Supplemental Figure Legends

Supplemental Figure 1: PPP phylogenetic analysis in yeasts, mouse, and human.

Phylogenetic analysis of PPP family members from yeast, mouse, and human. YEAST - *S. cerevisiae*, SCHPO - *S.pombe*, CANAL - *C. albicans*, and NEUCR - *N.crassa.* PPP family members identified in PIB pulldowns are highlighted.

Supplemental Figure 2: Determination of PIB binding capacity.

A, Workflow to determine PIB capacity. PIBs were incubated with increased amounts of recombinant PP1 (0.5 µg to 60 µg), washed, and eluted. B, Ten percent of eluted PP1 was resolved on SDS-PAGE and analyzed by Coomassie Brilliant Blue staining.

Supplemental Figure 3: Western blot analysis of PPP catalytic subunits bound to PIB

Western plot of PIB pulldowns from control and MCLR-treated cell lysates. The 37kDa mass marker is shown.

Supplemental Figure 4: Competitor titration curves for MCLR.

MCLR competitive binding assays in 293FT cell lysates with increasing amounts of MCLR (10 fM to 10 µM). Titration curves for PP1α (A), PP1β (B), PP1γ (C), PP4C (D), PP6C (E), PP2A (F), and PP5C (G). Error bars indicate the standard deviation of triplicate analyses. Curve fitting for the binding of PPP catalytic subunits to PIBs versus free MCLR was performed using a least-squares nonlinear regression model.

Supplemental Figure 5: Identification of PPP interacting proteins in mouse tissue

Volcano plots of PIB-MS analyses of six mouse tissue lysates control- or MCLR-treated. Green dots indicate specifically bound proteins in control versus MCLR-treated lysates and are listed in Supp. Table 6.

Supplemental Tables

Supplemental Table 1:

PIB pulldowns from HeLa cells in the presence and absence of MCLR.

Supplemental Table 2:

Competitive binding assays in 293FT cell lysates with increasing amounts of MCLR.

Supplemental Table 3:

PIB pulldowns from HeLa cells in the presence and absence of MCLR or OA.

Supplemental Table 4:

Breast cancer and glioblastoma cell lines analysis.

Supplemental Table 5:

Relative iBAQ abundances of regulatory subunits and endogenous inhibitors in PPP catalytic subunit purifications from “total” and PIB “depleted” 293FT lysates.

Supplemental Table 6:

PPPome analysis in mouse tissues by TMT-PIB-MS.

Supplemental Table 7:

PPPome analysis in yeast by TMT-PIB-MS.

