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NeuroD1 AAV-Based Gene Therapy for Functional Brain Repair after Ischemic Injury through In Vivo Astrocyte-to-Neuron Conversion.

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NeuroD1 AAV-Based Gene Therapy for Functional Brain Repair after Ischemic Injury through In Vivo Astrocyte-to-Neuron Conversion

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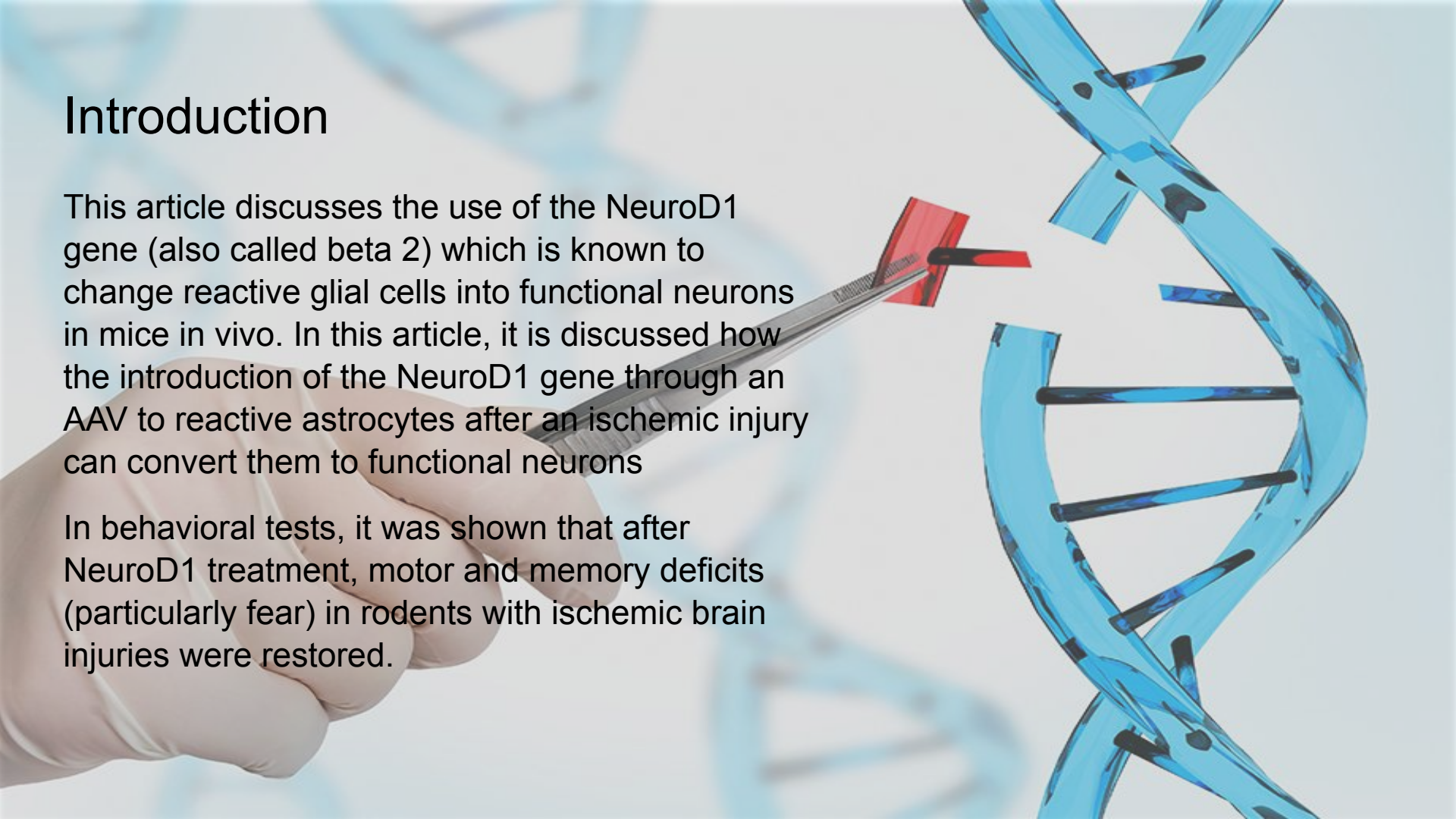
Introduction

This article discusses the use of the NeuroD1 gene (also called beta 2) which is known to change reactive glial cells into functional neurons in mice in vivo. In this article, it is discussed how the introduction of the NeuroD1 gene through an AAV to reactive astrocytes after an ischemic injury can convert them to functional neurons

