

Modular-based mapping between HPO and MPO provides a new approach to decipher phenotypic mechanisms

Yunxiang Liang, Jinmeng Jia, Dongming Guo, Yige Hu, Tieliu Shi*

The Center for Bioinformatics and Computational Biology, Shanghai Key Laboratory of Regulatory Biology, the Institute of Biomedical Sciences and School of Life Sciences, East China Normal University, Shanghai 200241, China

Abstract

Mapping human phenotypes to model organism phenotypes plays an important role in the study of disease mechanisms. Mouse and other mammals have been used as models to decipher the underlying mechanisms of various human phenotypes, including diseases. Great efforts have been made to generate the Mammalian Phenotype Ontology (MPO) to standard the phenotypes of mammals. Similarly, Human Phenotype Ontology (HPO) has been designed to systematically describe the corresponding human phenotypes. Mapping between MPO and HPO has been regarded as an effective approach to interpret the potential functions of human genes. Currently, the mapping between HPO phenotypes and MPO phenotypes are generally based on two approaches – connecting human phenotypes to mammalian phenotypes based on their corresponding homologous genes, or finding associations through semantic similarities between phenotypic terms from HPO and MPO. However, given that the different representation models of mutant mouse phenotypes and human disease abnormalities as well as their inconsistency of hierarchical structures, the results of the two methods have shown a very limited overlaps. Here, we proposed a modular recognition method which can recognize significant module-module correlations of HPO and MPO phenotypes. The phenotype modules were developed by grouping phenotypes which showed a steady underlying mechanism interactions in the phenotype-based disease network. The connections between HPO and MPO phenotype modules were built by linking their corresponding homologous genes based on gene-based disease network. As a result, 17,424 phenotype associations between HPO and MPO modules are built. Statistical methods and manual analysis were adopted to validate our mapping results, which showed that the modularized approach can generate reliable mapping between phenotypes from HPO and MPO. Analyses on those particular modules provided an important resources for the underlying mechanism investigation of human phenotypes.

Key words: HPO and MPO mapping, Phenotype network, Module mapping