

Scientific Poster Session



Nano-rare Patient
Colloquium 2025

Monday, October 20 | 5:15 – 6:15 pm EST

DYRK1A, a Discovery Case's Evolution from Research to High-throughput Scalability

The current DYRK1A program has evolved from designing a small number of candidate ASOs to leveraging n-Lorem's high-throughput n-of-1 Discovery pipeline. This work has enabled us to conduct rapid, rigorous and high-quality screening combined with functional studies to specifically target the pathogenic mechanism of this nano-rare disorder.

Craig McIntosh, Ph.D.

Associate Director, ASO Discovery, n-Lorem

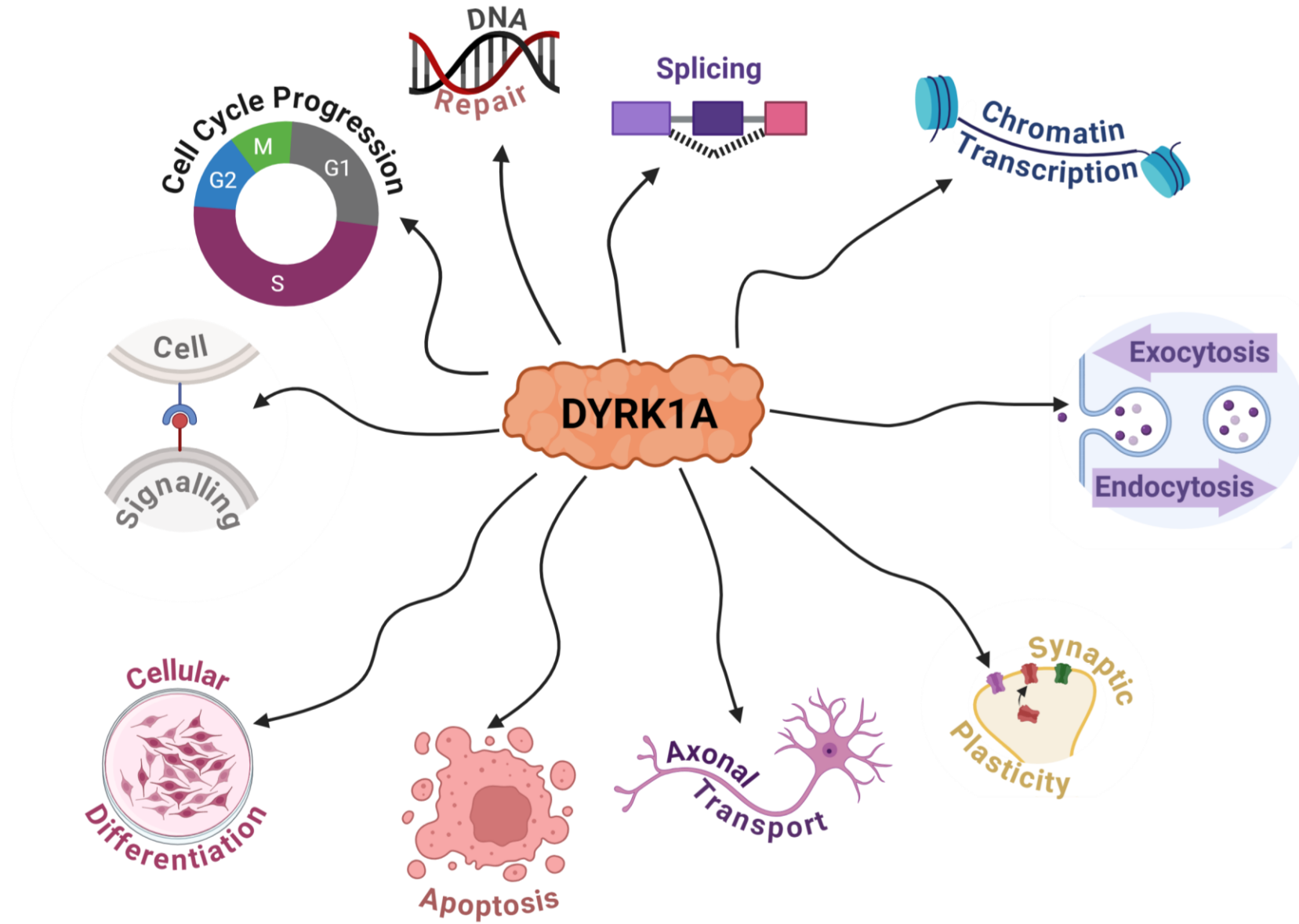


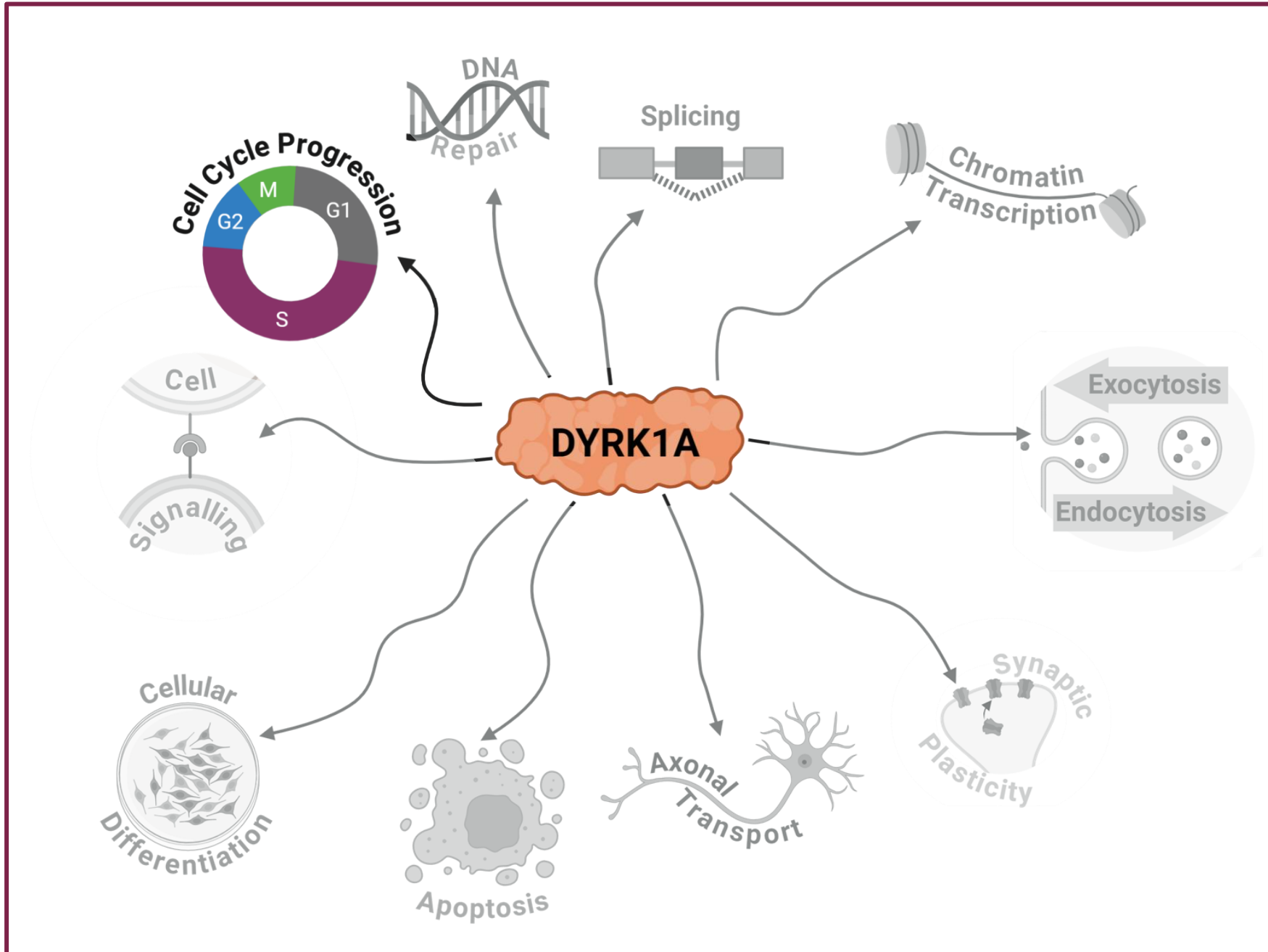
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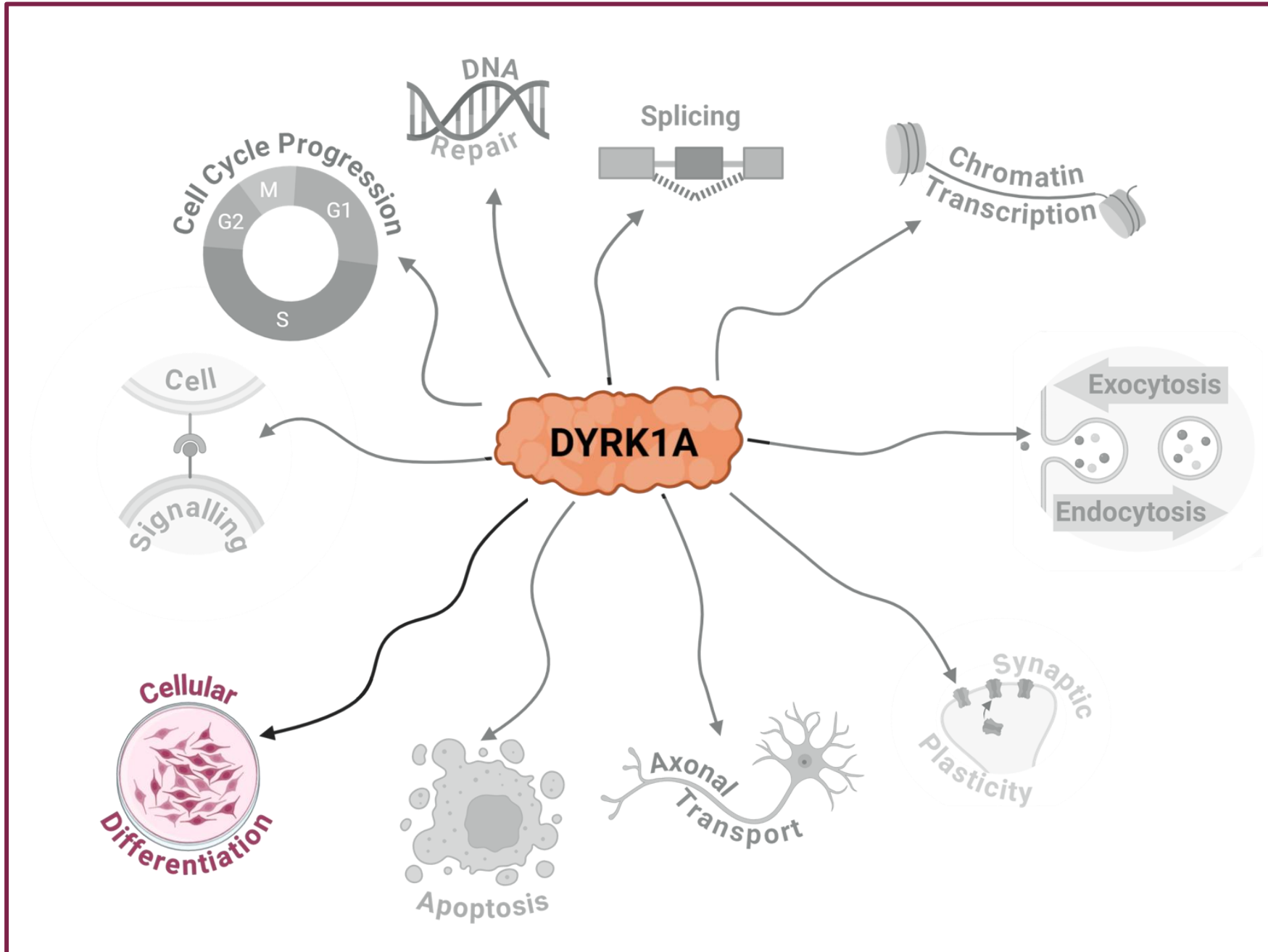


