Table S1 – Biotin-PIF binds the G12 fraction in mouse embryo extracts

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Description** | **Accession** | **Coverage** | **# Peptides** | **# AAs** | **MW [kDa]** | **calc. pI** | **Score** |
| HBS1-iso 3 | IPI:IPI00275176.3 | 3.10 | 14 | 612 | 67.5 | 5.64 | 7.32 |
| HBS1-iso2 | IPI:IPI00464282.4 | 2.84 | 11 | 599 | 65.2 | 8.34 | 7.32 |
| PRDX4 | IPI:IPI00108426.2 | 16.96 | 10 | 112 | 12.7 | 10.27 | 7.00 |
| DENN/MADD domain 5B | IPI:IPI00889876.2 | 0.67 | 3 | 1042 | 118.7 | 6.55 | 4.97 |
| Actin-related protein 6 | IPI:IPI00110922.2 | 3.28 | 4 | 396 | 45.8 | 5.03 | 4.77 |
| Iso1 Activating signal coin1 | IPI:IPI00135240.1 | 4.48 | 27 | 581 | 66.2 | 7.55 | 4.73 |
| Iso 2 Centlein | IPI:IPI00621351.1 | 2.20 | 3 | 318 | 35.7 | 8.48 | 4.52 |
| Cytochrome P450 26A1 | IPI:IPI00115829.1 | 1.41 | 3 | 497 | 56.1 | 8.60 | 4.49 |
| scleraxis | IPI:IPI00381245.2 | 5.80 | 3 | 207 | 22.2 | 10.14 | 3.71 |
| dynein, axon, heavy11 | IPI:IPI00622122.5 | 0.80 | 9 | 4488 | 516.0 | 6.16 | 1.72 |
| Iso 1 of Nischarin | IPI:IPI00110435.2 | 1.51 | 12 | 1593 | 174.9 | 5.16 | 1.61 |
| RAB12 | IPI:IPI00169699.4 | 2.41 | 1 | 291 | 32.2 | 8.84 | 1.61 |
| Iso1Phostensin | IPI:IPI00607928.1 | 3.03 | 4 | 594 | 65.6 | 5.39 | 1.54 |
| DDB1/ CuL4- factor 6 | IPI:IPI00120084.1 | 2.40 | 3 | 876 | 97.5 | 5.22 | 0.00 |
| Cadherin EGF LAG 7-GR 1 | IPI:IPI00127701.1 | 0.73 | 3 | 3034 | 330.3 | 5.91 | 0.00 |
| Iso 2Glutamate decarbo- 1 | IPI:IPI00316617.8 | 4.37 | 4 | 526 | 59.8 | 7.25 | 0.00 |
| Gm10414 | IPI:IPI00654290.1 | 6.11 | 1 | 131 | 14.0 | 10.62 | 0.00 |
| collagen,XXII, a 1 | IPI:IPI00944073.1 | 1.61 | 6 | 1613 | 159.8 | 7.21 | 0.00 |

Table S2 Biotin-PIF binds the B9 fraction in mouse embryo extracts.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Description** | **Accession** | **Coverage** | **# Peptides** | **# AAs** | **MW [kDa]** | **calc. pI** | **Score** |
| Hb Y embryonic | IPI:IPI00133148.2 | 30.61 | 10 | 147 | 16.1 | 8.19 | 75.19 |
| 14-3-3 protein gamma | IPI:IPI00230707.6 | 17.41 | 14 | 247 | 28.3 | 4.89 | 104.91 |
| 14-3-3 protein sigma | IPI:IPI00118286.1 | 13.31 | 9 | 248 | 27.7 | 4.83 | 62.26 |
| 78 kDa glucose-regulated protein | IPI:IPI00319992.1 | 14.81 | 15 | 655 | 72.4 | 5.16 | 78.17 |
| Actin, alpha skeletal muscle | IPI:IPI00110827.1 | 19.10 | 41 | 377 | 42.0 | 5.39 | 261.66 |
| ADP-ribosylation factor 1 | IPI:IPI00221613.5 | 27.62 | 12 | 181 | 20.7 | 6.80 | 61.57 |
| Alpha-actinin-1 | IPI:IPI00380436.1 | 7.51 | 10 | 892 | 103.0 | 5.38 | 58.37 |
| Annexin A2 | IPI:IPI00468203.3 | 15.63 | 11 | 339 | 38.7 | 7.69 | 63.68 |
| ATP synthase subunit beta, mitochondrial | IPI:IPI00468481.2 | 27.03 | 33 | 529 | 56.3 | 5.34 | 167.15 |
