Exocytotic properties of astrocytic vesicles

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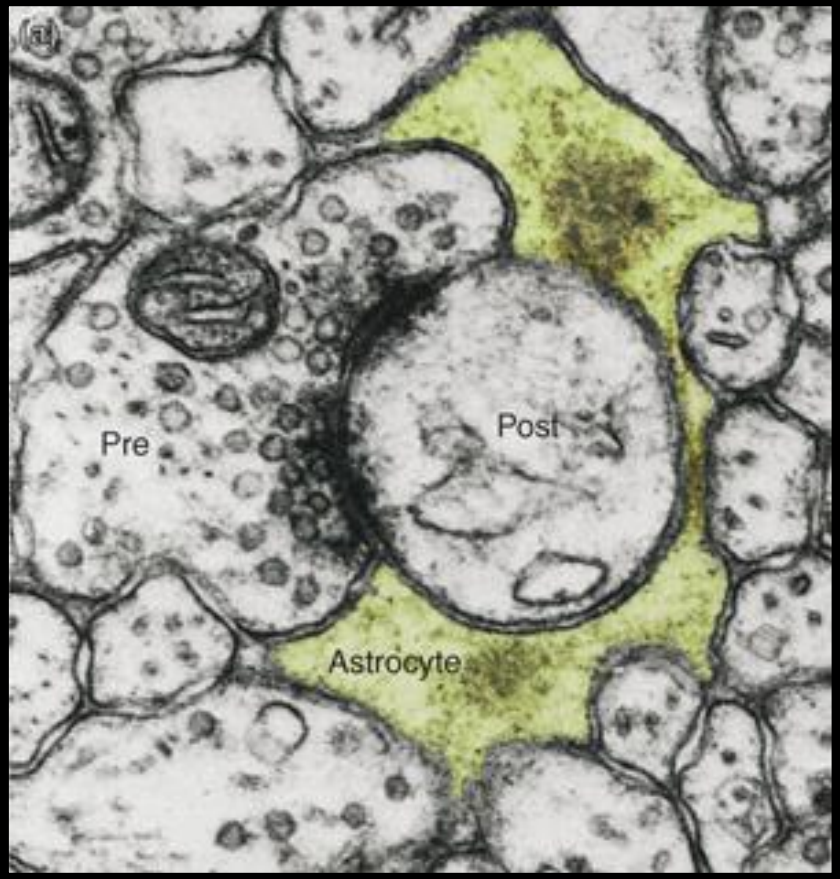
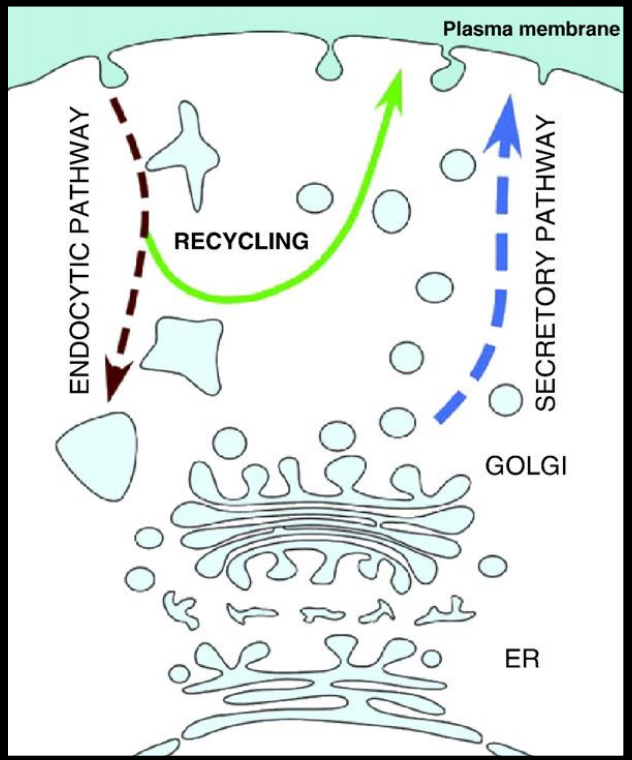
Astrocytes and vesicular gliotransmitters



Halassa et al., 2007

Exocytotitc release of gliotransmitters:
(i) amino acids: glutamate, D-serine
(ii) nucleotides: adenosine 5´triphosphate (ATP)
(iii) peptides: atrial natriuretic peptide (ANP), brain-derived neurotrophic factor (BDNF)



Parpura and Zorec, 2009

Overview

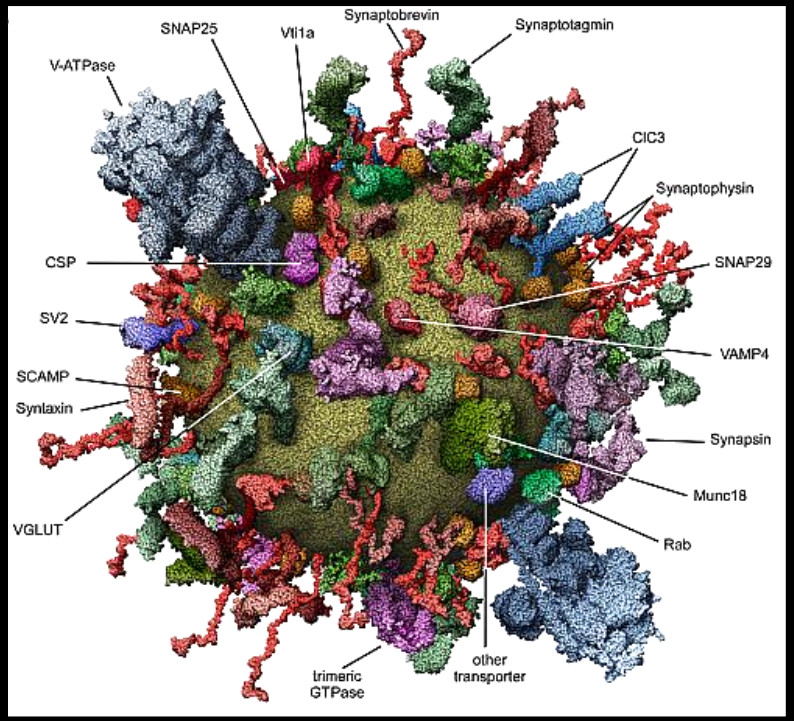
1. The anatomy of single vesicles in astrocytes