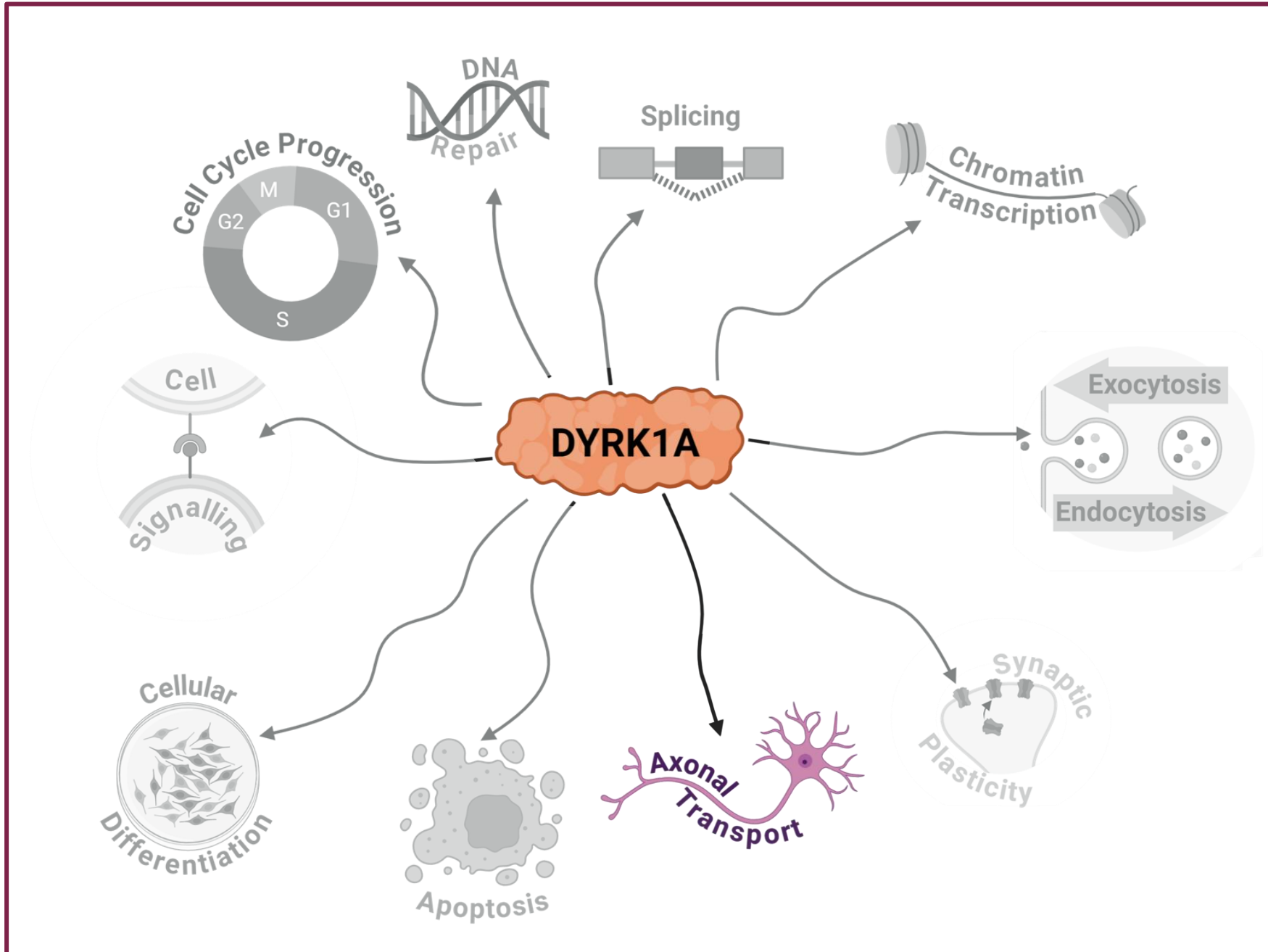
Introduction

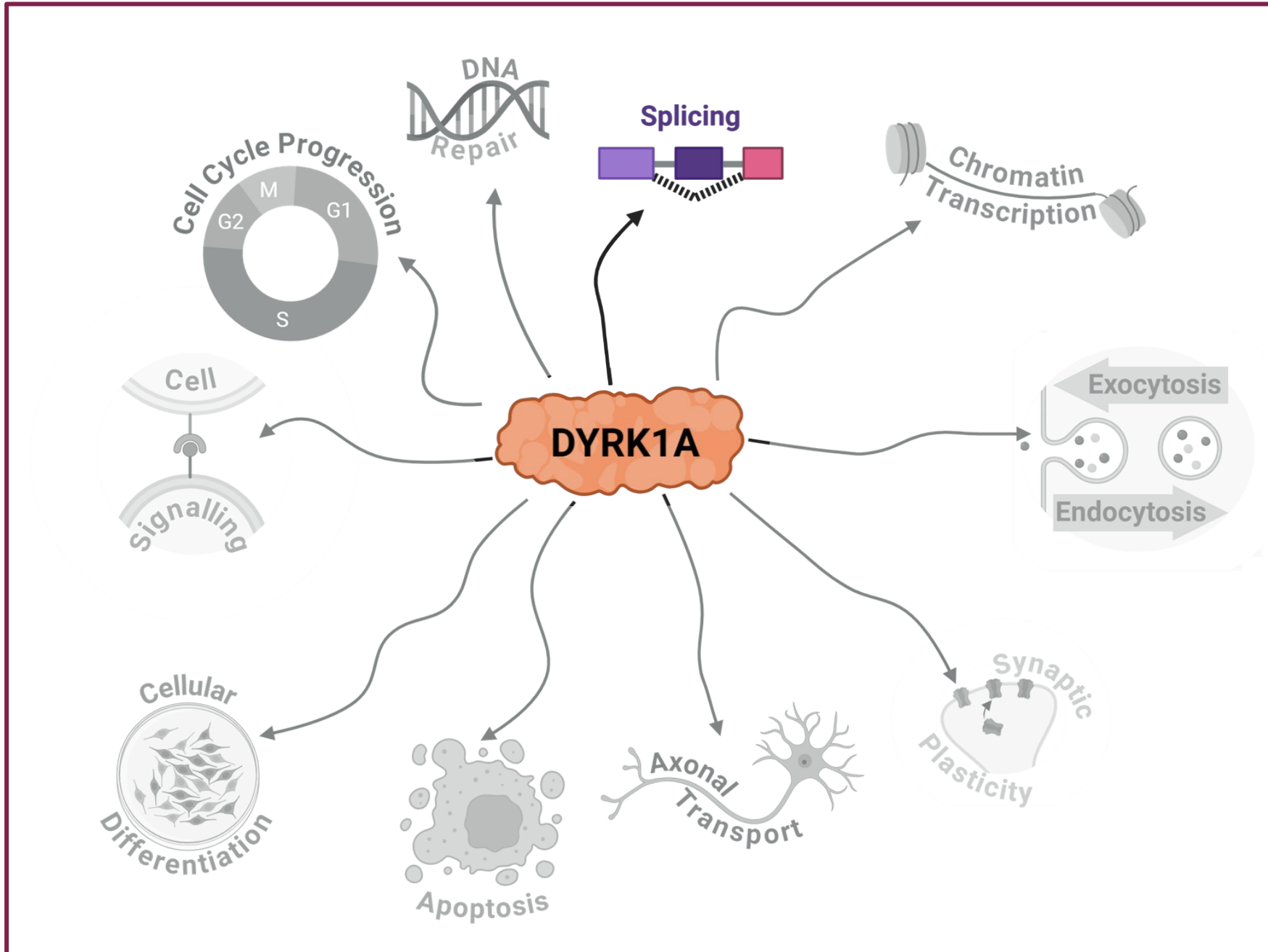
DYRK1A Syndrome is an autosomal dominant, rare neurodevelopmental disorder caused by loss of function mutations within the **DYRK1A** (dual specificity tyrosine-phosphorylation-regulated kinase 1A) gene, leading to what is known as **haploinsufficiency of DYRK1A**.

