



The Neuronal Gene Arc Encodes a Repurposed Retrotransposon Gag Protein that Mediates Intercellular RNA Transfer

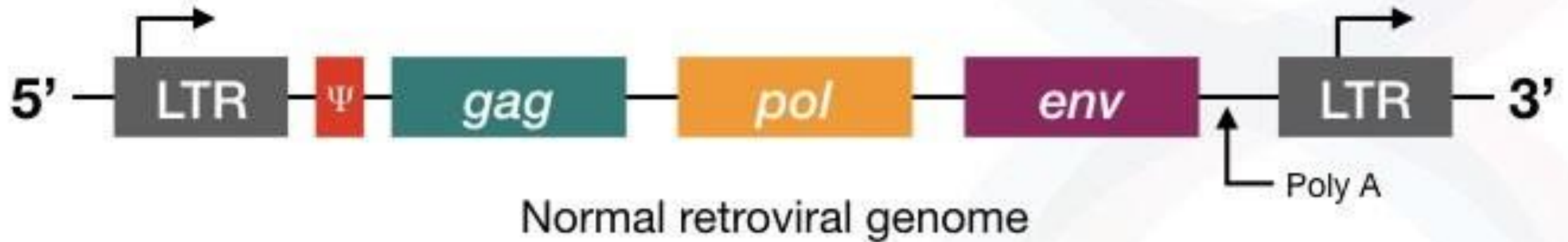
(Pastuzyn, et al., 2018)

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[illegible]

DNA-

What does a basic retrovirus look like?



An RNA virus that inserts a DNA copy into a host's genome

Gag = Capsid proteins

Pol = Replication machinery and Reverse Transcriptase

Env = Protective lipid envelope

What is Arc?



**A neuronal gene essential for
memory and synaptic plasticity**

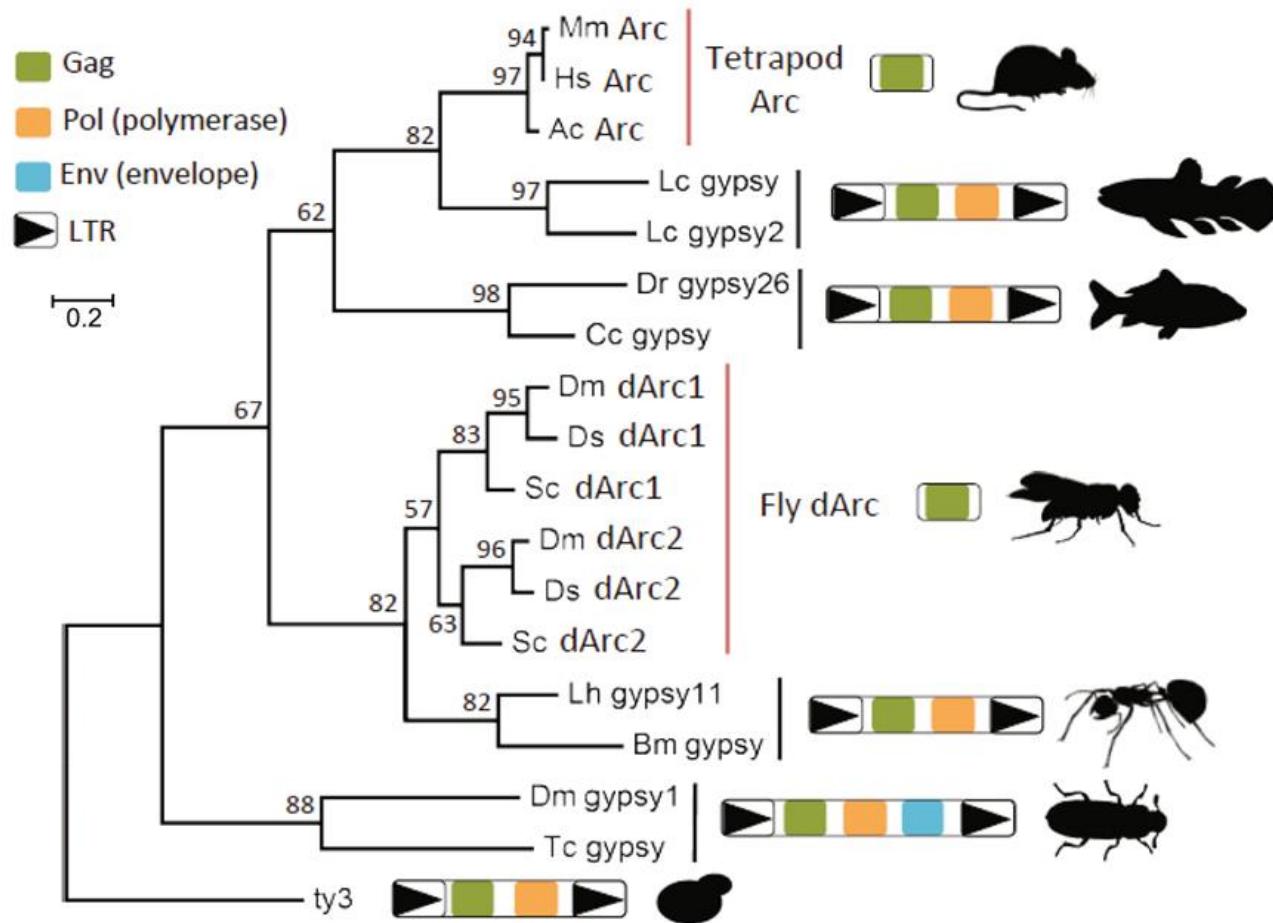
MA = Matrix

**CA-NTD = Capsid N-terminal
domain**

**CA-CTD = Capsid C-terminal
domain**

What are the evolutionary origins of Arc?

