Investigating the impact of the E200K mutation on Creutzfeldt-Jakob Disease

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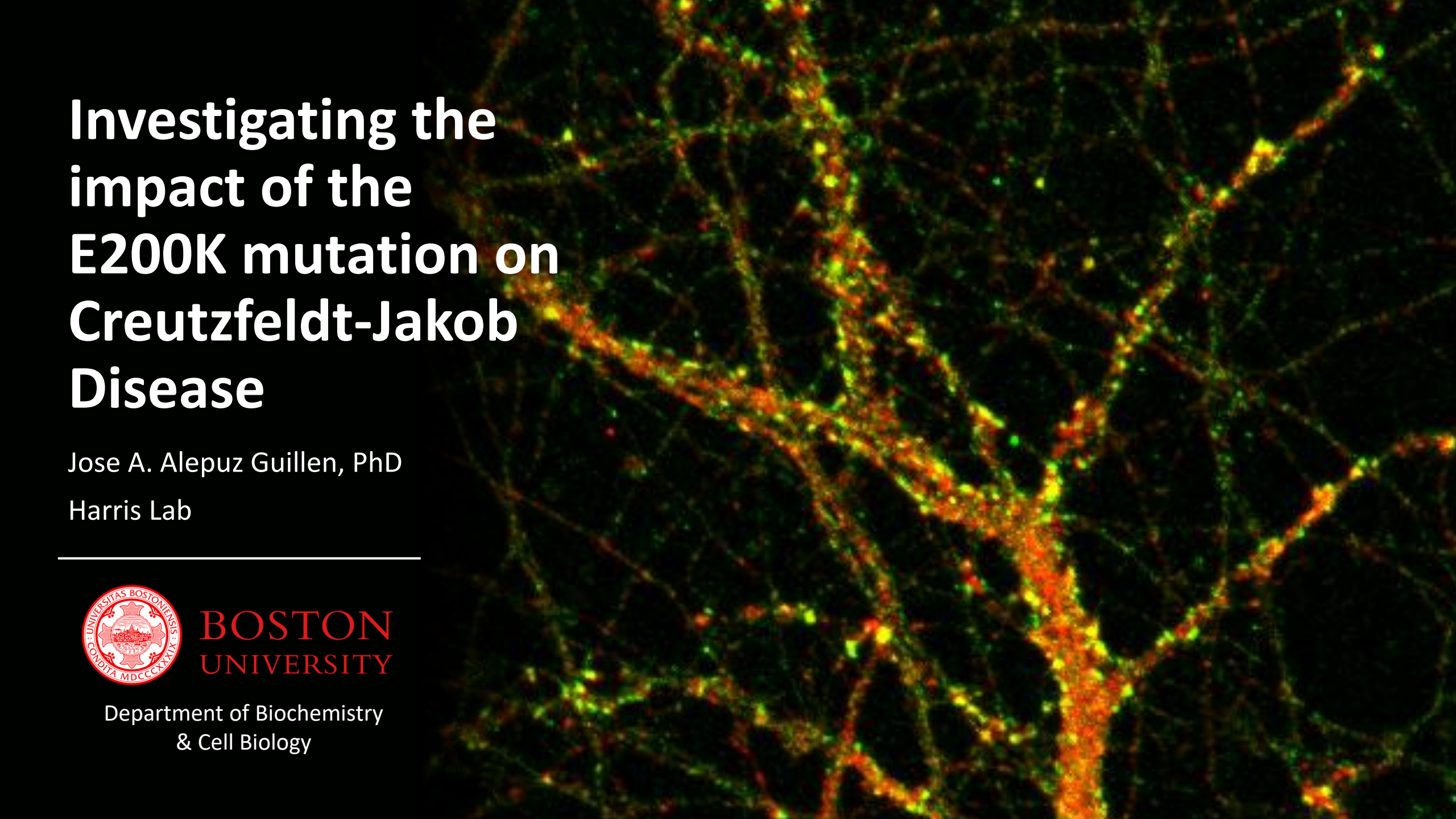
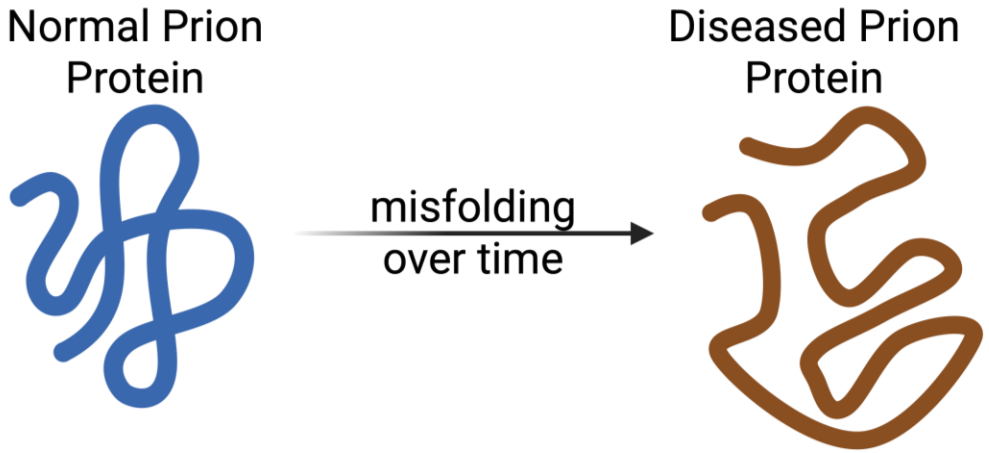
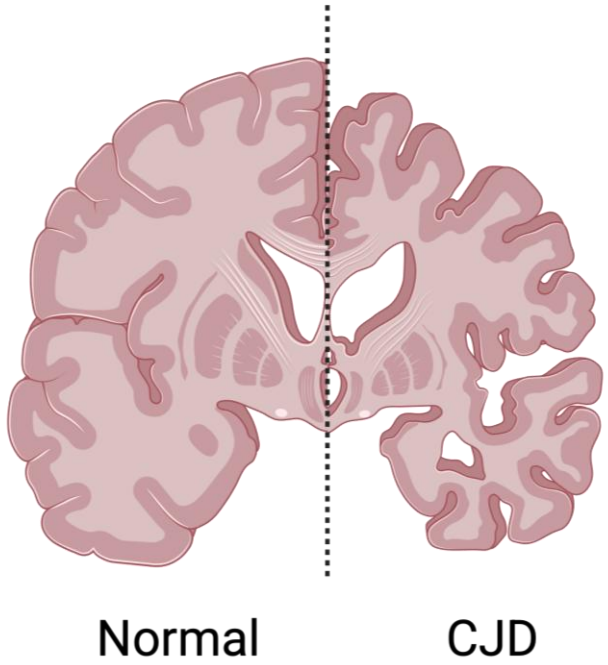


