

## Supplementary Information (Tables S1 through S4)

**Table S1.** Summary of Prx knockdown studies.

| Organism/ΔEnzyme/s                    | Reference                                 | Brief Phenotypic Observations <sup>a</sup>                        |
|---------------------------------------|---|---|
| <i>Homo sapiens</i> -PrxI             | <i>Hoshino</i> 2005 <sup>55</sup>         | Diminished FK228 antitumor properties.                            |
| <i>Homo sapiens</i> -PrxII            | <i>Stresing</i> 2013 <sup>49</sup>        | +H <sub>2</sub> O <sub>2</sub> sensitivity, -metastasis to lungs. |
| <i>Homo sapiens</i> -PrxIII           | <i>De Simoni</i> 2007 <sup>47</sup>       | +Protein carbonylation, + neuronal apoptosis.                     |
| <i>Homo sapiens</i> -PrxIII           | <i>Mukhopadhyay</i> 2006 <sup>50</sup>    | +Myocin-c sensitivity.  |
| <i>Homo sapiens</i> -PrxIV            | <i>Tavender</i> 2010 <sup>51</sup>        | +ER stress sensitivity.   |
| <i>Homo sapiens</i> -PrxIV            | <i>Tavender</i> 2008 <sup>52</sup>        | ++H <sub>2</sub> O <sub>2</sub> sensitivity.                      |
| <i>Homo sapiens</i> -PrxV             | <i>De Simoni</i> 2007 <sup>47</sup>       | +Protein carbonylation, + neuronal apoptosis.                     |
| <i>Homo sapiens</i> -PrxV             | <i>Kropotov</i> 2006 <sup>48</sup>        | +DNA ox., + non-coding DNA transcription.                         |
| <i>Homo sapiens</i> -PrxVI            | <i>Chang</i> 2007 <sup>53</sup>           | -Breast cancer growth, -metastases.                               |
| <i>Homo sapiens</i> -PrxVI            | <i>Kim</i> 2001 <sup>54</sup>             | + Apoptosis, -IL-1B production.                                   |
| <i>Mus musculus</i> -PrxII            | <i>Agrawal-Singh</i> 2011 <sup>136</sup>  | +Myeloblast-like cell growth.                                     |
| <i>Mus musculus</i> -PrxVI            | <i>Manevich</i> 2005 <sup>61</sup>        | +Lipid oxidation, + apoptosis.                                    |
| <i>Mus musculus</i> -PrxVI            | <i>Fatma</i> 2011 <sup>132</sup>          | +UPR, +apoptosis in lens epithelial/aging cells.                  |
| <i>Caenorhabditis elegans</i> -PrxII  | <i>Isermann</i> 2004 <sup>73</sup>        | Retarded development, -70% brood size.                            |
| <i>Caenorhabditis elegans</i> -PrxIII | <i>Ranjan</i> 2013 <sup>74</sup>          | -Motility, - brood size.  |
| <i>Schistosoma mansoni</i> -Prx1a     | <i>Sayed</i> 2006 <sup>75</sup>           | -Survival, + albumin and actin oxidation                          |
| <i>Schistosoma mansoni</i> -Prx1a/b   | <i>De Moraes</i> 2009 <sup>76</sup>       | Decreased larval size.  |
| <i>Schistosoma japonicum</i> -Prx1    | <i>Kumagai</i> 2009 <sup>77</sup>         | +H <sub>2</sub> O <sub>2</sub> , CHP, and TBP sensitivity.        |
| <i>Trypanosoma brucei</i> -TbCPX      | <i>Wilkinson</i> 2003 <sup>78</sup>       | +16-fold more H <sub>2</sub> O <sub>2</sub> sensitivity           |
| <i>Mycobacterium bovis</i> -AhpC      | <i>Wilson</i> 1998 <sup>96</sup>          | Reduced infectivity.  |
| <i>Arabidopsis thaliana</i> -“2-CP”   | <i>Baier</i> 2000 <sup>86</sup>           | +Foliar ascorbate oxidation.                                      |
| <i>Arabidopsis thaliana</i> -PrxQ     | <i>Lamkemeyer</i> 2006 <sup>87</sup>      | -PSII and cytochrome-b6 content.                                  |
| <i>Arabidopsis thaliana</i> -PrxII    | <i>Romero-Puertas</i> 2007 <sup>137</sup> | +lipid oxidation, +protein nitrosylation.                         |

<sup>a</sup> Abbreviations for cumene hydroperoxide (CHP) and tert-butyl hydroperoxide (TBP).

