

**Table S1. Details of the genomes used in this study.**

| <b>Species</b>                       | <b>Phyla</b> | <b>Website/source</b>                                                                                                                                                 |
|--------------------------------------|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Amphimedon queenslandica</i>      | Porifera     | <a href="http://metazoa.ensembl.org/Amphimedon_queenslandica/Info/Index">http://metazoa.ensembl.org/Amphimedon_queenslandica/Info/Index</a>                           |
| <i>Xestospongia bergquistia</i>      | Porifera     | Data available from the authors on request                                                                                                                            |
| <i>Tethya wilhelma</i>               | Porifera     | <a href="http://tethya.spongebase.net/">http://tethya.spongebase.net/</a>                                                                                             |
| <i>Ephydatia muelleri</i>            | Porifera     | <a href="https://spaces.facsci.ualberta.ca/ephybase/">https://spaces.facsci.ualberta.ca/ephybase/</a>                                                                 |
| <i>Oscarella carmela</i>             | Porifera     | <a href="http://compagen.unit.oist.jp/index.html">http://compagen.unit.oist.jp/index.html</a>                                                                         |
| <i>Sycon ciliatum</i>                | Porifera     | <a href="http://compagen.unit.oist.jp/index.html">http://compagen.unit.oist.jp/index.html</a>                                                                         |
| <i>Mnemiopsis leidyi</i>             | Ctenophora   | <a href="https://research.nhgri.nih.gov/mnemiopsis/">https://research.nhgri.nih.gov/mnemiopsis/</a>                                                                   |
| <i>Nematostella vectensis</i>        | Cnidaria     | <a href="https://www.ebi.ac.uk/ena/browser/view/GCA_000209225.1?show=blobtoolkit">https://www.ebi.ac.uk/ena/browser/view/GCA_000209225.1?show=blobtoolkit</a>         |
| <i>Acanthaster planci</i>            | Echinoderm   | <a href="https://marinegenomics.oist.jp/cots/viewer/info?project_id=46">https://marinegenomics.oist.jp/cots/viewer/info?project_id=46</a>                             |
| <i>Strongylocentrotus purpuratus</i> | Echinoderm   | <a href="https://www.ebi.ac.uk/ena/browser/view/GCA_000002235.4?show=blobtoolkit">https://www.ebi.ac.uk/ena/browser/view/GCA_000002235.4?show=blobtoolkit</a>         |
| <i>Branchiostoma floridae</i>        | Chordata     | <a href="https://mycocosm.jgi.doe.gov/Brafl1/Brafl1.home.html">https://mycocosm.jgi.doe.gov/Brafl1/Brafl1.home.html</a>                                               |
| <i>Ciona intestinalis</i>            | Chordata     | <a href="https://www.ebi.ac.uk/ena/browser/view/GCA_000224145.1">https://www.ebi.ac.uk/ena/browser/view/GCA_000224145.1</a>                                           |
| <i>Capitella teleta</i>              | Annelida     | <a href="https://www.ebi.ac.uk/ena/browser/view/GCA_000328365.1?show=blobtoolkit">https://www.ebi.ac.uk/ena/browser/view/GCA_000328365.1?show=blobtoolkit</a>         |
| <i>Lingula anatina</i>               | Brachipoda   | <a href="https://www.ebi.ac.uk/ena/browser/view/GCA_001039355.1">https://www.ebi.ac.uk/ena/browser/view/GCA_001039355.1</a>                                           |
| <i>Caenorhabditis elegans</i>        | Nematoda     | <a href="https://downloads.wormbase.org/releases/WS279/species/c_elegans/PRJNA13758/">https://downloads.wormbase.org/releases/WS279/species/c_elegans/PRJNA13758/</a> |
| <i>Drosophila melanogaster</i>       | Arthropoda   | <a href="https://flybase.org/">https://flybase.org/</a> (release dmel_r6.32 (FB2020_01))                                                                              |
| <i>Danio rerio</i>                   | Chordata     | <a href="https://www.ncbi.nlm.nih.gov/grc/zebrafish">https://www.ncbi.nlm.nih.gov/grc/zebrafish</a>                                                                   |
| <i>Xenopus tropicalis</i>            | Chordata     | <a href="http://www.xenbase.org/">http://www.xenbase.org/</a>                                                                                                         |
| <i>Homo sapiens</i>                  | Chordata     | <a href="https://www.ncbi.nlm.nih.gov/grc/human">https://www.ncbi.nlm.nih.gov/grc/human</a>                                                                           |