2. Regulated exocytosis in astrocytes

3. Vesicle mobility in astrocytes

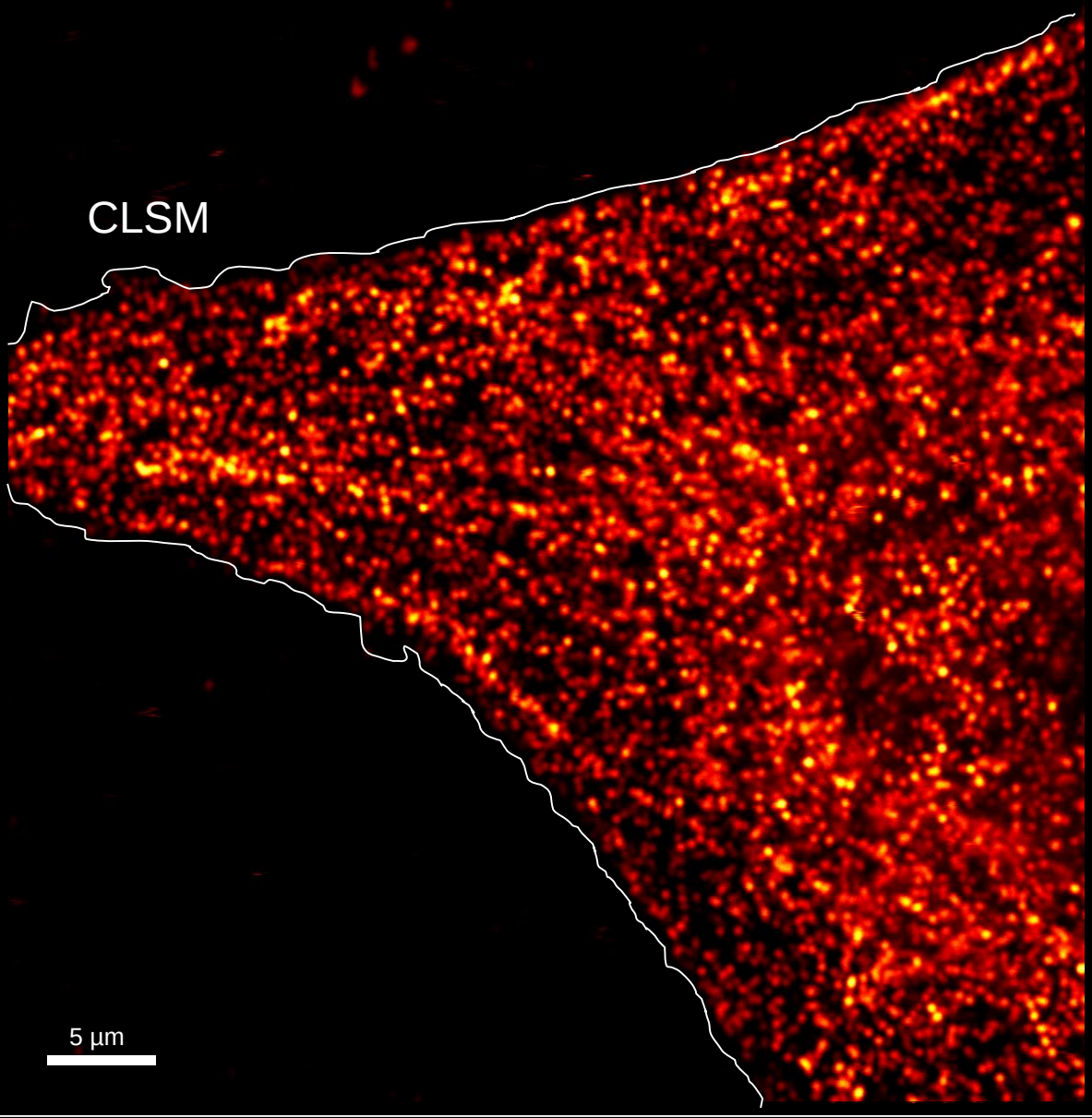
Overview

1. The anatomy of single vesicles in astrocytes

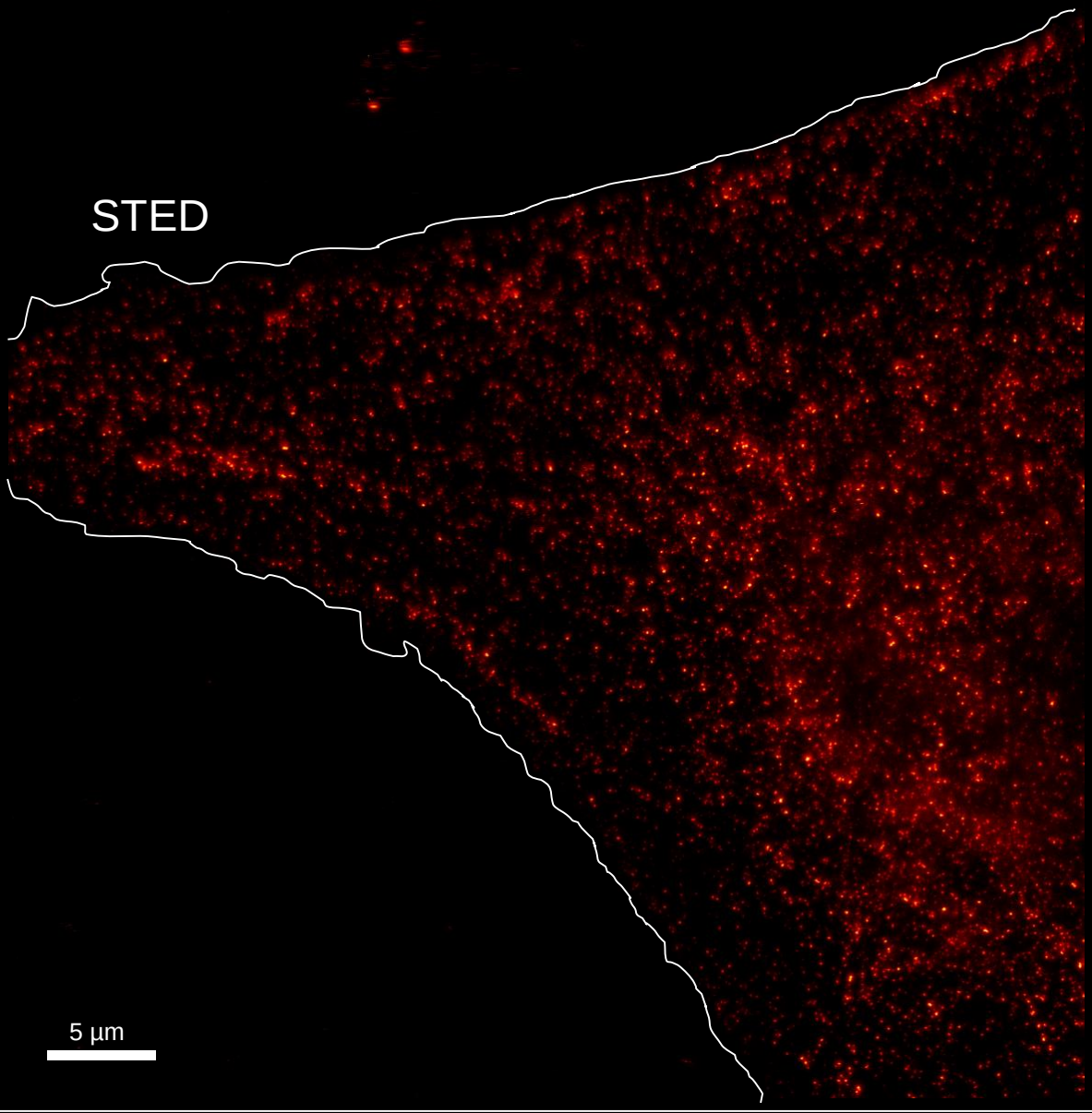


Takamori et al. 2006

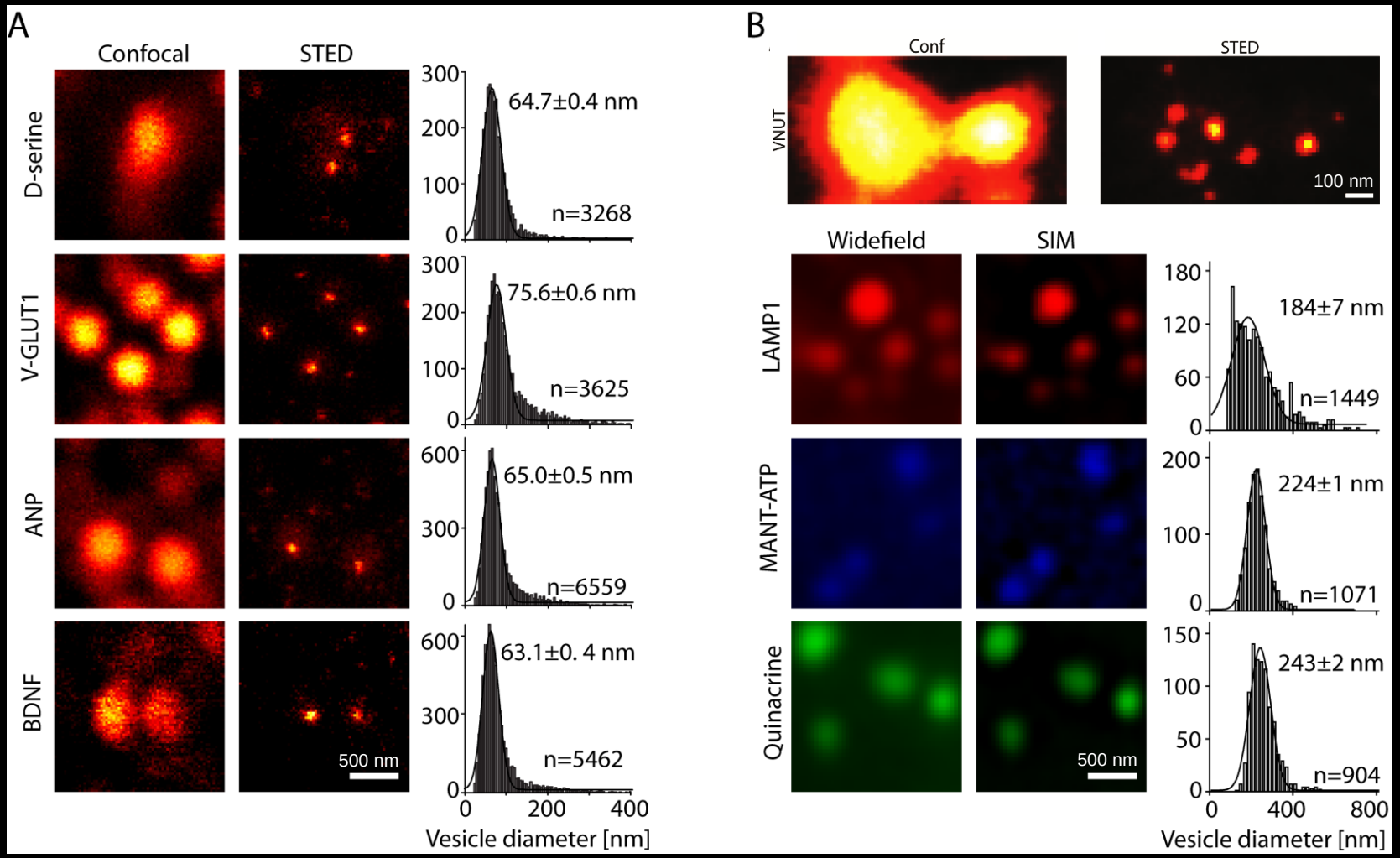
Astrocytic vesicles - STED



Astrocytic vesicles - STED



Astrocytic vesicles - STED