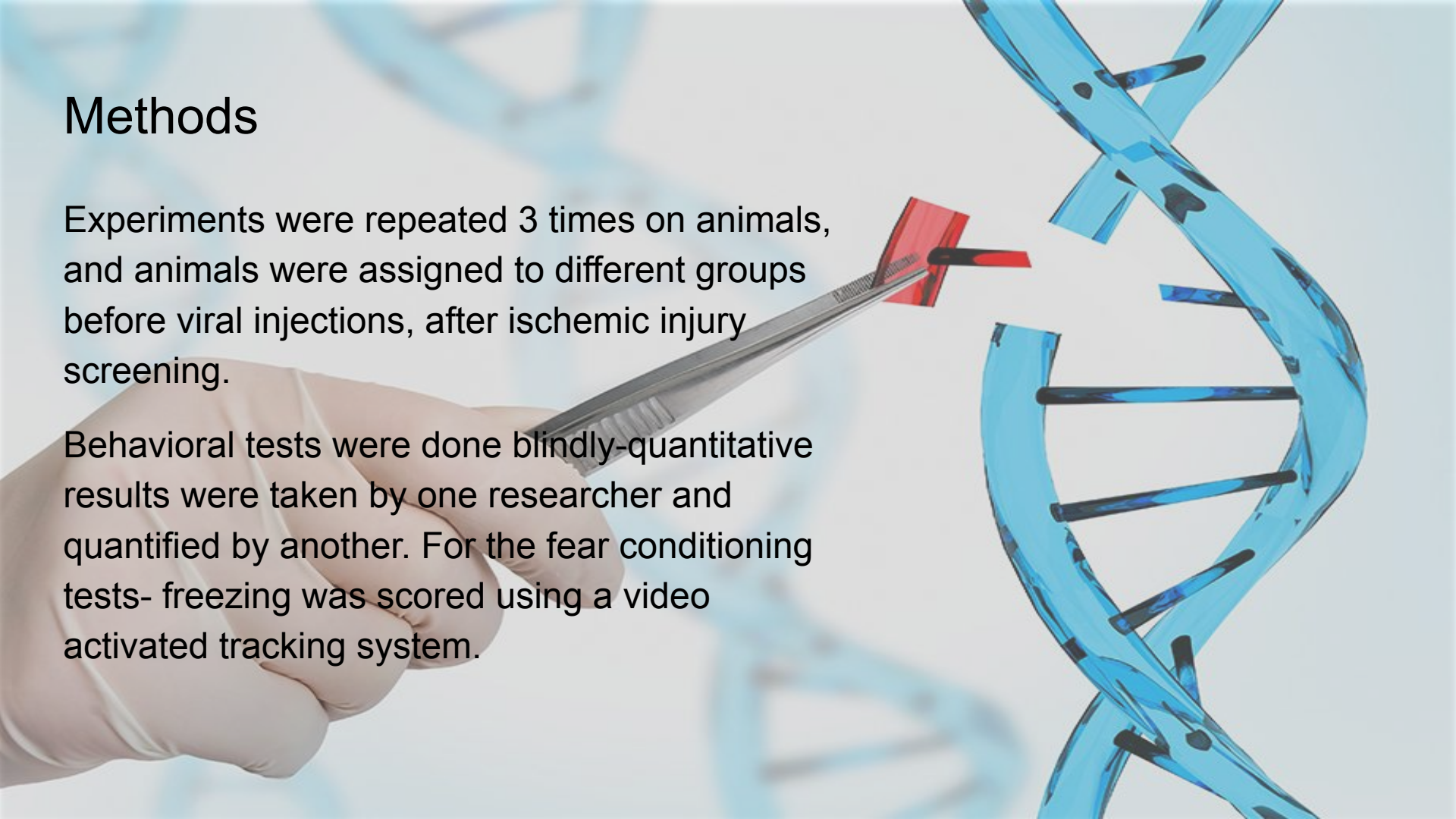
In behavioral tests, it was shown that after NeuroD1 treatment, motor and memory deficits (particularly fear) in rodents with ischemic brain injuries were restored.



Methods

Experiments were repeated 3 times on animals, and animals were assigned to different groups before viral injections, after ischemic injury screening.

Behavioral tests were done blindly-quantitative results were taken by one researcher and quantified by another. For the fear conditioning tests- freezing was scored using a video activated tracking system.