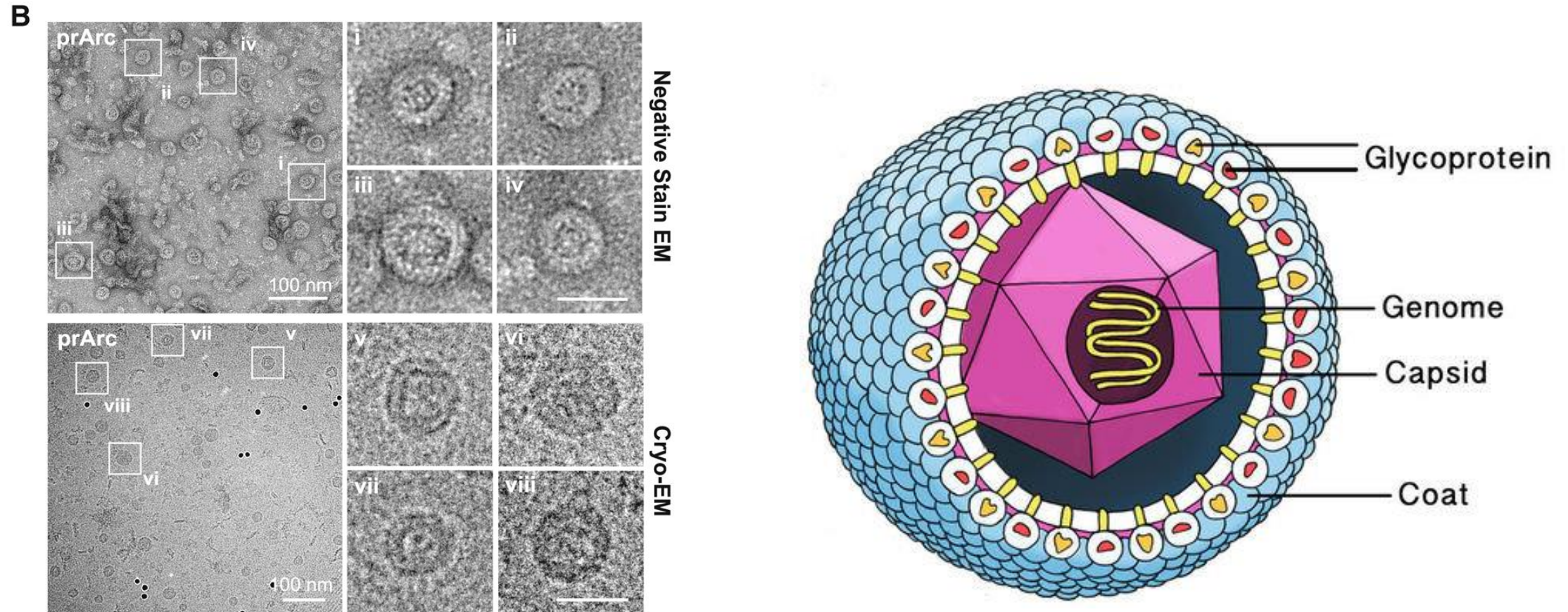
A



**Ty3/gypsy
retrotransposons!**

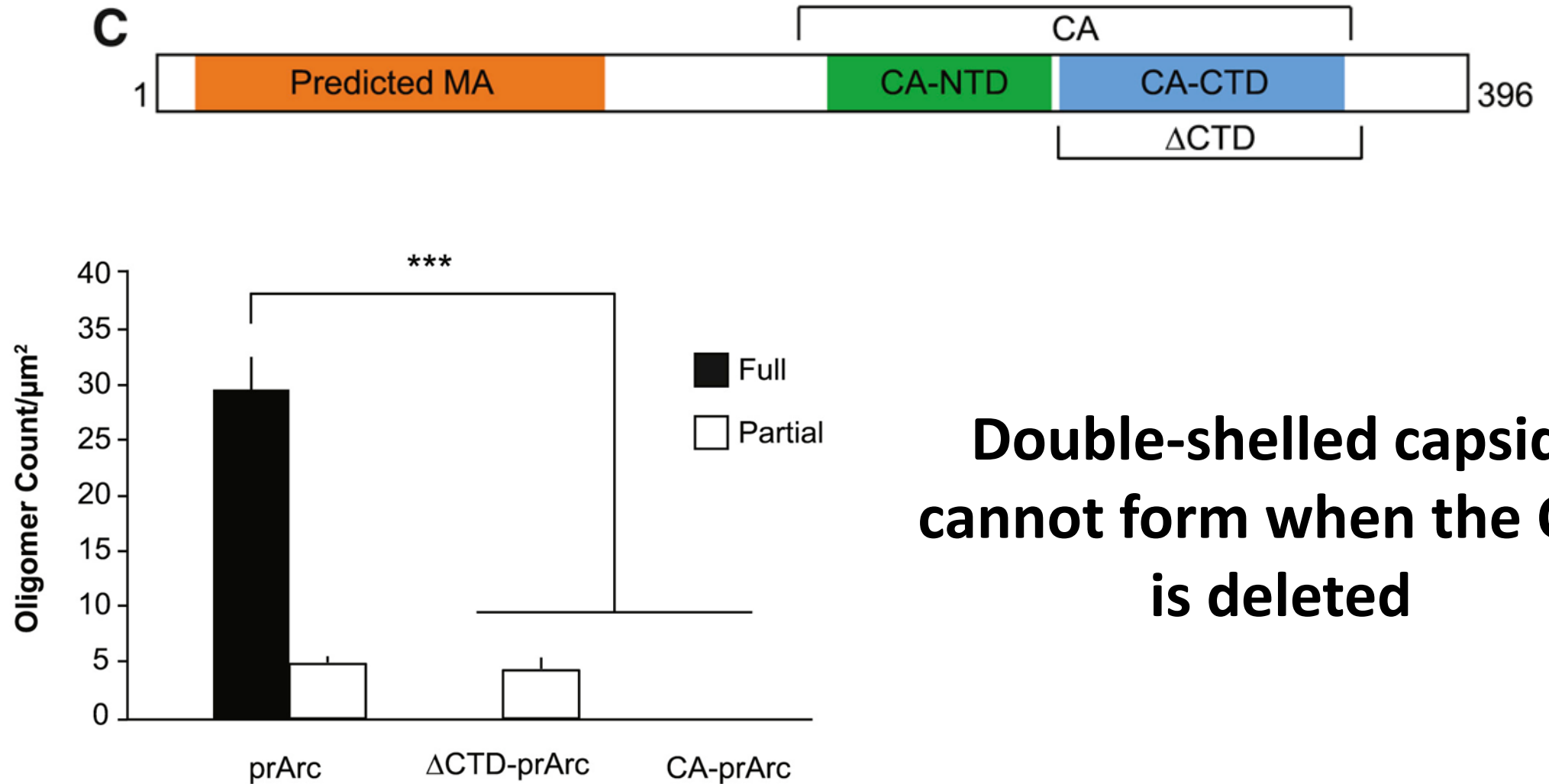
**Retroviral Gag
domain!**

Does Arc protein self-assemble into virus-like capsids?