**Table S2.** Summary of Prx knockout studies in other eukaryotes.

| <b>Organism/ΔEnzyme/s</b>                          | <b>Reference</b>                 | <b>Brief Phenotypic Observations<sup>a</sup></b>    |
|--|----------------------------------|---|
| <i>Saccharomyces cerevisiae</i> ( <i>Sc</i> )-Prx1 | Wong 2004 <sup>83</sup>          | +ROS/RNS sensitivity, +DNA mutation.                |
| <i>Sc</i> -Tsa1,Tsa2                               | Wong 2004 <sup>83</sup>          | +ROS/RNS sensitivity, ++DNA mutation.               |
| <i>Sc</i> -Tsa1,Tsa2                               | Ogusucu 2008 <sup>138</sup>      | +1-hydroxyethyl radical in the presence of ethanol. |
| <i>Sc</i> -Tsa1,Tsa2,Dot5                          | Wong 2004 <sup>83</sup>          | ++ROS/RNS sensitivity, ++DNA mutation.              |
| <i>Sc</i> -Tsa1,Tsa2,Prx1                          | Wong 2004 <sup>83</sup>          | ++ROS/RNS sensitivity, ++DNA mutation.              |
| <i>Sc</i> -Tsa1,Tsa2,Prx1,Dot5                     | Wong 2004 <sup>83</sup>          | ++ROS/RNS sensitivity, ++DNA mutation.              |
| <i>Sc</i> -Tsa1,Tsa2,Prx1,Ahp1                     | Wong 2004 <sup>83</sup>          | ++ROS/RNS sensitivity, ++DNA mutation rate.         |
| <i>Sc</i> -Tsa1,Tsa2,Prx1,Dot5,Ahp1                | Wong 2004 <sup>83</sup>          | -Growth rate, +++ROS/RNS sensitivity.               |
| <i>Sc</i> -Tsa1/2,Ahp1,nPrx,mPrx,Gpx1,Gpx2,Gpx3    | Fomenko 2010 <sup>84</sup>       | Relicative lifespan of strain decreased by ~50%.    |
| <i>Schizosaccharomyces pombe</i> -Tpx1             | Jara 2007 <sup>139</sup>         | No aerobic growth.                                  |
| <i>Neurospora crassa</i> -2Prx                     | Edgar 2012 <sup>85</sup>         | Lengthened circadian period with altered phase.     |
| <i>Plasmodium falciparum</i> -Tpx1                 | Komaki-Yasuda 2003 <sup>80</sup> | +Paraquat/sodium nitroprusside sensitivity.         |
| <i>Plasmodium berghei</i> -Tpx1                    | Yano 2006 <sup>81</sup>          | 60% fewer gametocytes, delayed gaetocytoma.         |
| <i>Plasmodium berghei</i> -Tpx1                    | Yano 2008 <sup>82</sup>          | Decreased infectivity in mice.                      |
| <i>Leishmania infantum</i> -mTxnPx                 | Castro 2011 <sup>79</sup>        | Decreased infectivity in mice.                      |
| <i>Arabidopsis thaliana</i> -2CysPrxA,2CysPrxB     | Edgar 2012 <sup>85</sup>         | Altered circadium rhythm in phase and amplitude.    |

<sup>a</sup> Abbreviations for reactive oxygen species (ROS), reactive nitrogen species (RNS), cumene hydroperoxide (CHP) and tert-butyl hydroperoxide (TBP).

