**Abstract**

Candidate gene associated with diseases could be ranked by the reconstruction of PPI Network. In current biomedical research, the prioritization of candidate gene is the most essential issue. A reliable heterogeneous network was used for candidate gene prioritization for diseases. This network was constructed by fusion of reconstructed Protein-Protein Interaction (PPI) network by topological similarity, relationship between diseases and genes of proteins and phenotype similarity network. Then, the candidate genes were prioritized by Random Walker on the Reliable Heterogeneous Network (RWRHN) which is a random walk-based algorithm. PPI network reconstruction by protein characteristic further improved the prediction accuracy of disease genes. In this paper, the prioritization of candidate gene for diseases is further improved by proposed Random Walker on Optimized Trustworthy Heterogeneous Network (RW-OTHN) which additionally considering the protein sequence similarity and gene expression profile similarity while reconstructing PPI network. The protein sequence similarity is calculated by piecewise linear regression model. The gene expression profile similarity is calculated by applying sub space clustering on high dimensional gene expression profile data. The subspace clustering is processed by multi objective BAT algorithm and K means clustering. The prioritization of candidate gene is improved with the consideration of protein sequence similarity and gene expression profile similarity in PPI network reconstruction