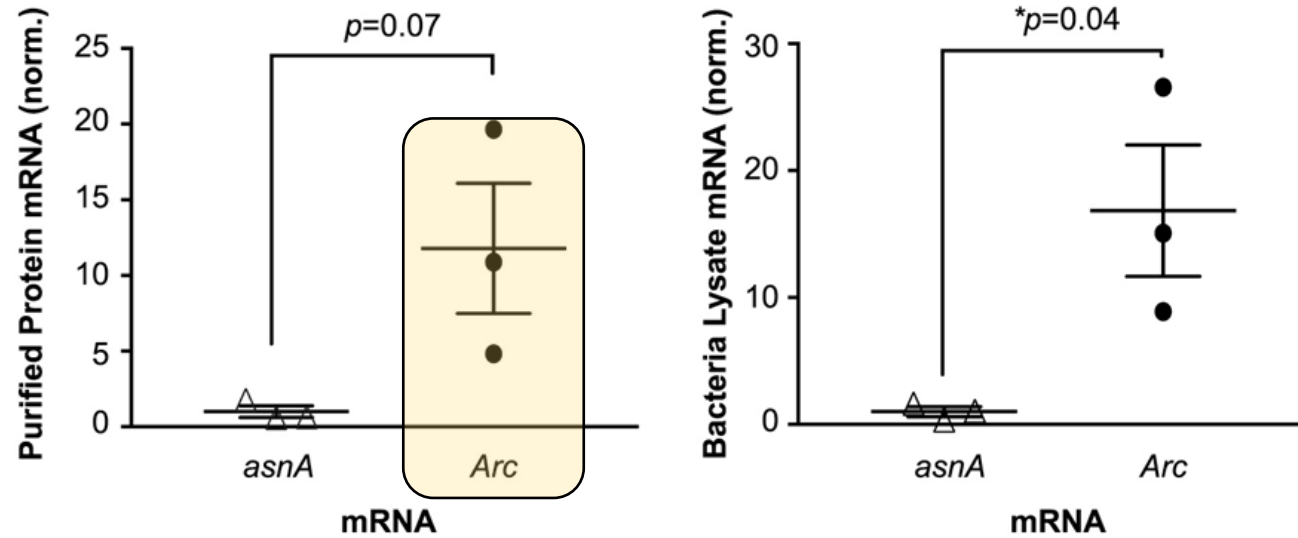
Viral capsid-like, double shell protein formations are seen in purified Arc

Is the CA-CTD Region Necessary for Capsid Assembly?



