**Supplementary file 1A: Comparison of the 5PPase domain of human Synj1 (Synj1528-873) with the corresponding 5PPase domain of the other human inositol polyphosphate 5-phosphatases and SPSynj.** The root-mean-square deviation (rmsd) after superposition of the structures was determined using CCP4 SUPERPOSE. Furthermore, the sequence identity was determined using Clustal Omega.

|  |  |  |  |
| --- | --- | --- | --- |
| **5PPase domain of** | **PDB code** | **Rmsd** | **Sequence identity** |
| **INPP5B** | 3N9V | 1.15 Å(for 273 superposed residues) | 39.60% |
| **SHIP2** | 3NR8 | 1.24 Å(for 269 superposed residues) | 29.24% |
| **OCRL** | 4CMN | 1.22 Å(for 283 superposed residues) | 38.26% |
| **INPP5E or Pharbin** | 2XSW | 1.35 Å(for 276 superposed residues) | 34.36% |
| **SPSynj** | 1I9Y | 1.20 Å (for 281 superposed residues) | 41.95% |
| **SHIP1** | / | / | 31.56 |
| **Synj2** | / | / | 63.01% |
| **INPP5J or PIPP** | / | / | 23.15% |
| **SKIP** | / | / | 29.94% |
| **INPP5A** | / | / | 21.48% |

**Supplementary file 1B: Residues interacting with the diC8-PI(3,4,5)P3 substrate in Synj1528-873 and the corresponding residues in the other nine human 5PPases and SPSynj.** Completely conserved residues are written in white with a red background and similar residues are written in red.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Synj1** | **Synj2** | **SPSynj** | **INPP5B** | **OCRL** | **SHIP1** | **SHIP2** | **INPP5A** | **INPP5E** | **INPP5J** | **SKIP** |
| **1P interacting residues** | N668**K669** | N664**K665** | N678**K679** | N379**K380** | N354**K355** | N519**K520** | N540**K541** | R162**K163** | T403**K404** | N540**K541** | N128**K129** |
| **4P interacting residues** | K798R800Y784 | K794R796Y780 | K808R810Y794 | K516R518Y502 | K491R493Y477 | K665N667Y644 | R682N684Y661 | N340R342Y326 | K548R550Y534 | K673R675F659 | K261R263Y247 |
| **5P interacting residues** | **H689****R734****H859** | **H685****R730****H855** | **H699****R744****H839** | **H400****R451****H549** | **H375****R426****H524** | **H540****R591****H701** | **H561****R611****H718** | **H183****R235****H384** | **H424****R481****H584** | **H561****R608****H722** | **H149****R196****H311** |
| **Residues involved in nucleophilic attack** | **D730****N732** | **D726****N728** | **D740****N742** | **D447****N449** | **D422****N424** | **D587****N589** | **D607****N609** | **D231****N233** | **D477****N479** | **D604****N606** | **D192****N194** |
| **Mg2+-coordinating****residues** | N543**E591** | N540**E587** | N568**E597** | N275**E303** | N250**E278** | G414**E453** | G434**E473** | G19**E54** | Q309**E340** | G434**E466** | A24**E54** |