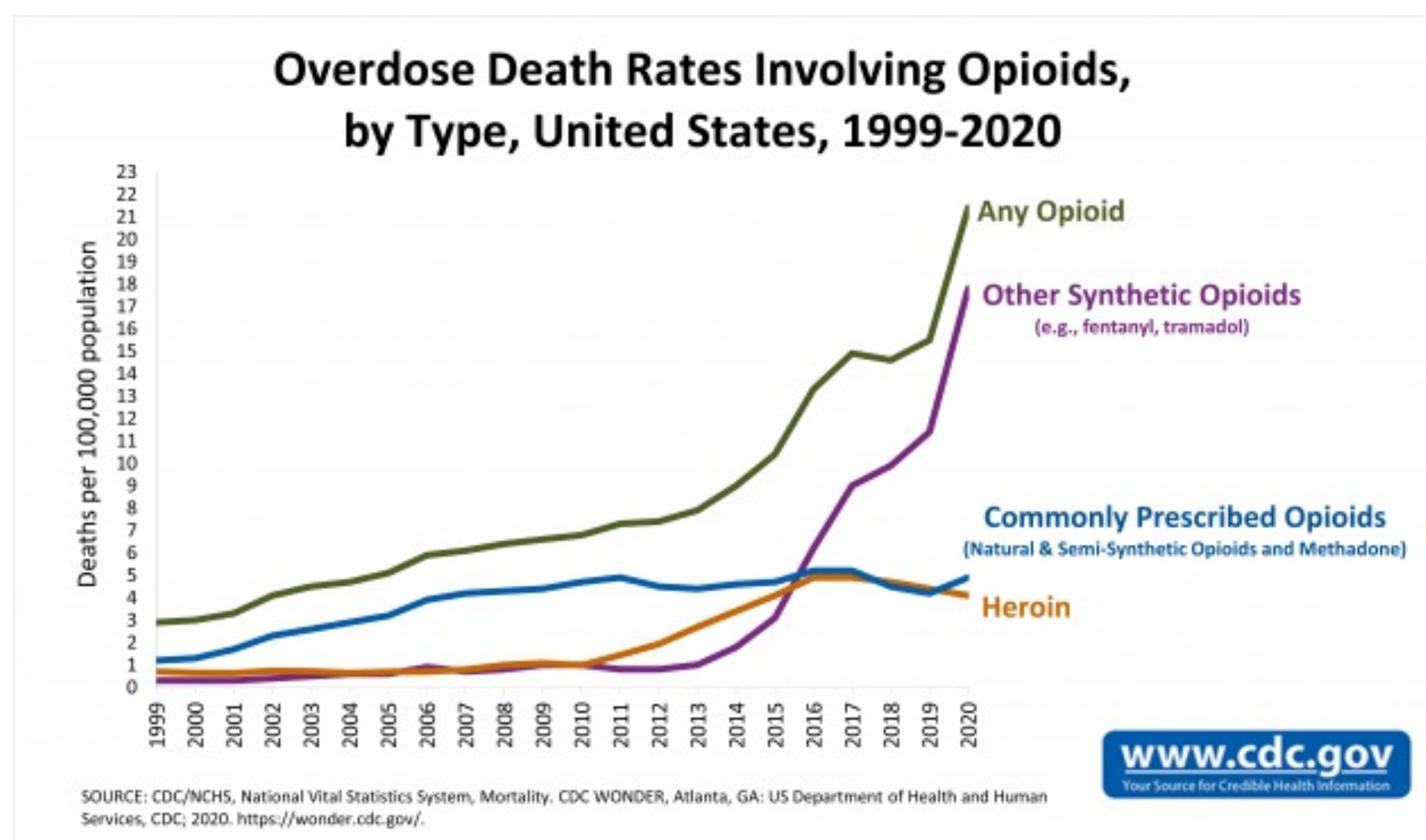


Perinatal fentanyl exposure disrupts brain mTOR pathways

Krystal Flores-Felix^{1,2}, John Page³, Janice Babus³, Philip H. Iffland II^{2,3}, and Asaf Keller²
University of Maryland School of Medicine, STAR-PREP¹, Anatomy and Neurobiology department², Neurology department³