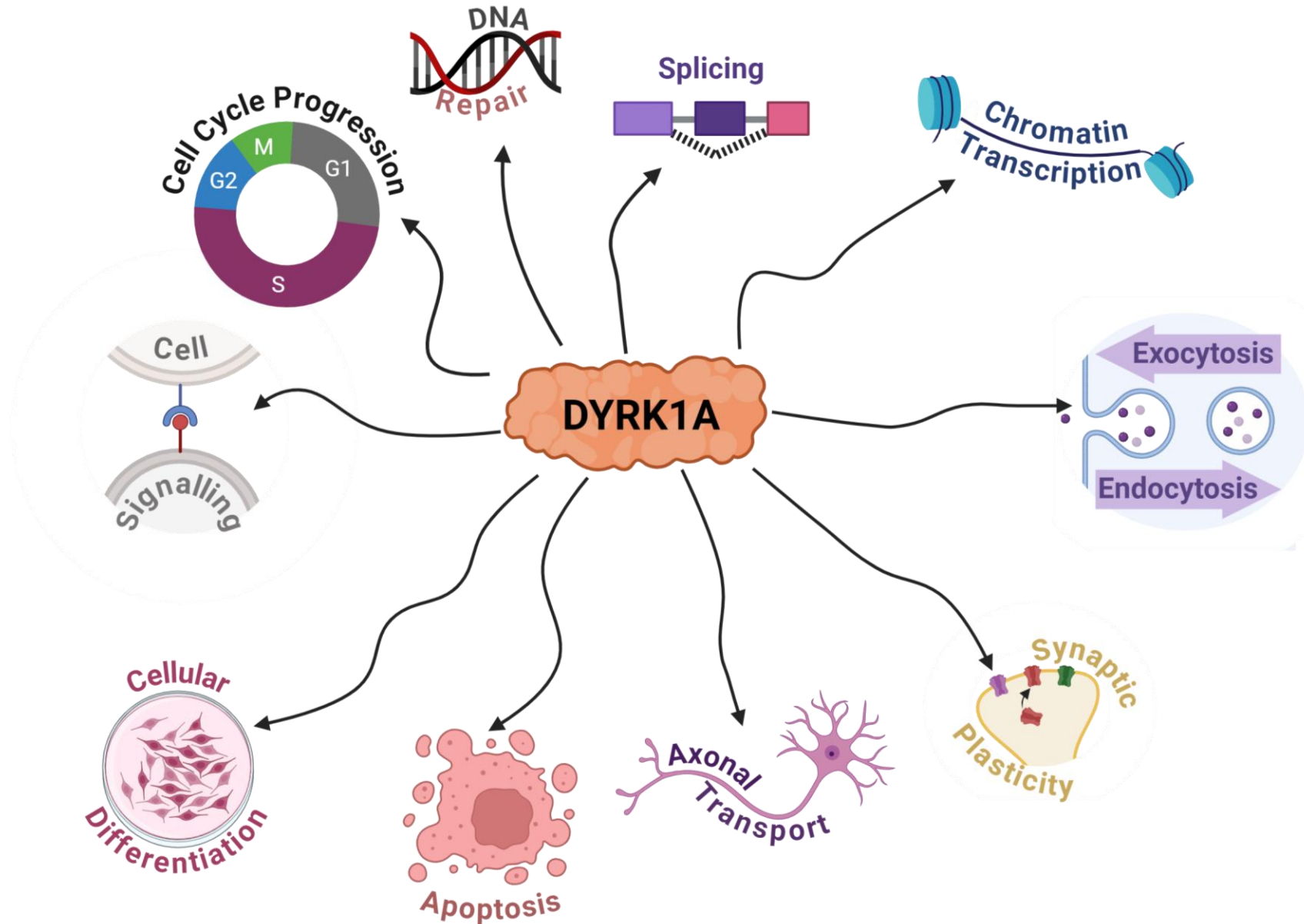












COMMON DYRK1A SYNDROME PHENOTYPES

EYES:

Deep set eyes, Optic nerve hypoplasia, eye abnormalities

UPPER BODY:

Gross & motor skill difficulties, Scoliosis, delayed growth low birth weight

BRAIN:

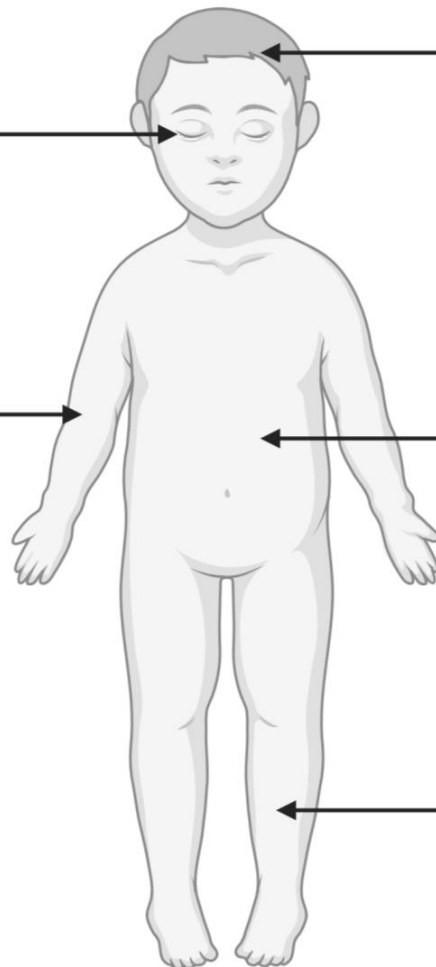
Microcephaly, Intellectual disability, ASD, Seizures and Speech Delay