**Table S2. Details of sequences used from species for evolutionary comparison.** Sequences were obtained from the UniProt data base <https://www.uniprot.org/>

| ID                                  | Phylum           | Gene | Accession (UniProt) |
|-------------------------------------|------------------|------|---------------------|
| Algoriphagus.machipongonensis_1     | Bacteroidetes    | PRX  | A3HSR4_9BACT        |
| Algoriphagus.machipongonensis_2     | Bacteroidetes    | PRX  | A3HY26_9BACT        |
| Algoriphagus.machipongonensis_3     | Bacteroidetes    | PRX  | A3HRY5_9BACT        |
| Algoriphagus.machipongonensis_1_GPx | Bacteroidetes    | GPX  | A3HYP7_9BACT        |
| Algoriphagus.machipongonensis_2_GPx | Bacteroidetes    | GPX  | A3HTQ2_9BACT        |
| Arabidopsis.thaliana_CAT3           | Spermatophyta    | CAT  | CATA3_ARATH         |
| Arabidopsis.thaliana_CAT2           | Spermatophyta    | CAT  | CATA2_ARATH         |
| Arabidopsis.thaliana_CAT1           | Spermatophyta    | CAT  | CATA1_ARATH         |
| Podospira.anserina_CAT_B            | Ascomycota       | KatB | Q9HDP5_PODAS        |
| Podospira.anserina_CAT_A            | Ascomycota       | KatA | Q9HDP6_PODAS        |
| Podospira.anserina_CAT              | Ascomycota       | CAT  | B2AVW1_PODAN        |
| Podospira.anserina_1                | Ascomycota       | PRX  | B2AMP3_PODAN        |
| Podospira.anserina_2                | Ascomycota       | PRX  | B2AKR1_PODAN        |
| Podospira.anserina_3                | Ascomycota       | PRX  | B2AT30_PODAN        |
| Podospira.anserina_GPx              | Ascomycota       | GPX  | B2B6Q1_PODAN        |
| Phaeosphaeria.nodorum_1_CAT         | Ascomycota       | CAT  | Q0U013_PHANO        |
| Phaeosphaeria.nodorum_2_CAT         | Ascomycota       | CAT3 | Q0UYJ1_PHANO        |
| Phaeosphaeria.nodorum_3_CAT         | Ascomycota       | CAT2 | Q0U1W6_PHANO        |
| Chondrus.crispus_1_CAT              | Rhodophyta       | CAT  | R7QFJ3_CHOCCR       |
| Chondrus.crispus_2_CAT              | Rhodophyta       | CAT  | S0F3T7_CHOCCR       |
| Chondrus.crispus_PRX3               | Rhodophyta       | PRX  | R7Q3P5_CHOCCR       |
| Chondrus.crispus_PRX1               | Rhodophyta       | PRX  | R7Q3N0_CHOCCR       |
| Chondrus.crispus_1                  | Rhodophyta       | PRX  | M5DDG0_CHOCCR       |
| Chondrus.crispus_2                  | Rhodophyta       | PRX  | R7Q5I9_CHOCCR       |
| Chondrus.crispus_3                  | Rhodophyta       | PRX  | R7QGR8_CHOCCR       |
| Chondrus.crispus_4                  | Rhodophyta       | PRX  | R7QBP3_CHOCCR       |
| Chondrus.crispus_1_GPx              | Rhodophyta       | GPX  | R7QCZ5_CHOCCR       |
| Pyropia.yezoensis_CAT               | Rhodophyta       | CAT  | E7DDY7_PYRYE        |
| Pyropia.yezoensis_1                 | Rhodophyta       | PRX  | YCF42_PYRYE         |
| Pyropia.yezoensis_2                 | Rhodophyta       | PRX  | M4QIZ7_PYRYE        |
| Pyropia.haitanensis_3               | Rhodophyta       | PRX  | M9PQP2_PYRHA        |
| Dictyostelium.discoideum_CAT_A      | Amoebozoa        | CATA | CATA_DICDI          |
| Dictyostelium.discoideum_CAT_B      | Amoebozoa        | CATB | CATB_DICDI          |
| Dictyostelium.discoideum_PRX4       | Amoebozoa        | PRX  | PRDX4_DICDI         |
| Dictyostelium.discoideum_1Cys       | Amoebozoa        | PRX  | PRDXL_DICDI         |
| Monosiga.brevicollis_CAT            | Choanoflagellata | CAT  | A9UW79_MONBE        |
| Monosiga.brevicollis_1              | Choanoflagellata | PRX  | A9VEN1_MONBE        |
| Monosiga.brevicollis_2              | Choanoflagellata | PRX  | A9USG5_MONBE        |
| Monosiga.brevicollis_3              | Choanoflagellata | PRX  | A9UXC8_MONBE        |
| Monosiga.brevicollis_4              | Choanoflagellata | PRX  | A9VBU1_MONBE        |
| Monosiga.brevicollis_5              | Choanoflagellata | PRX  | A9VD18_MONBE        |
| Monosiga.brevicollis_6              | Choanoflagellata | PRX  | A9V1X1_MONBE        |
| Monosiga.brevicollis_1_GPx          | Choanoflagellata | GPX  | A9UXZ2_MONBE        |
| Monosiga.brevicollis_2_GPx          | Choanoflagellata | GPX  | A9V6S1_MONBE        |
| Trichoplax.adhaerens_CAT            | Placozoa         | CAT  | B3SC13_TRIAD        |
| Trichoplax.adhaerens_PRX5a          | Placozoa         | PRX  | B3RM02_TRIAD        |