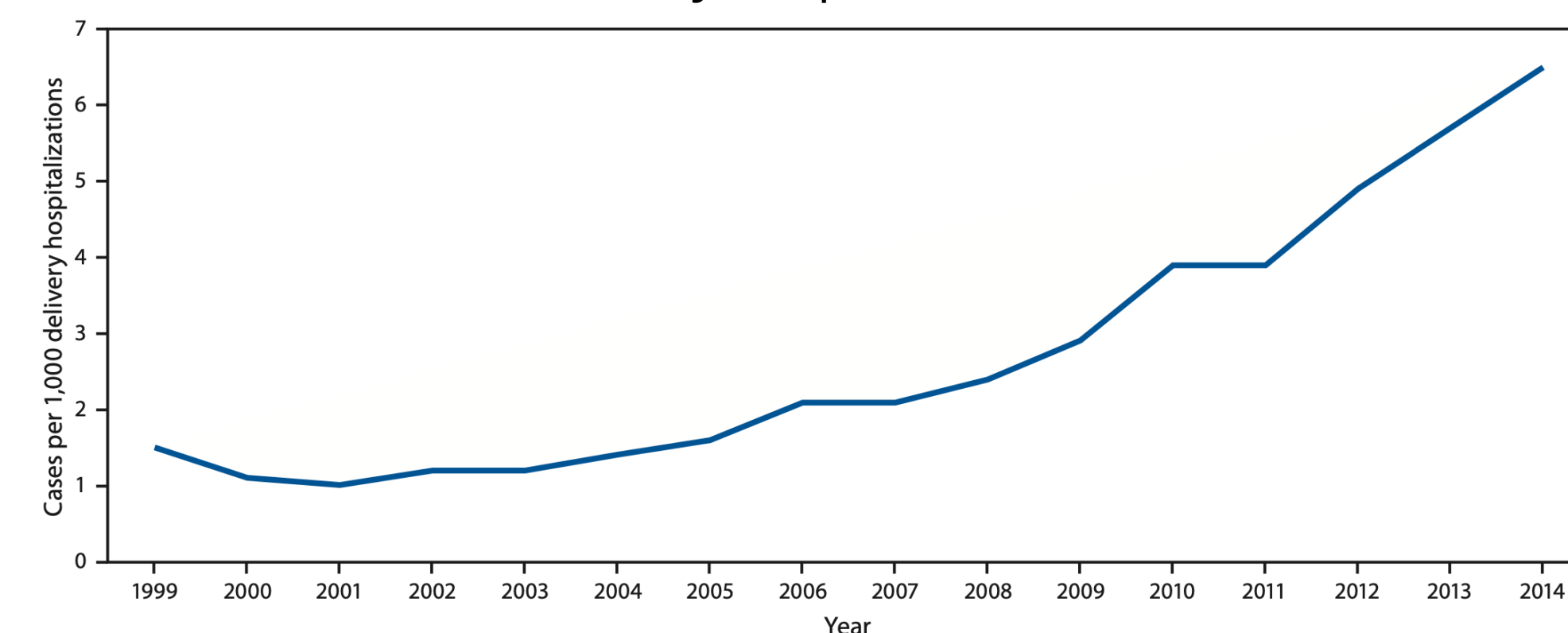
Introduction

- Fentanyl is a synthetic opioid 50 to 100 times more potent than morphine.