| Beta-actin-like protein 2 | IPI:IPI00221528.1 | 11.97 | 19 | 376 | 42.0 | 5.49 | 131.32 |
| Cholesterol side-chain cleavage enzyme, mitochondrial | IPI:IPI00136928.3 | 12.74 | 10 | 526 | 60.3 | 9.39 | 56.56 |
| Cytoskeleton-associated protein 4 | IPI:IPI00223047.2 | 14.96 | 13 | 575 | 63.7 | 5.64 | 89.56 |
| D-3-phosphoglycerate dehydrogenase | IPI:IPI00225961.5 | 11.63 | 9 | 533 | 56.5 | 6.54 | 46.88 |
| Dolichyl-diphosphooligosaccharide-glycosyltransferase 1 | IPI:IPI00309035.2 | 13.82 | 13 | 608 | 68.5 | 6.46 | 83.05 |
| Elongation factor 1-alpha 1 | IPI:IPI00307837.6 | 10.82 | 11 | 462 | 50.1 | 9.01 | 55.06 |
| Elongation factor 2 | IPI:IPI00466069.3 | 6.76 | 12 | 858 | 95.3 | 6.83 | 101.49 |
| Endoplasmin | IPI:IPI00129526.1 | 8.10 | 15 | 802 | 92.4 | 4.82 | 85.31 |
| Eukaryotic initiation factor 4A-I | IPI:IPI00118676.3 | 19.21 | 19 | 406 | 46.1 | 5.48 | 108.38 |
| Glucose-6-phosphate isomerase | IPI:IPI00669556.2 | 12.50 | 11 | 344 | 38.3 | 8.48 | 60.58 |
| Heat shock cognate 71 kDa protein | IPI:IPI00323357.3 | 27.24 | 38 | 646 | 70.8 | 5.52 | 191.68 |
| Heat shock protein HSP 90-alpha | IPI:IPI00330804.4 | 23.74 | 57 | 733 | 84.7 | 5.01 | 335.51 |
| Inositol-3-phosphate synthase 1 | IPI:IPI00119886.1 | 6.10 | 12 | 557 | 60.9 | 6.42 | 59.49 |
| Isoform 1 of 60 kDa heat shock protein, mitochondrial | IPI:IPI00308885.6 | 10.12 | 12 | 573 | 60.9 | 6.18 | 63.27 |
| IsoL Complement C3 (Fragment) | IPI:IPI00323624.3 | 11.00 | 26 | 1663 | 186.4 | 6.81 | 215.82 |
| L-lactate dehydrogenase A chain | IPI:IPI00319994.6 | 17.47 | 9 | 332 | 36.5 | 7.74 | 143.66 |
| Myosin-9 | IPI:IPI00123181.4 | 11.43 | 29 | 1960 | 226.2 | 5.66 | 200.11 |
| Nicotinamide Pribosyltransferase | IPI:IPI00320188.5 | 14.66 | 9 | 491 | 55.4 | 7.15 | 50.16 |
| Perilipin-3 | IPI:IPI00319270.2 | 19.91 | 13 | 437 | 47.2 | 5.62 | 60.60 |
| Plastin-2 | IPI:IPI00118892.6 | 18.82 | 29 | 627 | 70.1 | 5.33 | 175.17 |
| Profilin actin binder | IPI:IPI00650039.1 | 39.29 | 10 | 112 | 11.8 | 4.88 | 46.89 |
| Putative uncharacterized protein | IPI:IPI00473320.2 | 17.65 | 41 | 374 | 41.8 | 6.30 | 264.45 |
| Atp5a1 | IPI:IPI00857439.1 | 16.50 | 11 | 503 | 54.6 | 8.24 | 78.49 |
| Ribonucleoside-diP reductase M2 | IPI:IPI00112645.1 | 16.67 | 10 | 390 | 45.1 | 5.45 | 48.67 |
| Serine protease inhibitor A3K | IPI:IPI00131830.1 | 16.51 | 14 | 418 | 46.8 | 5.16 | 74.91 |
| similar to Eef 4AI isoform 1 | IPI:IPI00462110.2 | 10.90 | 10 | 376 | 42.7 | 5.29 | 62.50 |
| similar (GAPDH) 3isoform 2 | IPI:IPI00850243.1 | 13.89 | 10 | 288 | 30.8 | 7.75 | 53.84 |
| T-complex protein 1 subunit beta | IPI:IPI00320217.9 | 17.20 | 15 | 535 | 57.4 | 6.40 | 80.58 |
| Tubulin alpha-1C chain | IPI:IPI00403810.2 | 12.92 | 11 | 449 | 49.9 | 5.10 | 89.40 |
