

Supplementary Information

Propagation of PrPSc in mice reveals impact of aggregate composition on prion disease pathogenesis

Sheng Chun Chang^{1,2*}, Samia Hannaoui^{1,2*}, Maria Immaculata Arifin^{1,2}, Yuan-Hung Huang^{1,2},
Xinli Tang³, Holger Wille^{3,4}, Sabine Gilch^{1,2+}

*These authors contributed equally

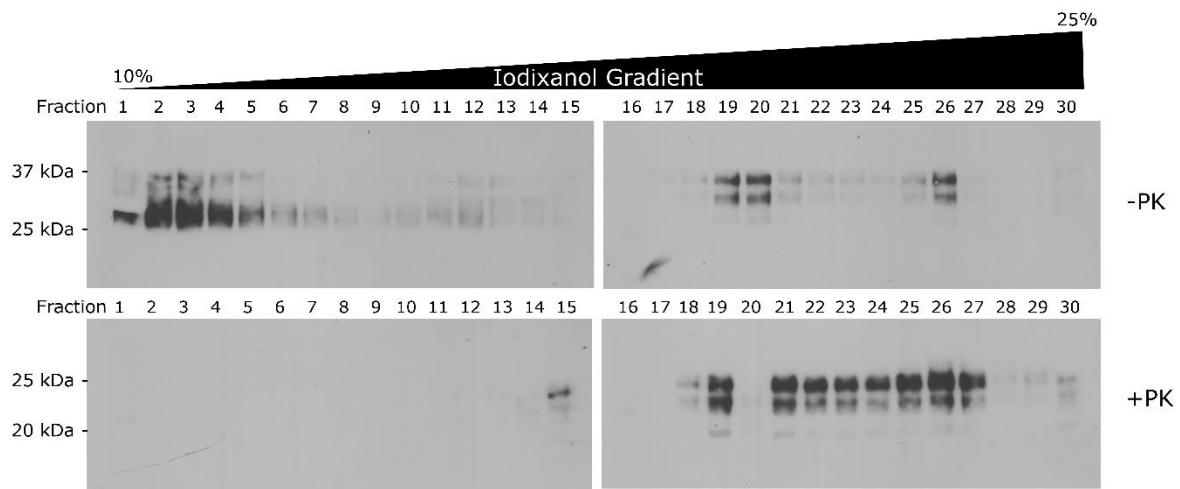
¹ Dept. of Comparative Biology and Experimental Medicine, Faculty of Veterinary Medicine,
University of Calgary, Calgary, Canada

² Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary,
Canada

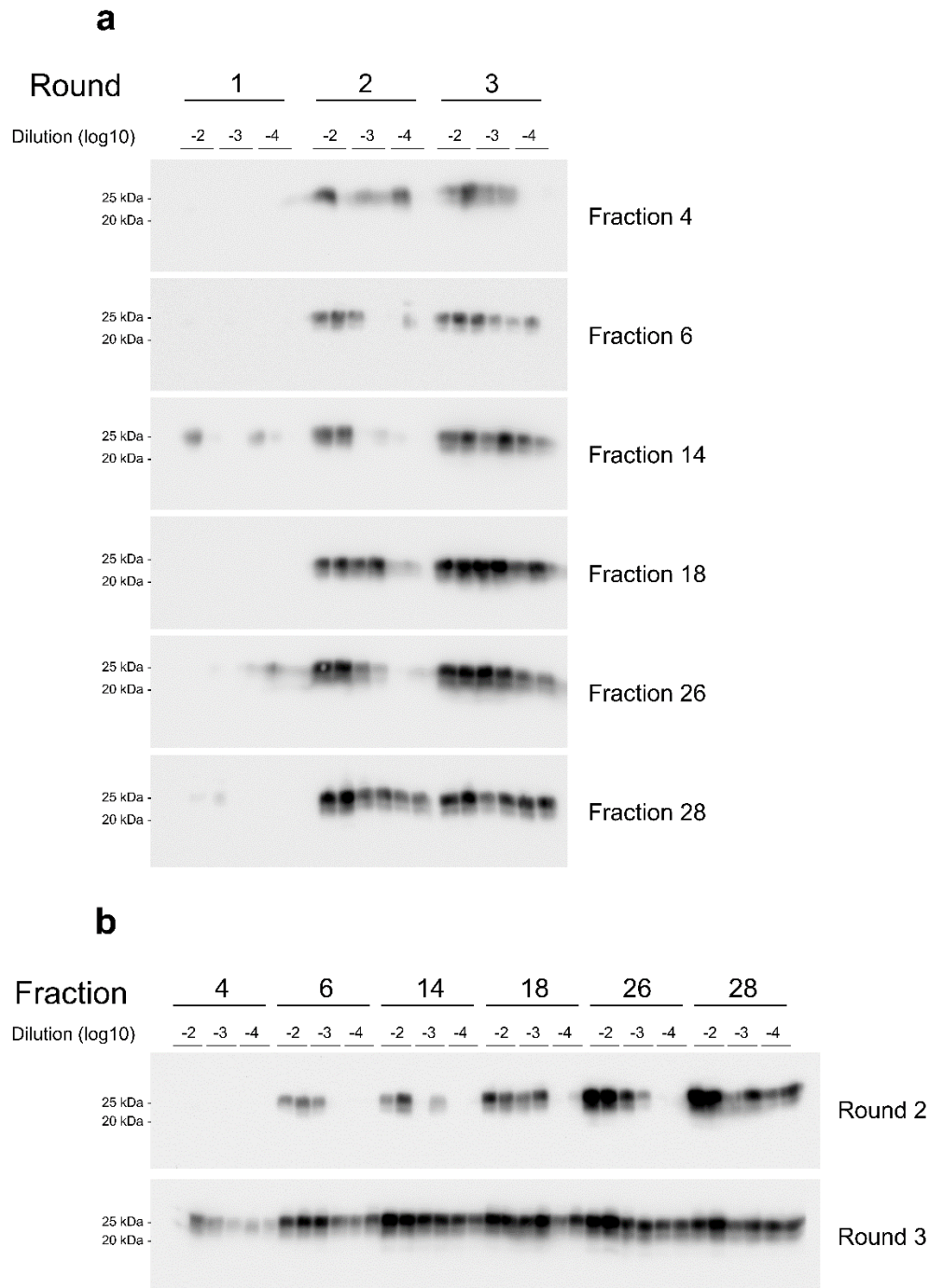
³ Department of Biochemistry, Center for Prions and Protein Folding Diseases, University of
Alberta, Edmonton, Canada

⁴ Neuroscience and Mental Health Institute, University of Alberta, Edmonton, Canada