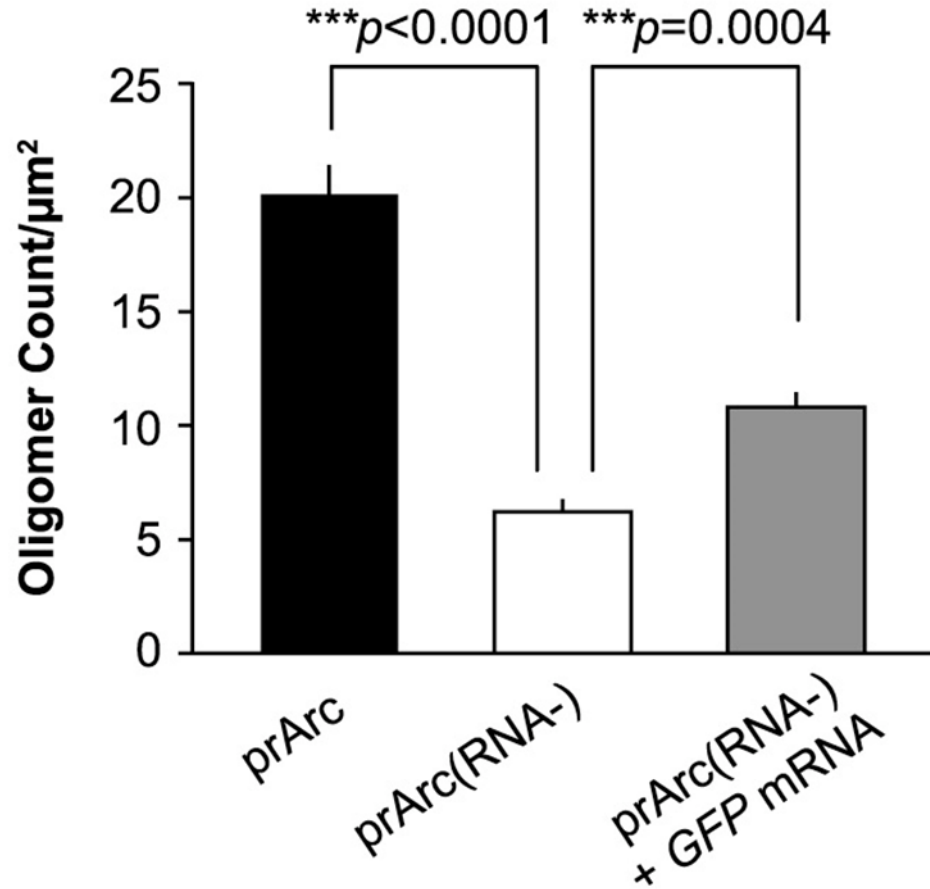
Does Arc bind and encapsulate mRNA?

A



Arc generally binds and encapsulates mRNA depending on stoichiometry and protects it from degradation

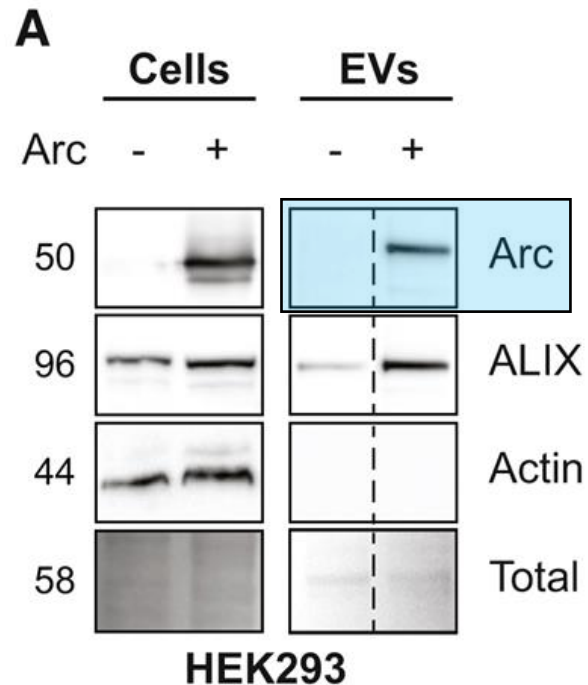
Does Arc require RNA for proper assembly?



**Stripping of RNA bases from
RNA decreased overall
proper capsid formation**

**Addition of general mRNA
increases proper capsid
formation**

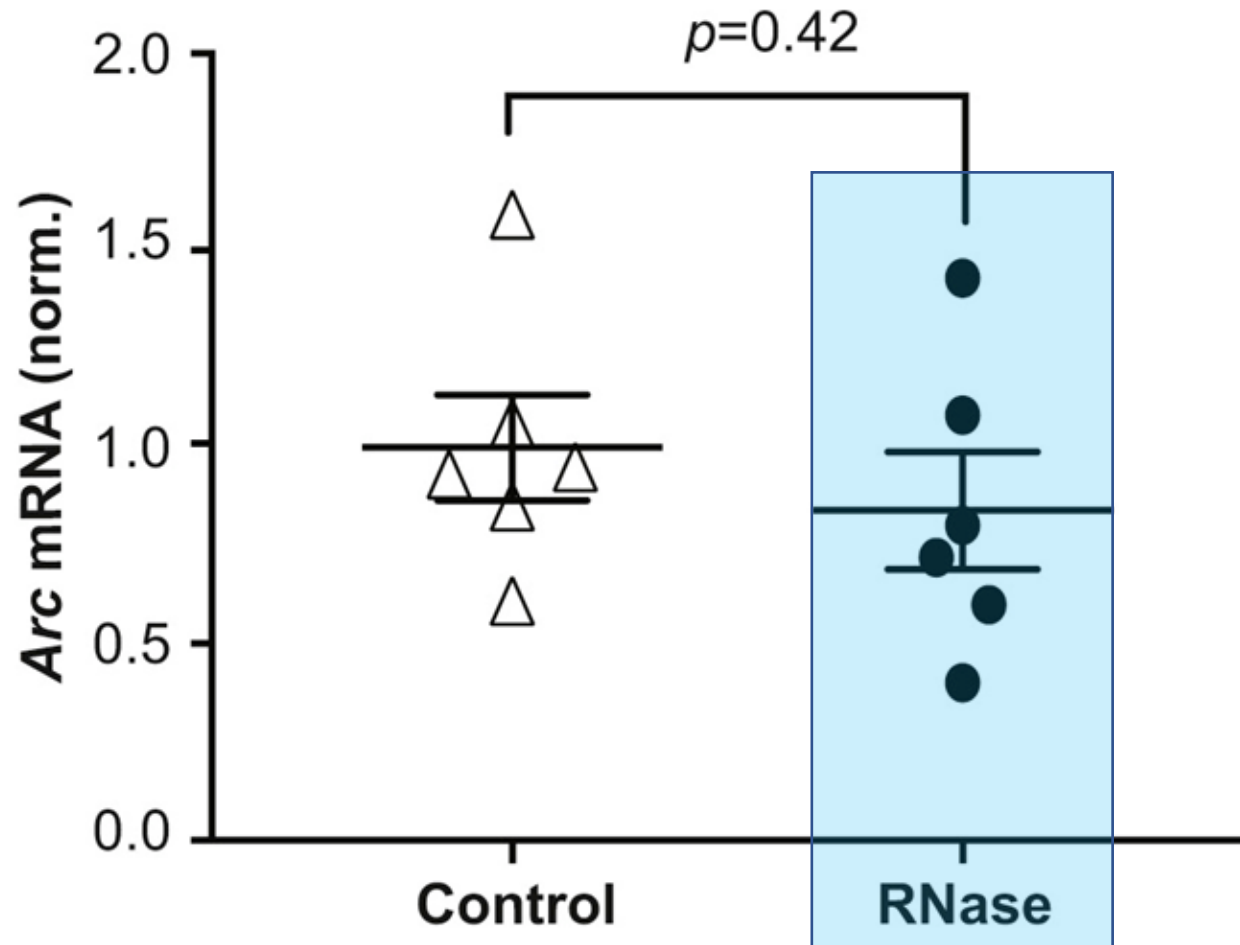
Is Arc mRNA found in extracellular vesicles (EVs) outside of the neuron?