| Tubulin beta-2A chain | IPI:IPI00338039.1 | 24.27 | 25 | 445 | 49.9 | 4.89 | 145.11 |
| Tubulin beta-2C chain | IPI:IPI00169463.1 | 28.99 | 27 | 445 | 49.8 | 4.89 | 163.10 |
| Tubulin beta-4 chain | IPI:IPI00109073.5 | 19.59 | 17 | 444 | 49.6 | 4.88 | 106.20 |
| Tubulin beta-5 chain | IPI:IPI00117352.1 | 28.60 | 34 | 444 | 49.6 | 4.89 | 183.97 |
| Tubulin beta-6 chain | IPI:IPI00122928.1 | 15.88 | 16 | 447 | 50.1 | 4.89 | 115.88 |
| Ubiquitin-like modr-activ enzyme 1 | IPI:IPI00123313.1 | 13.99 | 25 | 1058 | 117.7 | 5.66 | 128.44 |
| UDP-gluc:glycoprot glucosyltrans 1 | IPI:IPI00762897.2 | 6.51 | 12 | 1551 | 176.3 | 5.64 | 83.77 |
| Vincµlin | IPI:IPI00405227.3 | 5.63 | 11 | 1066 | 116.6 | 6.00 | 51.27 |
| Xaa-Pro aminopeptidase 1 | IPI:IPI00875027.1 | 12.04 | 17 | 623 | 69.5 | 5.54 | 80.68 |

Table S3 – Biotin-PIF binds the A9 fraction in mouse embryo extracts

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Description** | **Accession** | **Coverage** | **# Peptides** | **# AAs** | **MW [kDa]** | **calc. pI** | **Score** |
| Putative unchar. prot | IPI:IPI00229224.1 | 10.09 | 5 | 109 | 12.5 | 6.52 | 20.22 |
| Tubulin beta-5 chain | IPI:IPI00117352.1 | 2.70 | 3 | 444 | 49.6 | 4.89 | 12.35 |
| Integrin beta-3 | IPI:IPI00266264.1 | 1.91 | 3 | 787 | 86.6 | 5.27 | 11.00 |
| Liver carboxylesterase N | IPI:IPI00138342.3 | 2.17 | 2 | 554 | 61.1 | 5.21 | 9.04 |
| Polyphosphoinositide phospha | IPI:IPI00128101.1 | 1.32 | 1 | 907 | 103.4 | 6.98 | 8.86 |
| IsoLComplement C3 | IPI:IPI00323624.3 | 0.72 | 2 | 1663 | 186.4 | 6.81 | 7.94 |
| Vinculin | IPI:IPI00405227.3 | 1.41 | 2 | 1066 | 116.6 | 6.00 | 7.14 |
| Eef1a1 | IPI:IPI00831184.1 | 5.91 | 2 | 186 | 20.7 | 8.59 | 7.09 |
| Iso-non-muscle myosin alkali L | IPI:IPI00850361.1 | 4.31 | 1 | 116 | 13.0 | 4.65 | 5.77 |
| Putative uncharac protein | IPI:IPI00229080.7 | 1.52 | 3 | 724 | 83.2 | 5.03 | 3.55 |
| Isoform 2 of Myosin-11 | IPI:IPI00227865.1 | 0.77 | 1 | 1938 | 223.1 | 5.47 | 3.06 |

Table S4 (additional proteins identified from Table 4)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **MISCELLANEOUS** |  |  | First | Second |
| Prothymosin alpha | IPI00224784 | 12 kDa | 5 | 4 |
| Calmodulin | IPI00467841 (+1) | 22 kDa | 2 | 5 |
| **Elongation factor 1-alpha 1** | **IPI00307837** | **50 kDa** | **1** | **3** |
| Iso1Plasminogen activator inhibitor 1 RNA-bind | IPI00471475 (+3) | 45 kDa | 2 | 3 |
| Nuclease-sensitive element-BP 1 | IPI00120886 (+1) | 36 kDa | 4 | 3 |
| **Nucleolin** | **IPI00317794** | **77 kDa** | **2** | **5** |
| Granzyme F | IPI00137496 | 28 kDa | 2 | 3 |
| **Endoplasmin** | **IPI00129526** | **92 kDa** | **5** | **10** |
| Desmin | IPI00130102 | 53 kDa | 1 | 3 |
| Isoform 1 of Filamin-A | IPI00131138 (+2) | 281 kDa | 0 | 3 |
