

# Supporting Materials for Evolution of Specificity in Protein-Protein Interactions

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Table S1. A List of the PPIs considered in the analysis of the SIN database. We note the type of protein (*Multi*-, *Singlish*- and Non-hub), its Uniport ID, the PDB file ID and the specific chains involved in the interaction.

| Type  | Uniprot ID  | PDB ID | chain 1 (hub) | chain 2 (partner) |
|-------|-------------|--------|---------------|-------------------|
| Multi | 2DRA_HUMAN  | 1FV1   | A             | C                 |
| Multi | APC_HUMAN   | 1EMU   | B             | A                 |
| Multi | CABIN_HUMAN | 1N6J   | A             | G                 |
| Multi | CDK2_HUMAN  | 1FQ1   | B             | A                 |
| Multi | CDK2_HUMAN  | 1BUH   | A             | B                 |
| Multi | CDK6_HUMAN  | 1BI8   | A             | B                 |
| Multi | CO3_HUMAN   | 3OED   | A             | C                 |
| Multi | CTNB1_HUMAN | 1LUJ   | A             | B                 |
| Multi | FIBA_HUMAN  | 1FZA   | A             | B                 |
| Multi | FIBA_HUMAN  | 1FZA   | A             | C                 |
| Multi | FKB1A_HUMAN | 1FAP   | A             | B                 |
| Multi | HBA_HUMAN   | 1Y01   | B             | A                 |
| Multi | HBA_HUMAN   | 1A00   | A             | B                 |
| Multi | HBA_HUMAN   | 1A9W   | A             | E                 |
| Multi | HFE_HUMAN   | 1A6Z   | A             | B                 |
| Multi | IL6RB_HUMAN | 1P9M   | A             | C                 |
| Multi | IL6RB_HUMAN | 1P9M   | A             | B                 |
| Multi | IL6RB_HUMAN | 1PVH   | A             | B                 |
| Multi | IMB1_HUMAN  | 1QGK   | A             | B                 |
| Multi | IMB1_HUMAN  | 1M5N   | S             | Q                 |
| Multi | INHBA_HUMAN | 3B4V   | B             | D                 |
| Multi | NCBP1_HUMAN | 1H2T   | C             | Z                 |
| Multi | NCF2_HUMAN  | 1OEY   | A             | J                 |
| Multi | NFKB1_HUMAN | 1MDI   | B             | A                 |
| Multi | NFYB_HUMAN  | 1N1J   | A             | B                 |
| Multi | PO2F1_HUMAN | 1CQT   | A             | I                 |
| Multi | PO2F1_HUMAN | 1O4X   | A             | B                 |
| Multi | RAN_HUMAN   | 1RRP   | B             | A                 |
| Multi | RAN_HUMAN   | 1QBK   | C             | B                 |
| Multi | RENT2_HUMAN | 1UW4   | A             | B                 |
| Multi | RFA1_HUMAN  | 1L1O   | B             | C                 |