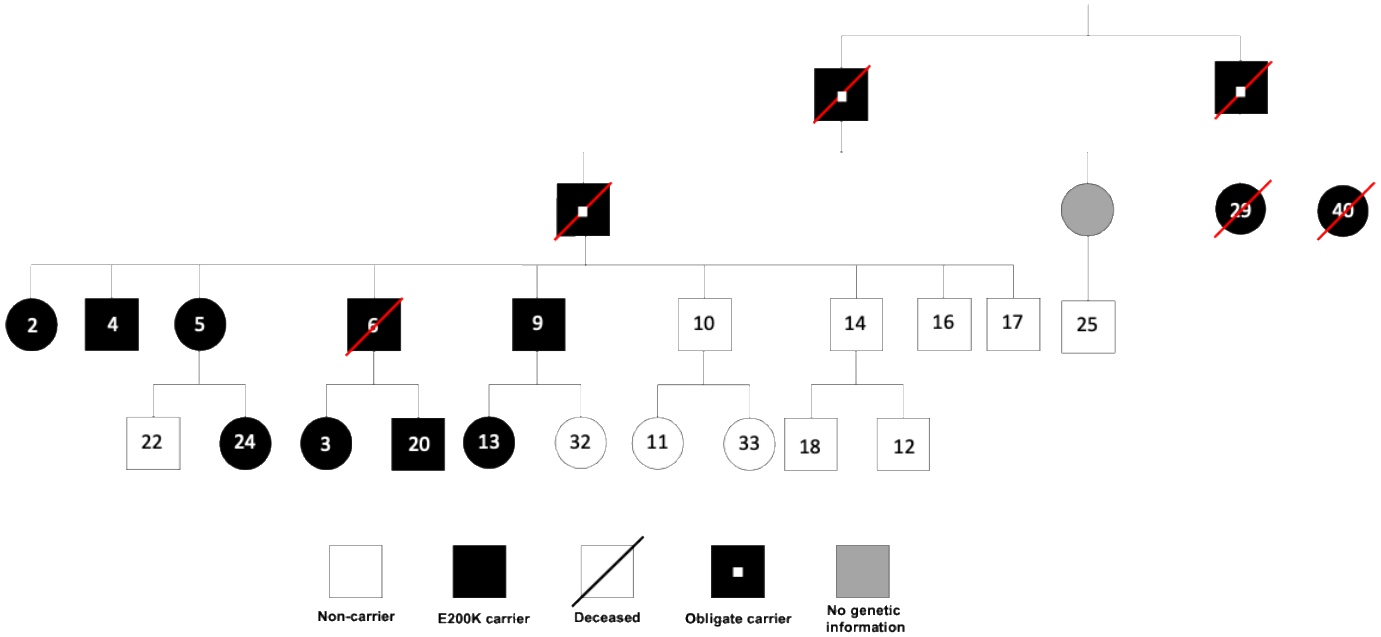
How does the E200K mutation alter neurons in the human brain?

E200K PRNP mutation is the most prevalent mutation in genetic CJD





Our approach: human-derived E200K neurons



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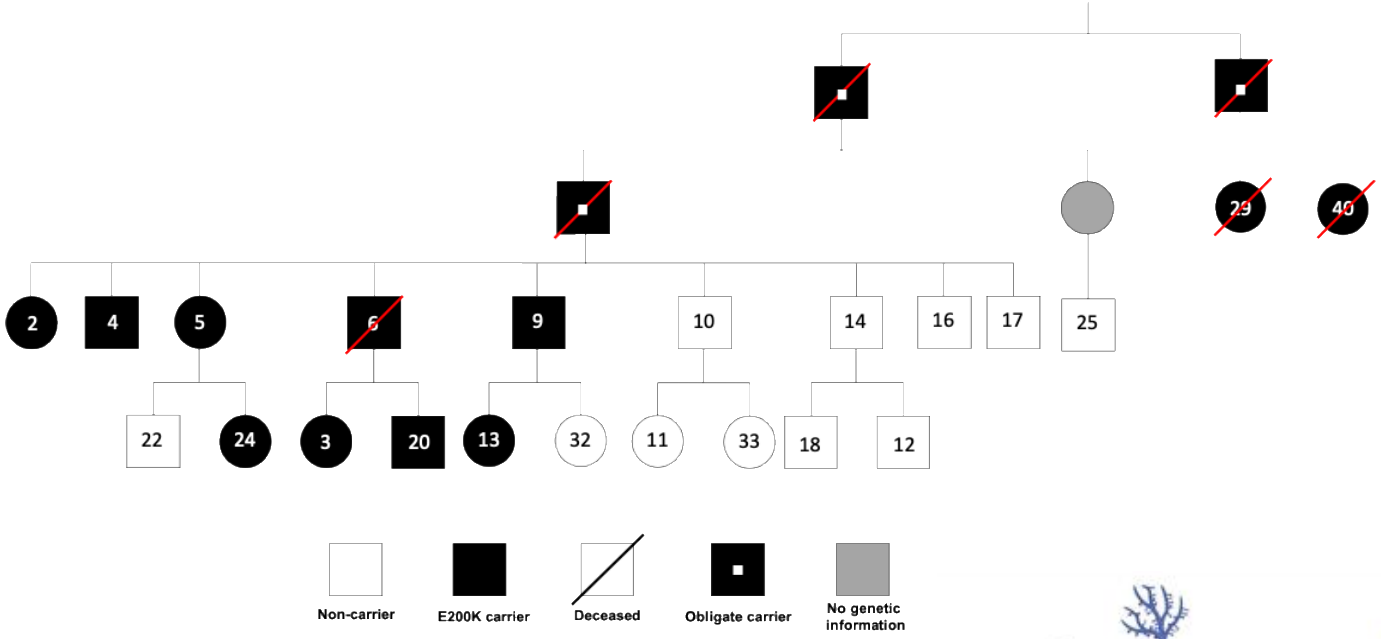
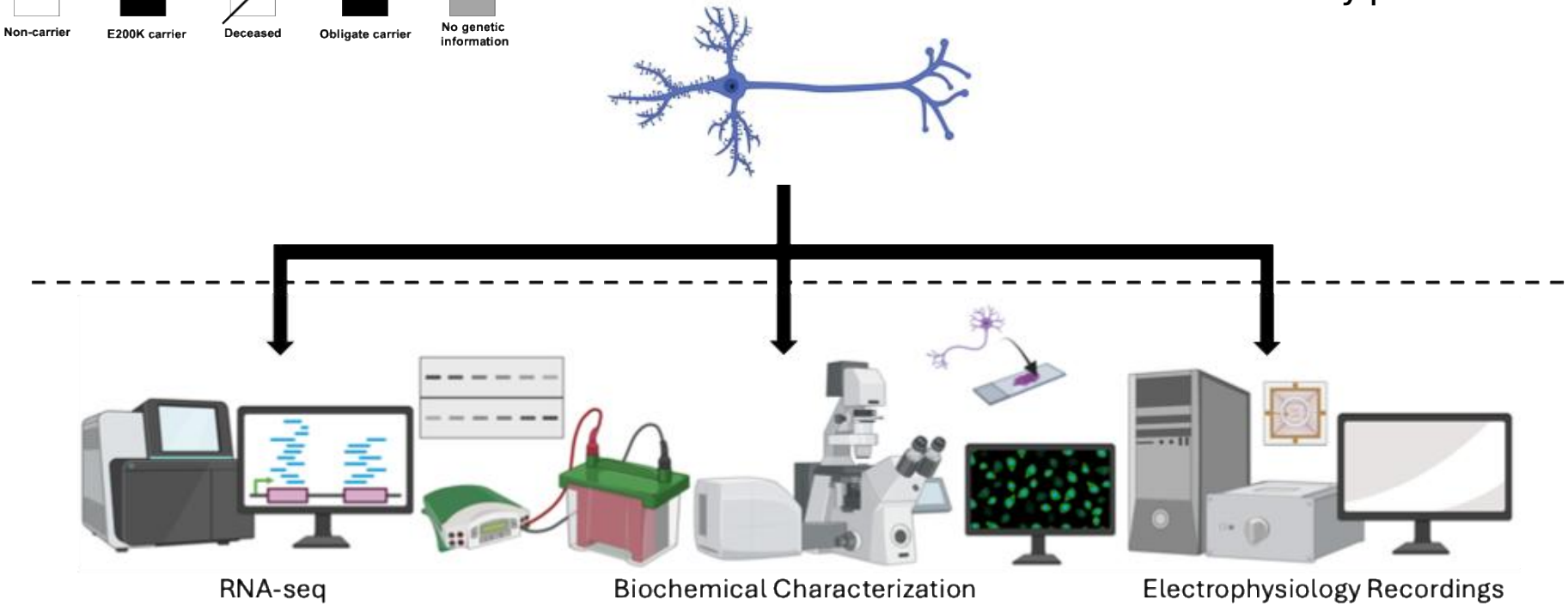