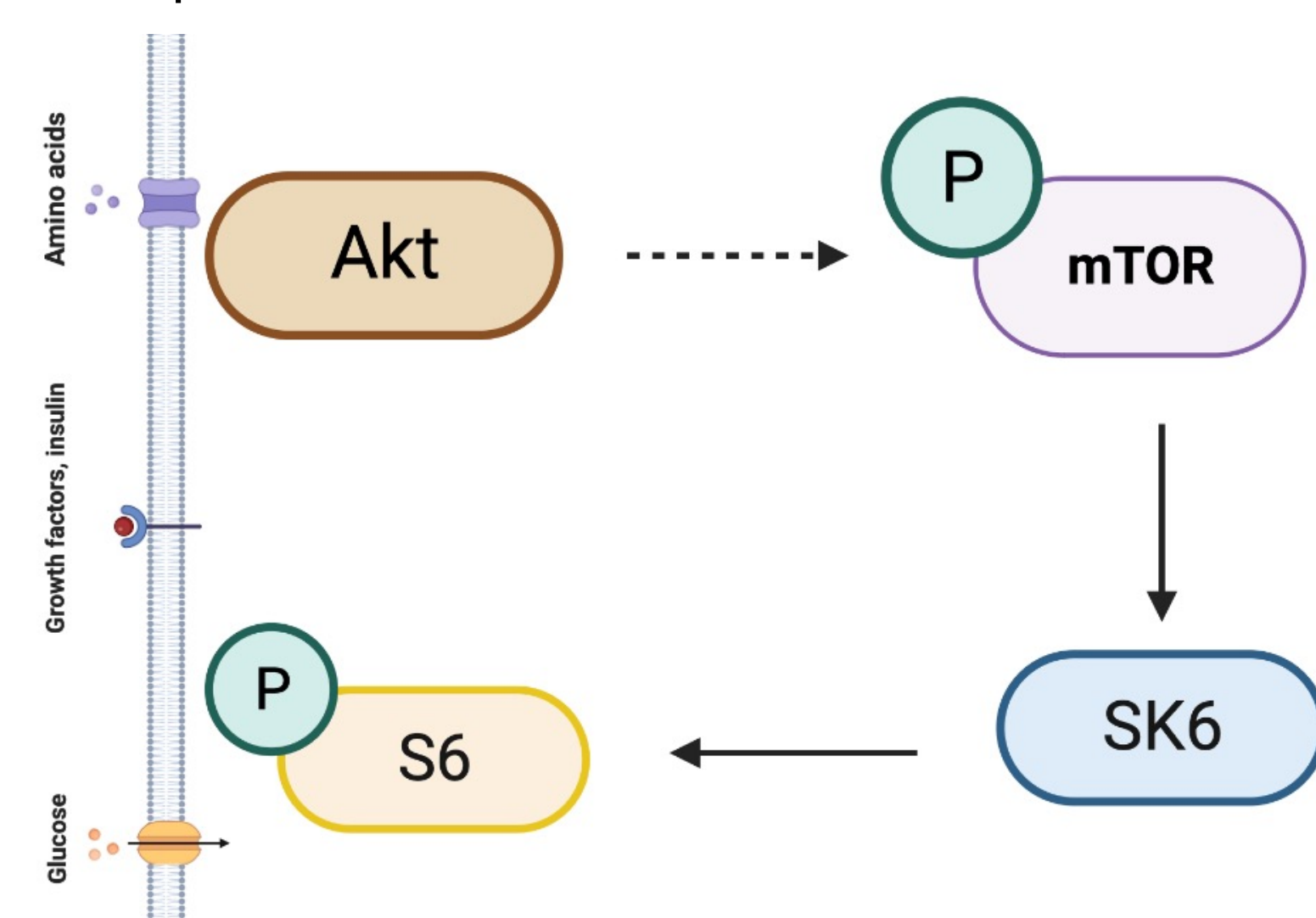


- Opioid related diagnosis in women have increased 131% from 2010-2017.

National prevalence of opioid use disorder per 1,000 delivery hospitalizations



- The mechanistic target of rapamycin (mTOR) pathway is a cell signaling pathway critically involved in brain development.



Hypothesis

- Lasting effects of perinatal fentanyl exposure are mediated by increased signaling in mTOR pathway.
- Prediction:** perinatal fentanyl exposure affects phosphorylation of ribosomal S6, a phospho-target of mTORC1.