Arc mRNA is found in extracellular vesicles. Amount decreases when CTD is altered

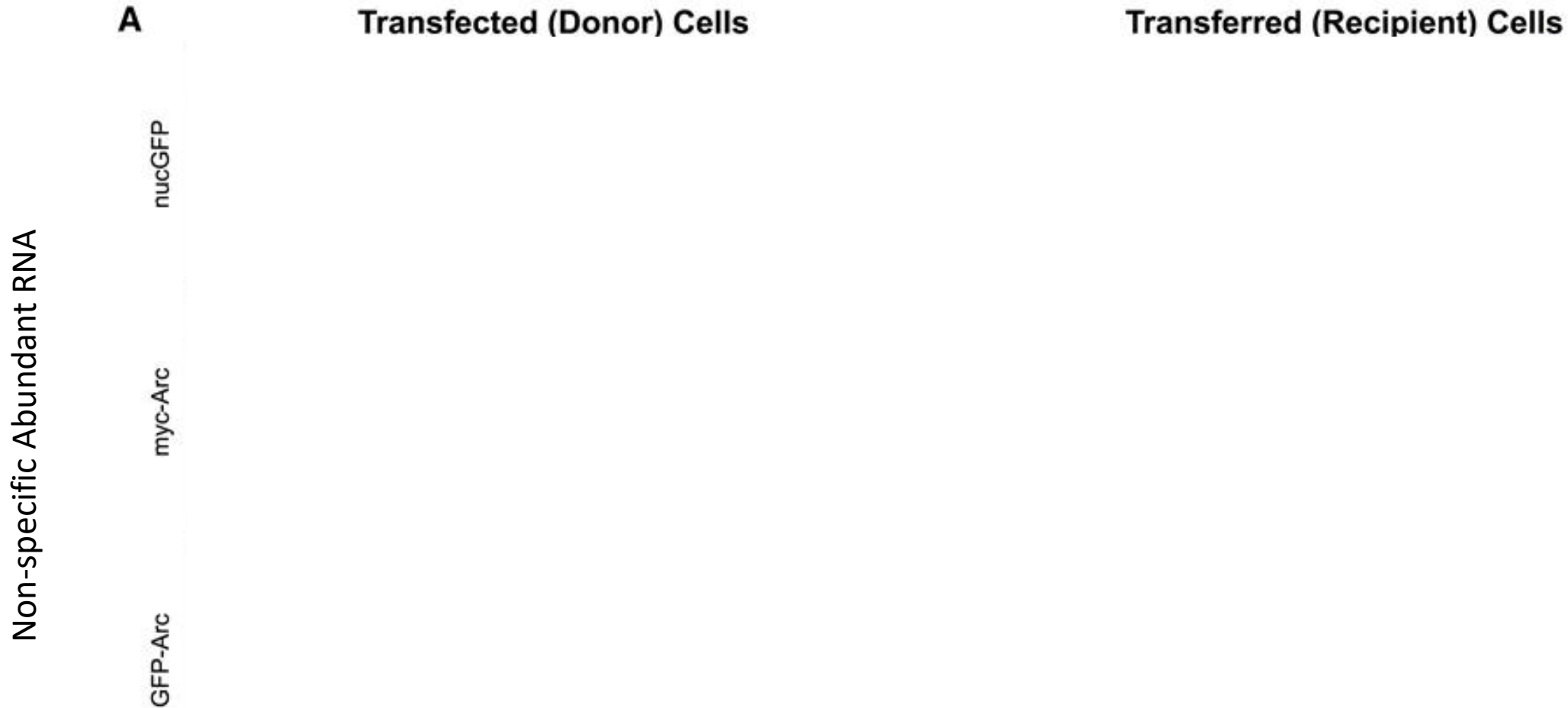
Do EVs degrade outside of the neuron?