**Table S3.** Summary of Prx knockout studies in prokaryotes.

| <b>Organism/ΔEnzyme/s</b>               | <b>Reference</b>                  | <b>Brief Phenotypic Observations<sup>a</sup></b>                                       |
|---|-----------------------------------|--|
| <i>Helicobacter pylori</i> -AhpC        | Baker 2001 <sup>93</sup>          | No colony growth in microaerobic conditions.   |
| <i>Helicobacter pylori</i> -AhpC        | Olczak 2003 <sup>94</sup>         | 100% reduction in mouse stomach colonization.  |
| <i>Helicobacter pylori</i> -Tpx         | Olczak 2003 <sup>94</sup>         | +H <sub>2</sub> O <sub>2</sub> /O <sub>2</sub> sensitivity, -94% stomach colonization. |
| <i>Helicobacter cinaedi</i> -AhpC       | Charoenlap 2011 <sup>140</sup>    | +Susceptibility to killing by macrophage.  |
| <i>Legionella pneumophila</i> -AhpC     | Rankin 2002 <sup>141</sup>        | Normal phenotype, but not extensively studied.   |
| <i>Legionella pneumophila</i> -AhpC     | LeBlanc 2006 <sup>142</sup>       | +H <sub>2</sub> O <sub>2</sub> , CHP, TBP, and paraquat sensitivity                    |
| <i>Mycobacterium tuberculosis</i> -AhpC | Springer 2001 <sup>143</sup>      | +CHP sensitivity.  |
| <i>Porphyromonas gingivalis</i> -AhpC   | Johnson 2004 <sup>144</sup>       | +H <sub>2</sub> O <sub>2</sub> sensitivity.  |
| <i>Bacteroides fragilis</i> -AhpC       | Rocha 1999 <sup>145</sup>         | -10,000-fold survival in aerobic conditions.   |
| <i>Staphylococcus aureus</i> -AhpC      | Cosgrove 2006 <sup>95</sup>       | -10-fold tolerance to desiccation, -colonization.                                      |
| <i>Salmonella typhimurium</i> -AhpC     | Chen 1998 <sup>146</sup>          | +CHP and RNI sensitivity, -10,000-fold survival.                                       |
| <i>Salmonella typhimurium</i> -AhpC     | Storz 1989 <sup>147</sup>         | +CHP sensitivity.  |
| <i>Escherichia coli</i> -AhpC           | Storz 1989 <sup>147</sup>         | +CHP sensitivity.  |
| <i>Escherichia coli</i> -PrxQ           | Jeong 2000 <sup>148</sup>         | +H <sub>2</sub> O <sub>2</sub> , TBP, linoleic acid peroxide sensitivity.              |
| <i>Xanthomonas campestris</i> -AhpC     | Mongkolsuk 2000 <sup>149</sup>    | +TBP sensitivity, +catalase expression.  |
| <i>Xanthomonas campestris</i> -AhpC     | Vattanaviboon 2003 <sup>150</sup> | +Menadione sensitivity.  |
| <i>Vibrio parahaemolyticus</i> -AhpC1   | Wang 2013 <sup>97</sup>           | -Colony formation with organic peroxides.  |
| <i>Vibrio parahaemolyticus</i> -AhpC2   | Wang 2013 <sup>97</sup>           | Rapid induction of “viable but nonculturable state.”                                   |
| <i>Vibrio parahaemolyticus</i> -AhpC1/2 | Wang 2013 <sup>97</sup>           | -Colony formation.   |
| <i>Brucella abortus</i> -AhpC           | Steele 2010 <sup>92</sup>         | +H <sub>2</sub> O <sub>2</sub> sensitivity.  |
| <i>Brucella abortus</i> -AhpC, KatE     | Steele 2010 <sup>92</sup>         | -Virulence to mice, +H <sub>2</sub> O <sub>2</sub> sensitivity.                        |
| <i>Synechococcus elongatus</i> -2CysPrx | Edgar 2012 <sup>85</sup>          | Altered circadian rhythm in phase and amplitude.                                       |
| <i>Campylobacter jejuni</i> -PrxQ       | Atack 2008 <sup>151</sup>         | Slightly reduced growth.   |
| <i>Campylobacter jejuni</i> -Tpx        | Atack 2008 <sup>151</sup>         | Slightly reduced growth.   |
| <i>Campylobacter jejuni</i> -PrxQ, Tpx  | Atack 2008 <sup>151</sup>         | Zero growth at high aeration, +DNA damage.   |
| <i>Anabaena PCC 7120</i> -PrxQ-A        | Latifi 2007 <sup>152</sup>        | Hypersensitive to oxidative stress.  |

<sup>a</sup> Abbreviations for reactive nitrogen intermediates (RNI), cumene hydroperoxide (CHP) and tert-butyl hydroperoxide (TBP).

**Table S4.** Eukaryotes that lack Srx but possess Prxs containing GGLG/YF-like sequences.<sup>a</sup>

|  |      |    |
|--|------|----|
| <i>Xenopus tropicalis</i>                    | GGLG | YF |
| <i>Caenorhabditis elegans</i>                | GGLG | YF |
| <i>Schistosoma mansoni</i>                   | GGLG | FF |
| <i>Nematostella vectensis</i>                | GGLG | YF |
| <i>Trichoplax adhaerens</i>                  | GGLG | FF |
| <i>Amphimedon queenslandica</i>              | GGLG | YF |
| <i>Phaeosphaeria nodorum</i>                 | GGLG | YL |
| <i>Tuber melanosporum</i>                    | GGLG | YF |
| <i>Laccaria bicolor</i>                      | GGLG | YF |
| <i>Encephalitozoon cuniculi</i> <sup>b</sup> | GVLG | -- |
| <i>Monosiga brevicollis</i>                  | GGLA | YF |
| <i>Entamoeba histolytica</i>                 | GGVG | YL |
| <i>Plasmodium falciparum</i>                 | GGIG | YY |
| <i>Paramecium tetraurelia</i>                | GGLG | YW |
| <i>Phaeodactylum tricornutum</i>             | GGLE | YF |
| <i>Phytophthora infestans</i>                | GGLG | YF |
| <i>Guillardia theta</i>                      | GGLG | FF |
| <i>Trypanosoma brucei</i>                    | GGLG | YF |
| <i>Trichomonas vaginalis</i>                 | GGLG | YF |
| <i>Giardia lamblia</i>                       | GGIG | YF |

<sup>a</sup> Shown are the sequences at the GGLG/YF motifs for representative Prxs from eukaryotes that lack Srx.

<sup>b</sup> This organism is included to show that the GGLG motif may be retained even if the YF is not.