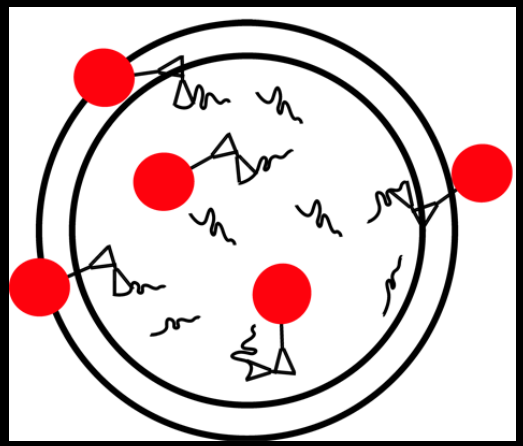


Guček, Jorgačevski et al., 2016

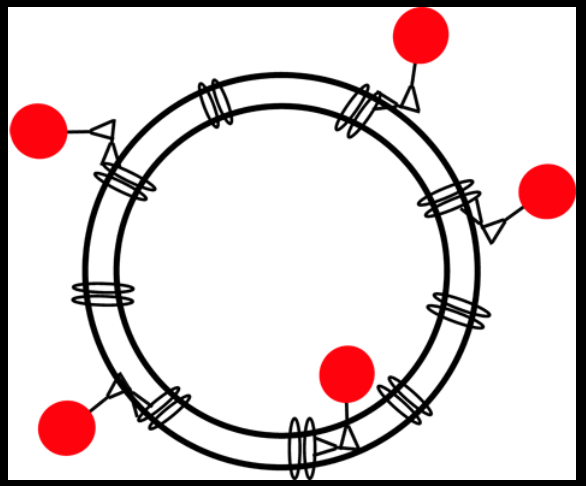
Vesicle diameters

Vesicles	EM (Literature)	STED
ANP	45 ± 2 nm (Potokar et al. 2008)	65 nm
BDNF	125 ± 22 nm (Bergami et al. 2008)	63 nm
D-serine	37 ± 11 nm (Bergersen et al. 2011)	65 nm
VGLUT1	30-50 nm (Bezzi et al. 2004, Stenovec et al. 2007)	76 nm