Methodology

Figure 1: Fentanyl exposure timeline

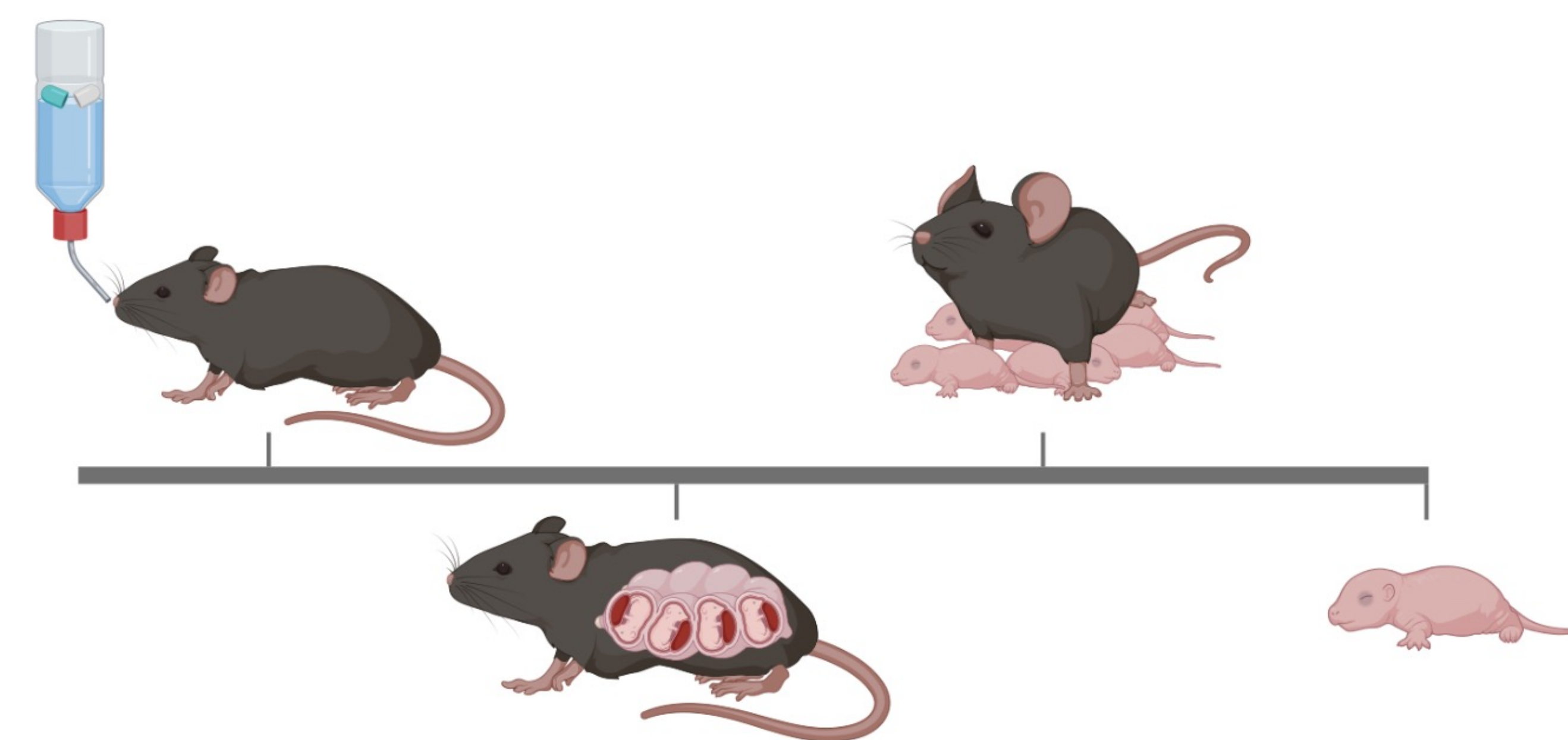