⁺corresponding author: sgilch@ucalgary.ca

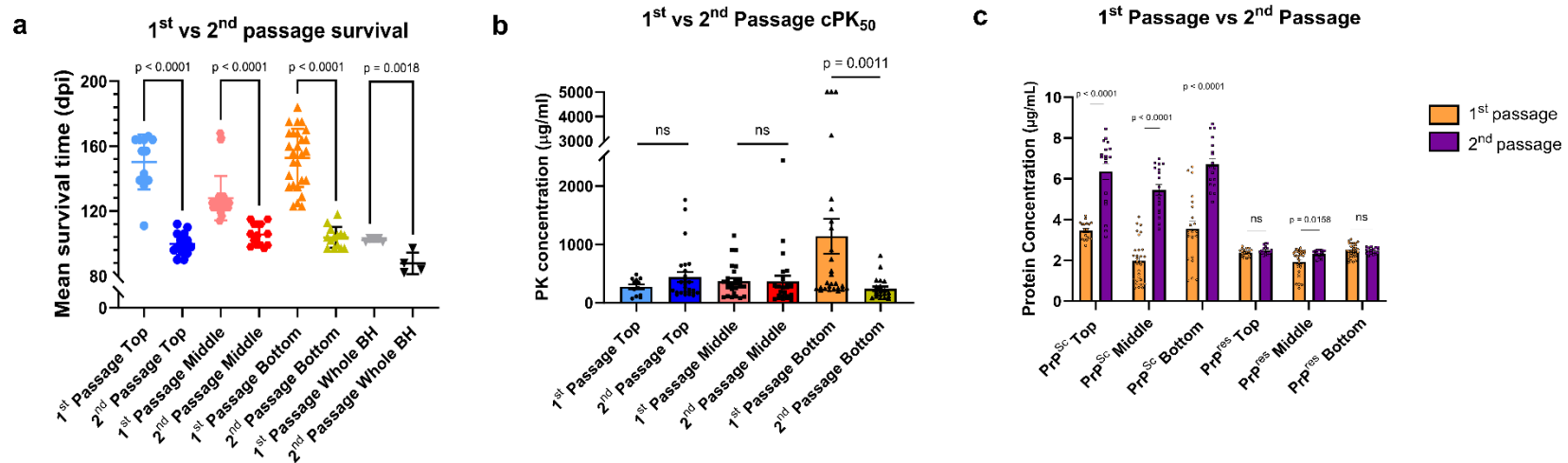


Supplementary Figure 1. Sedimentation velocity gradient of CWD-Elk fractions. (a) Representative western blot of the total PrP (top) and PrP^{res} (bottom) content depicting the total PrP and PrP^{res} of CWD-Elk prions solubilized and fractionated through sedimentation velocity ultracentrifugation. Total PrP content were greater at the top of the gradient, while PrP^{res} content were greater at the bottom of the gradient.



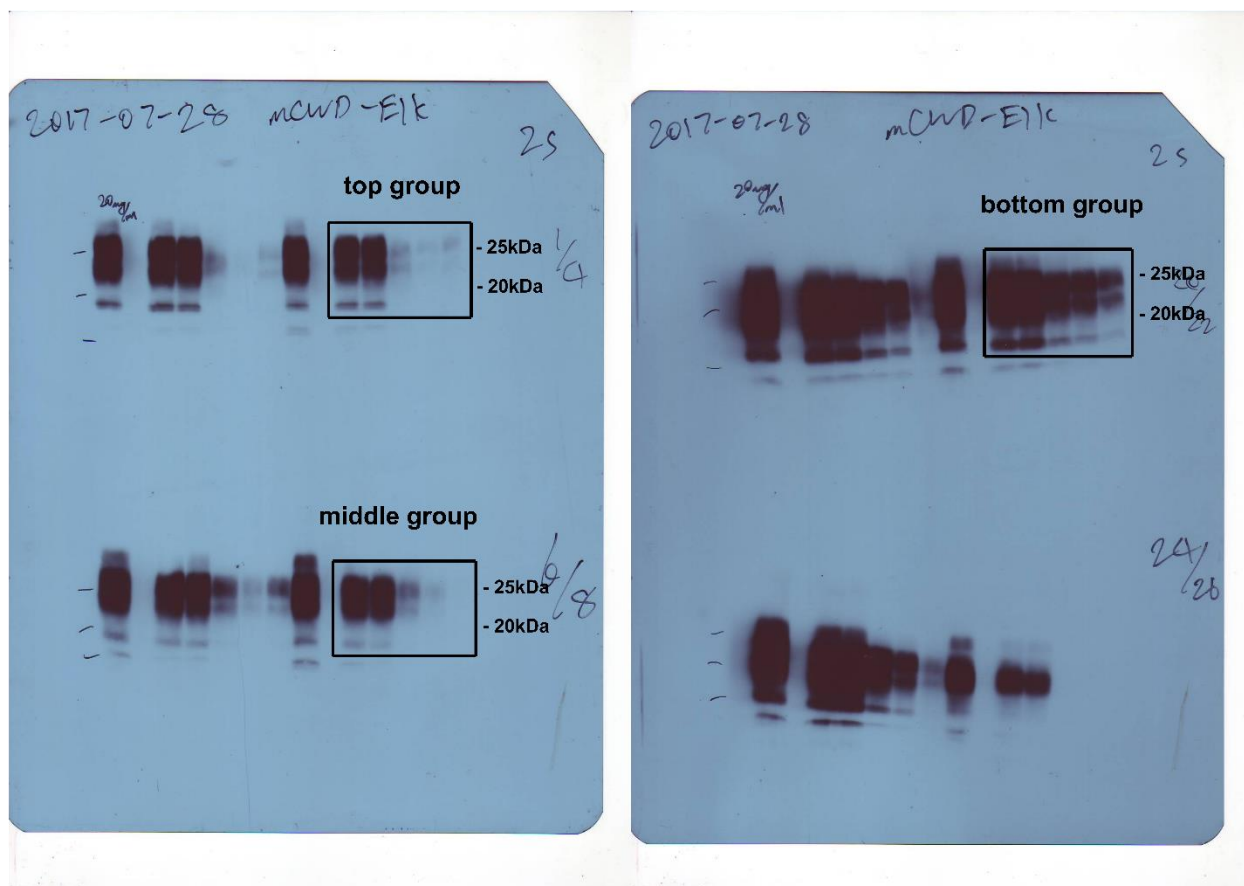
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42 **Supplementary Figure 2. Serial PMCA of fractionated CWD-elk brain homogenate.**
 43 Representative fractions were serially diluted and subjected to 3 rounds of PMCA. PrP^{res} generated
 44 in each round was analysed by western blot using anti-PrP mAb 4H11. (a) PMCA products
 45 generated over 3 rounds of PMCA from the specific fractions were compared. (b) Amount of PrP^{res}
 46 was compared in each round between the different fractions.