GI TRACT

Chronic constipation, Food sensitivities, Feeding tube

LOWER LIMBS

Hypertonia, Hypotonia, Small in stature, Feet abnormalities, Unsteady gait



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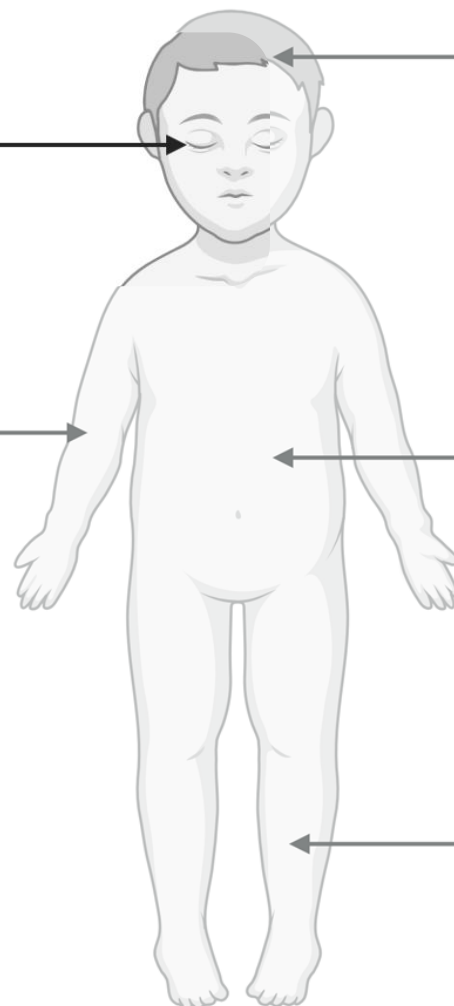
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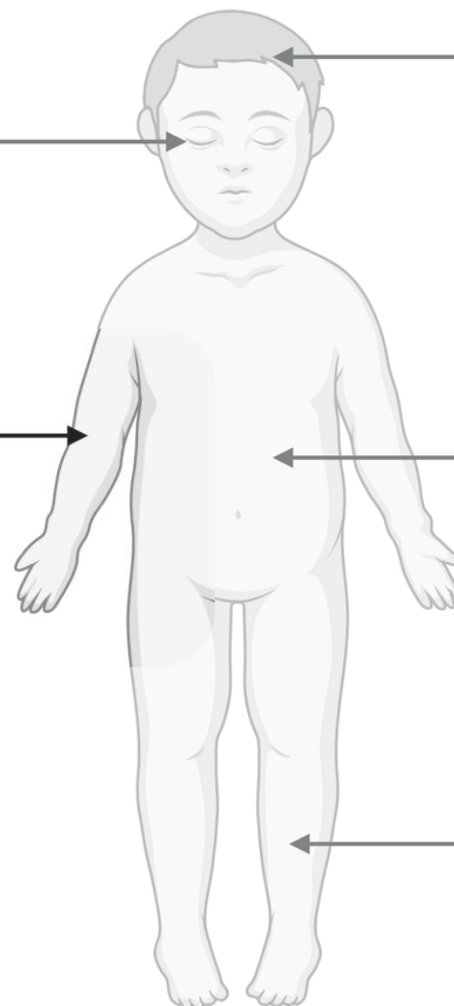
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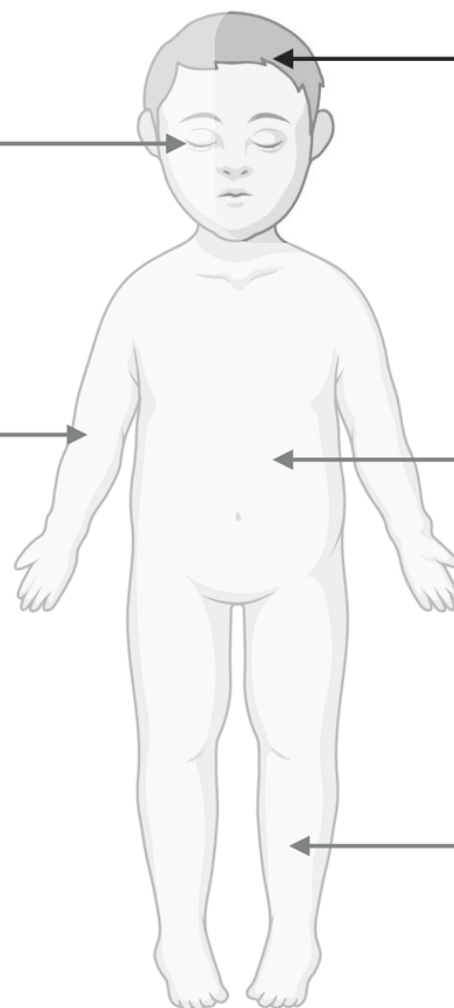
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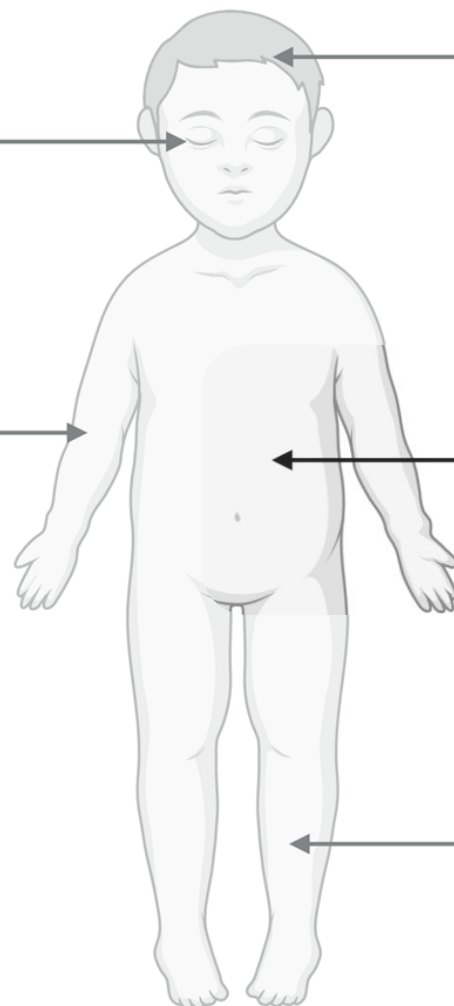
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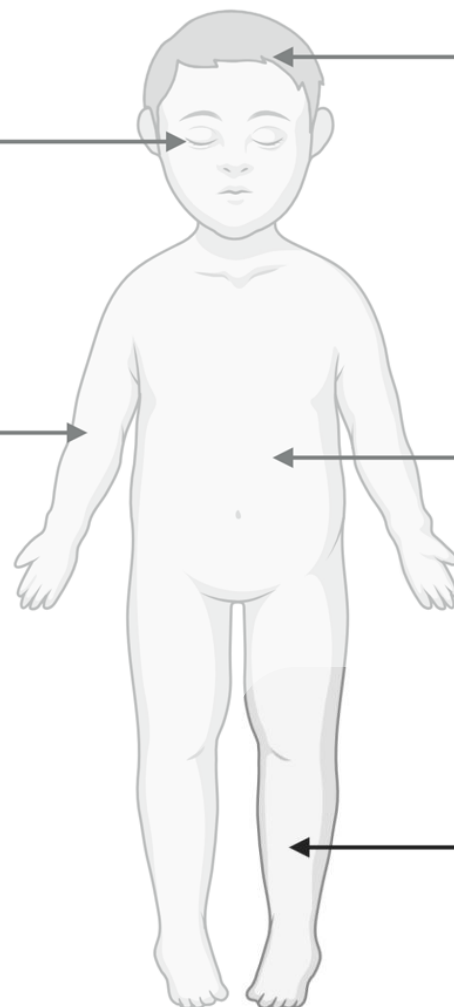
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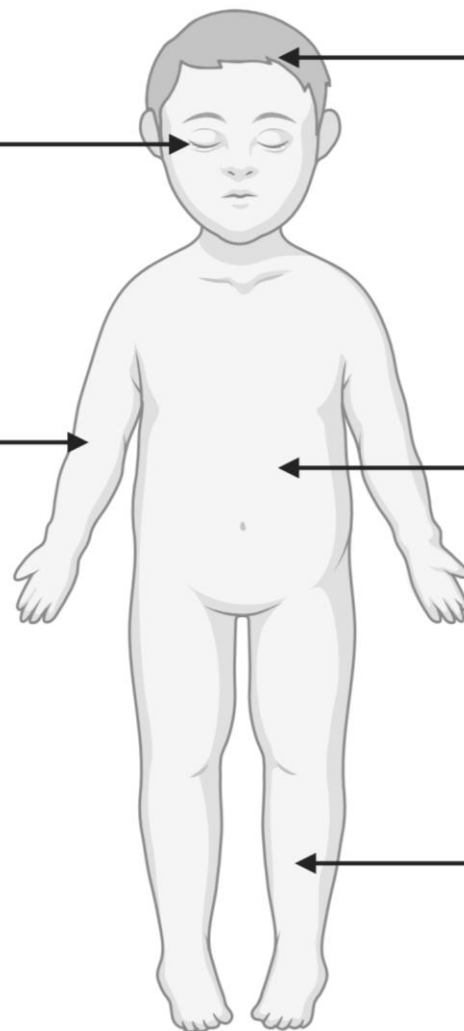
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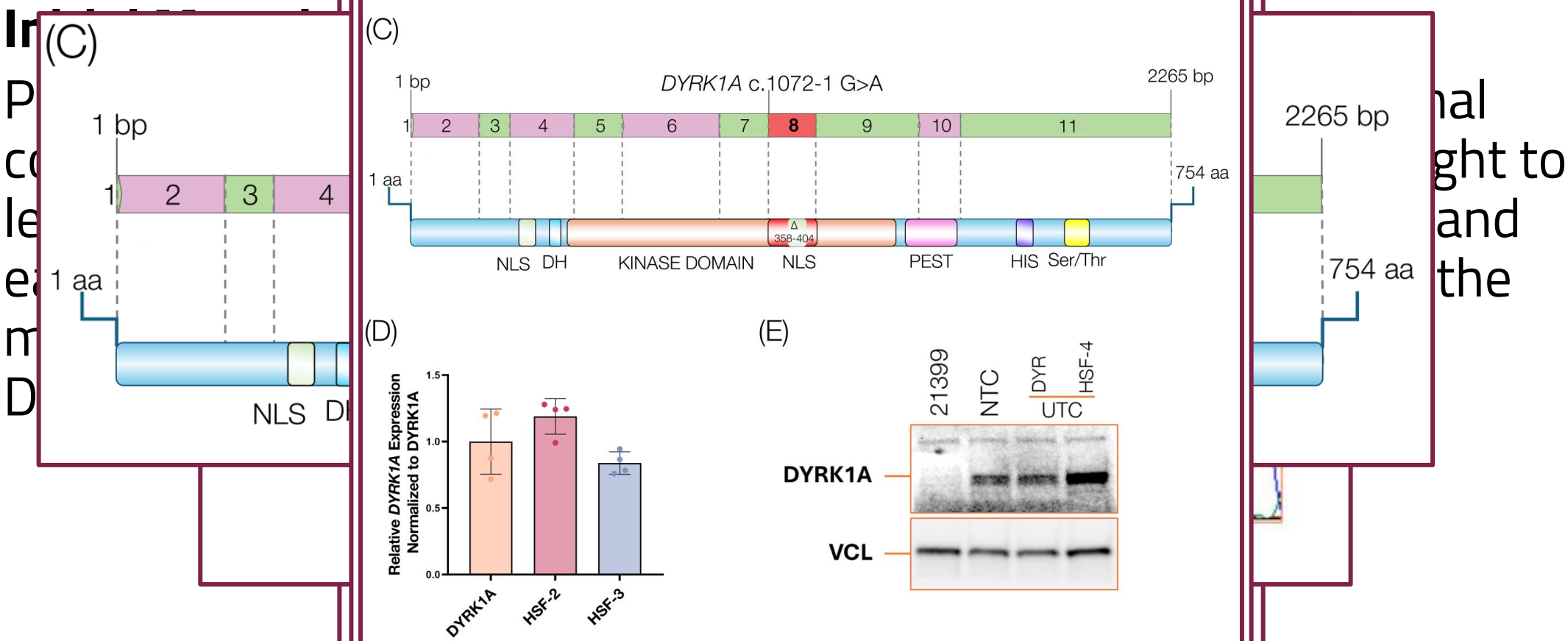
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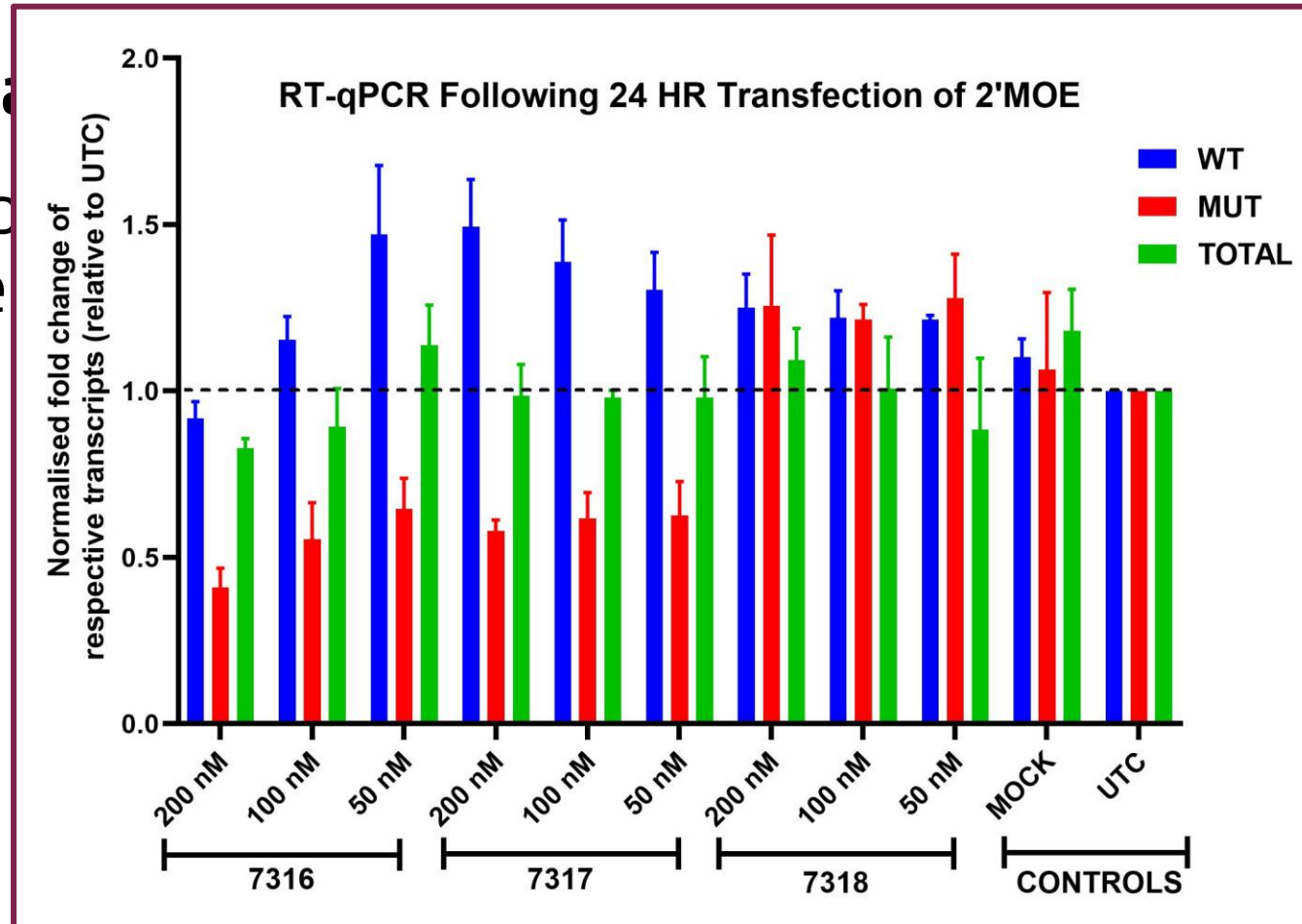
Data & Res



