**S3 Table. The ruleset for the standard filtering of the primary PPI datasets**.

The table indicates the evidence sets that are considered in the various quality classes regarding the probability of suggesting a direct PPI, based on the evidence attributes reported by each source database (shown in **S2 Table**).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Quality** | **Experimental Evidence Sets stored in PICKLE for cross-checking purposes only;**  **not included in the unfiltered PICKLE PPI network** | | | | | **Database** |
| **Interactor Type** | **Interaction Type** | **Experimental System (BioGRID) or**  **Detection Method (HPRD, MIntAct, DIP)** | **Throughput** | **Expansion**  **Method** |
| Quinary-class | Any applicable | Any applicable | Any of the following:   * + - * Protein-RNA       * Affinity Capture RNA | Any |  | BioGRID |
| Quinary-class | At least one interactor is not protein or peptide | Any applicable | Any applicable |  | Any | MIntAct |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Quality** | **Experimental Evidence Set included in the unfiltered PICKLE PPI network** | | | | **Database(s)** |
| **Interaction Type** | **Experimental System (BioGRID) or**  **Detection Method (HPRD, MIntAct, DIP)** | **Throughput** | **Expansion**  **Method** |
| First-class | 1. Any of the following:  * direct interaction * adp ribosylation reaction * acetylation reaction * cleavage reaction * covalent binding * deacetylation reaction * demethylation reaction * dephosphorylation reaction * deubiquitination reaction * enzymatic reaction * gtpase reaction * hydroxylation reaction * methylation reaction * neddylation reaction * palmitoylation reaction * phosphorylation reaction * phosphotransfer reaction * protein cleavage * ubiquitination reaction | Any | Any  (if applicable) | Any  (if applicable) | BioGRID, MInAct, DIP |
| First-class | 1. Any other interaction type than those mentioned in criterion 1 of first class above (among the evidence sets included in the unfiltered PICKLE PPI network). | Any of the following:   * PCA (BioGRID) * protein-peptide (BioGRID) * FRET (BioGRID) * two-hybrid (BioGRID) * reconstituted Complex (BioGRID) * biochemical activity (BioGRID) * antibody array * beta galactosidase complementation * bimolecular fluorescence complementation * bioluminescence resonance energy transfer * competition binding * deacetylase assay * dihydrofolate reductase reconstruction * enzymatic study * enzyme linked immunosorbent assay * equilibrium dialysis * far western blotting * filter binding * fluorescence polarization spectroscopy * fluorescence recovery after photobleaching * fluorescent resonance energy transfer * gal4 vp16 complementation * gtpase assay * isothermal titration calorimetry * lex-a dimerization assay * mammalian protein protein interaction trap * methyltransferase assay * methyltransferase radiometric assay * peptide array * phage display * protein array * protein kinase assay * reverse ras recruitment system * reverse two hybrid * split luciferase complementation * split renilla luciferase complementation * three-hybrid * tox-r dimerization assay * transcriptional complementation assay * two-hybrid (the only applicable to HPRD; should be one of the supporting detection methods) * two-hybrid array * ubiquitin reconstruction * x-ray crystallography * yeast display | Any  (if applicable) | Any  (if applicable) | BioGRID, MInAct, DIP |
| Second-class | Any other than interaction type than those mentioned in criterion 1 of first-class above. | Any other than experimental system (BioGRID) or detection method (MIntAct, DIP) than those mentioned in criterion 2 of first-class above; any set of supporting detection methods not including ‘two-hybrid’ (HPRD). | Low or  both (Low & High)  (when applicable) | No  (when applicable) | BioGRID, HPRD, MIntAct, DIP |
| Third-class | Any other than interaction type than those mentioned in criterion 1 of first-class above. | Any other than experimental system (BioGRID) or detection method (MIntAct, DIP) than those mentioned in criterion 2 of first-class above; any set of supporting detection methods not including ‘two-hybrid’ (HPRD). | High (only)  (when applicable) | Yes  (when applicable) | BioGRID, HPRD, MIntAct, DIP |