| Proteasome subunit alpha type-7 | IPI00131406 | 28 kDa | 1 | 4 |
| Isoform 1 of Glucosidase 2 subunit beta | IPI00115680 (+1) | 59 kDa | 1 | 3 |
| Alpha-2-macroglobulin-P | IPI00454052 | 164 kDa | 0 | 1 |
| Glyceraldehyde-3-phosphate dehydrogenase | IPI00271869 (+11) | 36 kDa | 0 | 3 |
| ATP synthase subunit beta, mitochondrial | IPI00468481 | 56 kDa | 0 | 3 |
| **Serum albumin** | **IPI00131695** | **69 kDa** | **8** | **14** |
| Hemoglobin subunit beta | IPI00762198 (+1) | 16 kDa | 2 | 4 |
| Hemoglobin subunit alpha | IPI00469114 (+1) | 15 kDa | 1 | 2 |
| 60S ribosomal protein L7a | IPI00330363 (+5) | 30 kDa | 4 | 4 |
| 60S ribosomal protein L6 | IPI00313222 (+1) | 34 kDa | 0 | 3 |
| 40S ribosomal protein S25 | IPI00137735 | 14 kDa | 2 | 3 |
| 40S ribosomal protein S3 | IPI00134599 | 27 kDa | 1 | 4 |
| **40S ribosomal protein S3a** | **IPI00331345 (+2)** | **30 kDa** | **1** | **3** |
| 40S ribosomal protein S10 | IPI00112448 | 19 kDa | 0 | 3 |

**Table S5. PepSite 2 prediction of PIF residues participating in targets binding site**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **PIF targets, binding score and probability** | | | **PIF1-10 residues and target residues positions** | | | | | | | | | |
| **PDI** | **SCORE** | **P-Value** | **M** | **V** | **R** | **I** | **K** | **P** | **G** | **S** | **A** | **N** |
| 4GSE | 80.10 | 0.003 | met-1::123 |  | arg-3::15 | ile-4::100 |  | pro-6::143 |  |  | ala-9::1 | asn-10::23 |
| 4GSF | 76.90 | 0.005 | met-1::122 | val-2::230 |  | ile-4::91 | lys-5::116 | pro-6::142 |  | ser-8::171 |  |  |
| 4GS8 | 76.70 | 0.005 | met-1::129 |  |  | ile-4::91 | lys-5::116 | pro-6::142 |  |  | ala-9::2 | asn-10::30 |
| 4DTT | 73.70 | 0.009 |  | val-2::225 | arg-3::16 | ile-4::99 |  | pro-6::145 |  |  | ala-9::5 | asn-10::26 |
| 3QZ2 | 73.20 | 0.010 | met-1::129 |  | arg-3::12 |  | lys-5::111 | pro-6::144 |  | ser-8::171 |  | asn-10::30 |
| 3E4A | 72.70 | 0.010 | met-1::130 |  | arg-3::15 | ile-4::97 | lys-5::111 | pro-6::141 |  |  | ala-9::10 |  |
| 3N57 | 72.50 | 0.011 | met-1::128 |  | arg-3::15 | ile-4::100 | lys-5::112 | pro-6::143 |  |  |  | asn-10::27 |
| 3OFI | 72.20 | 0.011 | met-1::123 | val-2::224 | arg-3::20 |  | lys-5::111 |  |  |  | ala-9::1 | asn-10::27 |
| 3CWW | 72.00 | 0.012 |  | val-2::221 | arg-3::13 | ile-4::92 |  |  |  | ser-8::175 | ala-9::1 | asn-10::26 |
| 4DWK | 71.50 | 0.013 | met-1::129 |  | arg-3::16 | ile-4::91 | lys-5::111 |  |  |  | ala-9::2 | asn-10::27 |
| 4GSC | 71.30 | 0.013 | met-1::126 |  | arg-3::11 |  | lys-5::120 | pro-6::142 | gly-7::77 | ser-8::174 |  |  |
| 4IOF | 70.80 | 0.014 |  |  | arg-3::15 |  | lys-5::111 | pro-6::141 | gly-7::76 | ser-8::178 | ala-9::10 |  |
| 2YUQ | 68.90 | 0.019 | met-1::126 | val-2::221 | arg-3::11 | ile-4::99 |  | pro-6::142 |  | ser-8::174 |  |  |
