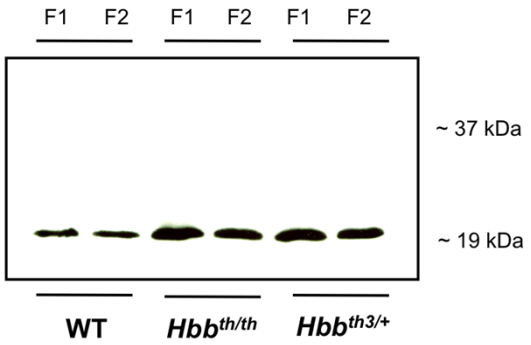
a



b

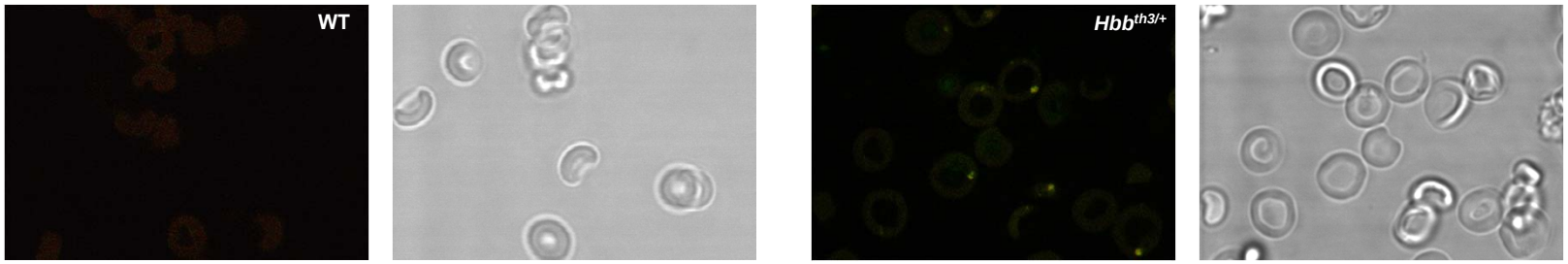


Fig. 1S: a. Immunoblot analysis with specific anti-Peroxiredoxin 2 (Prx2) antibody of total red cell lysate (8 • 10^6 cells) from normal (WT) and β thalassemic mice showing increased Prx2 levels compared to wild-type (WT) in both light dense red cells fraction (F1) and dense red cells fraction (F2). The immunoblot analysis was carried out in presence of β-mercaptoethanol. Shown is a representative experiment of 3 others performed with similar results. b. Confocal immunofluorescence using secondary antibody control (Alexa Fluor 594 goat anti-rabbit IgG) and corresponding brightfield images of fixed and permeabilized red cells from wild-type (WT) mice and the β thal mouse model *Hbb*$^{3th/+}$.