Supplemental References

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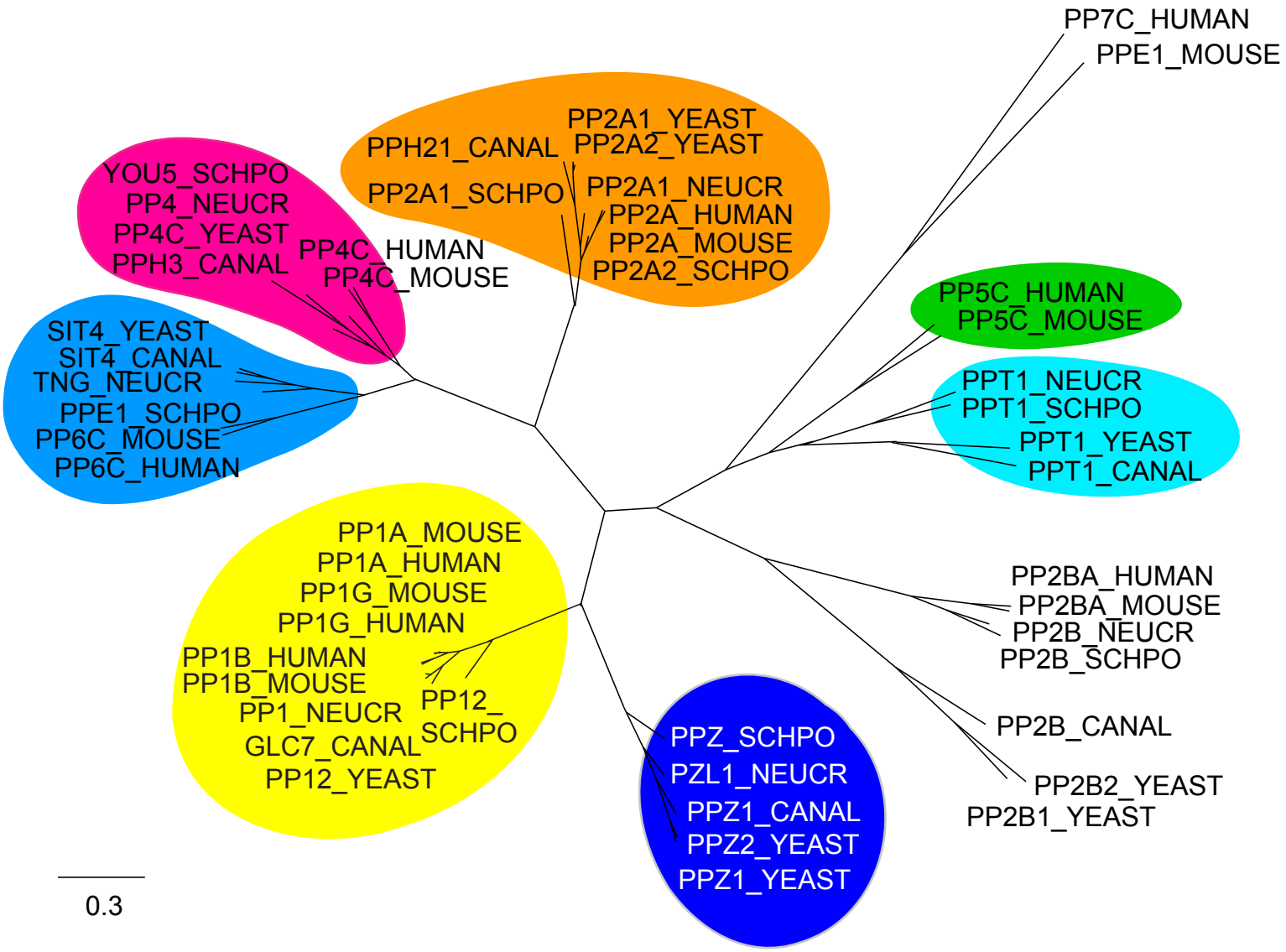
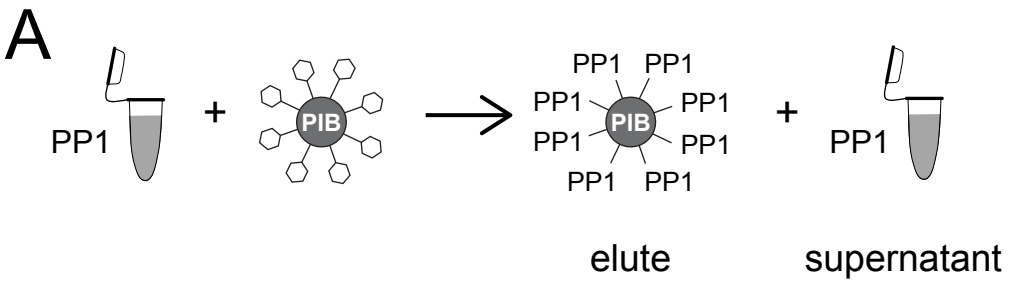
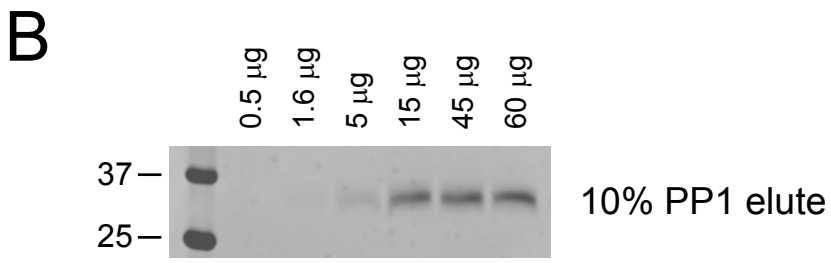


