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ARTICLE

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Retrovirus-like Gag Protein Arc1 Binds RNA and Traffics across Synaptic Boutons

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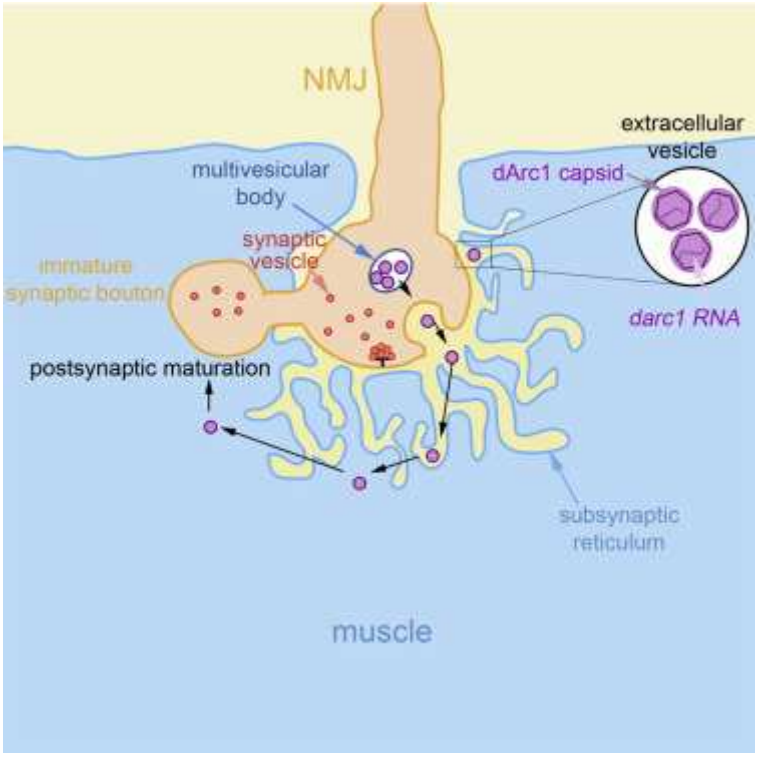

Summary

Arc/Arg3.1 isrequiredforsynapticplasticity and cognition, and mutations in this gene are linked to autism and schizophrenia. Arcbears a domainresembling retroviral/retrotransposon Gag-likeproteins, whichmultimerizeinto a capsidthatpackages viral RNA. Thesignificance of such a domain in a plasticitymoleculeisuncertain. Here, wereportthatthe *Drosophila* Arc1 proteinformscapsid-likestructuresthatbind *darc1* mRNA in neurons and is loadedintoextracellularvesiclesthat are transferredfrommotorneurons to muscles. Thisloading and transfer dependsonthe *darc1-mRNA* 3′ untranslatedregion, whichcontainsretrotransposon-likesequences. Disrupting transfer blocks synapticplasticity, suggestingthat transfer of dArc1 complexedwithitsmRNAisrequiredforthisfunction. Notably, culturedcellsalsoreleaseextracellularvesiclescontainingthe Gag region of the Copia

retrotransposoncomplexedwithitsownmRNA. Takentogether, ourresultspoint to a *trans*-synapticmRNAtransportmechanisminvolving retrovirus-likecapsids and extracellularvesicles.