We have been able to derive neurons from a family carrying the E200K mutation.

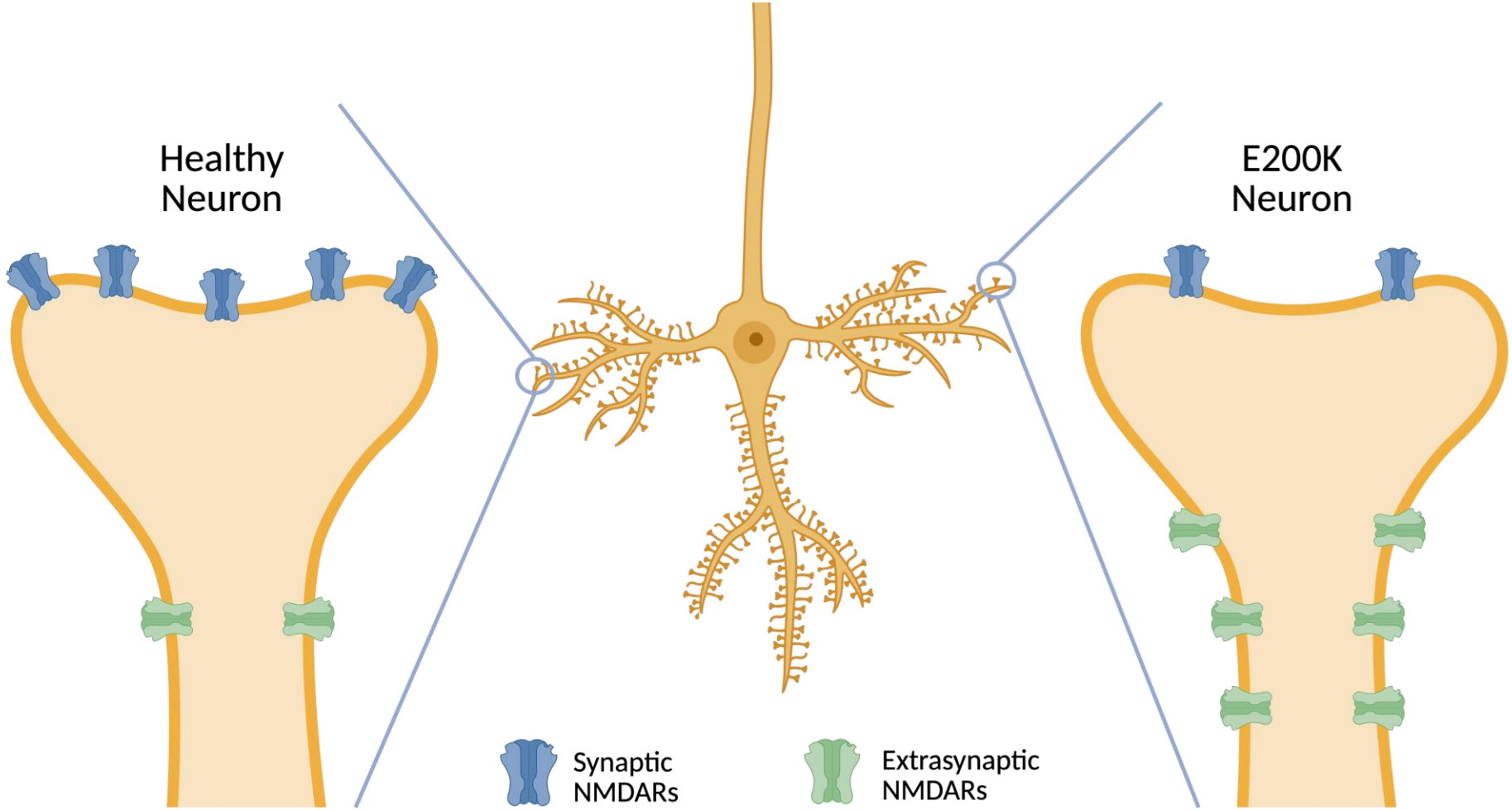
We used neurons carrying the mutation and neurons where the mutation was corrected to test different aspects of neuronal activity, such as:

- Gene expression
- Protein expression and location
- Electrical activity patterns



E200K mutation changes neuronal activity through receptor location

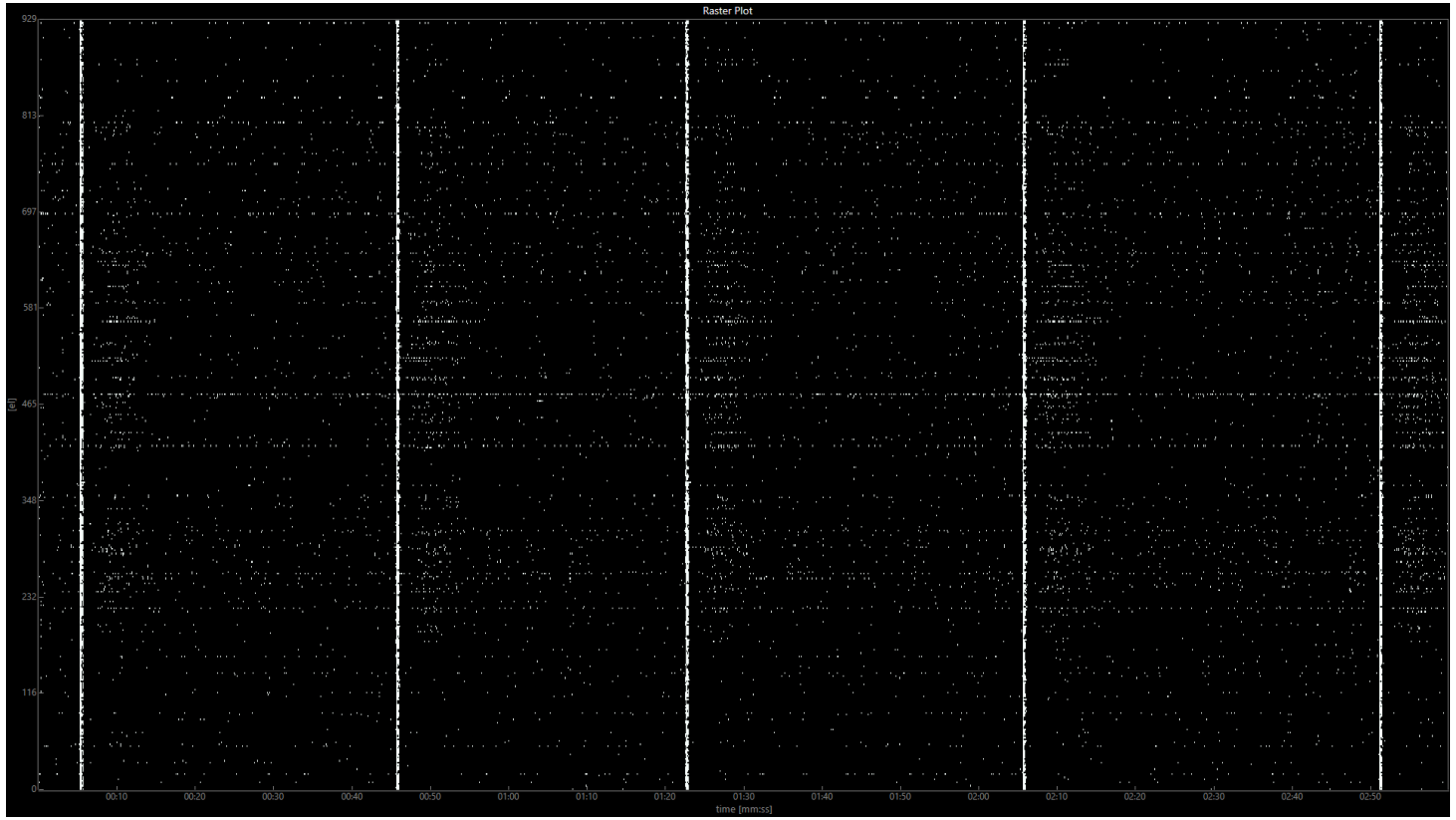
Neurons expressing the E200K prion mutation have a localization difference in receptors involved in neuronal electrical activity compared to healthy neurons.