Supp. Figure 1





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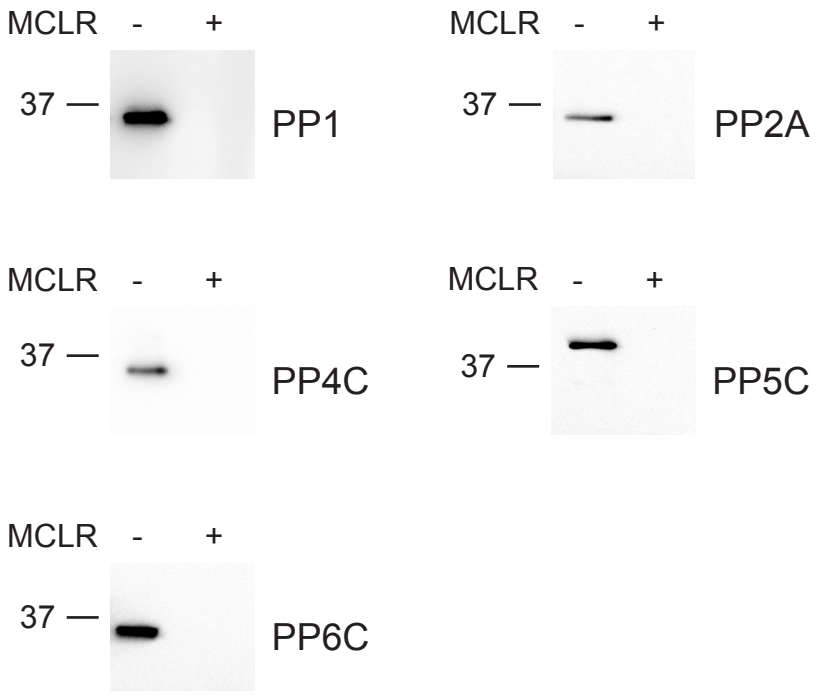