Vesicles	EM (Literature)	SIM
Lysosomes	100-1200 nm (Holtzmann E. 1989)	~200 nm

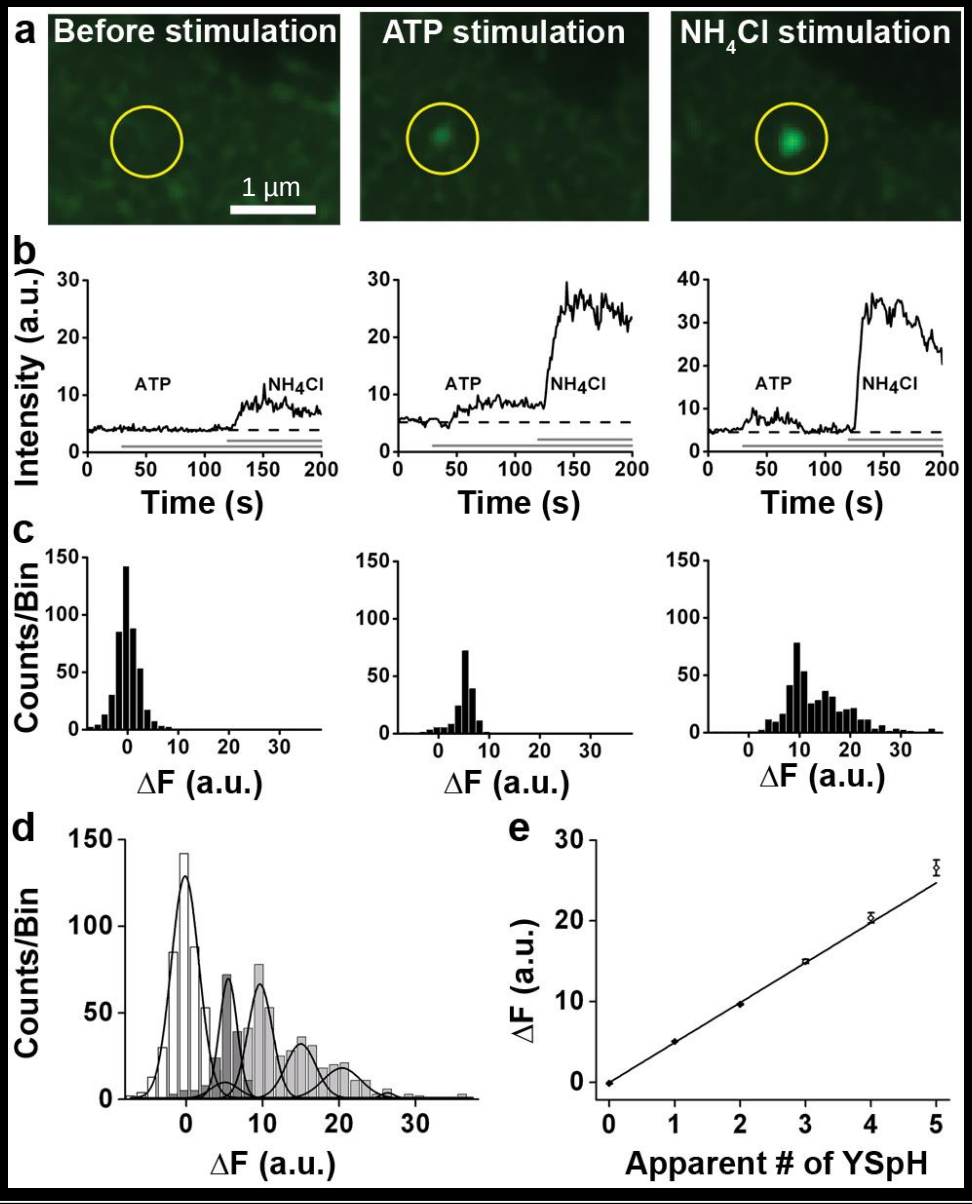


ANP



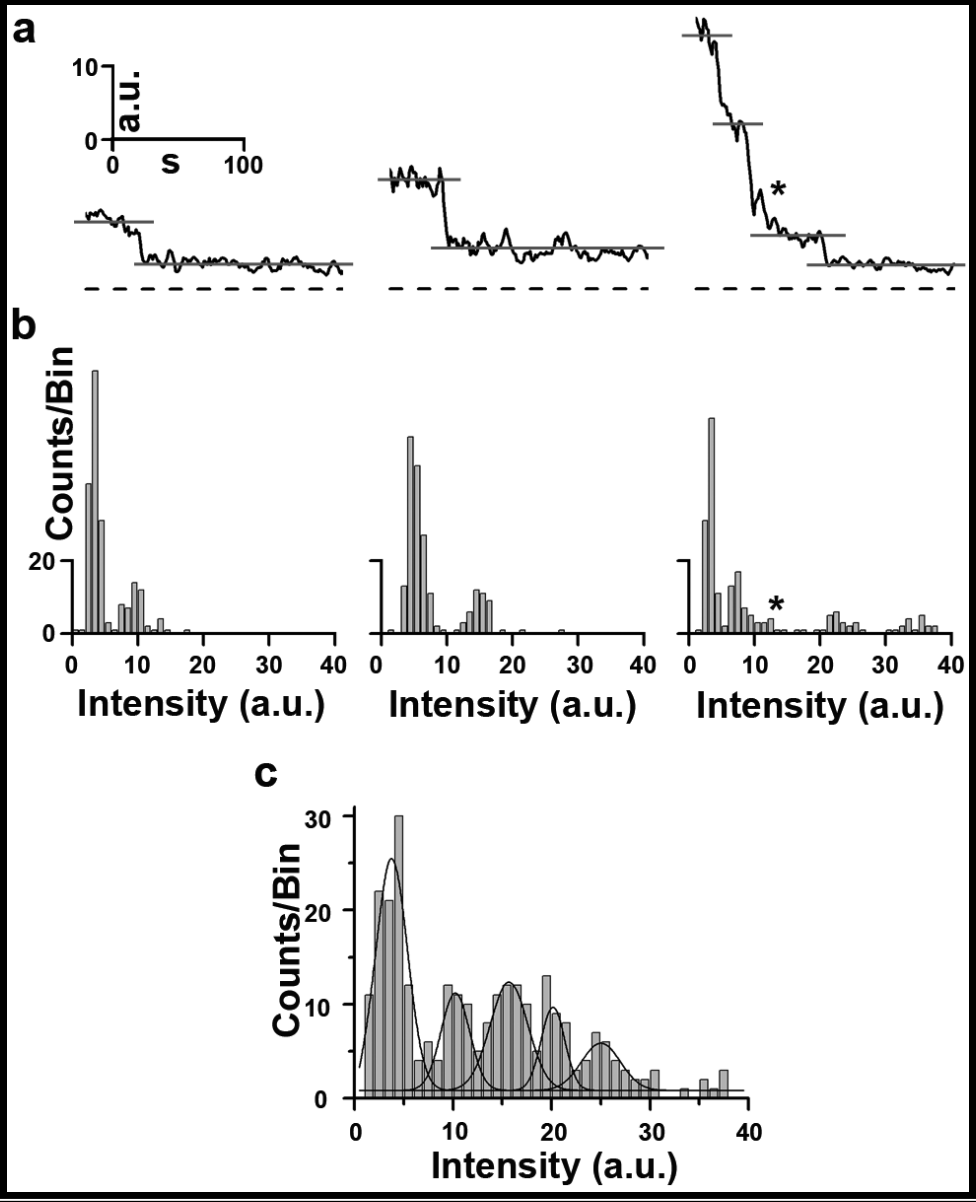
VGLUT1

The number of YspH per astrocytic vesicle



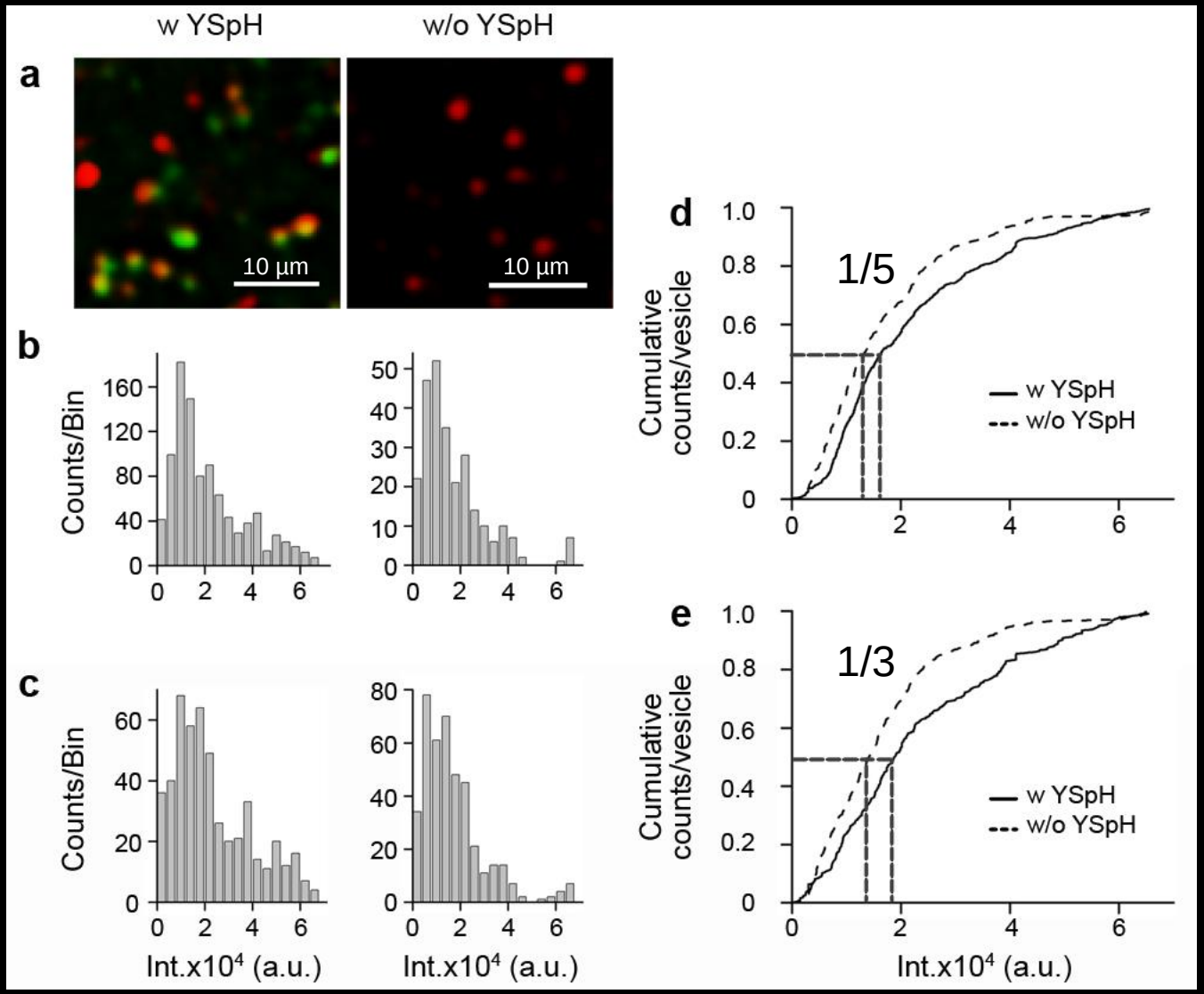
Singh et al., 2016