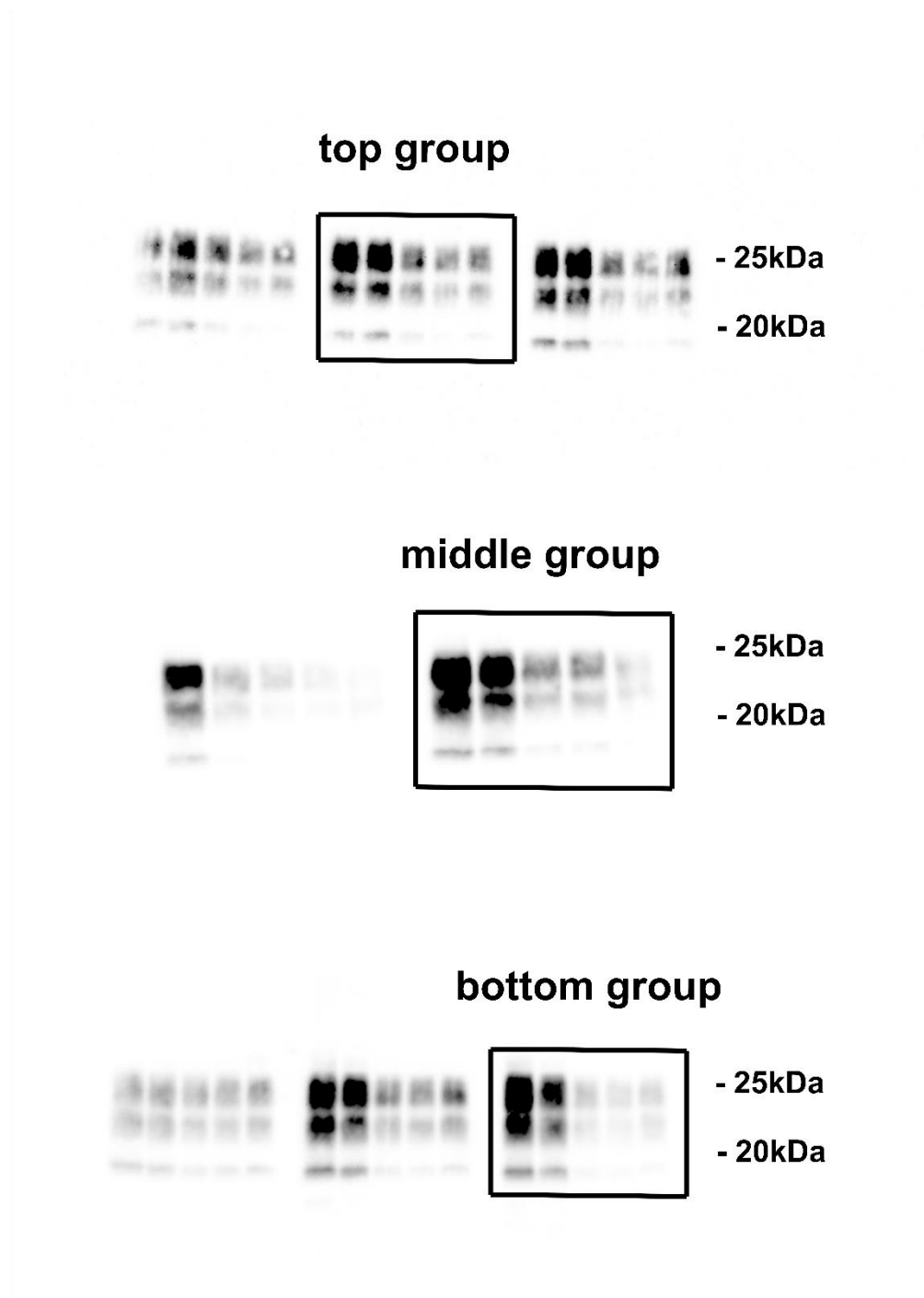


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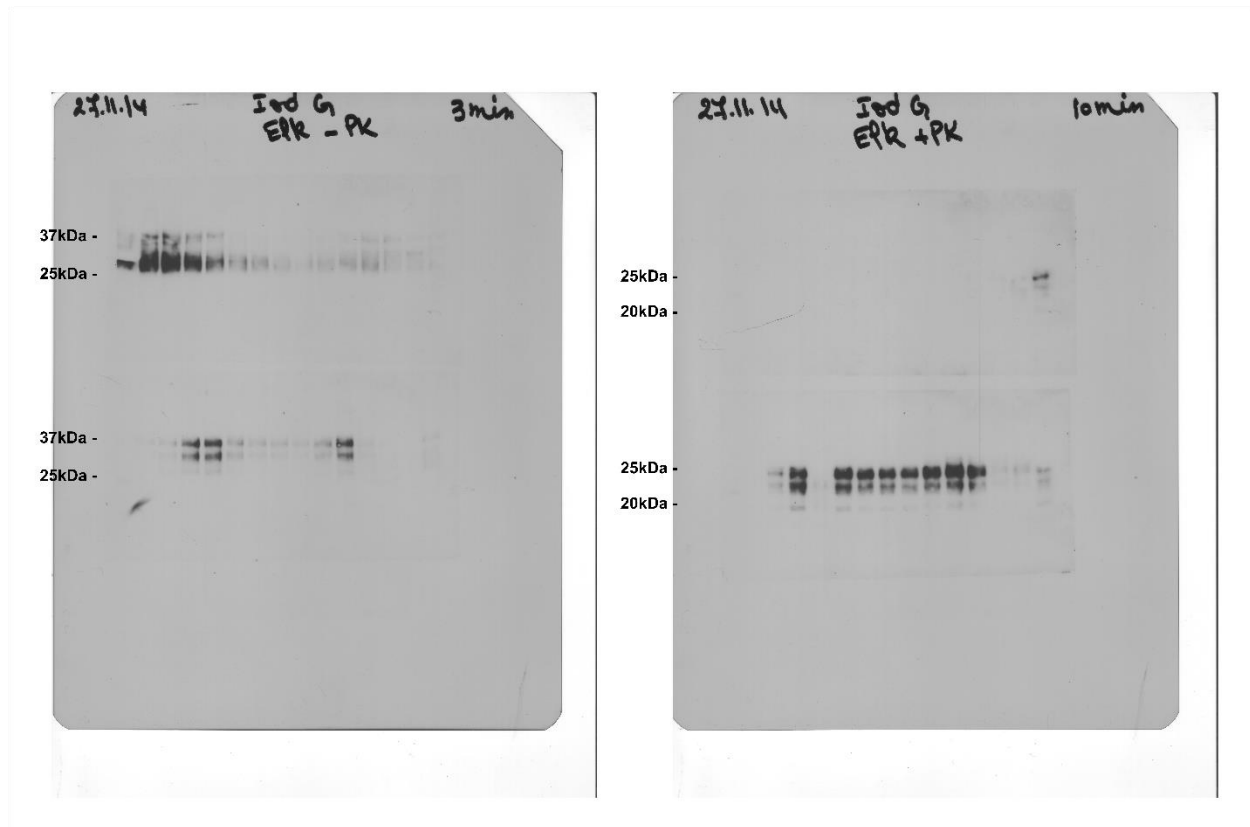
48 **Supplementary Figure 3. Comparison of first and second passage of fractionated prions in tgElk.** (a) Depiction of the survival,
 49 with an approximate 50-day decrease in the top and bottom groups and 20-day decrease in the middle group from the first to the second
 50 passage. (b) Depiction of the cPK₅₀, with an insignificant increase in the top group, no change in the middle group, and a significant
 51 decrease in the bottom group through passaging. (c) Depiction of the ELISA, with a drastic increase in PrP^{Sc} levels across all groups,
 52 and a slight PrP^{res} increase observed in the middle group, from first to second passage. Statistical analyses were performed with unpaired
 53 Student's *t*-test.