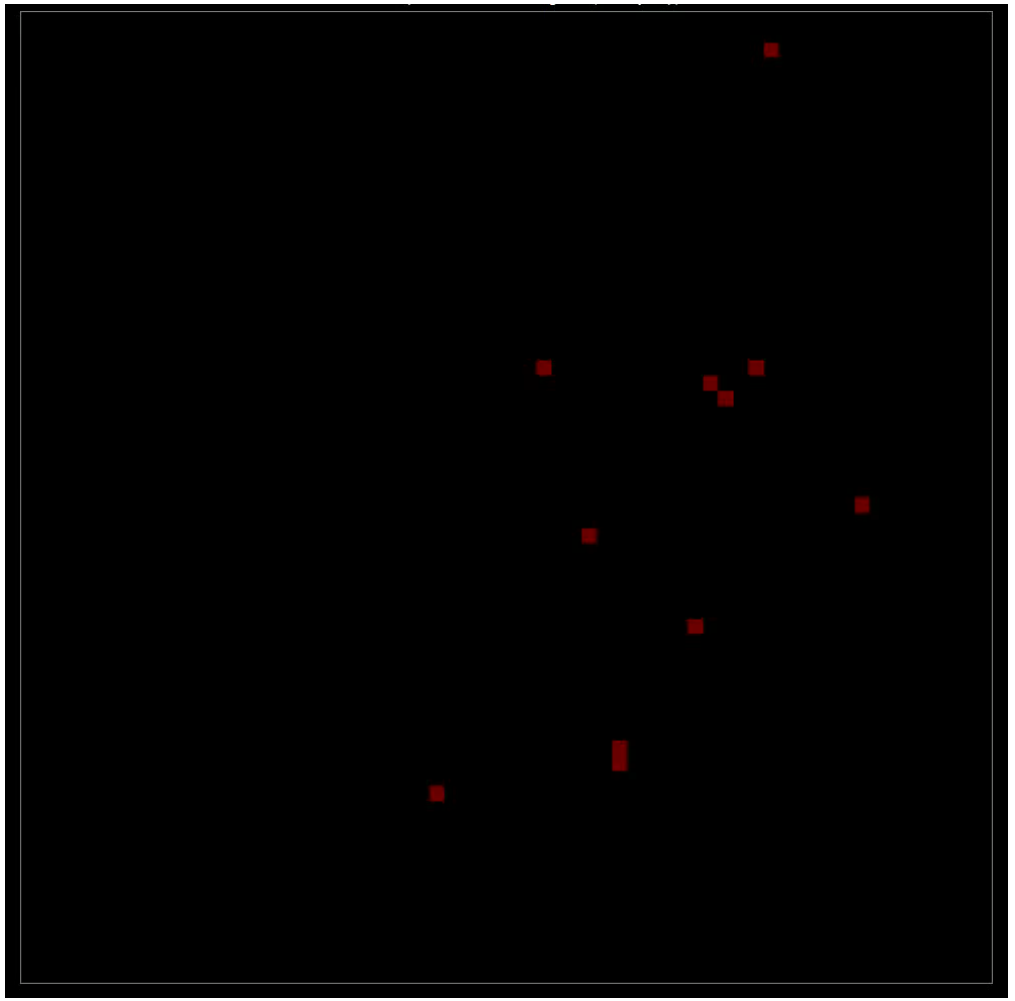


E200K mutation changes neuronal activity through receptor location

This location difference changes the electrical activity pattern of the neurons.