Data & Results

Initial ASO Val

From the above data, we determined that the ASOs were designed to be therapeutic.



Data & Results

n-Lorem's High Throughput Screening

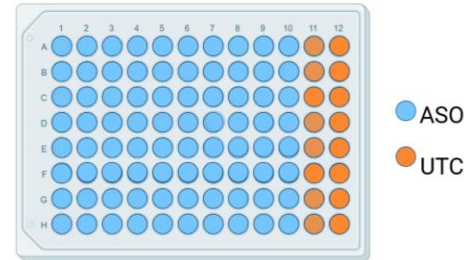
These paved the way for n-Lorem's Discovery pipeline for this truly n-of-1 mutation.

In-house AI-informed ASO design

Whole Genome Sequencing and
ASO Design



ASOs at Single Dose

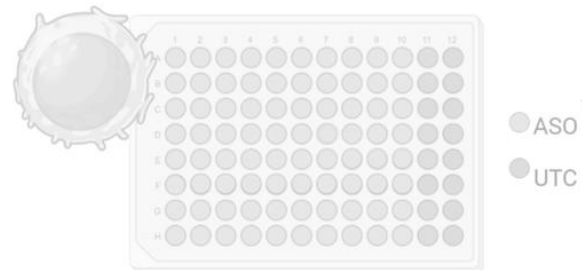


Fully automated high throughput ASO screening

ASO Dose Response



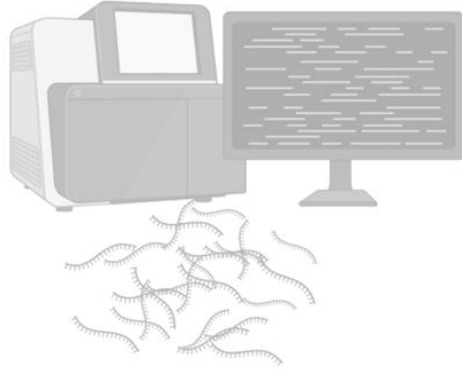
ASOs at Single Dose for
Innate Immune Activation



Candidate selection for in
vivo studies



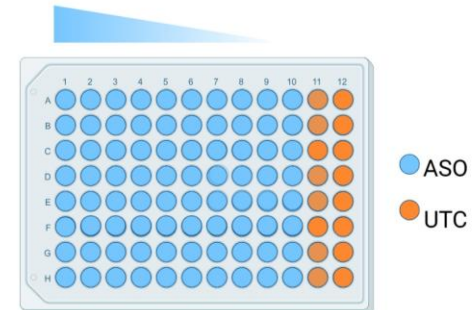
Whole Genome Sequencing and ASO Design



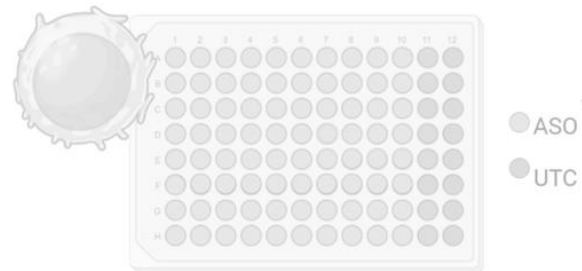
ASOs at Single Dose



ASO Dose Response



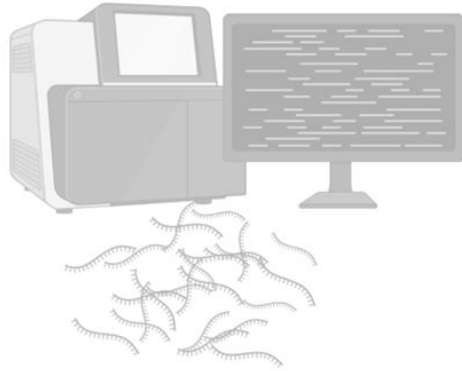
ASOs at Single Dose for Innate Immune Activation



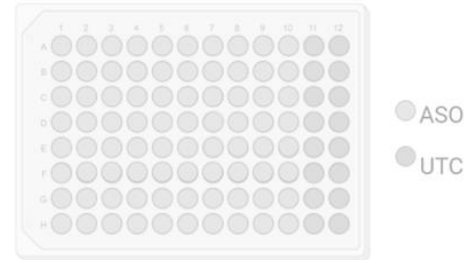
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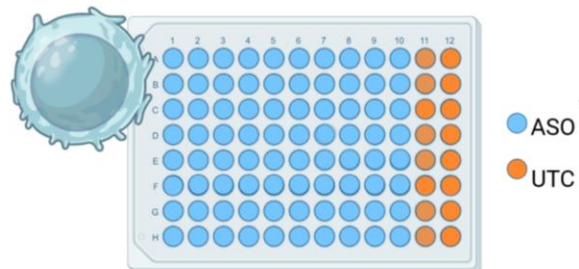
ASOs at Single Dose



ASO Dose Response



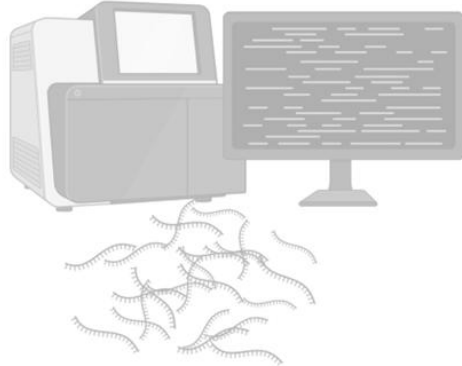
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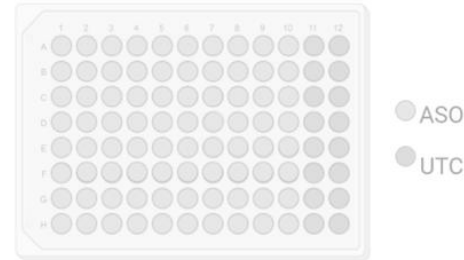
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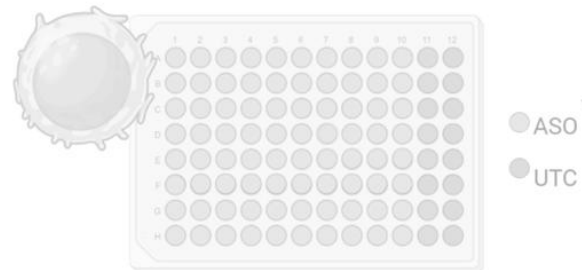