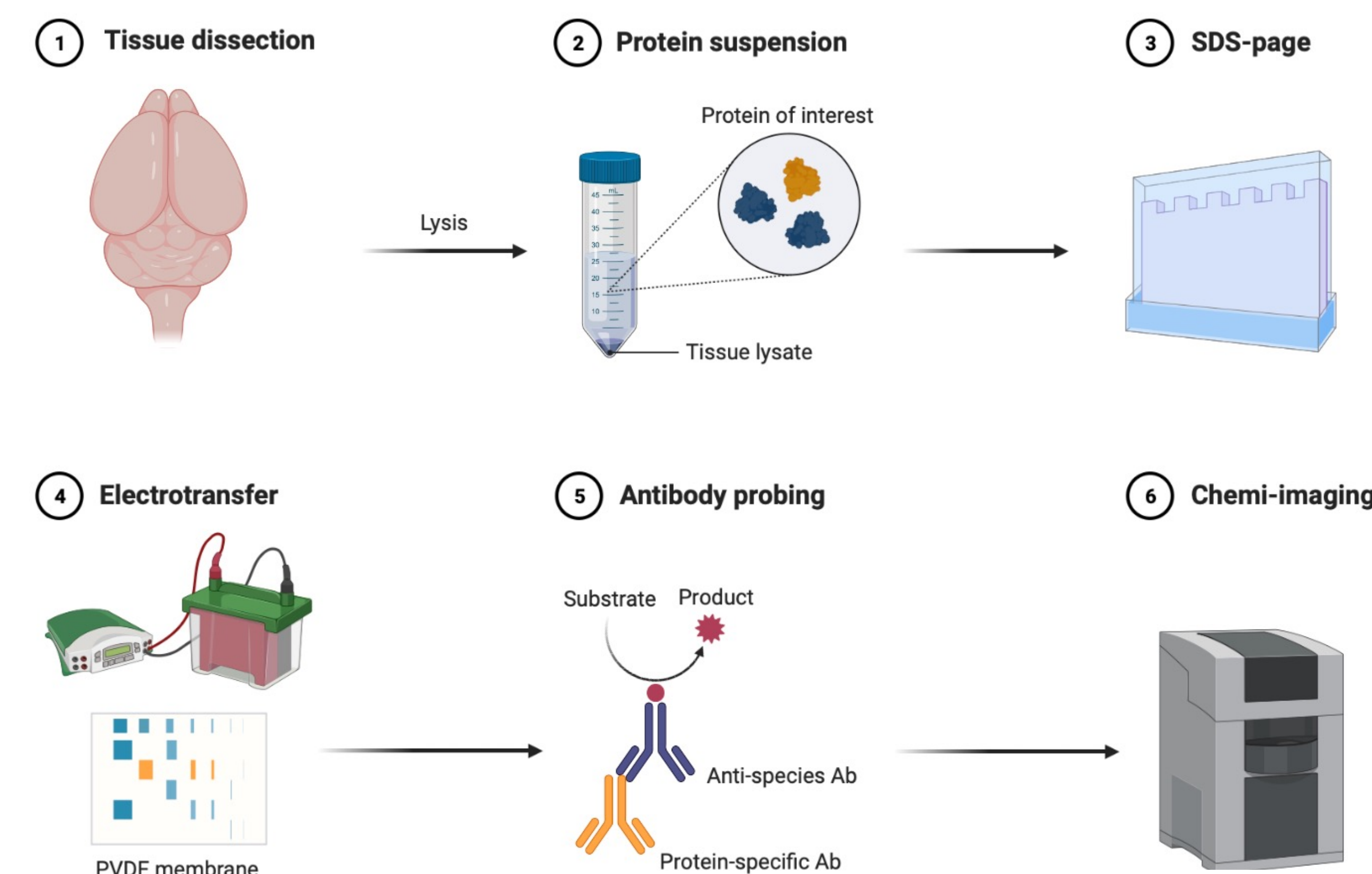
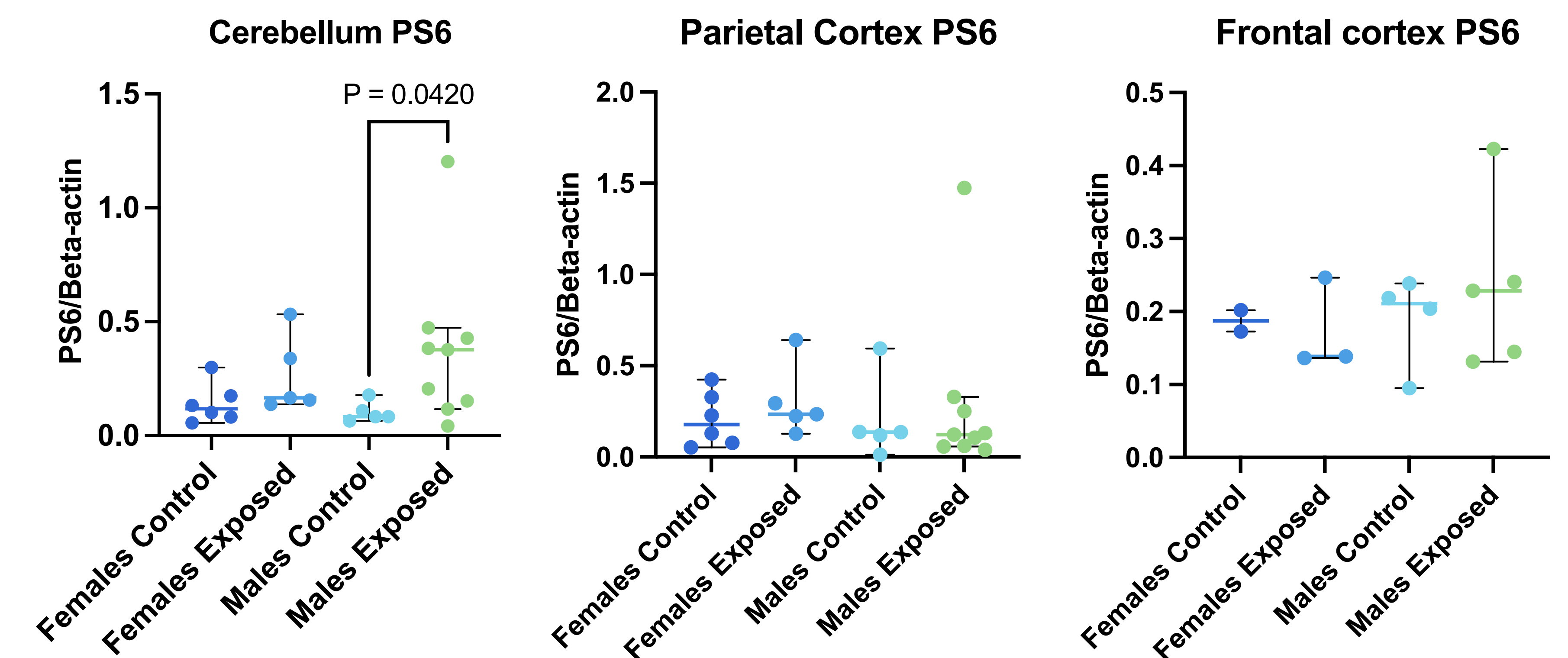