| 2JG4 | 68.90 | 0.020 | met-1::121 | val-2::223 | arg-3::13 |  | lys-5::117 |  |  |  | ala-9::8 | asn-10::25 |
| 2JG4 | 68.90 | 0.020 | met-1::121 | val-2::223 | arg-3::13 |  | lys-5::117 |  |  |  | ala-9::8 | asn-10::25 |
| 3QGW | 68.60 | 0.020 |  |  | arg-3::16 |  |  | pro-6::142 | gly-7::76 | ser-8::174 | ala-9::1 | asn-10::24 |
| 3N56 | 68.40 | 0.021 | met-1::124 |  | arg-3::17 | ile-4::99 |  |  |  | ser-8::173 | ala-9::5 | asn-10::25 |
| 2YPU | 68.00 | 0.022 | met-1::124 | val-2::229 | arg-3::12 |  | lys-5::112 |  |  | ser-8::175 | ala-9::4 |  |
| 1QRQ | 67.80 | 0.023 |  |  | arg-3::14 | ile-4::98 | lys-5::120 | pro-6::150 |  |  |  |  |
| 3HGZ | 62.60 | 0.054 | met-1::125 | val-2::222 | arg-3::15 | ile-4::93 | lys-5::117 |  |  |  |  | asn-10::30 |
| 3V5J | 59.90 | 0.083 | met-1::124 | val-2::223 |  | ile-4::91 | lys-5::111 | pro-6::142 | gly-7::80 |  |  |  |
| 3MJ2 | 59.80 | 0.084 | met-1::128 | val-2::224 | arg-3::12 | ile-4::91 | lys-5::111 | pro-6::141 |  |  |  |  |
| 2LMJ | 59.50 | 0.089 |  |  | arg-3::19 |  | lys-5::119 | pro-6::145 | gly-7::74 | ser-8::173 | ala-9::6 |  |
| 4B8Z | 58.90 | 0.096 | met-1::125 | val-2::228 | arg-3::14 |  |  |  |  |  | ala-9::9 | asn-10::26 |
| 3V8W | 58.50 | 0.102 |  |  | arg-3::11 | ile-4::95 | lys-5::113 | pro-6::142 |  |  | ala-9::10 | asn-10::22 |
| 3MJ1 | 57.70 | 0.115 | met-1::123 |  | arg-3::16 | ile-4::91 | lys-5::113 | pro-6::141 | gly-7::75 |  |  |  |
| 2G54 | 55.00 | 0.170 |  |  | arg-3::18 | ile-4::95 | lys-5::114 | pro-6::141 |  |  | ala-9::10 |  |
| 4HQU | 54.80 | 0.174 | met-1::128 |  | arg-3::18 |  |  | pro-6::144 |  | ser-8::180 | ala-9::3 | asn-10::27 |
| 4HQX | 54.70 | 0.176 | met-1::125 | val-2::226 | arg-3::11 | ile-4::95 | lys-5::111 | pro-6::146 |  |  |  |  |
| 2G49 | 54.60 | 0.179 |  | val-2::224 |  | ile-4::92 | lys-5::118 | pro-6::146 |  | ser-8::179 |  |  |
| 3QGY | 53.90 | 0.197 |  |  | arg-3::12 | ile-4::92 | lys-5::112 | pro-6::148 |  | ser-8::176 | ala-9::10 |  |
| 3V8T | 53.40 | 0.200 |  |  | arg-3::18 | ile-4::96 | lys-5::111 | pro-6::145 | gly-7::74 |  |  | asn-10::24 |
| 2E6I | 53.50 | 0.206 |  | val-2::230 | arg-3::15 | ile-4::93 | lys-5::118 | pro-6::141 |  |  |  |  |
| 3V5L | 53.40 | 0.209 | met-1::124 | val-2::221 | arg-3::15 | ile-4::91 |  | pro-6::145 |  |  |  |  |
| 1PDG | 52.60 | 0.230 | met-1::121 |  | arg-3::15 | ile-4::91 | lys-5::114 | pro-6::147 |  |  |  |  |
| 1PDG | 52.60 | 0.230 | met-1::121 |  | arg-3::15 | ile-4::91 | lys-5::114 | pro-6::147 |  |  |  |  |
| 4B8W | 51.40 | 0.241 | met-1::122 | val-2::225 | arg-3::19 |  |  |  |  |  | ala-9::1 | asn-10::22 |
| 2WBY | 51.90 | 0.250 | met-1::123 |  |  |  | lys-5::112 | pro-6::141 | gly-7::72 |  |  |  |