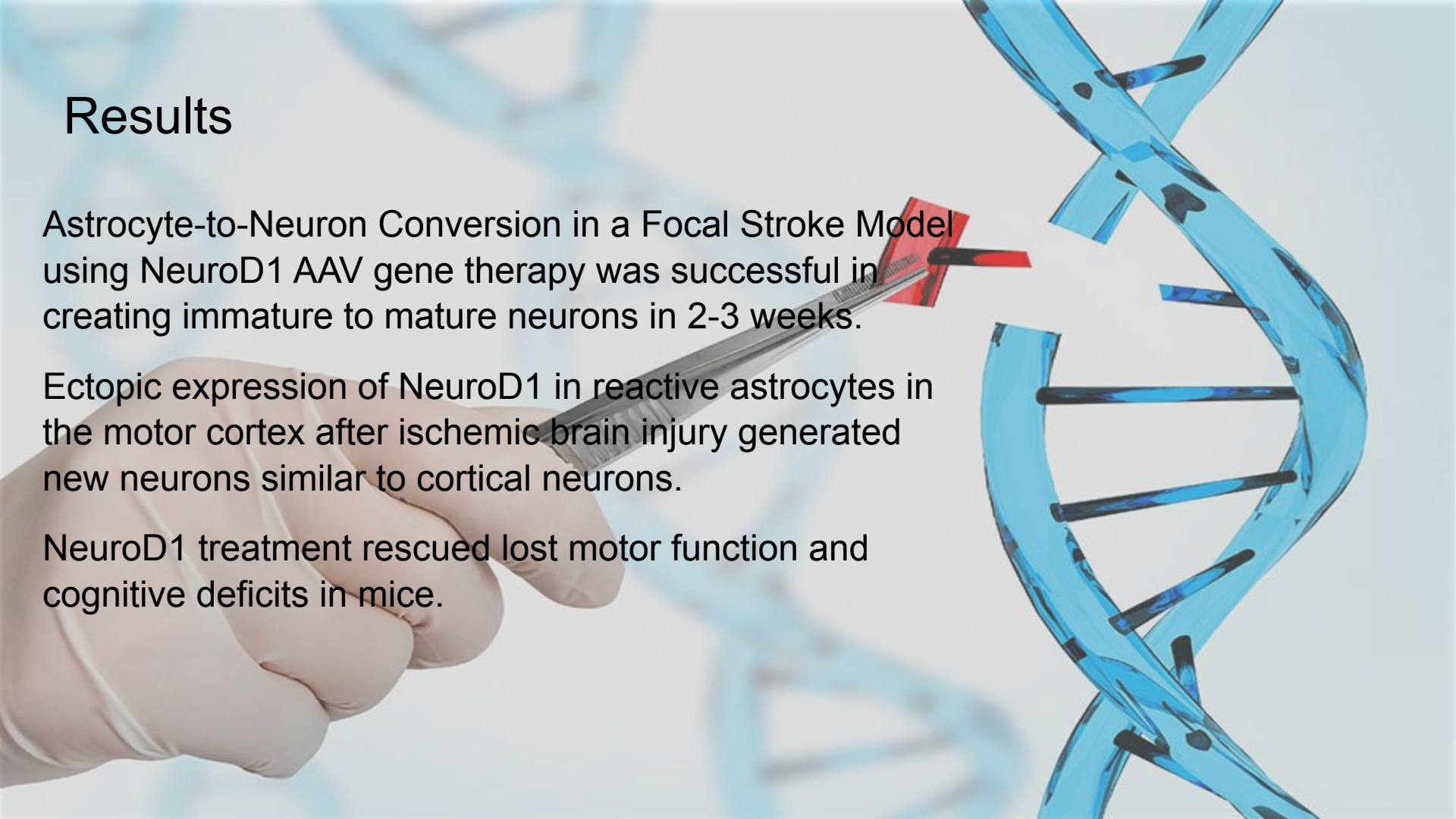


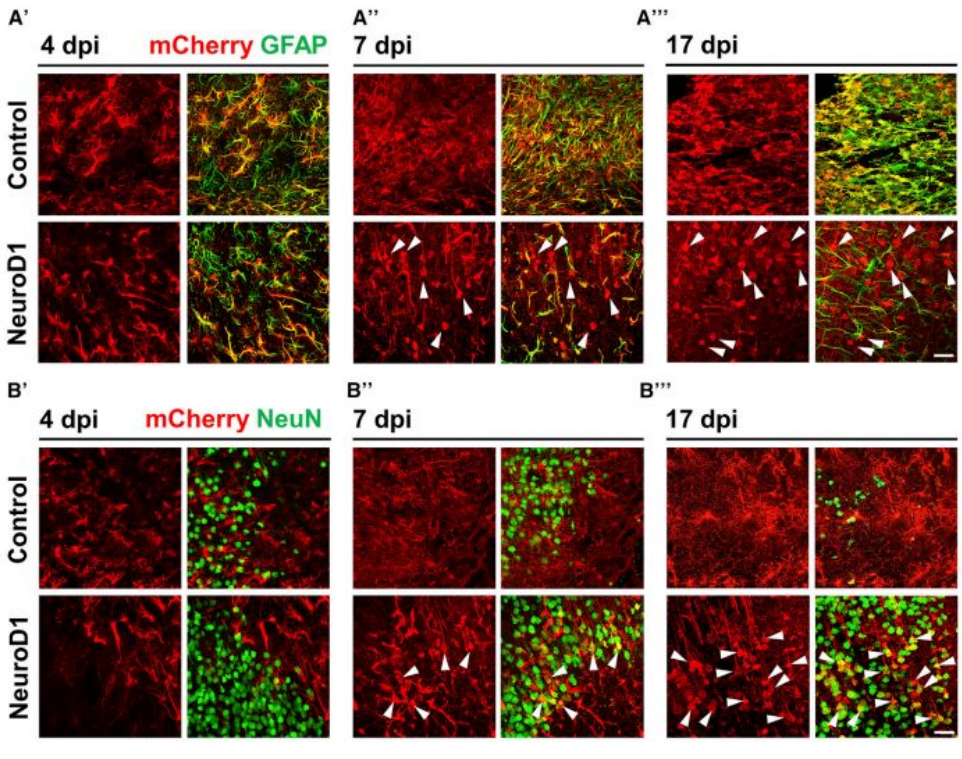
Results

Astrocyte-to-Neuron Conversion in a Focal Stroke Model using NeuroD1 AAV gene therapy was successful in creating immature to mature neurons in 2-3 weeks.

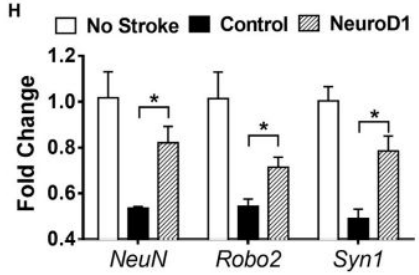
Ectopic expression of NeuroD1 in reactive astrocytes in the motor cortex after ischemic brain injury generated new neurons similar to cortical neurons.