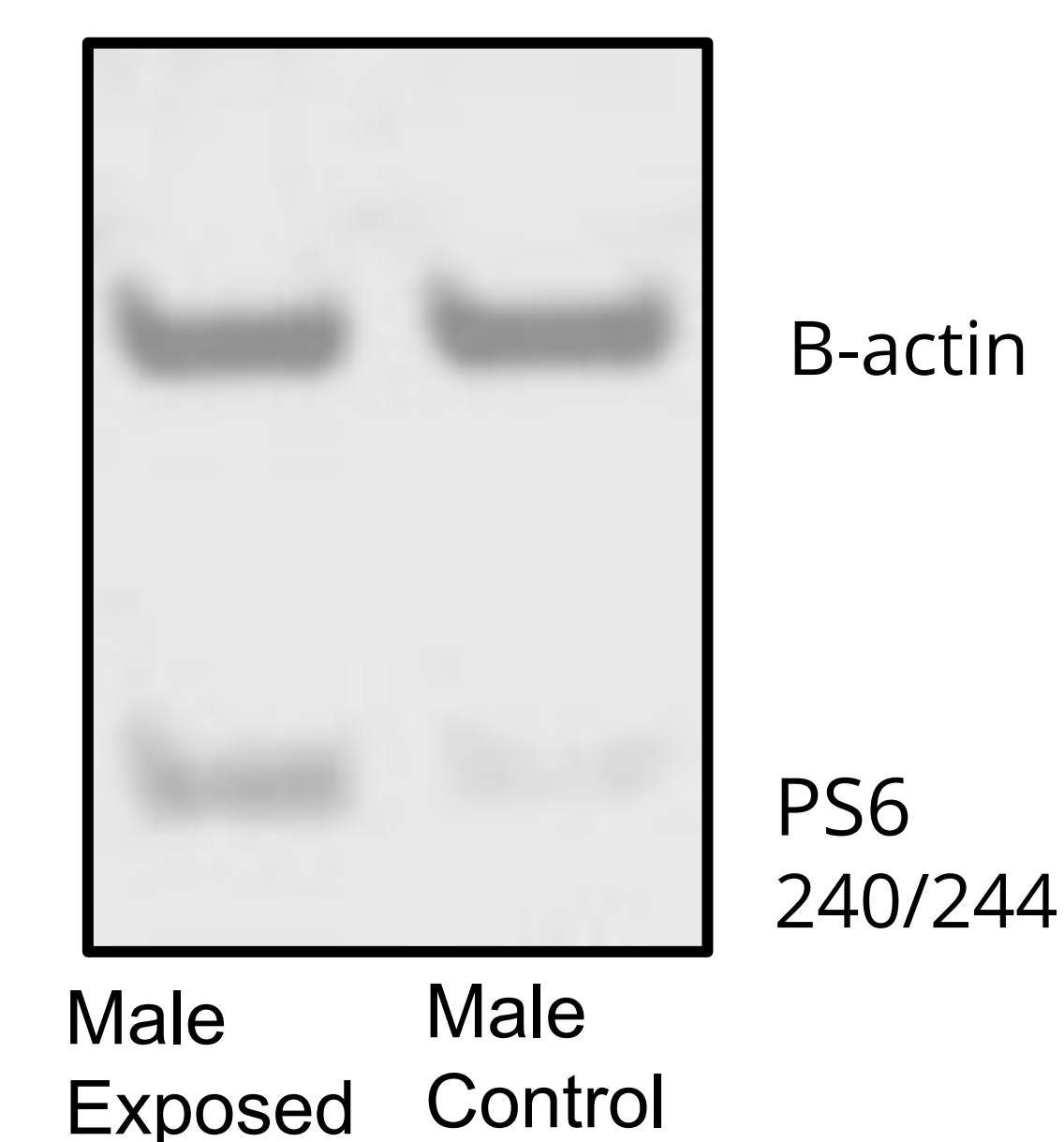
Figure 2: Western blot procedure



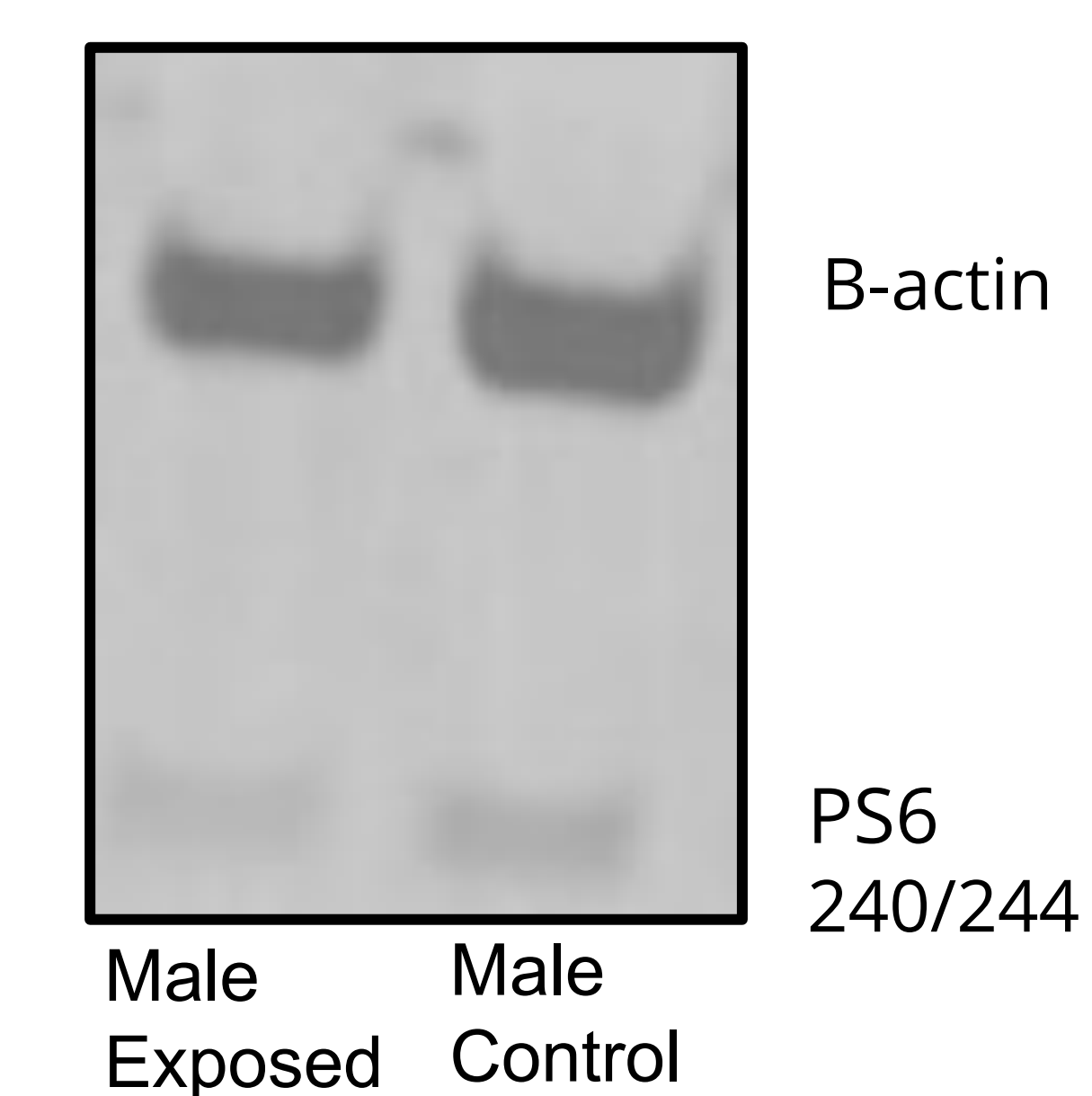
Results



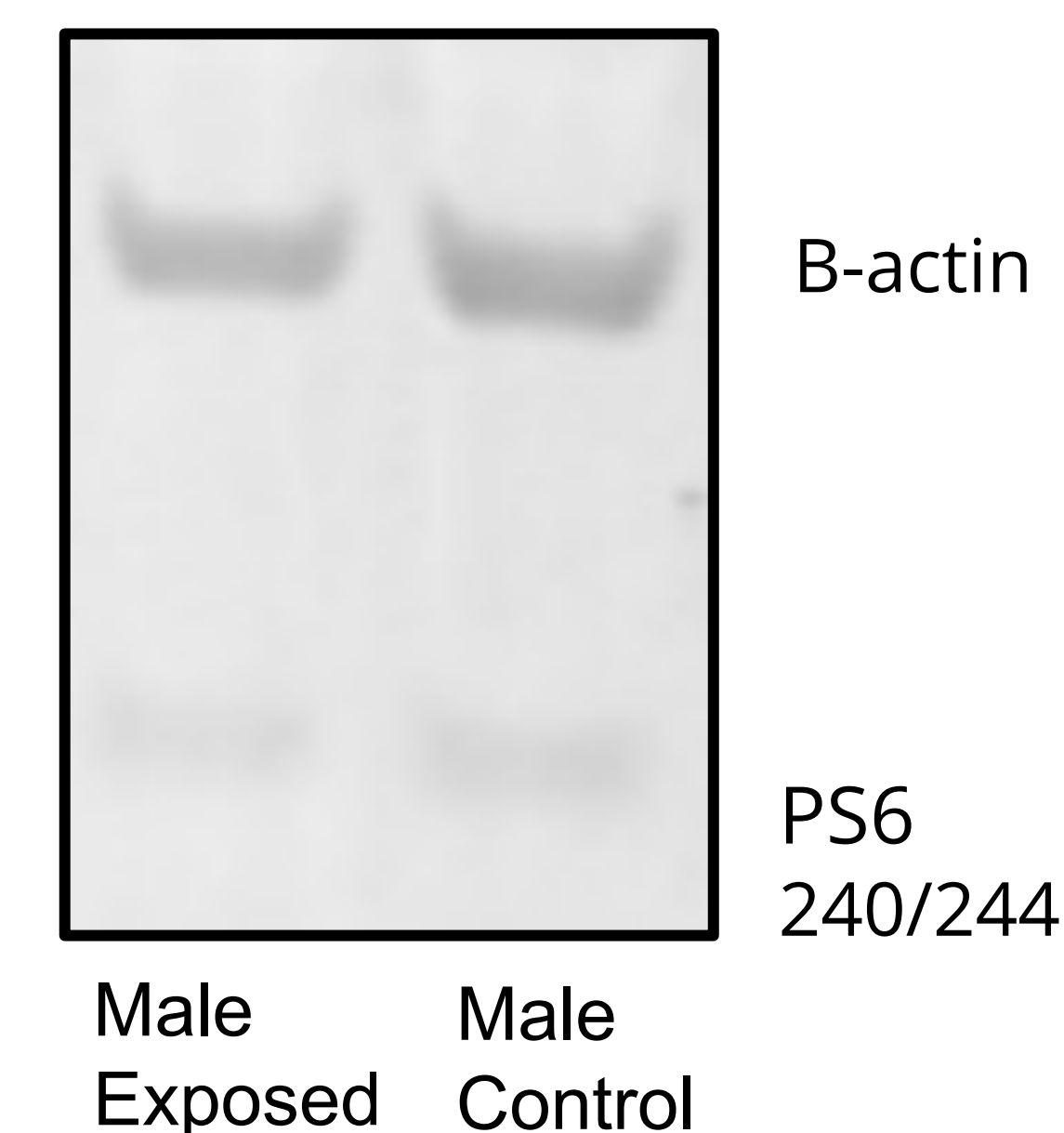
Cerebellum



Parietal Cortex



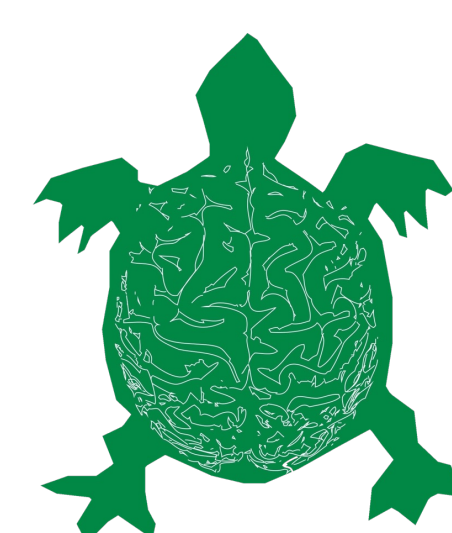
Frontal Cortex



Conclusion and future directions

- Taken together, our results suggest that perinatal fentanyl exposure results in increase levels of PS6, a downstream effector of mTOR.
- Histology analysis of mTOR downstream effector PS6 is also in the works.