C



**No, the mRNA
within stays
stable!**

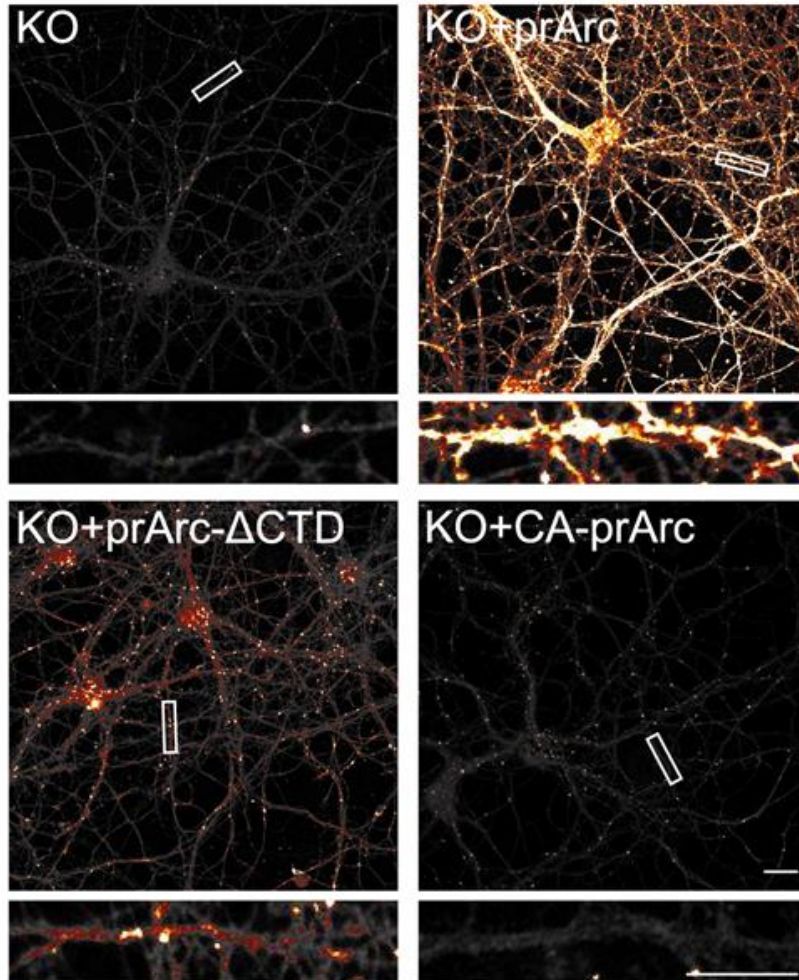
Can Arc transfer mRNA through encapsulated mRNA or arc-containing EVs?



Is Arc capsid required for neuron uptake?

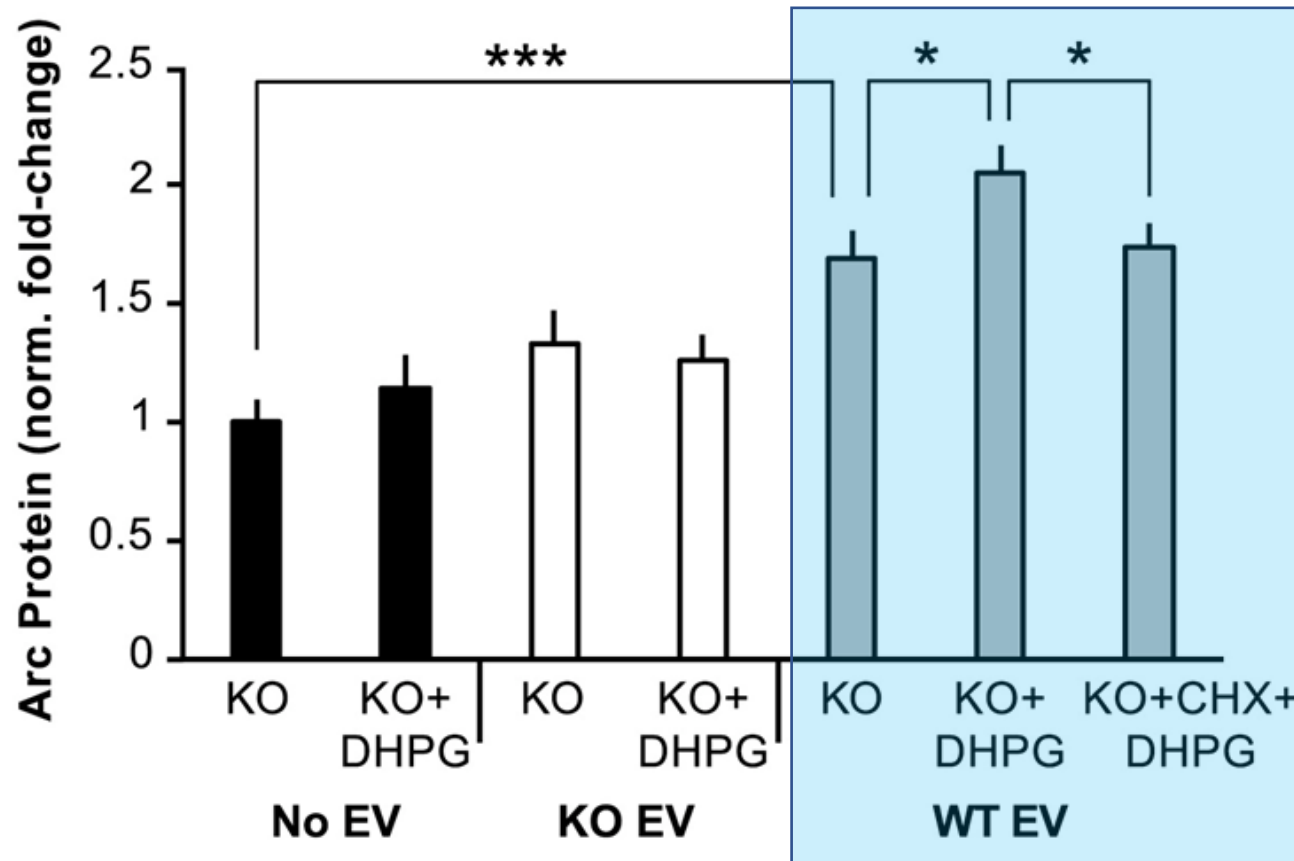
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D



Is Arc transferred mRNA available in the neurons for translation?