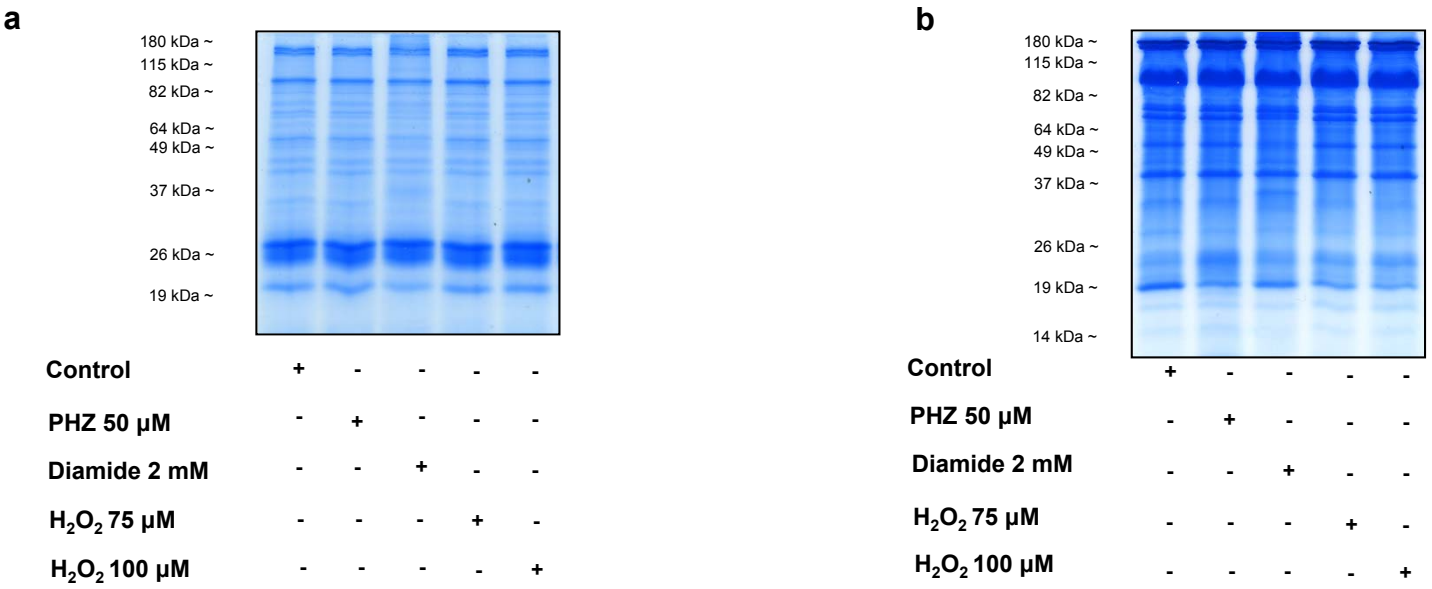


Fig. 2S: Tween colloidal Coomassie stained gels of Fig. 3 immuno-blot analysis with specific anti-Prx2 antibody of red cell cytosol fraction **(a)** and membrane (ghost) **(b)** from wild-type mouse red cells (control) with and without phenylhydrazine (PHZ, 50 µM), Diamide (2 mM), hydrogen peroxide (75- 100 µM) treatment. Shown is a representative experiment of 4 others performed with similar results.

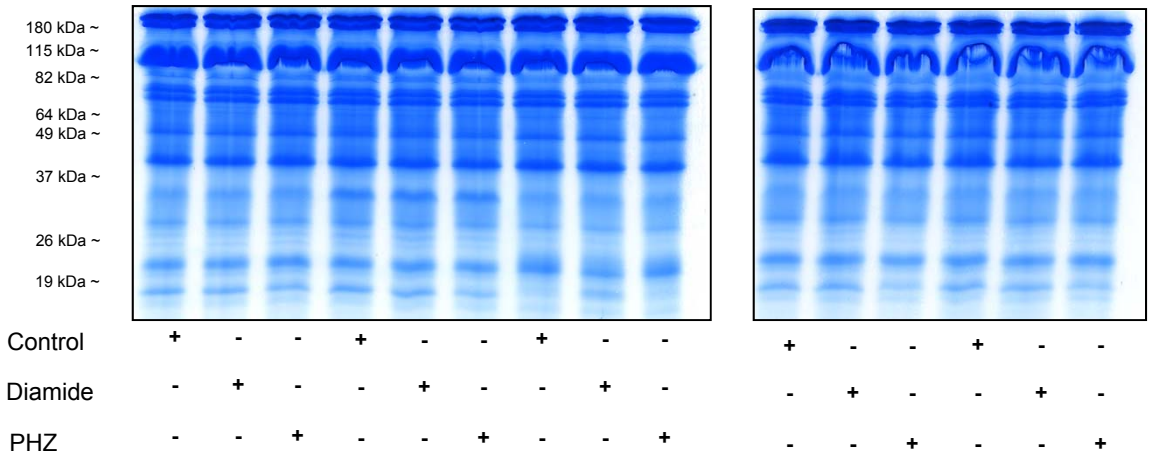


Fig. 3S: Tween colloidal Coomassie stained gels of Fig. 5 immunoblot analysis with specific anti-Prx2 antibody of red cell membrane from native red cells (control, lanes 1-3); red cells exposed to Diamide (2 mM, lanes 4-6) or phenylhydrazine (PHZ, 50 µM, lanes 7-9); isolated red cell membranes treated with diamide (2 mM, lanes 10-12) or PHZ (50 µM, lanes 13-15) incubated with cytoplasm fraction of either control or Diamide (2 mM) or PHZ (50 µM) treated red cells. Shown is a representative experiment of 3 others performed with similar results