|          |             |      |   |   |
|----------|-------------|------|---|---|
| Multi    | RFA3_HUMAN  | 1L1O | A | B |
| Multi    | S100B_HUMAN | 1MQ1 | A | C |
| Multi    | SKP1_HUMAN  | 2OVP | A | B |
| Multi    | SUMO1_HUMAN | 1TGZ | B | A |
| Multi    | TBP_HUMAN   | 1C9B | B | A |
| Singlish | ANPRC_HUMAN | 1YK1 | A | E |
| Singlish | ANPRC_HUMAN | 1JDP | A | H |
| Singlish | ANPRC_HUMAN | 1YK0 | A | E |
| Singlish | ARL1_HUMAN  | 1UPT | B | A |
| Singlish | B2MG_HUMAN  | 1ONQ | B | A |
| Singlish | B2MG_HUMAN  | 1GZP | B | A |
| Singlish | B2MG_HUMAN  | 1ZT4 | B | A |
| Singlish | B2MG_HUMAN  | 1EXU | B | A |
| Singlish | C1QA_HUMAN  | 1PK6 | C | A |
| Singlish | CY24A_HUMAN | 1WLP | A | B |
| Singlish | EP300_HUMAN | 1P4Q | A | B |
| Singlish | FGFR2_HUMAN | 1NUN | A | B |
| Singlish | GLHA_HUMAN  | 1HCN | A | B |
| Singlish | IF4E_HUMAN  | 1WKW | B | A |
| Singlish | IL1R1_HUMAN | 1ITB | B | A |
| Singlish | ITAL_HUMAN  | 1TOP | A | B |
| Singlish | ITAL_HUMAN  | 1MQ8 | B | A |
| Singlish | ITB3_HUMAN  | 1BP3 | A | B |
| Singlish | KLRD1_HUMAN | 1SYX | B | A |
| Singlish | NCOA1_HUMAN | 1KV6 | D | B |
| Singlish | NCOA1_HUMAN | 3BEJ | F | B |
| Singlish | NKG2D_HUMAN | 1KCG | A | C |
| Singlish | P53_HUMAN   | 1YCR | B | A |
| Singlish | PABP1_HUMAN | 1JH4 | B | A |
| Singlish | PCNA_HUMAN  | 1UL1 | A | X |
| Singlish | PEBB_HUMAN  | 1H9D | B | A |
| Singlish | RABE1_HUMAN | 1X79 | B | A |
| Singlish | RAC1_HUMAN  | 1I4D | D | A |
| Singlish | RAD51_HUMAN | 1NOW | A | B |
| Singlish | RBX1_HUMAN  | 3DPL | R | C |
| Singlish | RHOA_HUMAN  | 1XCG | A | B |
| Singlish | ROCK1_HUMAN | 2V55 | C | D |
| Singlish | SRF_HUMAN   | 1HBX | B | G |
| Singlish | TDG_HUMAN   | 2D07 | A | B |
| Singlish | TIMP1_HUMAN | 2J0T | A | D |
| Non-hub  | ANGI_HUMAN  | 1A4Y | B | A |

|         |             |      |   |   |
|---------|-------------|------|---|---|
| Non-hub | C1QB_HUMAN  | 1PK6 | B | A |
| Non-hub | CO4A1_HUMAN | 1LI1 | A | C |
| Non-hub | CSF3R_HUMAN | 2D9Q | B | A |
| Non-hub | CTDP1_HUMAN | 1F3U | B | A |
| Non-hub | CYBP_HUMAN  | 2A25 | B | A |
| Non-hub | EPOR_HUMAN  | 1AUI | A | B |
| Non-hub | FIBB_HUMAN  | 1FZA | B | C |
| Non-hub | GHR_HUMAN   | 1J7D | A | B |
| Non-hub | GSTM2_HUMAN | 3GTU | A | B |
| Non-hub | IFNG_HUMAN  | 1FG9 | A | C |
| Non-hub | IL4RA_HUMAN | 1IAR | B | A |
| Non-hub | IL6RA_HUMAN | 1P9M | B | A |
| Non-hub | KU70_HUMAN  | 1JEQ | B | A |
| Non-hub | MD1L1_HUMAN | 1GO4 | A | G |
| Non-hub | MDM2_HUMAN  | 2VJE | C | D |
| Non-hub | MGN_HUMAN   | 1P27 | A | B |
| Non-hub | ODBA_HUMAN  | 1DTW | A | B |
| Non-hub | ODPA_HUMAN  | 1NI4 | A | B |
| Non-hub | PM14_HUMAN  | 2F9D | A | P |
| Non-hub | PPIH_HUMAN  | 1MZW | A | B |
| Non-hub | PRLR_HUMAN  | 1BP3 | B | A |
| Non-hub | RINI_HUMAN  | 1Z7X | W | X |
| Non-hub | RPB4_HUMAN  | 2C35 | B | A |
| Non-hub | RU2A_HUMAN  | 1A9N | A | B |
| Non-hub | SENP2_HUMAN | 2IO1 | A | B |
| Non-hub | TAF11_HUMAN | 1BH8 | A | B |
| Non-hub | TAF12_HUMAN | 1H3O | B | A |
| Non-hub | TIM10_HUMAN | 2BSK | B | A |