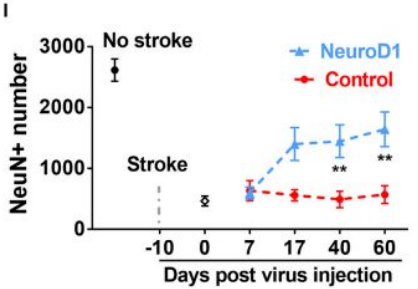
NeuroD1 treatment rescued lost motor function and cognitive deficits in mice.



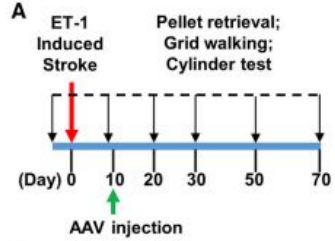


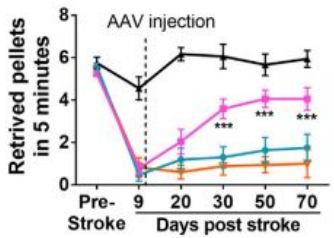
NeuroD1 Gradually Converts Reactive Astrocytes into Neurons after Stroke

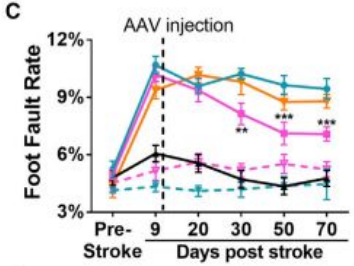


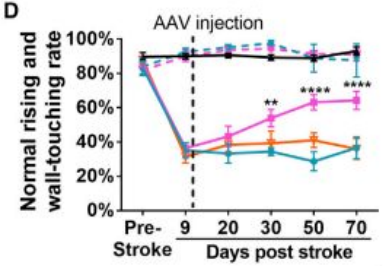


gh Efficiency of Neuroregeneration Achieved by NeuroD1-Mediated Astrocyte-to-Neuron Conversion