Potent, efficacious and safe ASOs

ASO Dose Response



ASOs at Single Dose for
Innate Immune Activation

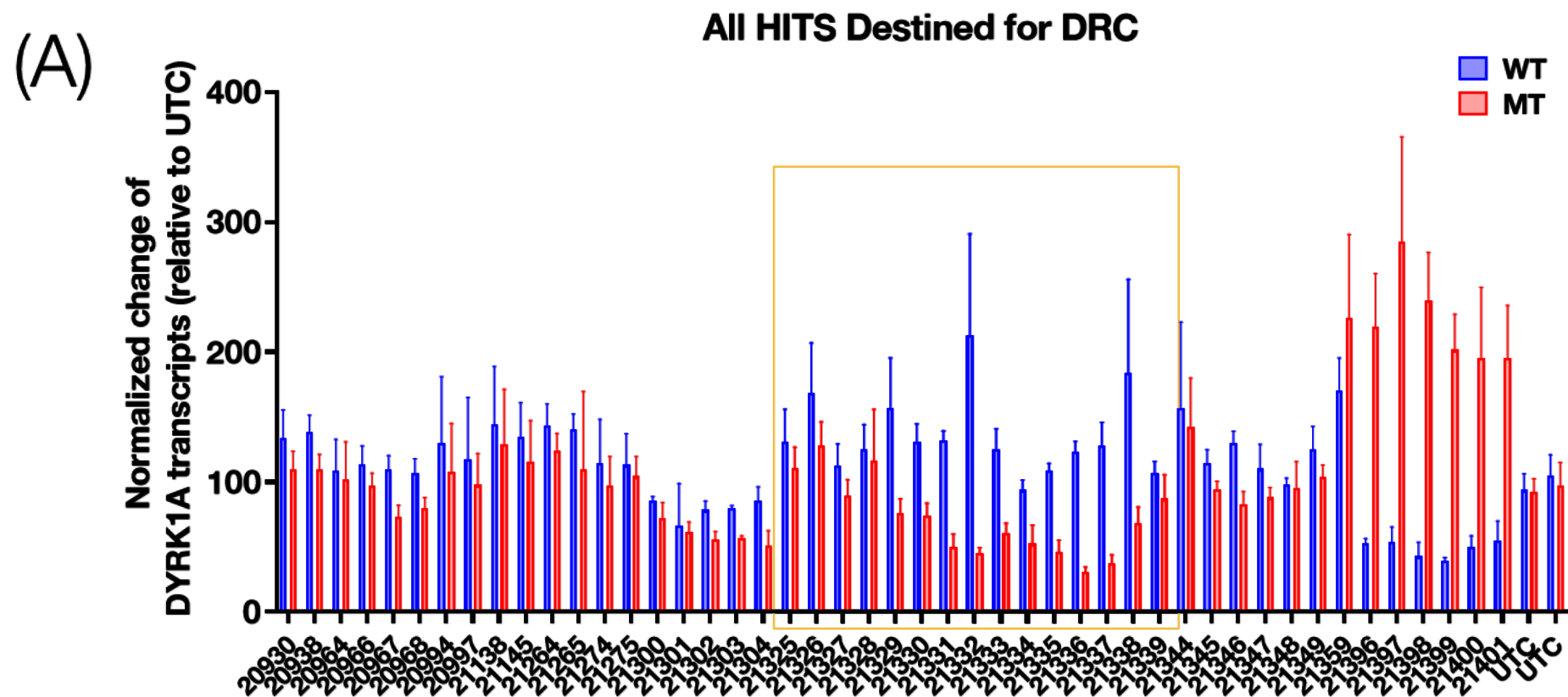


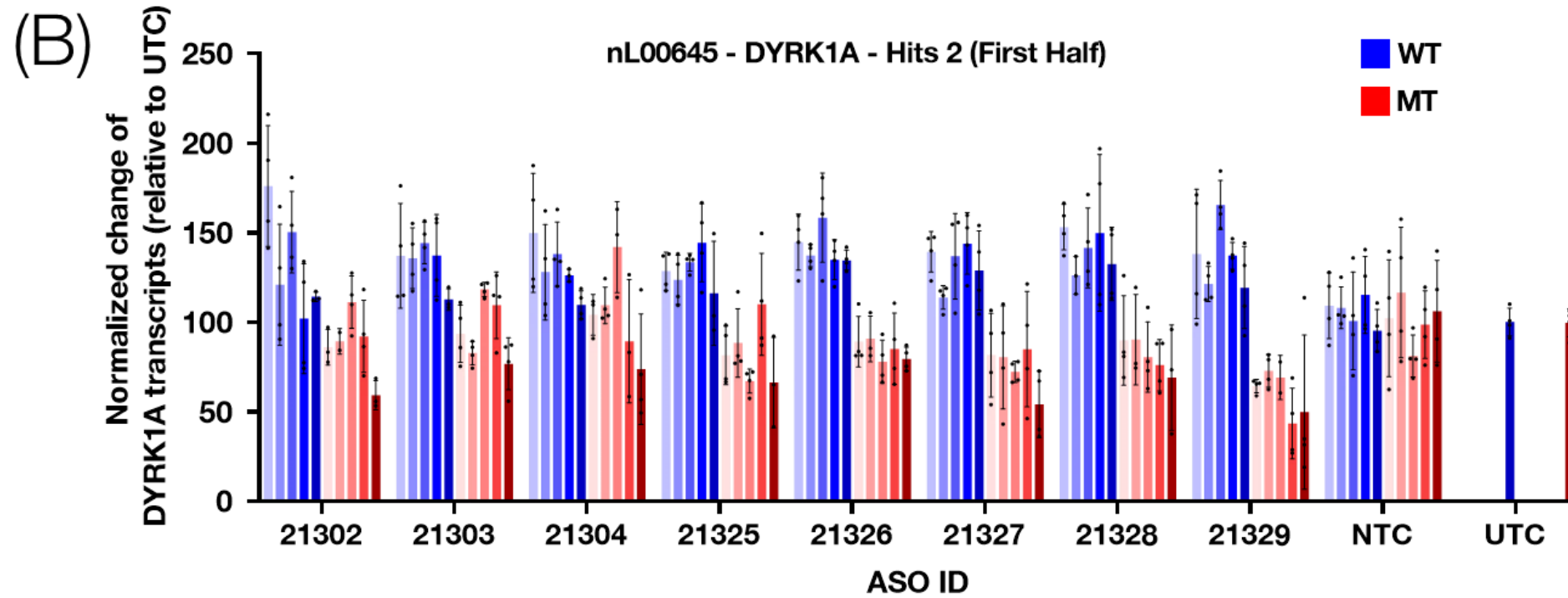
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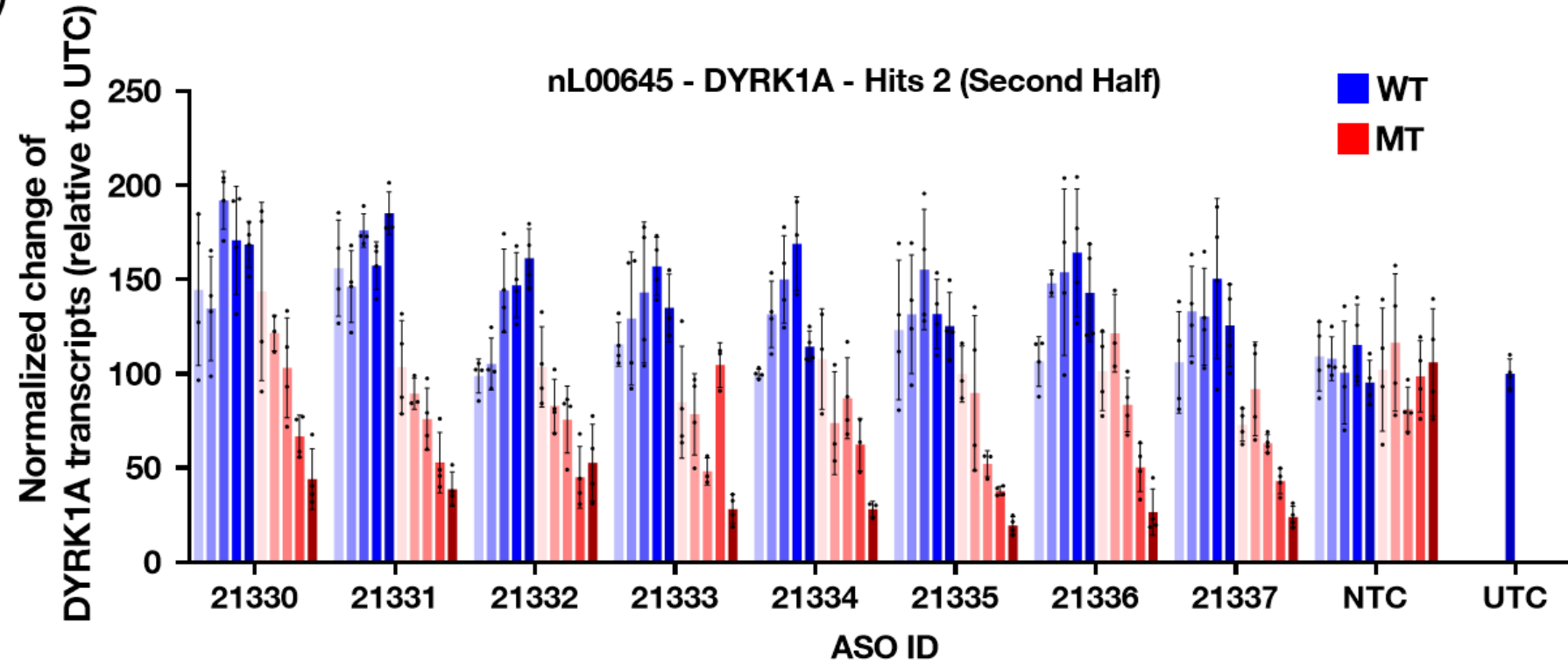
Data & Results

n-Lorem's Discovery Pipeline, included Single Dose, Dose Response Curve and BJAB Assay