Healthy Neurons





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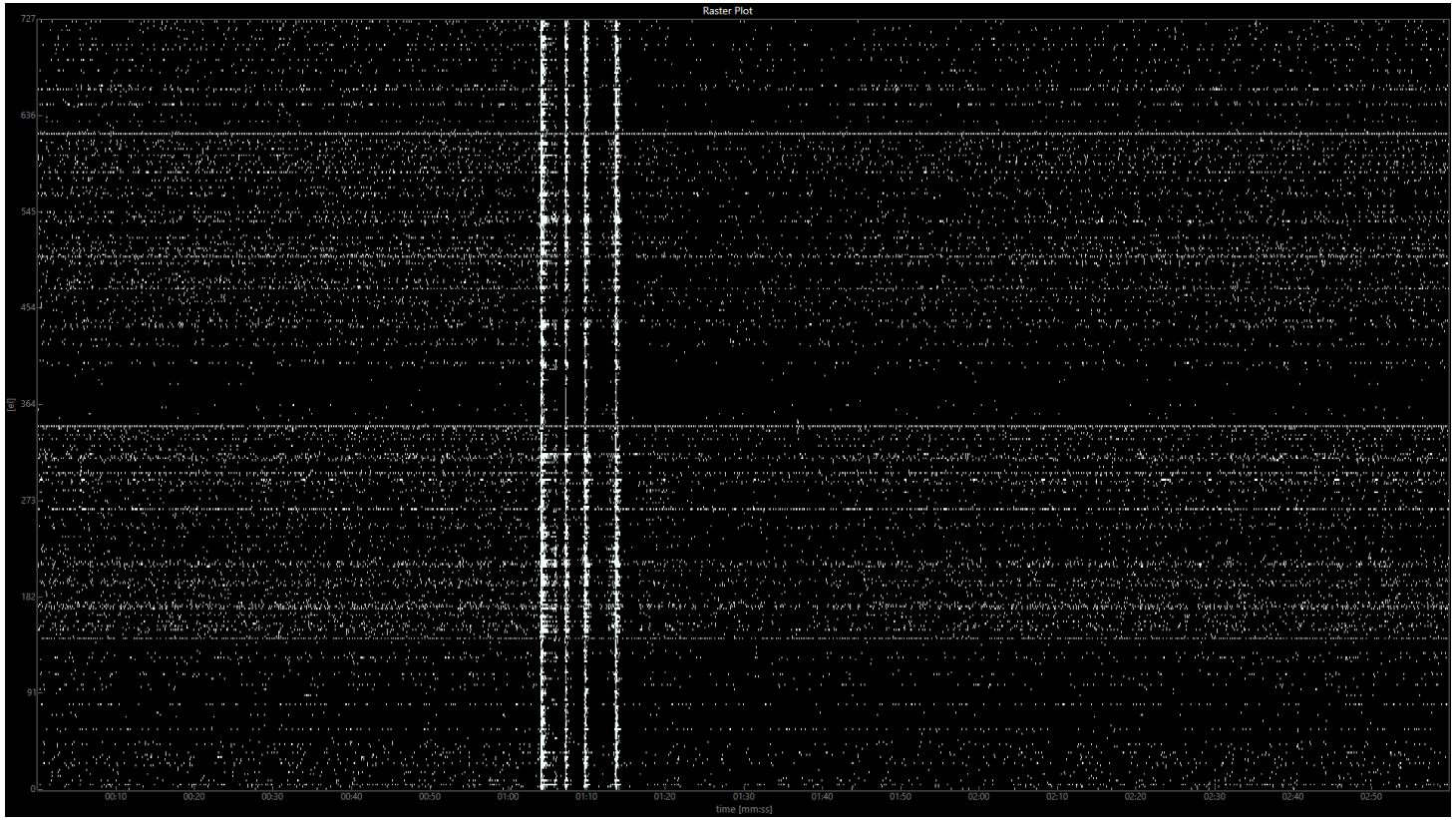
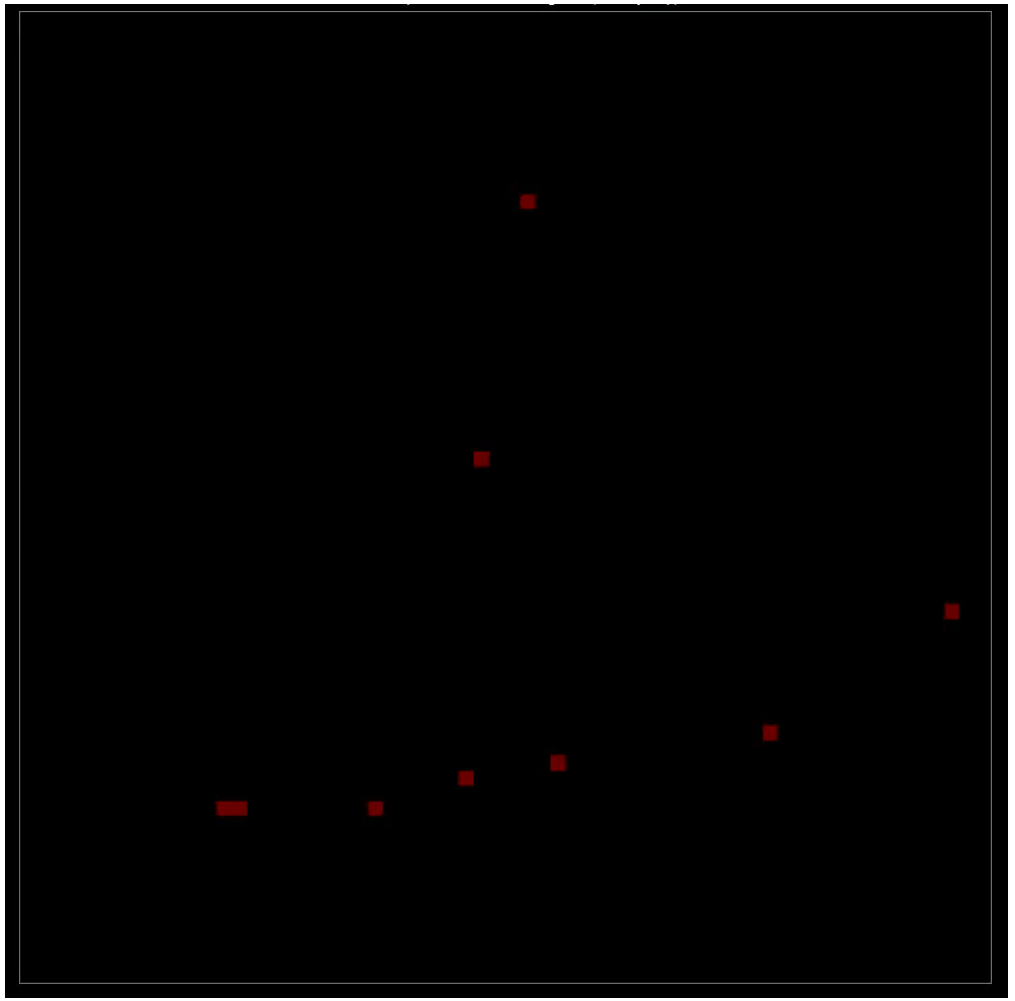
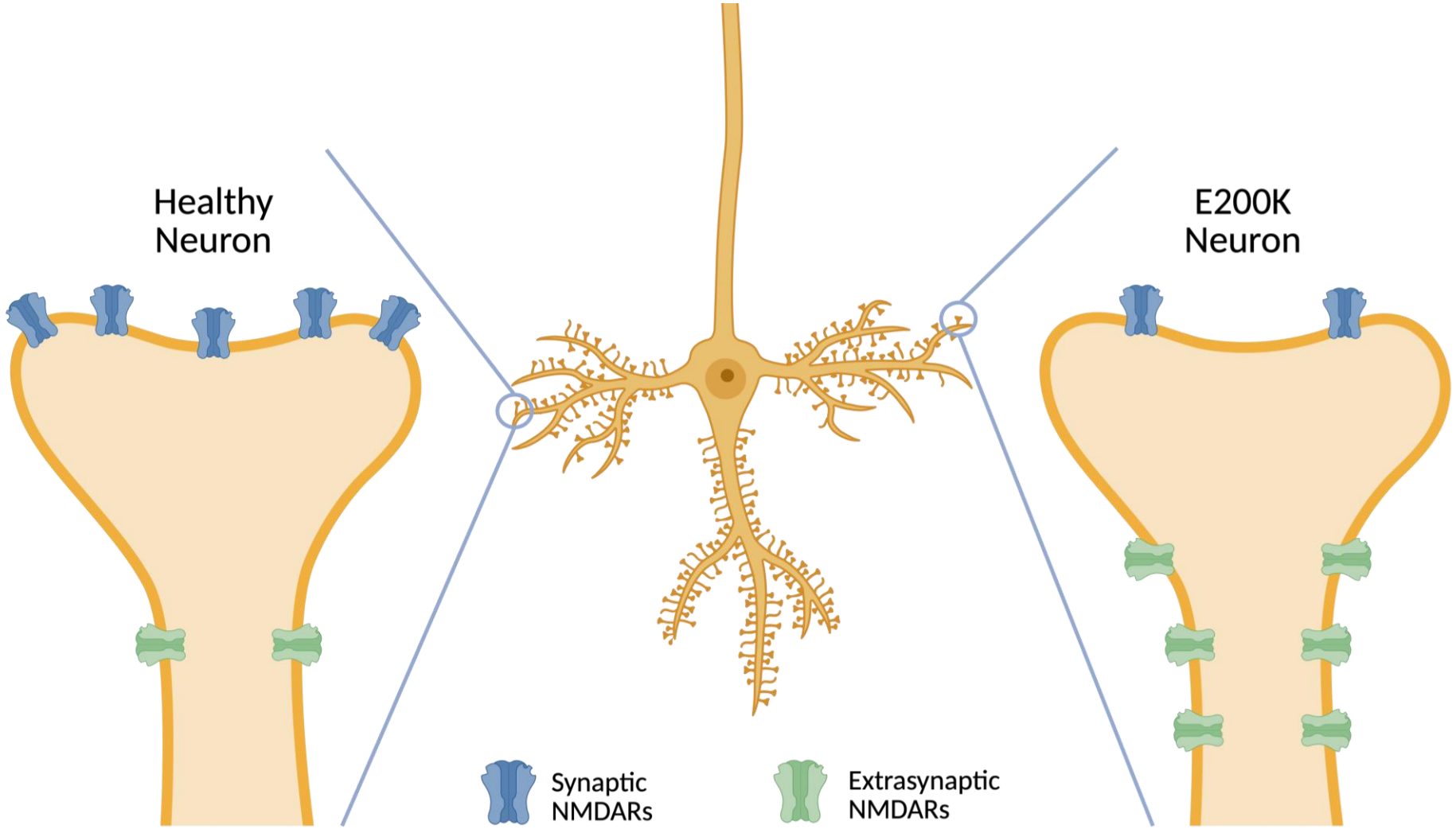
E200K Neurons





E200K mutation changes neuronal activity through receptor location

The mutation also changes the functionality of the neurons, specifically how they react to the same stimulus.