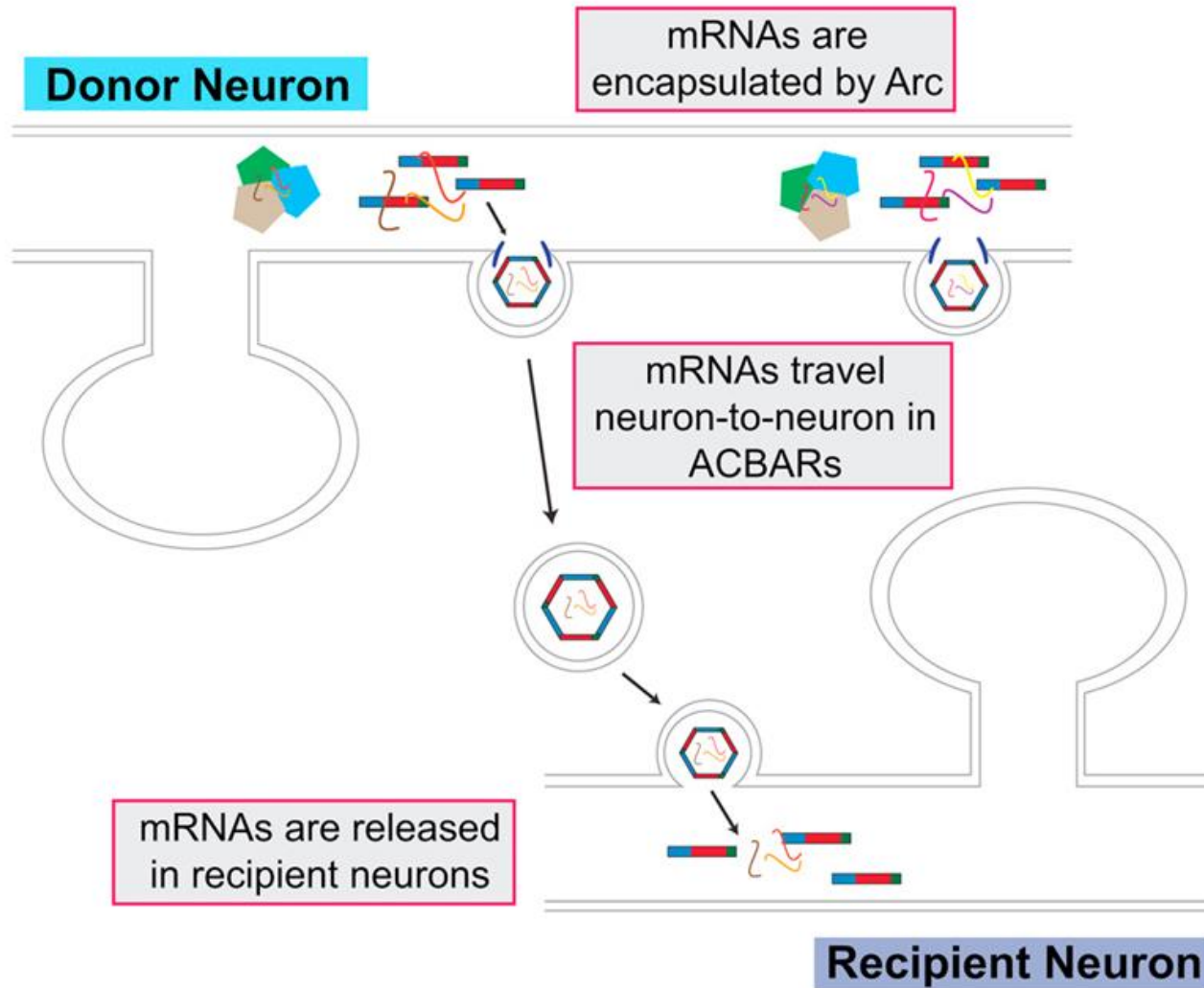
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**Induction with DHPG
increases translation
of Arc mRNA in
recipient neurons**

**Repression with CHX
decreases translation**

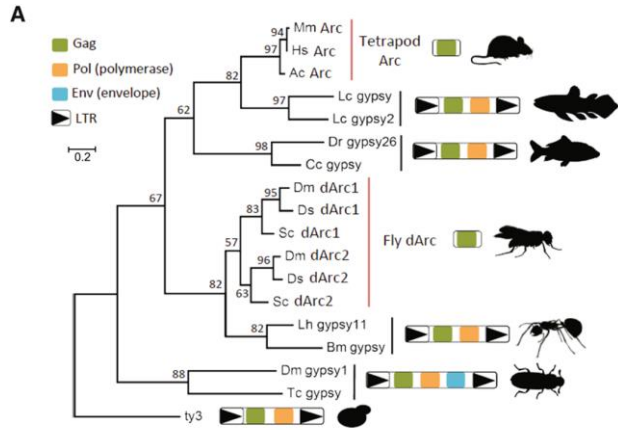
How does Arc work in the brain?