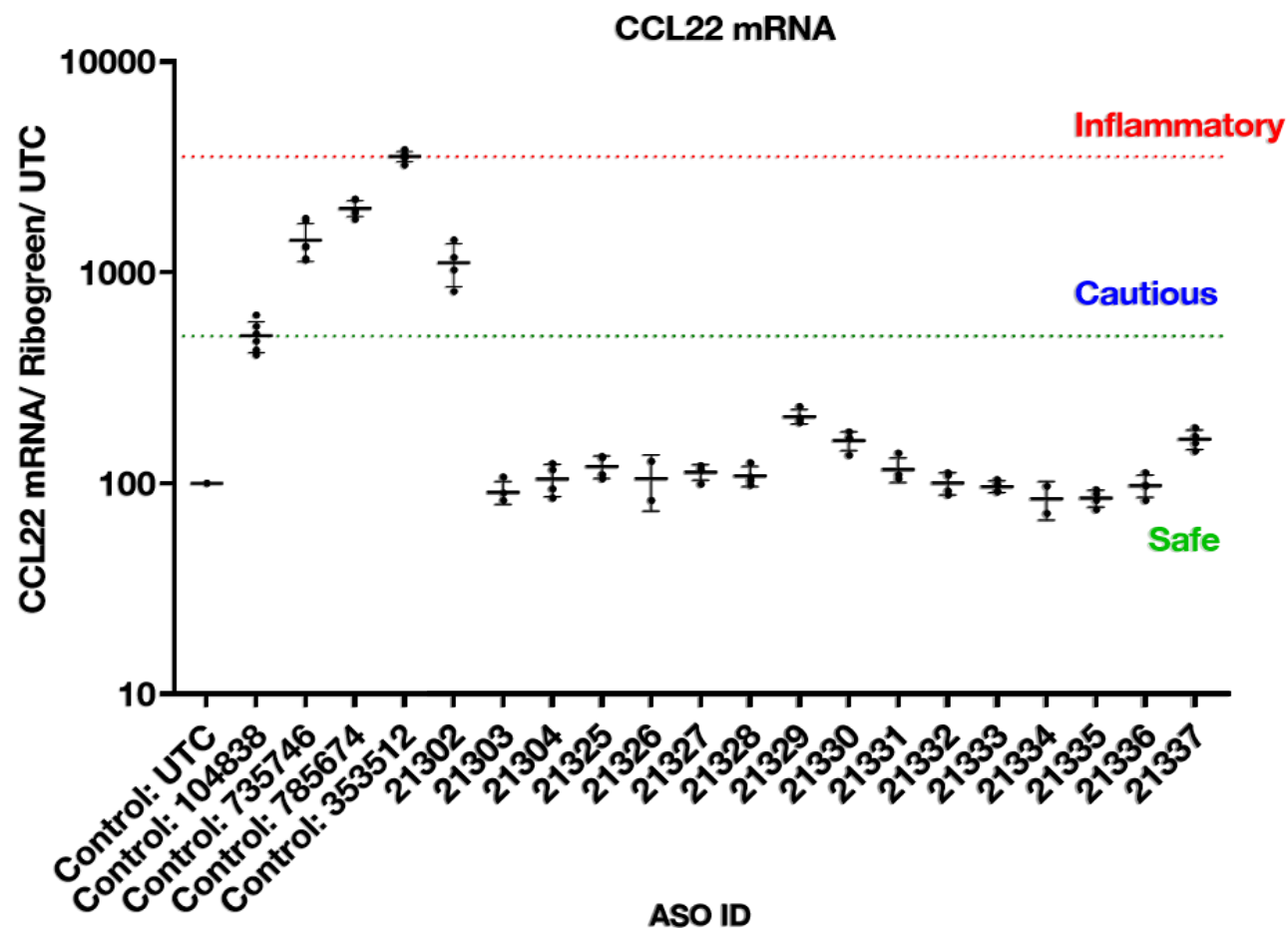




(C)



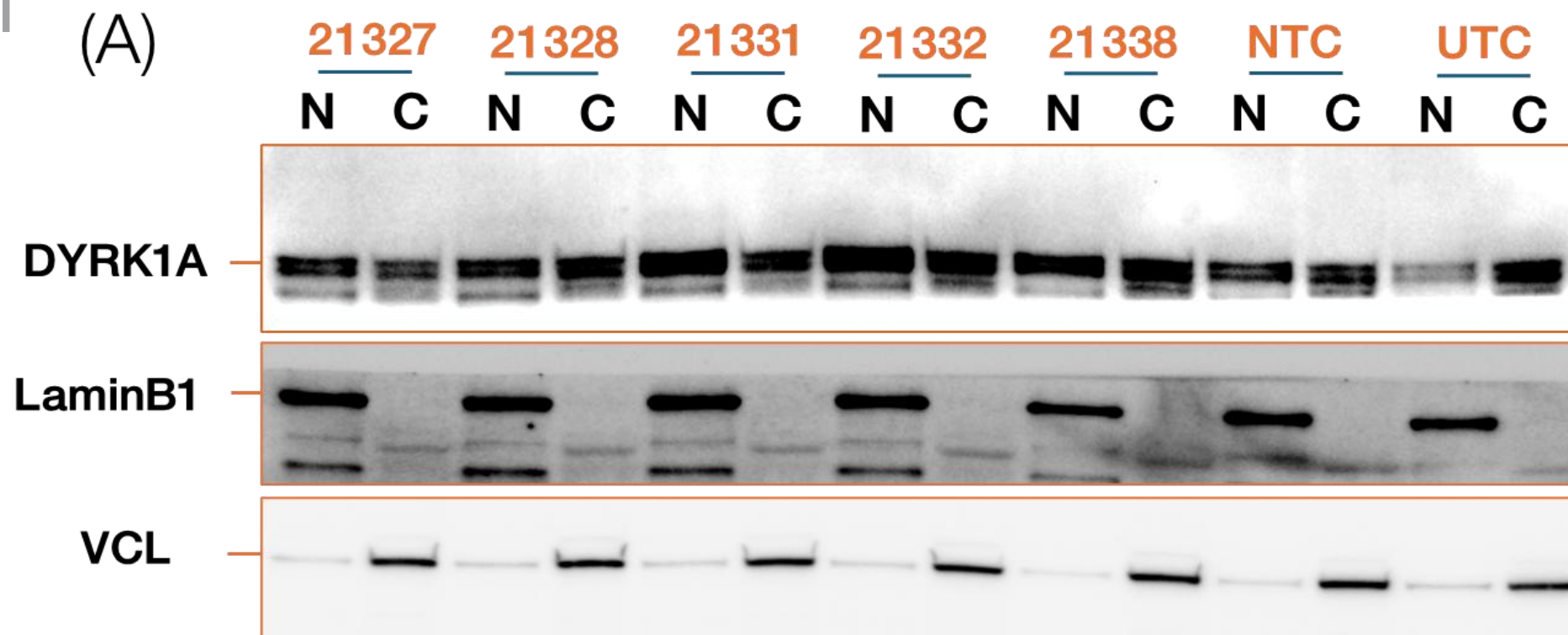
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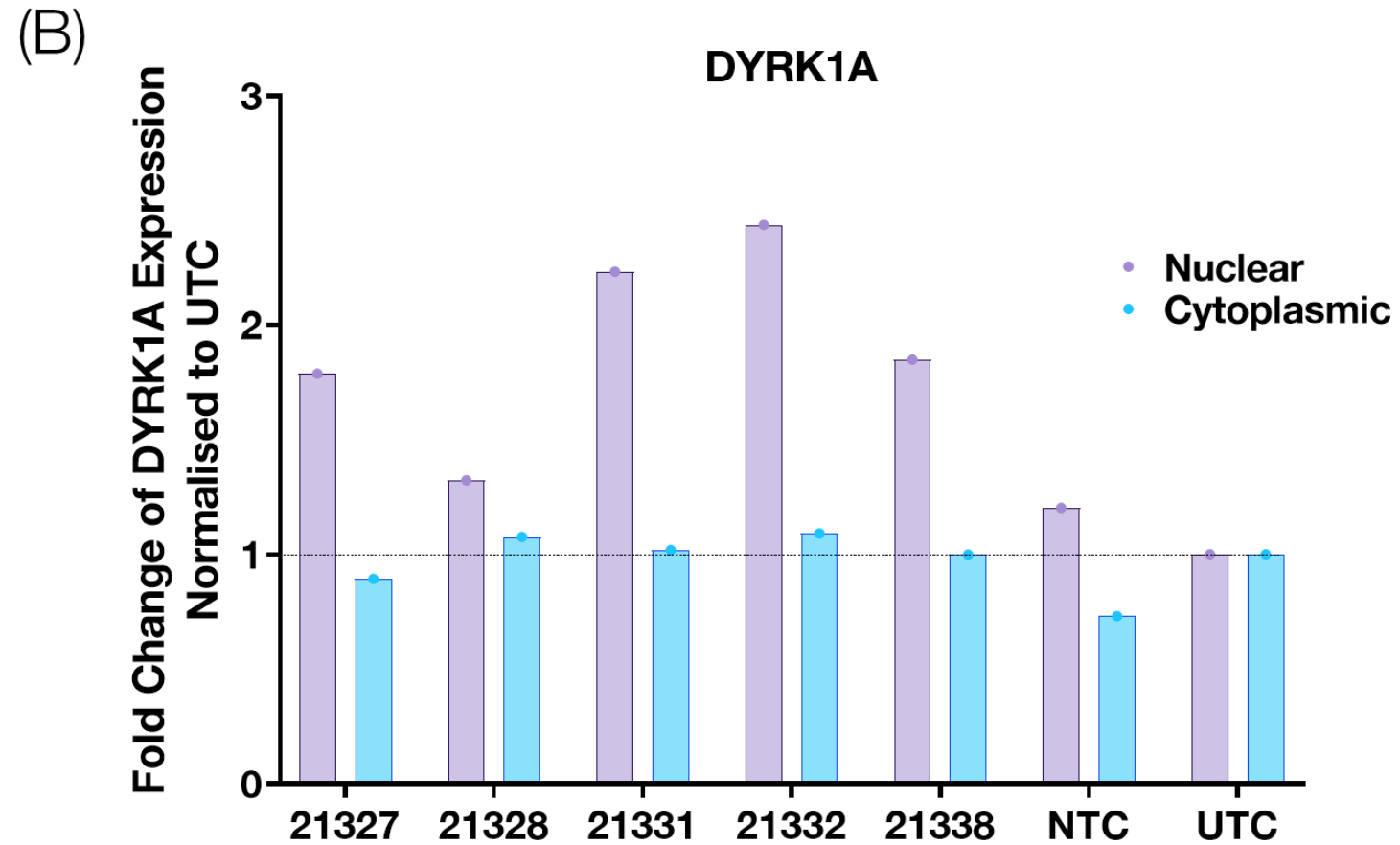