|                            |          |     |              |
|----------------------------|----------|-----|--------------|
| Trichoplax.adhaerens_PRX5b | Placozoa | PRX | B3RLY4_TRIAD |
| Trichoplax.adhaerens_3     | Placozoa | PRX | B3RP43_TRIAD |
| Trichoplax.adhaerens_4     | Placozoa | PRX | B3S1P8_TRIAD |
| Trichoplax.adhaerens_5     | Placozoa | PRX | B3RX50_TRIAD |
| Trichoplax.adhaerens_6     | Placozoa | PRX | B3RUE8_TRIAD |
| Trichoplax.adhaerens_GPx   | Placozoa | GPX | B3RVW7_TRIAD |

**Table S3. PRX classes and subfamilies named according to both profiling of the C<sub>p</sub> active site and that used previously (i.e., homology to mammalian named isoforms) classification systems.**

Conserved residues around the peroxidatic (C<sub>p</sub>) and resolving cysteine (C<sub>R</sub>) active sites based on 19 assessed metazoan species are indicated. Active sites shown are highly conserved across metazoan species assessed in this study, except for C<sub>R</sub> in PRX5, where there is some notable variation within phylum Porifera. Residues that deviated from the amino acid displayed within more than one metazoan sequence are underlined. Residues in bold are absolutely conserved residues. Motifs are not shown for non-animal PRX subclasses, denoted in italicised grey font.