The number of YspH per astrocytic vesicle



Singh et al., 2016

The number of Sb2 per astrocytic vesicle



Singh et al., 2016

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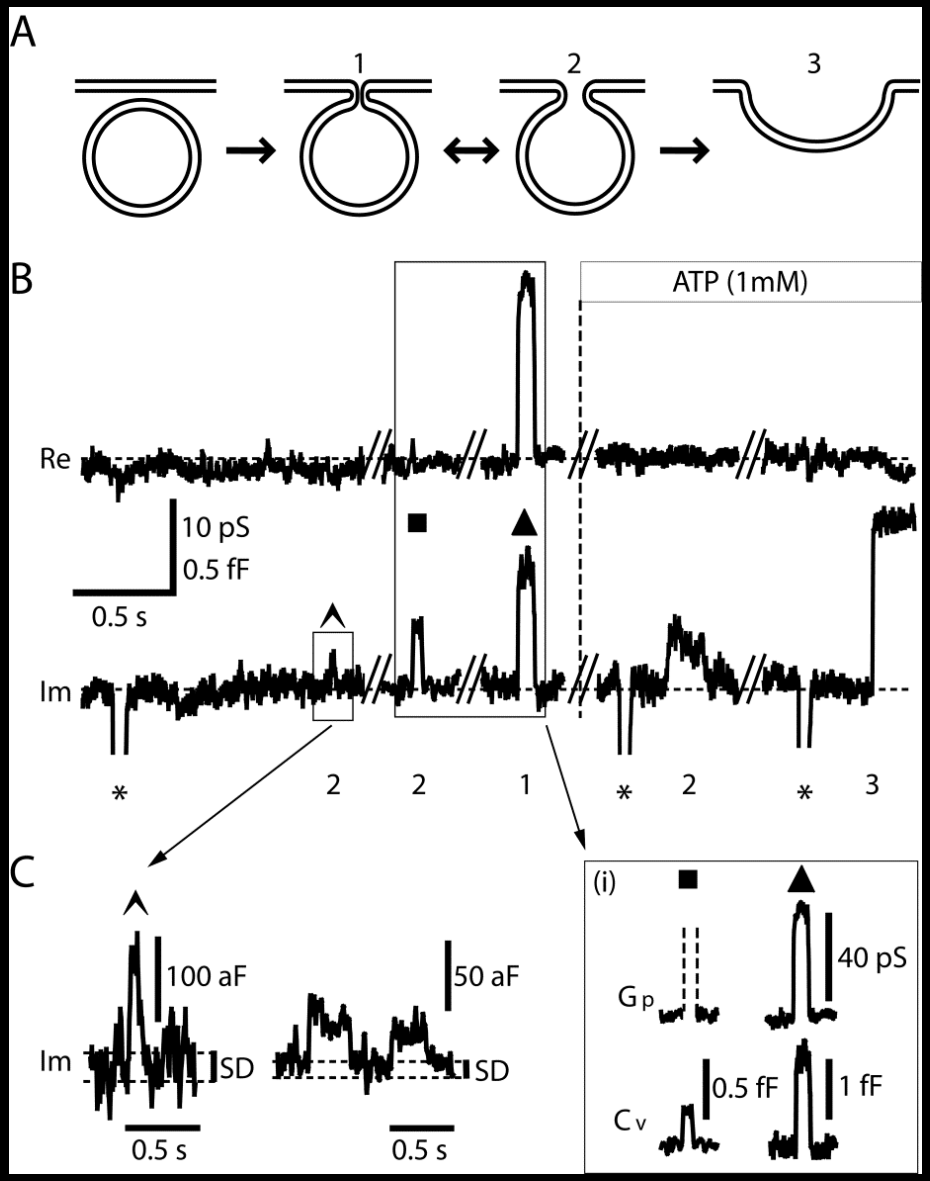
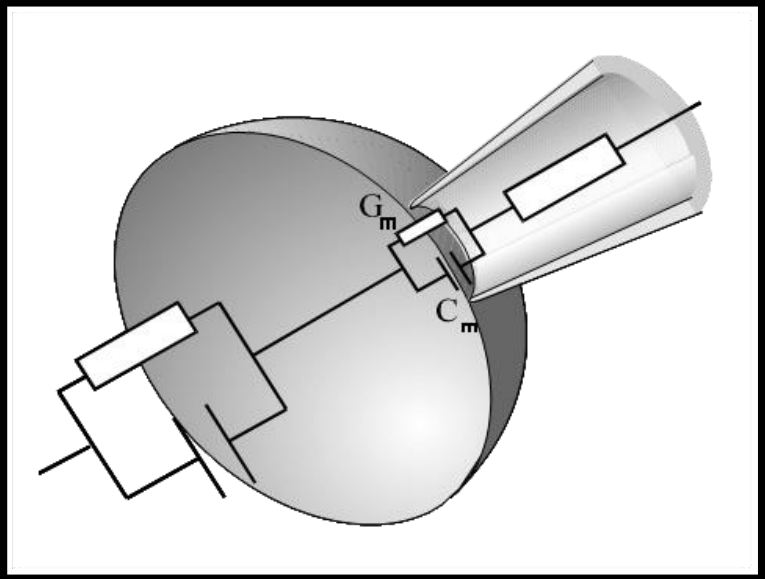
Overview