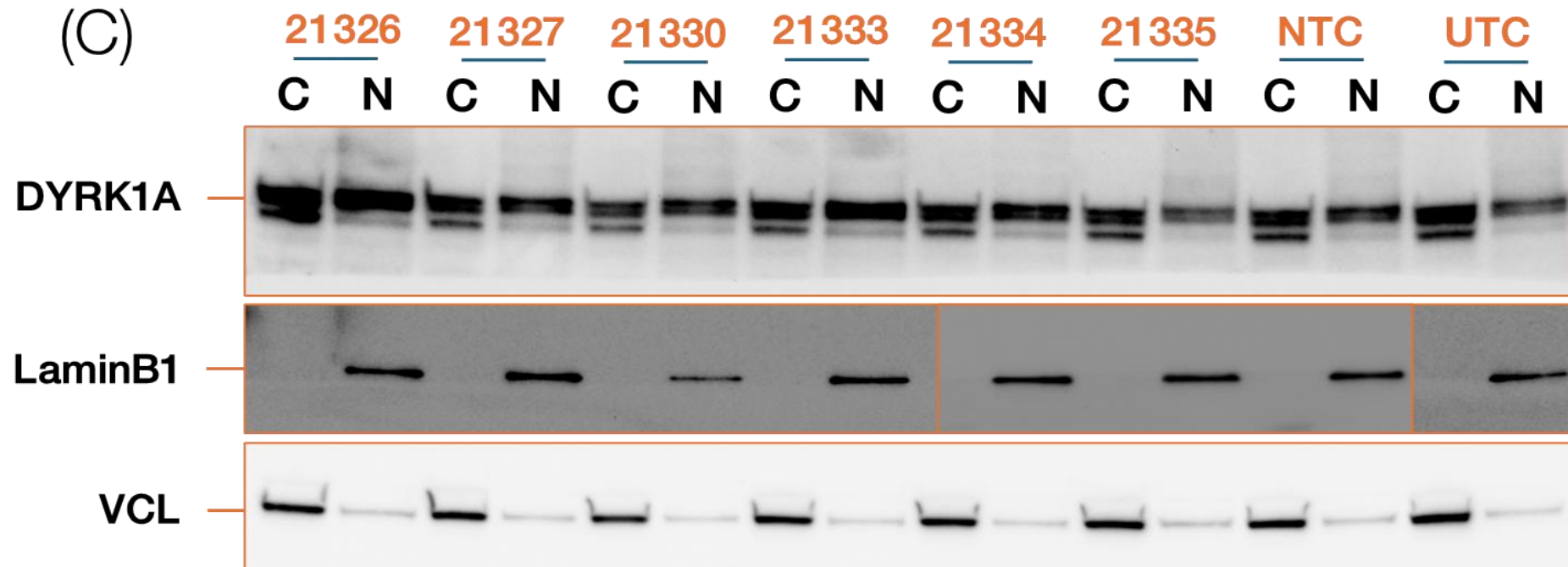
Data & Results

Immunoblot of DYRK1A Nuclear and Cytoplasmic Fractionated Samples

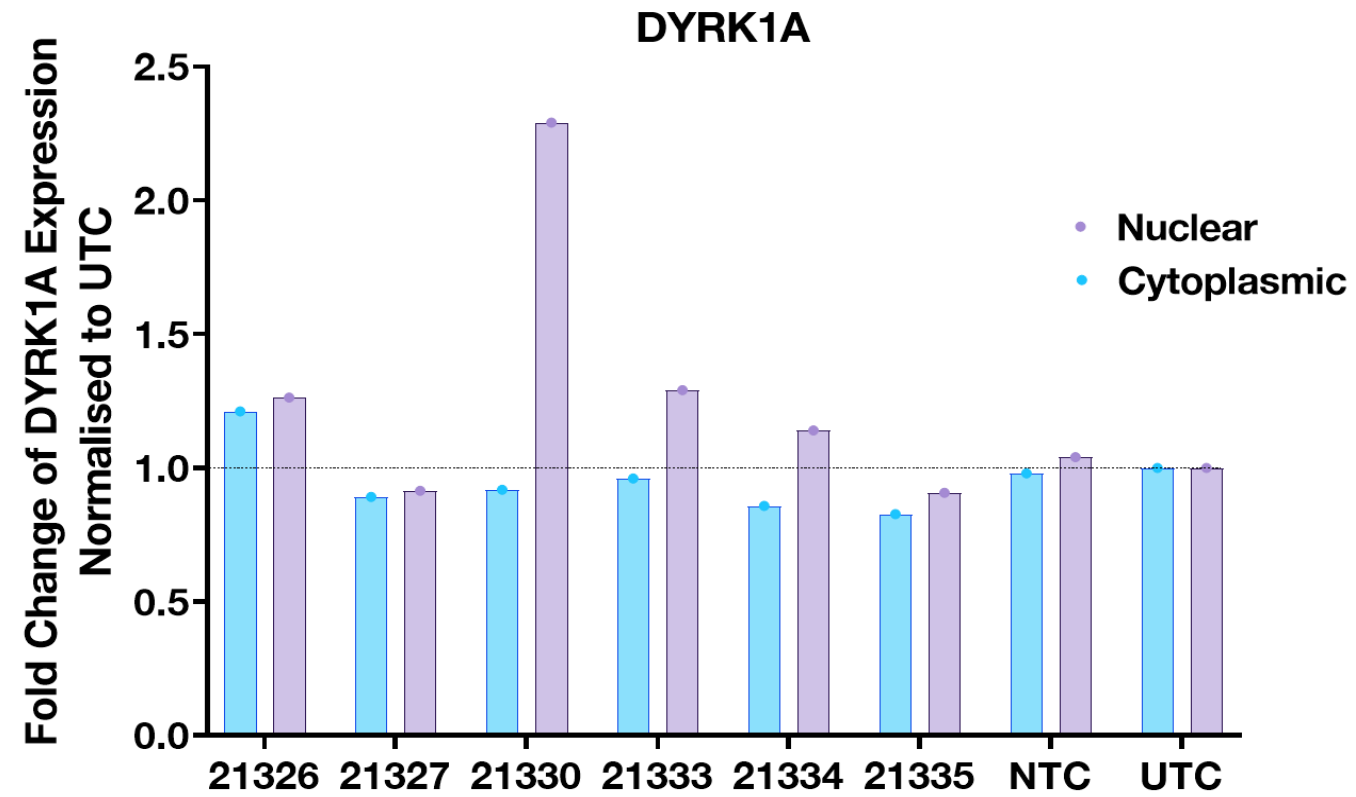
In splicing cases it is best practice to confirm splice-modulation at the transcript level has had a concomitant modulation of protein expression. In the case of our DYRK1A patient we expect to see an increase in DYRK1A protein and specifically, an increase in nuclear DYRK1A







(D)



Conclusion



Activities occur in parallel for efficiency



Leverages robots to ensure comprehensive design



High-throughput



Scalable with high-quality

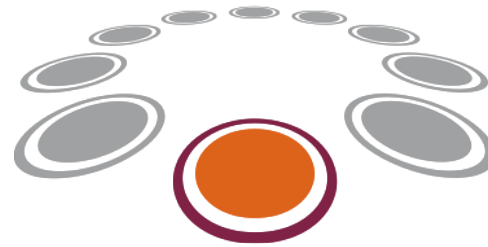


Efficient and more cost-effective

Acknowledgements

We would like to thank the **DYRK1A Syndrome International Association** for their grant funding that allowed a portion of the discovery program to be completed.

Thank you



n-lorem
FOUNDATION