| Class                 | Enzyme Classification | Subfamily classification |                    | C <sub>p</sub>                                             | C <sub>R</sub>             |
|-----------------------|-----------------------|--------------------------|--------------------|------------------------------------------------------------|----------------------------|
|                       |                       | Active site profile      | Mammalian homology |                                                            |                            |
| <b>Typical 2-Cys</b>  | EC 1.11.1.24          | AhpC-PRX1                | PRX1               | <u>FFYP</u> <u>LD</u> FTFVCPTEI                            | <u>GEVCPA</u>              |
|                       | EC 1.11.1.24          | AhpC-PRX1                | PRX2               | <u>FFYP</u> <u>LD</u> FTFVCPTEI                            | <u>GEVCPA</u>              |
|                       | EC 1.11.1.25          | AhpC-PRX1                | PRX3               | <u>FFYP</u> <u>LD</u> FTFVCPTEI                            | <u>GEVCPA</u>              |
|                       | EC 1.11.1.24          | AhpC-PRX1                | PRX4               | <u>FFYP</u> <u>LD</u> FTFVCPTEI                            | <u>GEVCPA</u>              |
|                       | EC 1.11.1.24          | AhpC-PRX1                | CNID-PRX*          | <u>FFYP</u> <u>LD</u> FTFVCPTEI                            | <u>GEVCPA</u>              |
|                       | <i>EC 1.11.1.26</i>   | <i>AhpC-PRX1</i>         | <i>AhpC</i>        |                                                            |                            |
| <b>Atypical 2-Cys</b> | EC 1.11.1.24          | PRX5                     | PRX5               | F <u>AV</u> P <u>G</u> AFT <u>P</u> <u>G</u> <u>C</u> SKTH | GL <u>I</u> CS <u>L</u> ** |
|                       | EC 1.11.1.24          | <u>PRXQ</u>              | <u>BCP</u>         |                                                            |                            |
|                       | EC 1.11.1.24          | <u>TPX</u>               | <u>TPX</u>         |                                                            |                            |
| <b>1-Cys</b>          | EC 1.11.1.27          | PRX6                     | PRX6               | FSHP <u>A</u> D <u>Y</u> TPVCTTEL                          | -                          |
|                       | <i>EC 1.11.1.29</i>   | <i>AhpE</i>              | <i>AhpE</i>        |                                                            |                            |

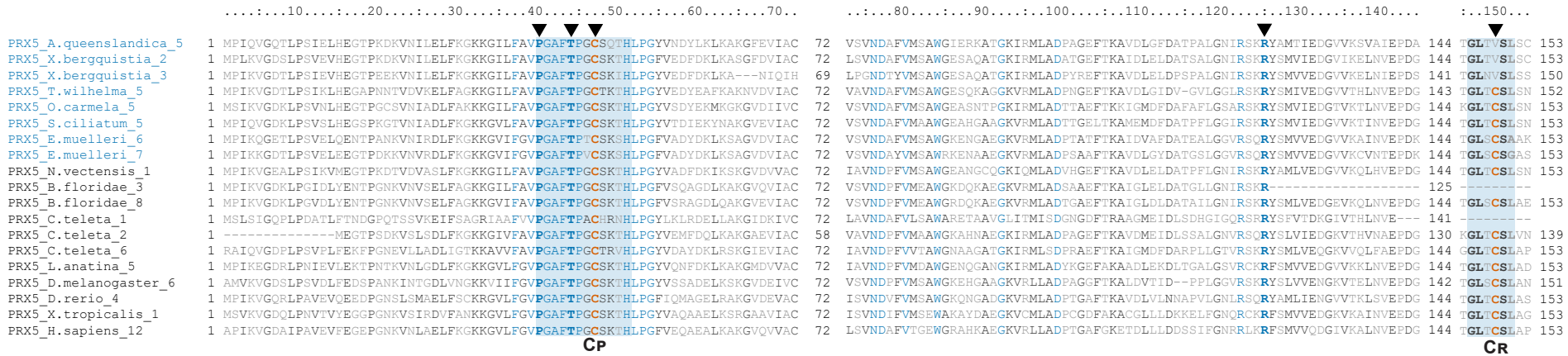
\*Recently established subfamily by [39], separated from human PRX4, based on presence in Cnidaria

\*\* For *A. queenslandica* and *X. bergquistia* PRX5, the C<sub>R</sub> is absent