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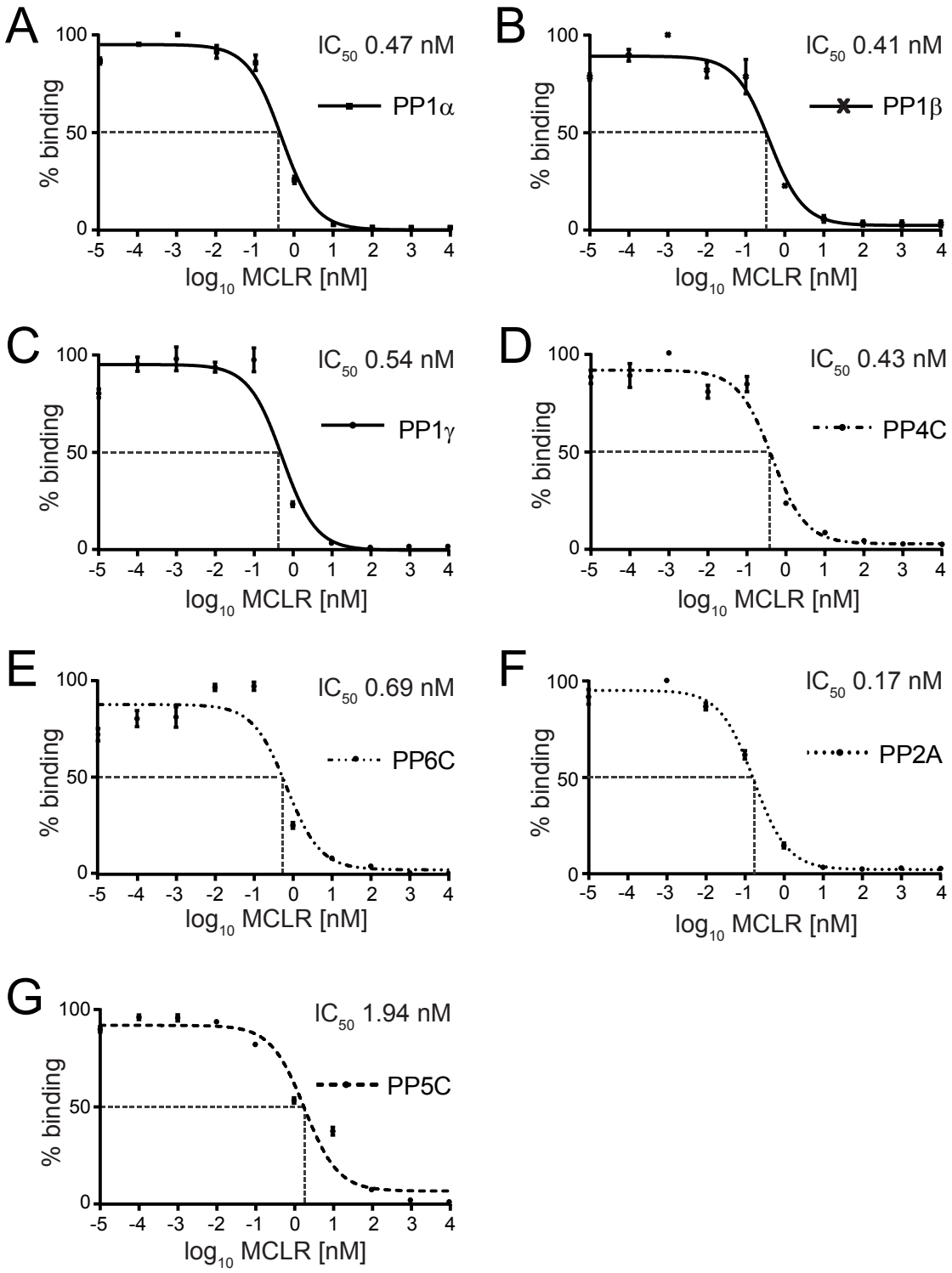
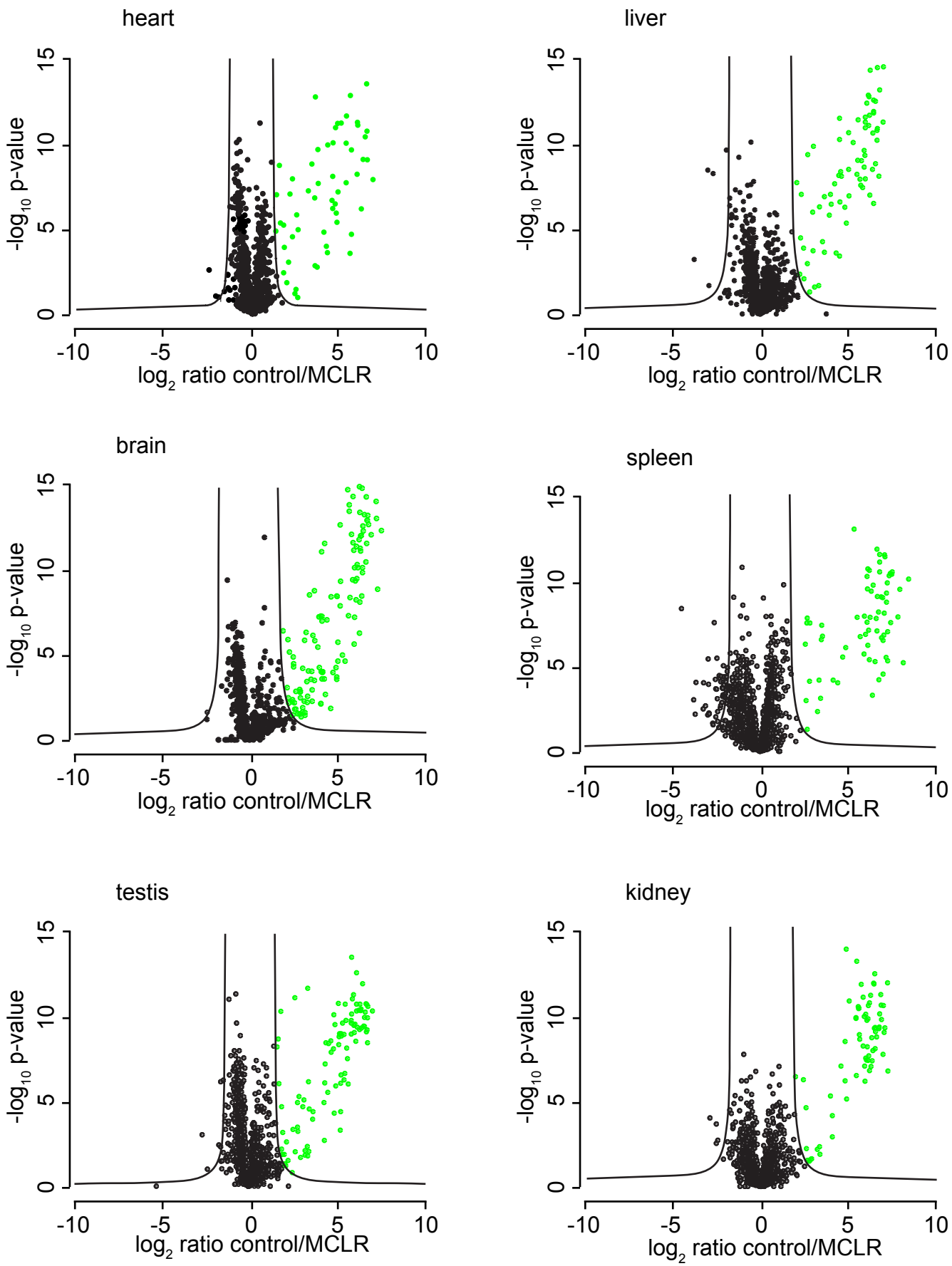


Supp. Figure 4



Supp. Figure 5