2. Regulated exocytosis in astrocytes

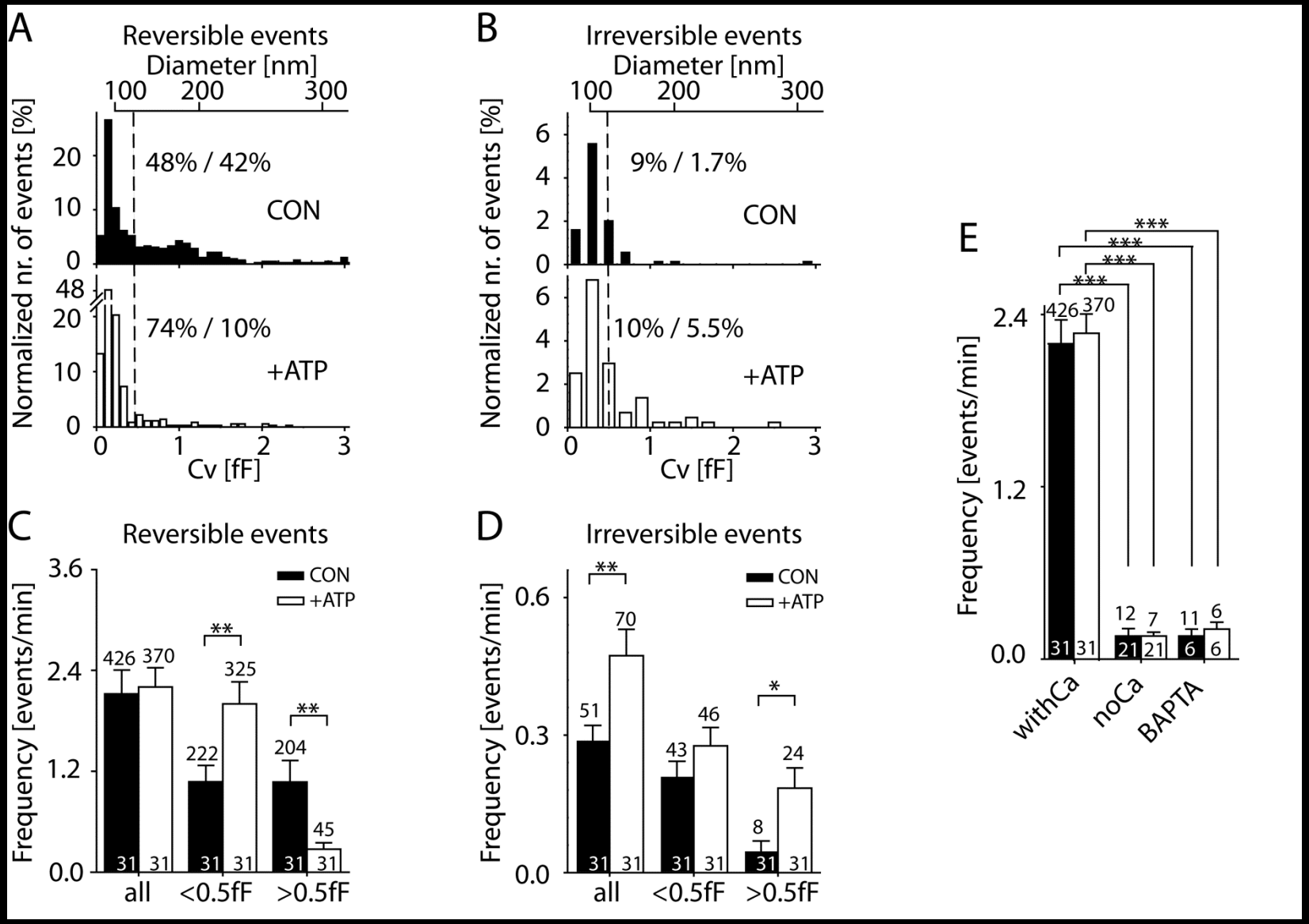
Exocytotic events in astrocytes



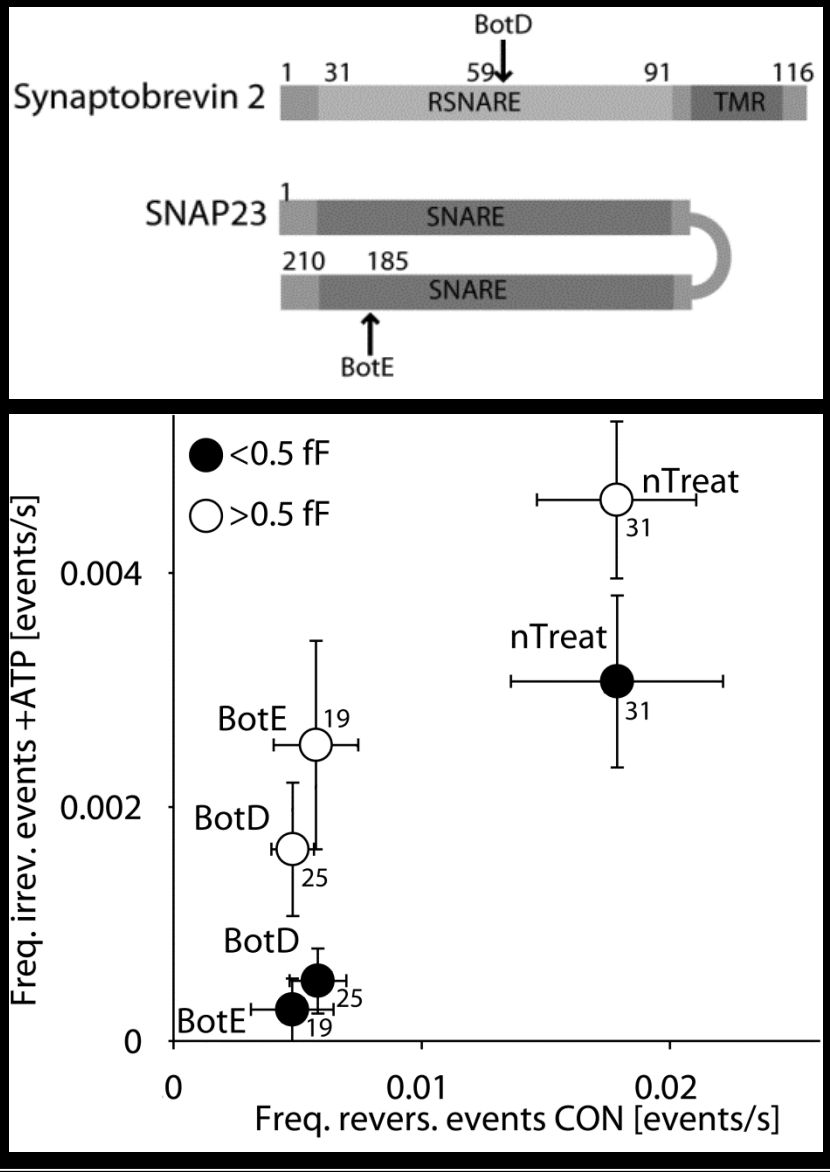


Guček, Jorgačevski et al., 2016

Properties of exocytotic events in astrocytes