| 4KIO | 51.80 | 0.250 | met-1::121 | val-2::222 | arg-3::16 | ile-4::95 |  | pro-6::143 |  |  |  |  |
| 2WBY | 51.90 | 0.250 | met-1::123 |  |  |  | lys-5::112 | pro-6::141 | gly-7::72 |  |  |  |
| 3MJG | 50.90 | 0.251 | met-1::122 |  | arg-3::15 | ile-4::94 | lys-5::112 | pro-6::142 |  |  |  |  |
| 2G48 | 50.60 | 0.260 |  | val-2::230 |  |  |  |  | gly-7::77 | ser-8::180 | ala-9::3 | asn-10::22 |
| 1SNX | 46.90 | 0.357 |  |  |  | ile-4::97 | lys-5::115 | pro-6::149 | gly-7::72 | ser-8::171 |  |  |
| 2G47 | 45.10 | 0.412 | met-1::123 |  |  |  |  | pro-6::141 |  | ser-8::172 | ala-9::2 |  |
| 2WK3 | 45.00 | 0.415 |  |  |  | ile-4::91 |  | pro-6::146 | gly-7::75 |  | ala-9::4 |  |
| 3MIY | 44.70 | 0.423 | met-1::121 | val-2::228 | arg-3::15 | ile-4::91 | lys-5::111 |  |  |  |  |  |
| 4HCV | 44.60 | 0.429 |  |  | arg-3::12 | ile-4::95 | lys-5::112 | pro-6::146 |  |  | ala-9::5 |  |
| 2WC0 | 44.10 | 0.445 |  |  |  |  | lys-5::120 |  |  | ser-8::171 | ala-9::3 | asn-10::23 |
| 3H44 | 43.60 | 0.460 | met-1::126 |  |  | ile-4::99 | lys-5::111 | pro-6::150 |  |  |  |  |
| 3E4Z | 40.90 | 0.560 | met-1::121 | val-2::221 |  |  |  |  |  |  | ala-9::1 | asn-10::26 |
| 2G56 | 40.80 | 0.562 | met-1::122 |  |  |  |  | pro-6::142 |  | ser-8::180 | ala-9::5 |  |
| 2JBU | 40.10 | 0.588 | met-1::128 |  |  | ile-4::99 | lys-5::112 | pro-6::148 |  |  |  |  |
| 4HCU | 39.40 | 0.615 | met-1::121 |  | arg-3::20 | ile-4::100 | lys-5::116 |  | gly-7::79 |  |  |  |
| 1SNU | 39.00 | 0.632 | met-1::124 |  |  | ile-4::97 |  | pro-6::141 | gly-7::71 |  |  |  |
| 4E5Y | 38.50 | 0.650 |  |  | arg-3::11 | ile-4::95 |  |  | gly-7::75 | ser-8::172 |  |  |
| 4HCT | 37.20 | 0.699 | met-1::122 |  |  | ile-4::96 | lys-5::112 | pro-6::143 |  |  |  |  |
| 4BKP | 35.20 | 0.772 |  |  |  | ile-4::94 |  | pro-6::141 | gly-7::79 |  |  |  |
| 1SM2 | 35.10 | 0.775 |  |  |  | ile-4::95 |  | pro-6::149 | gly-7::73 | ser-8::175 |  |  |
| 3T9T | 34.30 | 0.803 | met-1::123 |  | arg-3::12 |  |  |  |  |  | ala-9::1 | asn-10::25 |
| 2CRE | 28.10 | 0.954 | met-1::127 |  | arg-3::11 | ile-4::91 | lys-5::116 |  |  |  |  |  |

**Table S6. BeATMuSiC server predicted *in silico* mutagens disrupting the interface of the PIF docking models with several targets**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **PIF target** | **PDI** | **Highest ∆E [kcal/mol]** | **PIF1-15 residues and target residues positions** | | | | | | | | | | | | | | |
|  |  |  | **M** | **V** | **R** | **I** | **K** | **P** | **G** | **S** | **A** | **N** | **K** | **P** | **S** | **D** | **D** |
| oxidized PDI, chain A | 4EL1:A | **2.57** |  | **E** |  |  |  | **E** |  |  |  |  |  | **G** |  |  |  |
| oxidized PDI, chain B | 4EL1:B | **3.65** |  |  |  | **G** |  | **G** |  |  |  |  |  |  |  |  |  |