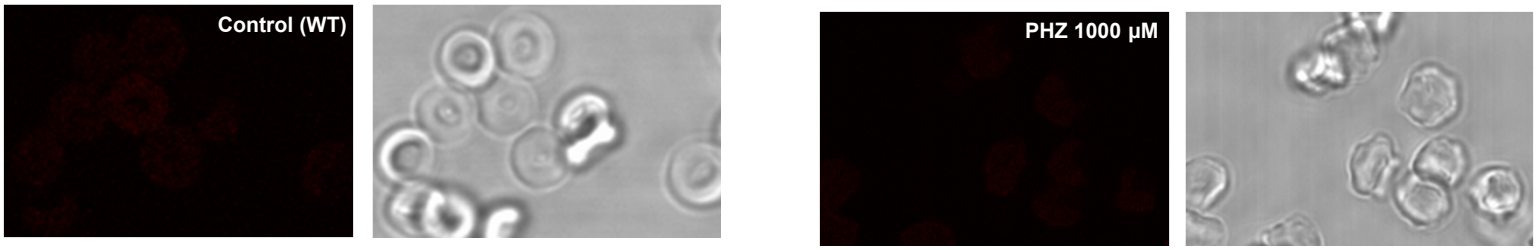


Fig. 4S: Confocal immunofluorescence using secondary antibody control (rabbit IgG isotypic control and Alexa Fluor 594 goat anti-rabbit IgG) and corresponding brightfield images of fixed and permeabilized red cells from wild-type (WT) untreated and treated with 1000 µM of PHZ.

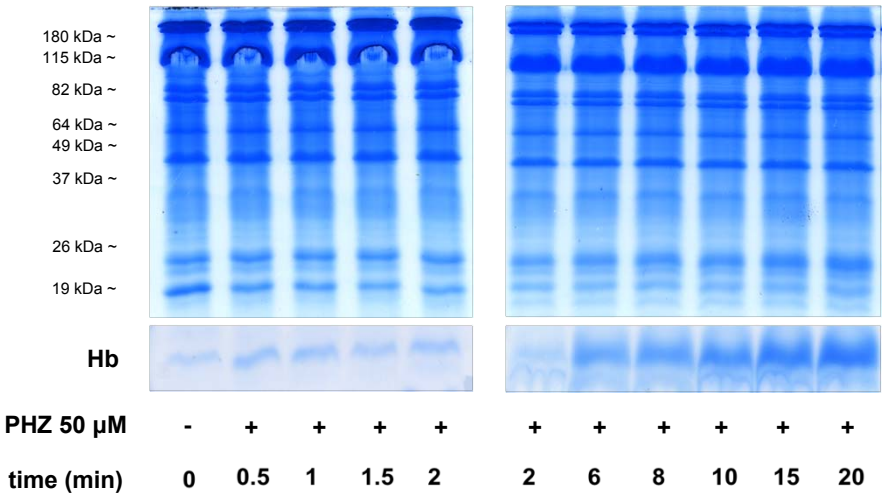


Fig. 5S: Tween colloidal Coomassie stained gel of Fig. 7. Time course effects of PHZ treatment (50 µM) on wild-type (WT) mouse red cells. In the lower panel, we showed the band corresponding to the hemoglobin (Hb) that progressively associated with ghosts during PHZ treatment (from the Coomassie stained gel loaded with the same samples). Shown is a representative experiment of 4 others performed with similar results.

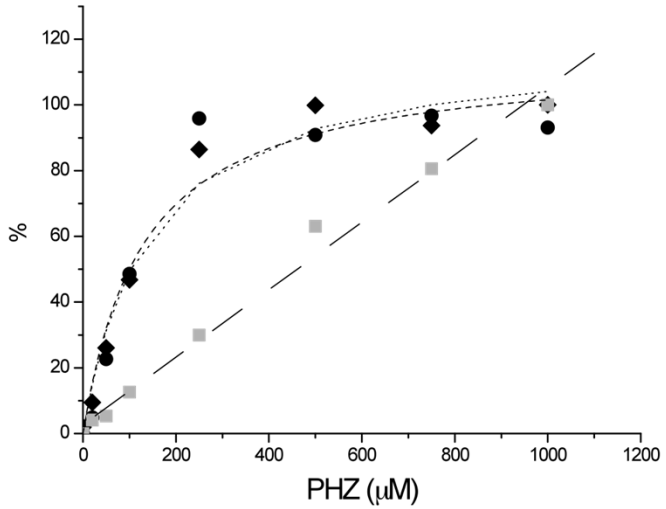


Fig. 6S: RBCs were treated with increasing concentrations of PHZ and Prx2 membrane displacement (●), MetHb content (◆) and hemichromes membrane binding (■) were measured as described in "Materials and Methods" section. The percentage of cells displaying Prx2 displacement and MetHb content exhibits a saturation behaviour as a function of PHZ concentration. Fitting to a hyperbola (dashed line for Prx2 displacement and dotted line for MetHb content, Eq. 2) allows us to estimate the Kd of the Prx2-PHZ-target complex (see "Results" and "Discussion"). The hemichromes membrane binding follows a linear dependence on PHZ concentration whose linear regression (dashed line) gives a second order constant which represents the slope of the regression line.