**Supplementary Table 1: Types of interactions between pairs of mutated proteins in RASopathy interactome.** The data in the table presents detailed explanation of the Figure 4. The table includes interactions with known directions of action.

|  |  |
| --- | --- |
| **Gene/protein name** | **Type of interaction with protein** |
| **Upregulates** | **Downregulates** | **Controls expression of** |
| **NF1** | HRAS | - | - |
| **PTPN11** | HRAS | NF1 | HRAS (post-translational modifications, catalysis) |
| KRAS | SOS1 | KRAS (post-translational modifications, catalysis) |
| MAP2K1 | - | NRAS (post-translational modifications, catalysis) |
| MAP2K2 | - | NF1 (expression) |
| NRAS | - | SPRED1 (post-translational modifications) |
| **RAF1** | MAP2K1 | - | MAP2K1 (reaction, catalysis, post-translational modifications) |
| MAP2K2 | - | MAP2K2 (reaction, catalysis) |
| - | - | HRAS (reaction, catalysis) |
| - | - | KRAS (reaction, catalysis) |
| - | - | NRAS (reaction, catalysis) |
| - | - | RIT1 (reaction, catalysis) |
| **BRAF** | MAP2K1 | - | MAP2K1 (reaction, catalysis) |
| MAP2K2 | - | MAP2K2 (reaction, catalysis) |
| - | - | HRAS (reaction, catalysis) |
| - | - | KRAS (reaction, catalysis) |
| - | - | NRAS (reaction, catalysis) |
| - | - | RIT1 (reaction, catalysis) |
| **SOS1** | HRAS | - | HRAS (reaction, catalysis) |
| KRAS | - | KRAS (reaction, catalysis) |
| MAP2K1 | - | NRAS (reaction, catalysis) |
| MAP2K2 | - | RIT1 (reaction, catalysis) |
| NRAS | - | - |
| **KRAS** | - | - | BRAF (reaction, catalysis) |
| - | - | HRAS (reaction, catalysis) |
| - | - | MAP2K1 (reaction, catalysis) |
| - | - | MAP2K2 (reaction, catalysis) |
| - | - | NRAS (reaction, catalysis) |
| - | - | RAF1 (reaction, catalysis) |
| - | - | SOS1 (reaction) |
| **NRAS** | BRAF | - | BRAF (reaction, catalysis) |
| RAF1 | - | RAF1 (reaction, catalysis) |
| - | - | HRAS (reaction, catalysis) |
| - | - | KRAS (reaction, catalysis) |
| - | - | MAP2K1 (reaction, catalysis) |
| - | - | MAP2K2 (reaction, catalysis) |
| - | - | SOS1 (reaction) |
| **HRAS** | BRAF | - | BRAF (reaction, catalysis) |
| RAF1 | - | RAF1 (reaction, catalysis) |
| - | - | KRAS (reaction, catalysis) |
| - | - | MAP2K1 (reaction, catalysis) |
| - | - | MAP2K2 (reaction, catalysis) |
| - | - | NRAS (reaction, catalysis) |
| - | - | SOS1 (reaction) |
| **MAP2K2** | - | - |  BRAF (reaction, catalysis) |
| - | - | HRAS (reaction, catalysis) |
| - | - | KRAS (reaction, catalysis) |
| - | - | MAP2K1 (reaction, catalysis) |
| - | - | NRAS (reaction, catalysis) |
| - | - | RAF1 (reaction, catalysis) |
| - | - | RIT1 (reaction, catalysis) |
| **MAP2K1** | - | - | BRAF (reaction, catalysis) |
| - | - | HRAS (reaction, catalysis) |
| - | - | KRAS (reaction, catalysis) |
| - | - | MAP2K2 (reaction, catalysis) |
| - | - | NRAS (reaction, catalysis) |
| - | - | RAF1 (reaction, catalysis) |
| - | - | RIT1 (reaction, catalysis) |
| **RIT1** | BRAF | - | BRAF (reaction, catalysis) |
| - | - | MAP2K1 (reaction, catalysis) |
| - | - | MAP2K2 (reaction, catalysis) |
| - | - | RAF1 (reaction, catalysis) |
| - | - | SOS1 (reaction) |