- Future direction include administering mTOR antagonist, rapamycin, to investigate the potential reversal effect of perinatal fentanyl exposure on the brain.

Acknowledgments



LABORATORY OF SENSORY
PERCEPTION



NATIONAL INSTITUTE OF
NEUROLOGICAL
DISORDERS AND STROKE

The Iffland Lab
STAR-PREP
Science Training for Advancing biomedical Research

References

- Alipio, J. B., Haga, C., Fox, M. E., Arakawa, K., Balaji, R., Cramer, N., ... & Keller, A. (2021). Perinatal fentanyl exposure leads to long-lasting impairments in somatosensory circuit function and behavior. *Journal of Neuroscience*, 41(15), 3400-3417.
- Center for Disease Control and Prevention. Drug overdose death data. Available at: <https://www.cdc.gov/drugoverdose/data/statedeaths.html>. Accessed July 25, 2022.
- Haight, S.C., Ko, J.Y., Tong, V.T., Bohm, M.K., Callaghan, W.M. Opioid Use Disorder Documented at Delivery Hospitalization — United States, 1999–2014. *MMWR Morb Mortal Wkly Rep* 2018;67:845–849. DOI: <https://dx.doi.org/10.15585/mmwr.mm6731a1>.
- National Institute of Drug Abuse. Overdose death rates. Available at: <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>. Accessed July 25, 2022.