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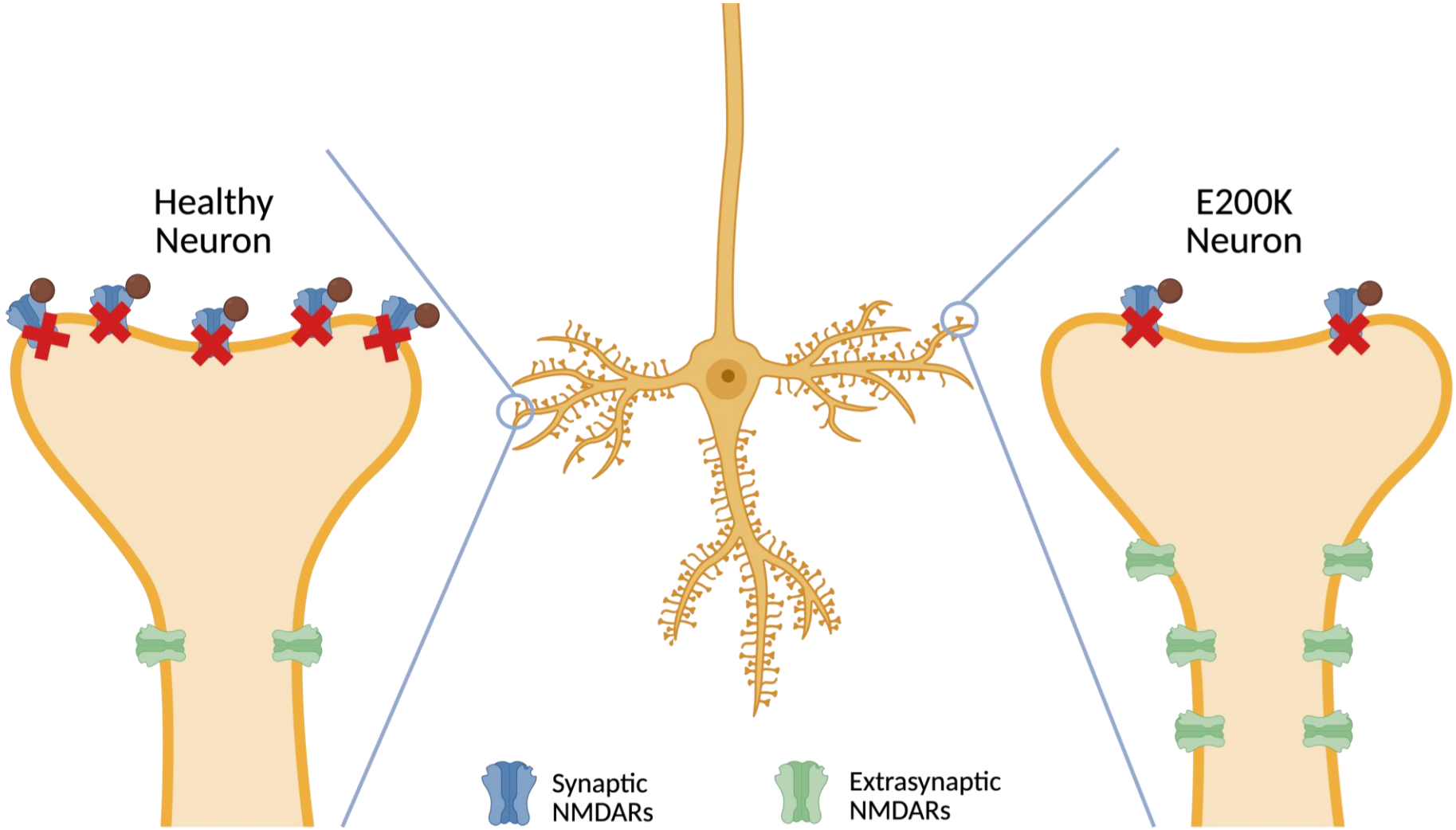

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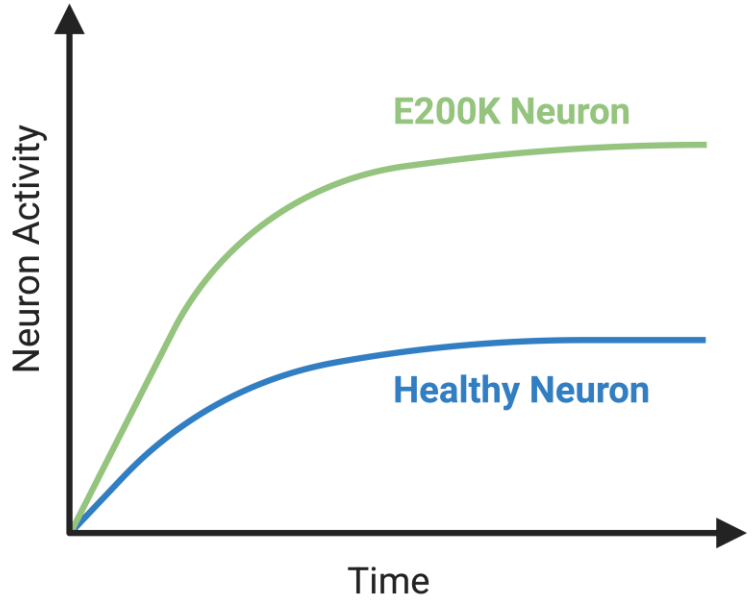