Exocytotic events in astrocytes



Guček, Jorgačevski et al., 2016

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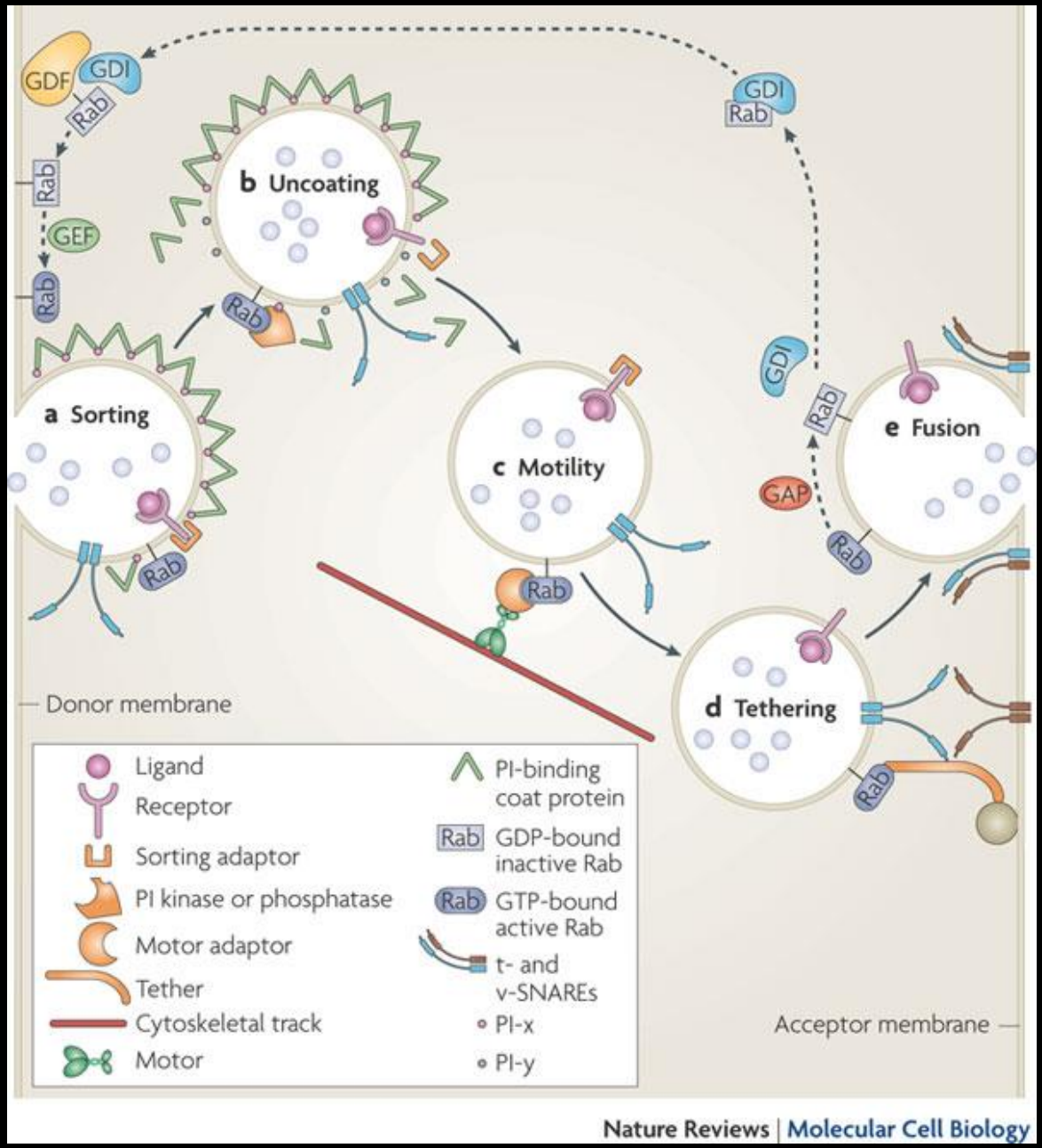
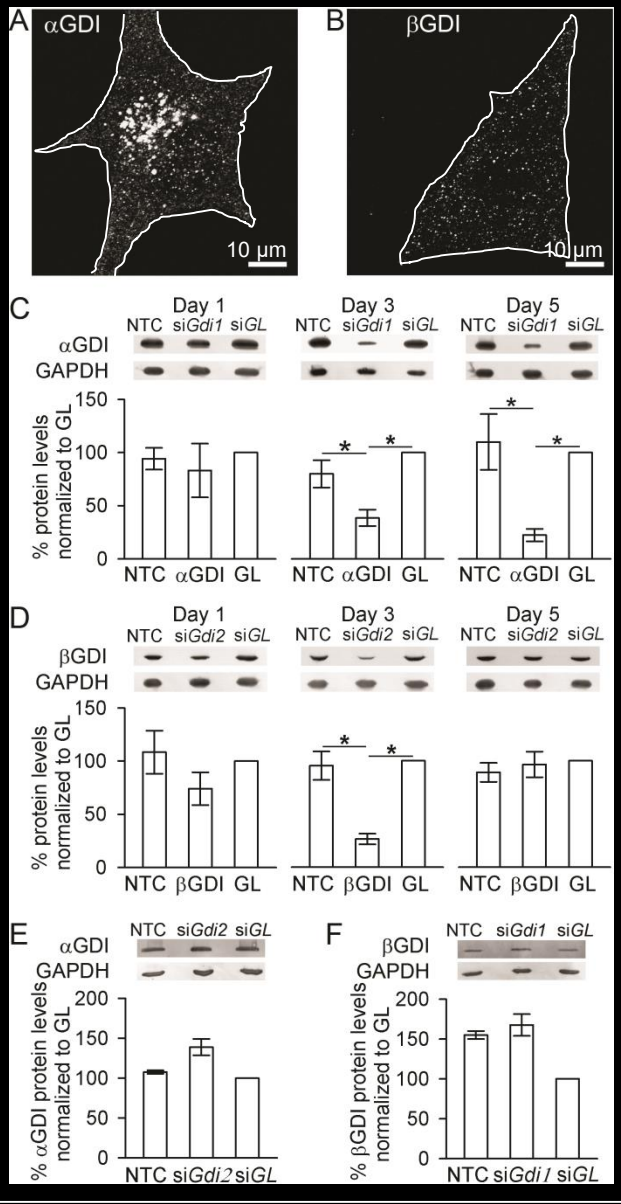
XLID