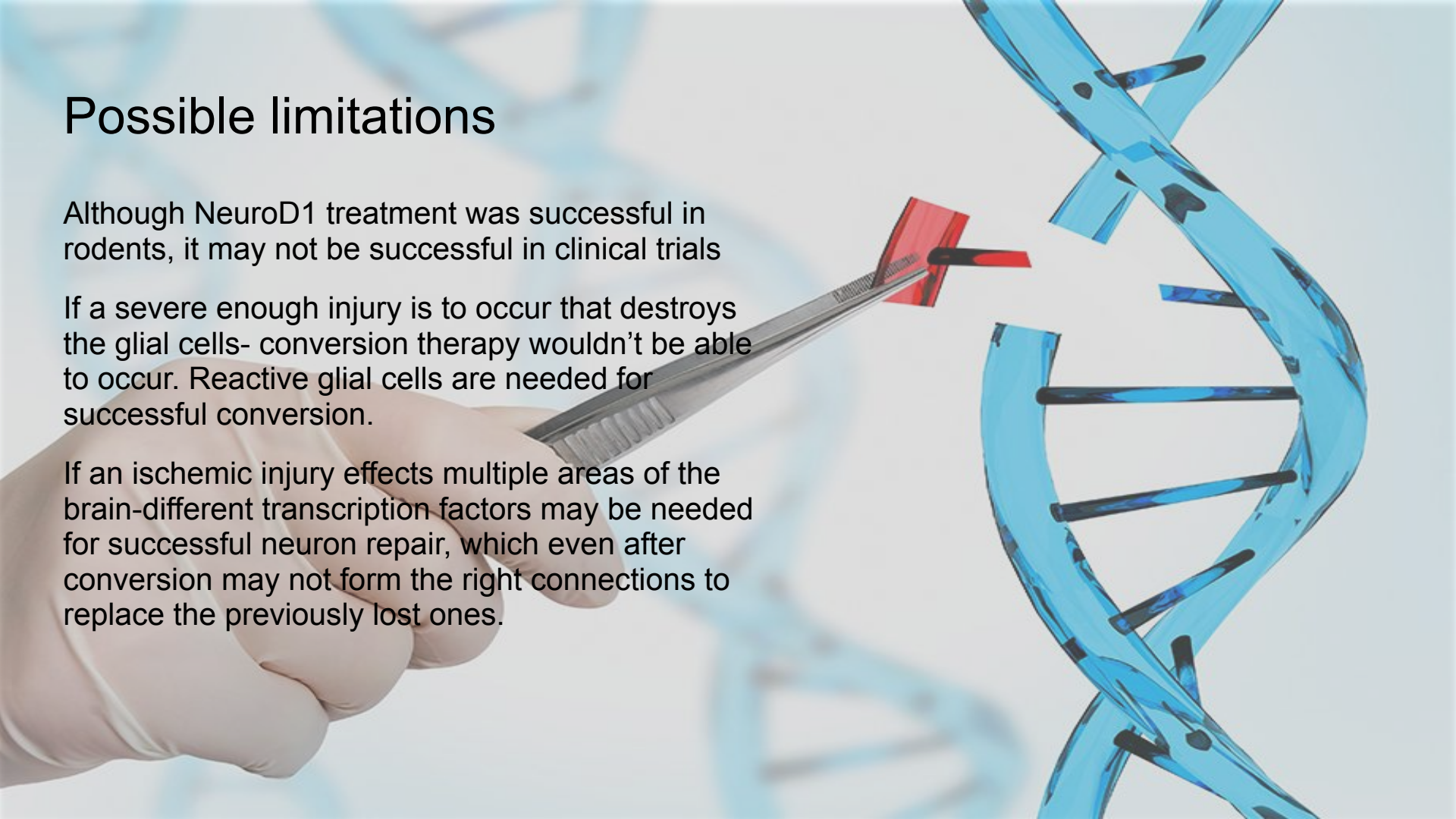
PBS Contral.
Stroke + NeuroD1 Contral.
Stroke + NeuroD1 Ipsil.
Stroke No Virus Contral.
Stroke + Control Contral.
Stroke + Control Ipsil.