Arc is similar to a retrovirus

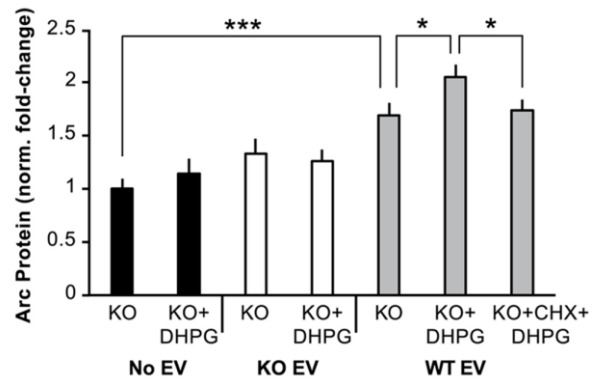
ACBARs = Arc Capsids Bearing Any RNA

Summary

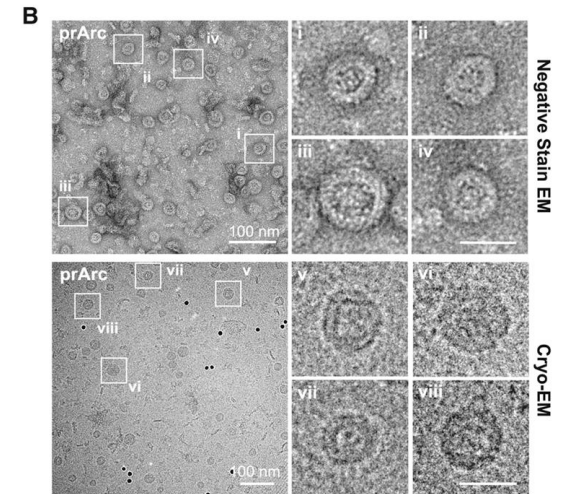


Arc exhibits similar properties to retroviral Gag proteins

Arc forms virus-like capsids



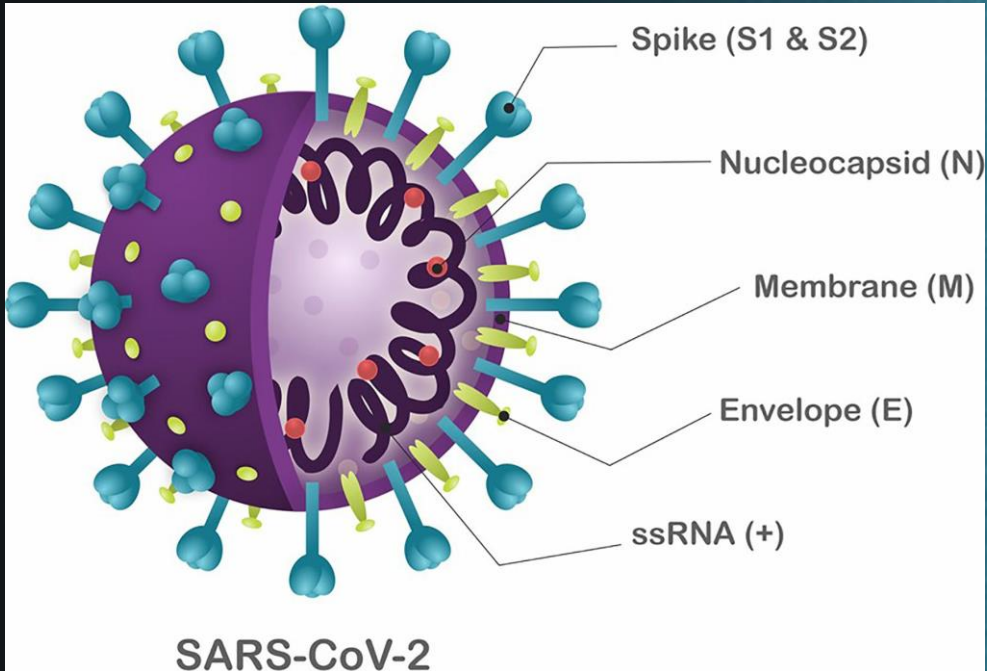
These capsids transfer mRNA across cells, implicating Arc in long-term information storage



Questions?



Future Directions



**What other cargo do
ACBARs contain?**

References

1) Pastuzyn ED, Day CE, Kearns RB, Kyrke-Smith M, Taibi AV, McCormick J, Yoder N, Belnap DM, Erlendsson S, Morado DR, Briggs JAG, Feschotte C, Shepherd JD. The Neuronal Gene Arc Encodes a Repurposed Retrotransposon Gag Protein that Mediates Intercellular RNA Transfer. Cell. 2018 Jan 11;172(1-2):275-288.e18. doi: 10.1016/j.cell.2017.12.024. Erratum in: Cell. 2018 Mar 22;173(1):275. PMID: 29328916; PMCID: PMC5884693.

Images:

<https://news.harvard.edu/gazette/story/2020/12/how-neurons-form-long-term-memories/>

<https://www.claromentis.com/blog/dont-let-a-lack-of-digital-knowledge-hold-back-your-business/>

<https://en.wikipedia.org/wiki/Retrotransposon>

<https://geneticeducation.co.in/gene-therapy-types-vectors-viral-and-non-viral-process-applications-and-limitations/>

<https://www.ck12.org/book/ck-12-biology-advanced-concepts/section/11.22/>

<https://www.forbes.com/sites/jarretjackson/2020/08/12/as-a-leader-are-you-asking-the-right-questions/?sh=63db96866e7d>

<https://www.frontiersin.org/articles/10.3389/fmicb.2020.01818/full>

<https://healthmatters.nyp.org/what-is-causing-covid-brain-fog/>