However, clinical heterogeneity among patients with similar genetic defects suggests that non-genetic factors, such as epigenetic modifications, may also play a role in disease progression. Histone modifications are key regulators of gene expression, and their dysregulation may influence immune cell function, inflammatory pathways, and susceptibility to immune-related complications. Despite their relevance, the epigenetic landscape of PIDs—particularly histone modifications—remains poorly characterized.

Methods:
The study utilized chromatin immunoprecipitation sequencing (ChIP-seq) data from neuronal precursor cells derived from 250 PID patients and matched healthy controls. Analysis focused on key histone modifications (e.g., H3K4me3, H3K27ac) at regulatory immune-related gene loci. These datasets were integrated with whole-genome sequencing and clinical metadata. Convolutional Neural Networks (CNNs) were applied to detect spatial patterns of histone modification peaks, while a Random Forest (RF) model was used to predict disease onset and severity by integrating epigenetic, genomic, and clinical variables. Stratified cross-validation was used to evaluate model performance and ensure reproducibility.

Results:
Distinct histone modification patterns were observed in PID patients with early disease onset and more aggressive progression. These alterations were especially pronounced near genes involved in neuronal signaling and immune regulation. The combined CNN-RF model achieved 88% accuracy in distinguishing early- from late-onset PID, with an area under the curve (AUC) of 0.94 and a mean absolute error of 2.3 years in predicting disease onset. A subset of patients with specific epigenetic signatures exhibited a 30% higher rate of disease progression.

Conclusion:
This study highlights the potential of machine learning tools to decode the epigenetic architecture of PIDs. Histone modification profiles may serve as early biomarkers and therapeutic targets, offering new avenues for personalized immunological care and advancing our understanding of PID pathogenesis.