**Supplementary Table 1: Comparison of degree values of central and non-central proteins**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Network** | **Pathogen/host** | **Number of central nodes** | **Mean Degree of central nodes** | **Mean degree of non-central nodes** |
| **wHPI** | Virus | 478 | 89 | 5 |
|  | Bacteria | 228 | 26 | 3 |
|  | Host interspecies network | 287 | 56 | 4 |
|  | Host intraspecies network | 285 | 211 | 32 |
| **cHPI** | Virus | 103 | 58 | 4 |
|  | Bacteria | 73 | 19 | 2 |
|  | Host interspecies network | 78 | 40 | 3 |
|  | Host intraspecies network | 81 | 157 | 22 |

**Supplementary Table 2: Biological characterization of central host proteins**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| S.No. | Category | Central proteins of cHPI network (inter-species) | Central proteins of cHPI network (intra-species) | Central proteins of wHPI network (inter-species) | Central proteins of wHPI network (intra-species) |
|  | Essential | 63/78 (82%) | 68/81 (85%) | 246/287 (86%) | 205/245 (84%) |
|  | Host Factor | 58/78 (75%) | 63/81 (79%) | 241/287 (84%) | 200/245 (82%) |
|  | Immune Related | 28/78 (36%) | 64/81 (80%) | 154/287 (54%) | 105/245 (60%) |
|  | Extracellular | 56/78 (72%) | 50/81 (62%) | 206/287 (72%) | 191/245 (78%) |

**Supplementary Table 3: List of enriched homologous domains between host and viral proteins**

|  |  |  |  |
| --- | --- | --- | --- |
| **S.No.** | **Viral protein domains** | **P-value (Hypergeometric test)** | **Fold enrichment** |
|  | FABD | 0.002942 | 417.414796 |
|  | IRF-3 | 0.000357 | 200.004044 |
|  | DED | 0.004399 | 167.066058 |
|  | DEXDc | 0.000169 | 155.60803 |
|  | Z alpha | 0.006406 | 150.404458 |
|  | HELICc | 3.77E-09 | 66.7314778 |
|  | S\_TKc | 8.11E-07 | 59.9518604 |
|  | ZnF\_C2HC | 7.85E-38 | 45.2121363 |
|  | AAA | 0.000173 | 35.9402294 |
|  | IRF | 0.000173 | 33.9673368 |
|  | PTPc\_motif | 0.044491 | 32.4401259 |
|  | RINGv | 1.82E-05 | 25.9586808 |
|  | BCL | 4.63E-06 | 23.6860941 |
|  | A1pp | 0.004903 | 21.2396356 |
|  | PDGF | 0.004903 | 17.3367168 |
|  | BACK | 0.001095 | 16.6888269 |
|  | TNFR | 8.06E-06 | 13.4778068 |
|  | SH2 | 0.000869 | 12.8850466 |
|  | UDG | 6.92E-05 | 11.7433577 |
|  | TyrKc | 6.92E-05 | 11.0619124 |
|  | Sema | 1.1E-07 | 10.7016895 |
|  | SERPIN | 0.019568 | 9.92909586 |
|  | Kelch | 0.006446 | 8.85741794 |
|  | POLBc | 0.006446 | 8.45024602 |
|  | DSPc | 0.011543 | 7.87612127 |
|  | DnaJ | 0.009619 | 7.83212305 |
|  | SCY | 7.85E-05 | 7.74131441 |
|  | CCP | 7.62E-05 | 7.53738158 |
|  | SH3 | 0.004821 | 6.28684071 |
|  | BTB | 0.009778 | 5.351049 |
|  | BRLZ | 0.010632 | 4.48794546 |
|  | SANT | 0.022681 | 3.83787737 |
|  | ANK | 3.69E-08 | 3.27569063 |
|  | DSRM | 3.77E-09 | 3.05446144 |
|  | RING | 0.001003 | 2.42200608 |
|  | IG | 0.001003 | 2.26861758 |

**Supplementary Table 4: List of enriched homologous domains between host and bacterial proteins**

|  |  |  |  |
| --- | --- | --- | --- |
| **S.No.** | **Bacterial Protein domains** | **P-value (Hypergeometric test)** | **Fold enrichment** |
|  | alkPPc | 1.87E-61 | 148.998674 |
|  | A2M | 8.23E-24 | 44.1865747 |
|  | LMWPc | 4.46E-27 | 31.2477587 |
|  | HELICc | 5.64E-19 | 22.4048876 |
|  | AAA | 3.77E-15 | 21.3083268 |
|  | DEXDc | 4.14E-31 | 21.3083268 |
|  | A2M\_N\_2 | 7.96E-17 | 20.9345621 |
|  | S\_TKc | 1.62E-19 | 19.2465632 |
|  | PTPc\_motif | 2.54E-09 | 18.645202 |
|  | CPSase\_L\_D3 | 8.08E-15 | 17.5485867 |
|  | THUMP | 1.55E-08 | 16.5738006 |
|  | PTPc | 0.045879 | 11.3653879 |
|  | LysM | 0.009691 | 10.2877285 |
|  | PlsC | 0.003194 | 9.32332929 |
|  | LRR\_TYP | 1.99E-21 | 8.99640975 |
|  | Gp\_dh\_N | 0.009564 | 8.0093912 |
|  | CPSase\_sm\_chain | 3.32E-09 | 7.50568758 |
|  | Enolase\_C | 1.92E-06 | 7.50568758 |
|  | Enolase\_N | 2.36E-11 | 7.50568758 |
|  | Arg\_tRNA\_synt\_N | 7.05E-11 | 7.48785266 |
|  | AdoHcyase | 0.000284 | 7.41245502 |
|  | AdoHcyase\_NAD | 7.99E-06 | 7.41245502 |
|  | DALR\_1 | 1.53E-08 | 7.02005401 |
|  | MUTSd | 2.89E-44 | 6.98550671 |
|  | MUTSac | 0.000382 | 6.78074759 |
|  | MGS | 1.75E-05 | 6.66711012 |
|  | Aamy | 5.44E-15 | 6.51272308 |
|  | EFG\_IV | 1.18E-07 | 5.64153378 |
|  | BRCT | 9.33E-08 | 5.57674587 |
|  | CSP | 6.8E-07 | 5.23432912 |
|  | EFG\_C | 0.014321 | 5.20705009 |
|  | Iso\_dh | 0.001126 | 5.20705009 |
|  | HDc | 5.25E-20 | 4.8923741 |
|  | DNA\_mis\_repair | 0.000458 | 4.73584137 |
|  | PGAM | 9.26E-15 | 4.71712337 |
|  | ClpB\_D2-small | 0.00055 | 4.68012777 |
|  | PKS\_ER | 0.004179 | 4.66184674 |
|  | KH | 7.09E-05 | 4.62570979 |
|  | Cpn10 | 7.85E-38 | 4.55509096 |
|  | NDK | 0.05388 | 4.51938971 |
|  | Tryp\_SPc | 0.036086 | 4.41285455 |
|  | RHOD | 0.002942 | 4.35877611 |
|  | Elp3 | 0.000357 | 4.35344108 |
|  | HATPase\_c | 0.004399 | 4.35344108 |