PICKLE 3.0: A standardized human and mouse protein-protein interaction (PPI) meta-database

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ABSTRACT

After more than fifteen years from the first high-throughput experiments for human protein-protein interaction (PPI) detection, we are still wondering how close the completion of the genome-scale human PPI network reconstruction is, what needs to be further explored, and whether biological insights gained from the holistic investigation of the current network are valid and useful. PICKLE (www.pickle.gr), a meta-database of the human (1) and mouse (2) experimentally-determined direct PPI network developed by our group, uses the UniProtKB/Swiss-Prot reviewed human and mouse complete proteomes (RHCP, RMCP) as the reference protein interactor sets, integrates PPI datasets via genetic information ontology, links human and mouse ontological networks *via* gene orthology by Mouse Genome Informatics (MGI, http://www.informatics.jax.org/), provides PPI networks at three filtering modes based on experimental evidence for PPIs being direct, and permits queries for multiple identifiers (1, 2). The unique structure of PICKLE, presently covering ~80% of RHCP, enables the evaluation of the interactome expansion by comparing PICKLE successive releases since 2013 (1). We observe a gradual overall increase of 182%, 39% and 67%, in PPIs, protein-nodes and supporting references, respectively. Our results indicate that, in recent years, (a) the PPI addition rate has decreased, (b) the new PPIs are largely determined by high-throughput experiments and mainly concern existing protein-nodes, and (c), as we had predicted earlier, most of the newly-added protein-nodes have a low degree (3). These observations, combined with a largely overlapping k-core between PICKLE releases and a network density increase, imply that an almost complete picture of a structurally defined network has been reached. Comparative unsupervised application of two clustering algorithms indicated that exploring the full interactome topology can reveal protein neighborhoods involved in same biological processes, as transcriptional regulation, cell signaling, and multiprotein complexes such as the connexon complex associated with cancer (3). Our results imply that an almost complete picture of a structurally defined human PPI network has been reached. A well-reconstructed human protein interactome is a powerful tool in network biology and medicine research forming the basis for multi-omic and dynamic analyses.

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