





A rare DNA methylation variant exhibits dramatically different methylation levels in a small group of individuals compared to the rest of the studied population. Recent studies show that rare DNA methylation variants are linked to several human diseases, such as cancer and congenital anomalies. Existing methods to compare rare DNA methylation variants between two groups of samples were mostly single-variant association tests. In this study, we introduced a procedure for multi-variant association analysis. The regional outlying methylation difference between two groups was measured by aggregating the group differences for each variant in that region. The performance of the proposed method was supported by a simulation study, and we have applied the method to multiple real datasets.