|  |  |  | **D** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **E** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **S** |  |  |  |  |  |  |  |  |  |  |  |
| reduced PDI | 4EKZ | **3.00** |  | **E** |  | **P** |  | **E** |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  | **D** |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  | **S** |  |  |  |  |  |  |  |  |  |
| Potassium Channel Kv Beta-subunit (KCNAB2) | 1ZSX | **3.21** | **A** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **G** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Voltage-dependent K+ channel β-subunit | 1QRQ:A | **4.30** |  |  |  | **G** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **E** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **S** |  |  |  |  |  |  |  |  |  |  |  |
| Voltage-dependent K+ channel β-subunit | 1QRQ:B | **2.99** | **A** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **S** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **G** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Voltage-dependent K+ channel β-subunit | 1QRQ:C | **3.28** |  | **E** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Voltage-dependent K+ channel β-subunit | 1QRQ:D | **2.36** |  |  |  |  |  | **A** |  |  |  | **P** |  |  |  |  |  |
|  |  |  |  |  | **E** |  |  |  | **G** |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  | **E** |  |  |  |  |  |
| Substrate free IDE – closed conformation | 2JG4:A | **3.03** |  |  |  | **G** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **D** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **E** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **A** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **S** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **K** |  |  |  |  |  |  |  |  |  |  |  |
| Substrate free IDE – closed conformation | 2JG4:B | **2.04** |  |  |  |  | **G** |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  | **D** |  |  |  |  |  |  |  |  |  |  |
| IDE bound to Insulin | 2WBY:A | **3.78** |  |  |  | **G** | **A** |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **G** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **E** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **D** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **S** |  |  |  |  |  |  |  |  |  |  |  |

**Table S7. PIF mutant models**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **PIF target** | **PDB** | **PIF mutated** | **Mutated Full Sequence** | **Mutation ID** |
| red PDI | 4EKZ | P6 ->E6 | MVRIKEGSANKPSDD | mut1 |
| red PDI | 4EKZ | I4 ->P4 | MVRPKPGSANKPSDD | mut2 |
| oxid PID, chain A | 4EL1:A | I4 -> G4 | MVRGKPGSANKPSDD | mut3 |
| oxid PID, chain B | 4EL1:B | V2 -> E2 | MERIKPGSANKPSDD | mut4 |