Possible limitations

Although NeuroD1 treatment was successful in rodents, it may not be successful in clinical trials

If a severe enough injury is to occur that destroys the glial cells- conversion therapy wouldn't be able to occur. Reactive glial cells are needed for successful conversion.

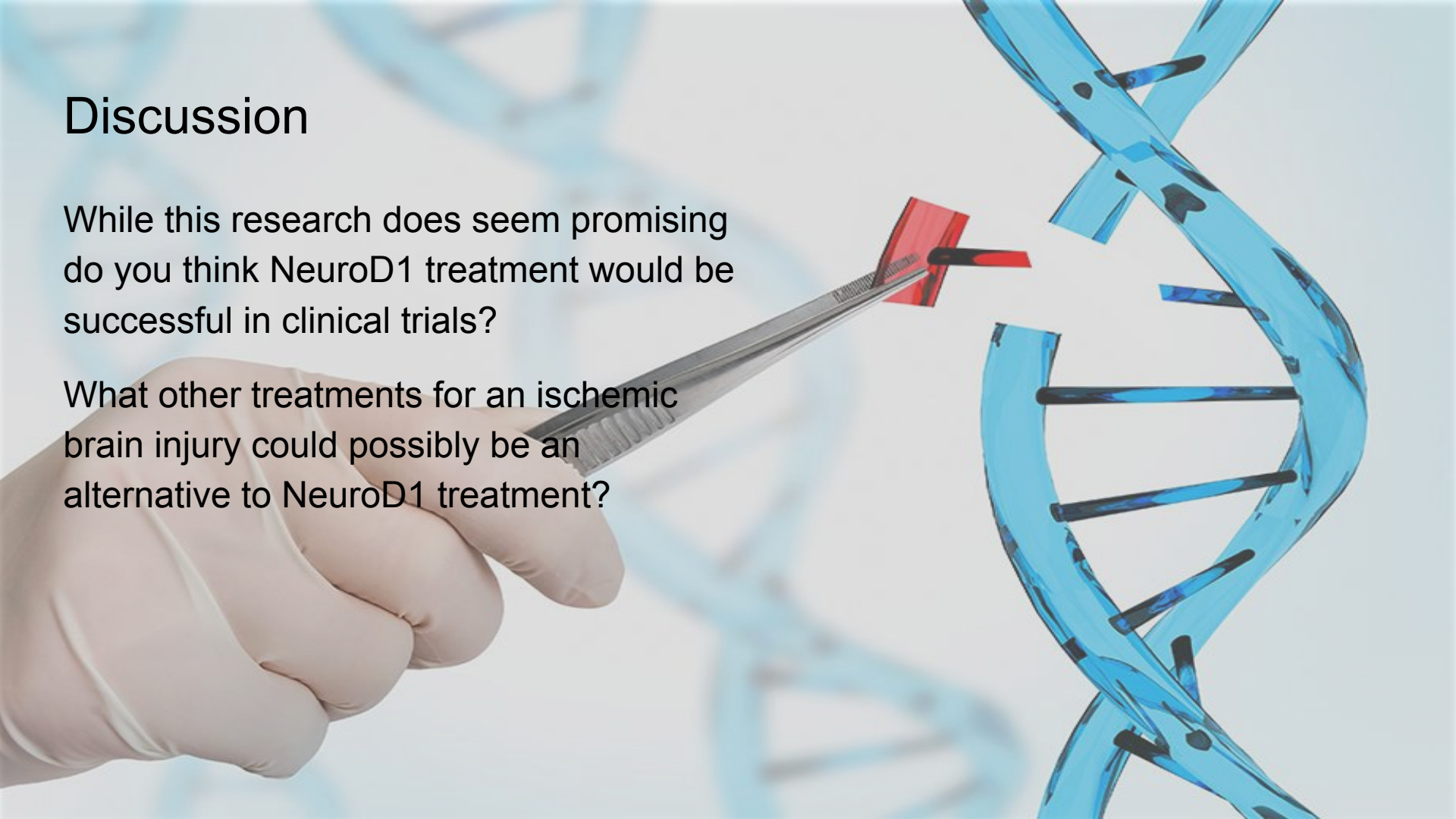
If an ischemic injury effects multiple areas of the brain-different transcription factors may be needed for successful neuron repair, which even after conversion may not form the right connections to replace the previously lost ones.



Discussion

While this research does seem promising do you think NeuroD1 treatment would be successful in clinical trials?

What other treatments for an ischemic brain injury could possibly be an alternative to NeuroD1 treatment?



Citations

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