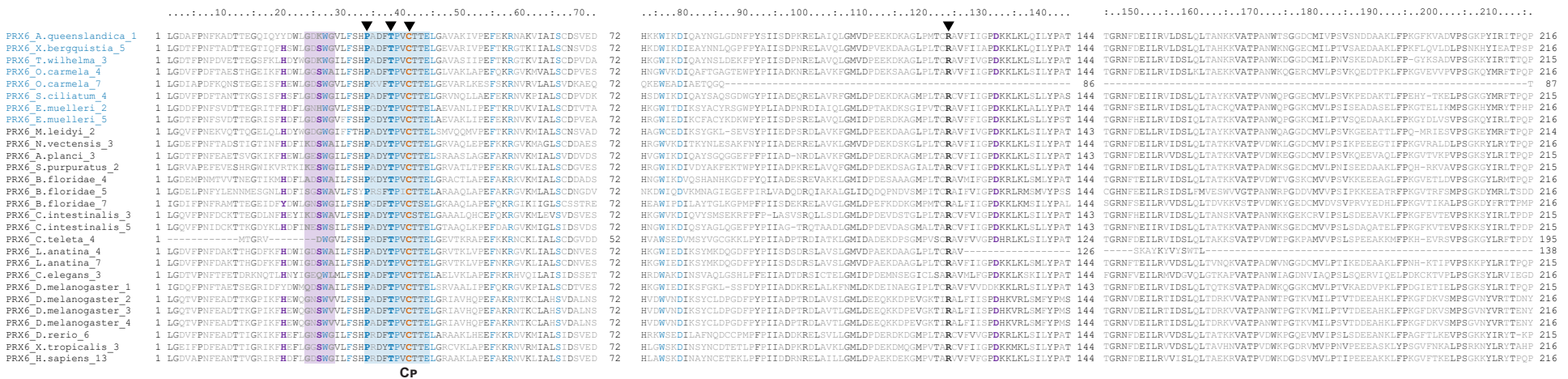
\*\*\*Previously EC 1.11.1.15, which only became redundant in 2020 and is still the main EC used in online database annotations.



**Figure S1.** Multiple sequence alignment for AhpC-PRX1 sequences identified from 19 metazoan species. Blue: identical residues, Orange: conserved Peroxidative (C<sub>p</sub>) and resolving (C<sub>r</sub>) Cysteine residues, Black: residues with 90% similarity. C<sub>p</sub> and C<sub>r</sub> conserved motifs highlighted in blue box. Motifs encoding "sensitive" PRX highlighted in bold in dark grey boxes, GGLG.... YF for which 41 of 51 metazoan AhpC-PRX1 sequences have the full motif. Arrowhead denotes absolutely conserved Arginine residue. Species names belong to phylum Porifera are in blue. Sequences aligned using MAFFT.



**Figure S2.** Multiple sequence alignment for PRX5 sequences identified from 19 metazoan. Blue: identical residues, Orange: conserved Peroxidatic (C<sub>p</sub>) and resolving (C<sub>r</sub>) Cysteine residues, Black: residues with 90% similarity. C<sub>p</sub> and C<sub>r</sub> conserved motifs highlighted in blue box. Arrowhead denotes absolutely conserved Arginine residue. Species names belong to phylum Porifera are in blue. Sequences aligned using MAFFT.



**Figure S3.** Multiple sequence alignment for PRX6 sequences identified from 19 metazoan species. Blue: identical residues, Orange: conserved Peroxidatic (C<sub>p</sub>) Cysteine residue, Purple: Phospholipase A<sub>2</sub> (PLA<sub>2</sub>) catalytic triad, Black: residues with 90% similarity. C<sub>p</sub> conserved motifs highlighted in blue box. Black arrowheads denote peroxidase catalytic triad and active site. Motifs encoding phospholipase/esterase (lipase) activity highlighted in bold, in purple box, **GXSXG**. Species names belong to phylum Porifera are in blue. Sequences aligned using MAFFT.