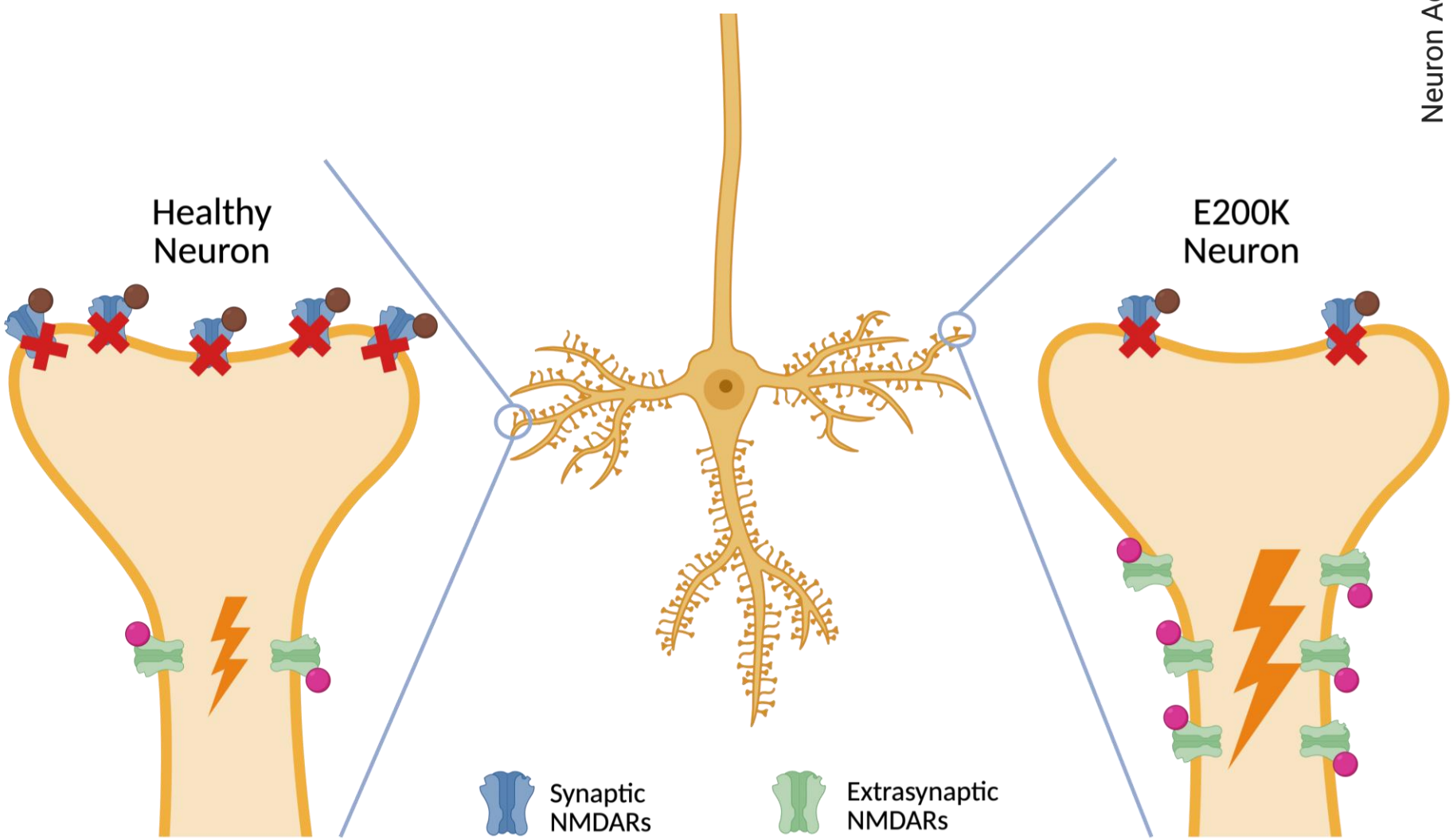

Implications and future work

We have identified how the E200K prion mutation affects neuronal activity, potentially causing some of the symptoms involved in CJD.

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By identifying its impact on synaptic receptors, we can target such receptors during disease to alleviate symptoms linked to these faulty receptors.

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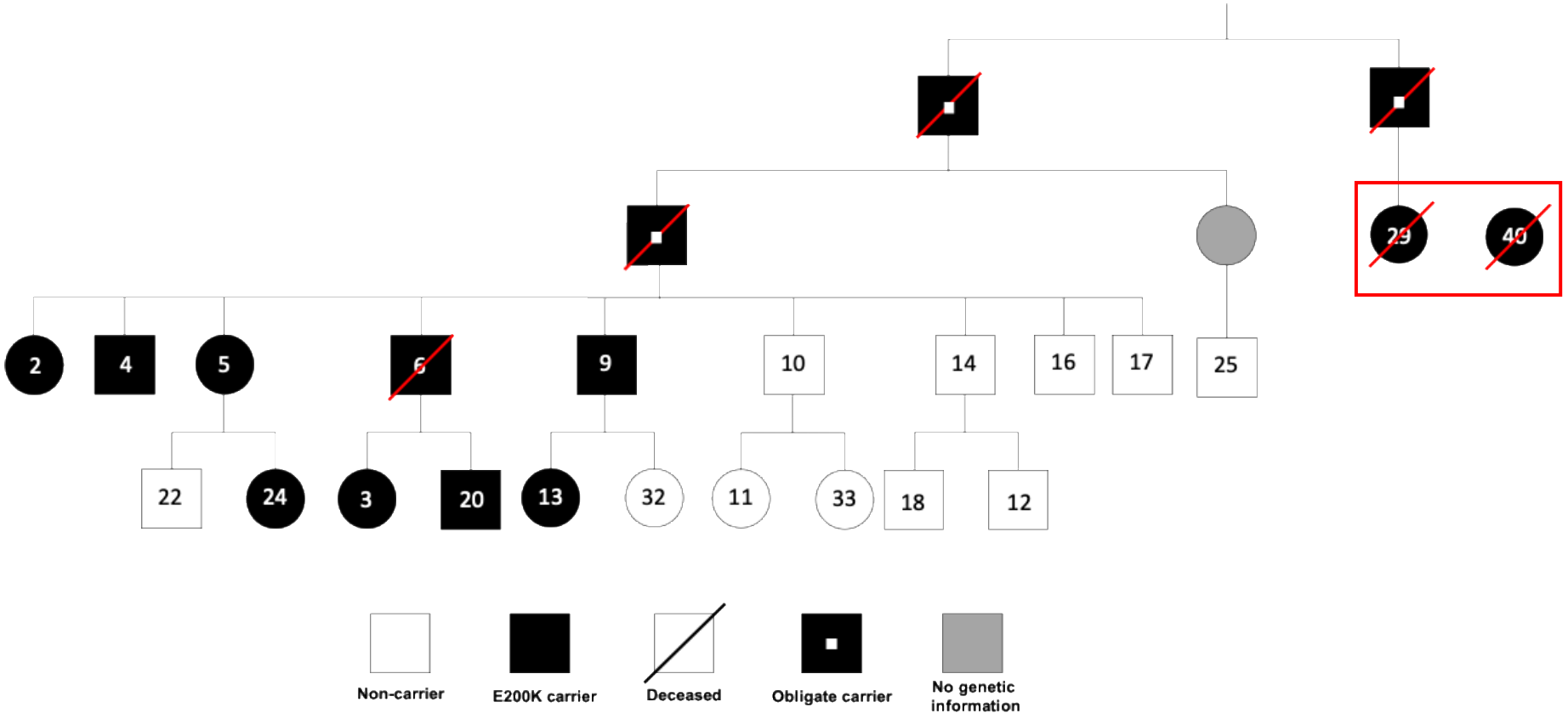
We also have neurons from other family members which carry the mutation; however, they died past the age of 90 with no signs of suffering from CJD.

These neurons will allow us to further investigate why these people carrying the E200K mutation did not die of CJD and point us towards a potential treatments for those carrying the mutation.



Acknowledgements

Harris Lab

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