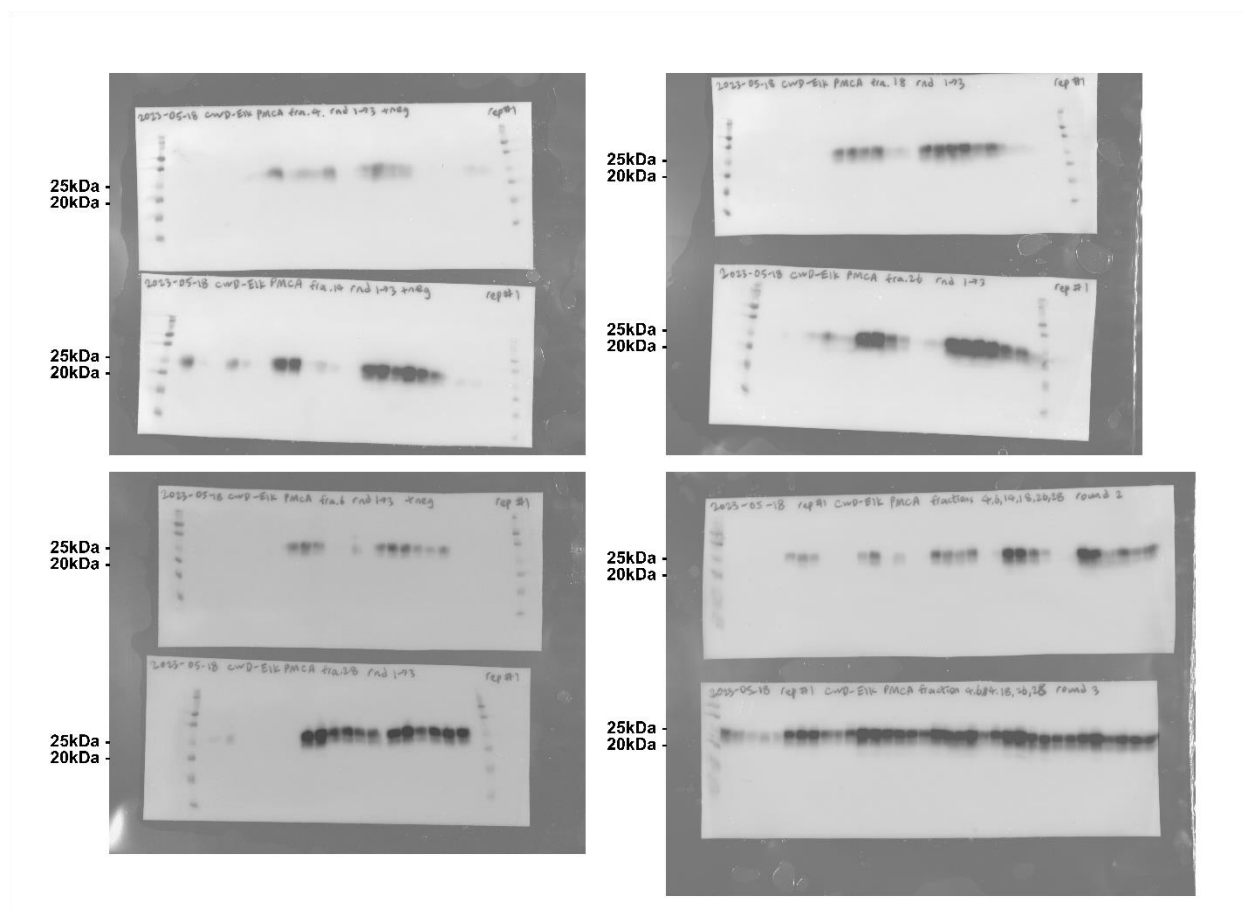
Supplementary Figure 4. Uncropped and unedited western blot of Fig. 3a.



Supplementary Figure 5. Uncropped and unedited western blot of Fig. 8a.



Supplementary Figure 6. Uncropped and unedited western blot of Supplementary Fig. 1.



Supplementary Figure 7. Uncropped and unedited western blot of Supplementary Fig. 2.