**Table S4. SRX identified from genome sequences of 19 metazoan species.** ParBc (PF02195) is the SRX domain.

| Species                              | Phylum     | Number of genes<br>encoding ParBc domain | SRX |
|--------------------------------------|------------|------------------------------------------|-----|
| <i>Amphimedon queenslandica</i>      | Porifera   | 3                                        | -   |
| <i>Xestospongia bergquistia</i>      | Porifera   | -                                        | -   |
| <i>Tethya wilhelma</i>               | Porifera   | 3                                        | -   |
| <i>Ephydatia muelleri</i>            | Porifera   | 3                                        | -   |
| <i>Oscarella carmela</i>             | Porifera   | -                                        | -   |
| <i>Sycon ciliatum</i>                | Porifera   | 3                                        | -   |
| <i>Mnemiopsis leidyi</i>             | Ctenophora | 1                                        | -   |
| <i>Nematostella vectensis</i>        | Cnidaria   | 5                                        | SRX |
| <i>Acanthaster planci</i>            | Echinoderm | 1                                        | SRX |
| <i>Strongylocentrotus purpuratus</i> | Echinoderm | 1                                        | SRX |
| <i>Branchiostoma floridae</i>        | Chordata   | 1                                        | SRX |
| <i>Ciona intestinalis</i>            | Chordata   | 3                                        | SRX |
| <i>Capitella teleta</i>              | Annelida   | 16                                       | -   |
| <i>Lingula anatina</i>               | Brachipoda | 2                                        | SRX |
| <i>Caenorhabditis elegans</i>        | Nematoda   | -                                        | -   |
| <i>Drosophila melanogaster</i>       | Arthropoda | 2                                        | SRX |
| <i>Danio rerio</i>                   | Chordata   | 1                                        | SRX |
| <i>Xenopus tropicalis</i>            | Chordata   | 2                                        | -   |
| <i>Homo sapiens</i>                  | Chordata   | 1                                        | SRX |

**Table S5. Showing presence of motifs, *a* and *b* [61] encoded within sensitive PRX4 sequences belonging to subfamily AhpC-PRX1.** Not having these amino acids makes the sequence more prone to hyperoxidation. Since, *C. elegans* does not encode PRX4, the motifs displayed for are for a PRX1/2 gene sequence. Rows highlighted in yellow denote species that do not encode SRX.

| PRX4                                 | A MOTIF |     |  |   |     | B MOTIF |     |
|--------------------------------------|---------|-----|--|---|-----|---------|-----|
| Species                              | D       | N/G |  | H | S/G | T       | S/T |
| <i>Amphimedon queenslandica</i>      | D       | N   |  | K | S   | T       | S   |
| <i>Xestospongia bergquistia</i>      | D       | N   |  | K | S   | T       | S   |
| <i>Tethya wilhelma</i>               | D       | N   |  | K | S   | T       | S   |
| <i>Ephydatia muelleri</i>            | D       | N   |  | K | A   | T       | S   |
| <i>Oscarella carmela</i>             | D       | N   |  | P | S   | T       | S   |
| <i>Sycon ciliatum</i>                | D       | N   |  | K | S   | T       | S   |
| <i>Mnemiopsis leidyi</i>             | D       | N   |  | K | S   | T       | S   |
| <i>Nematostella vectensis</i>        | D       | N   |  | E | S   | T       | S   |
| <i>Acanthaster planci</i>            | D       | N   |  | Q | S   | T       | S   |
| <i>Strongylocentrotus purpuratus</i> | D       | N   |  | Q | S   | T       | A   |
| <i>Branchiostoma floridae</i>        | E       | N   |  | Q | S   | T       | S   |
| <i>Ciona intestinalis</i>            | D       | N   |  | H | S   | T       | S   |
| <i>Capitella teleta</i>              | D       | N   |  | P | S   | S       | S   |
| <i>Lingula anatina</i>               | D       | N   |  | Q | S   | T       | S   |
| <i>Caenorhabditis elegans prx1/2</i> | D       | N   |  | V | A   | N       | S   |
| <i>Drosophila melanogaster</i>       | D       | K   |  | H | S   | T       | S   |
| <i>Danio rerio</i>                   | D       | N   |  | Q | S   | T       | S   |
| <i>Xenopus tropicalis</i>            | D       | N   |  | Q | S   | T       | S   |
| <i>Homo sapiens</i>                  | D       | N   |  | Q | S   | T       | S   |