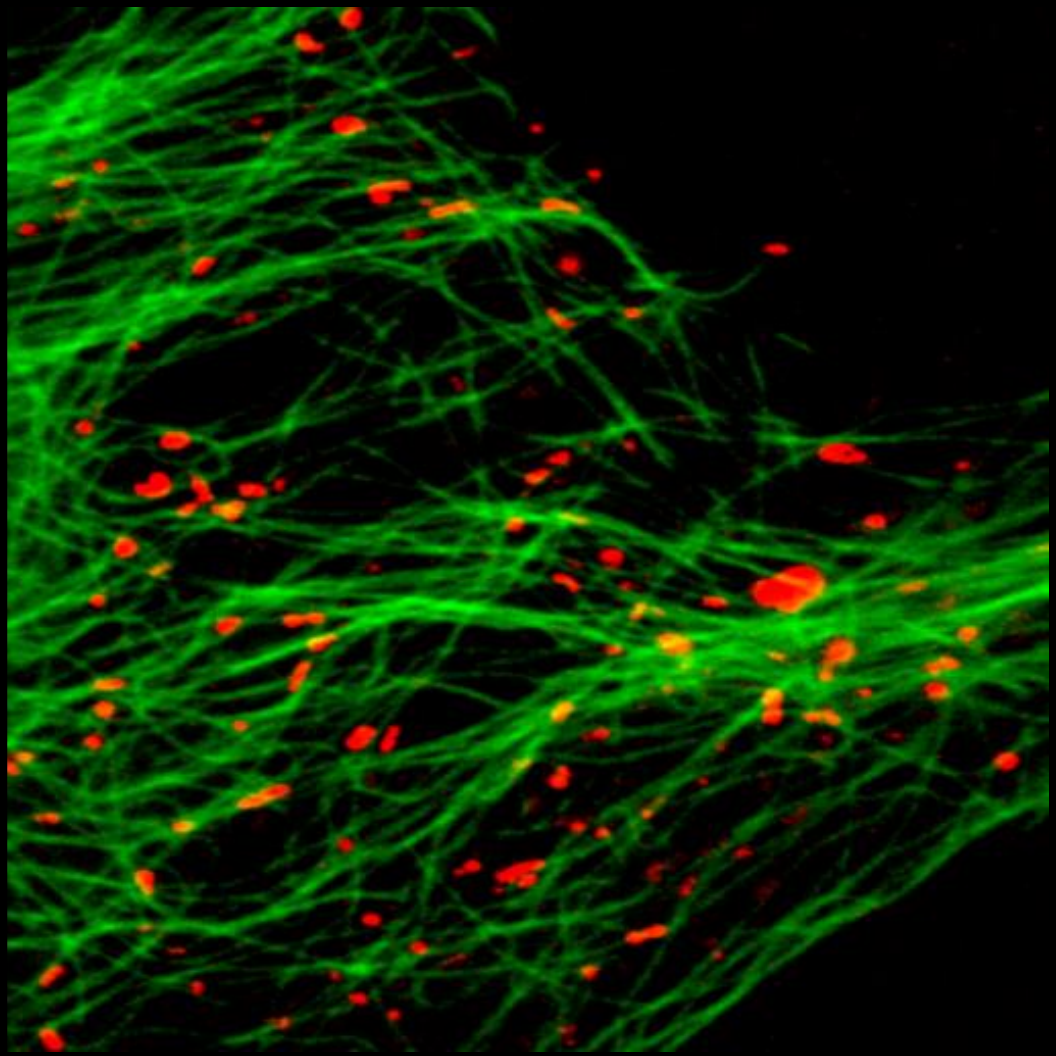
- ID - a non-progressive cognitive impairment affecting 1-3% of the Western population.
- Lifelong care at home or in welfare centers - enormous socioeconomic burdens.
- Syndromic and non-syndromic ID - environmental factors, genetic predisposition, or a combination of both.
- ~50% of moderate-to-severe cases have genetic origins and ~10% are due to XLID.
- ~820 genes responsible for ID; guanine nucleotide dissociation inhibitor (*GDI1*) was one of the first identified.

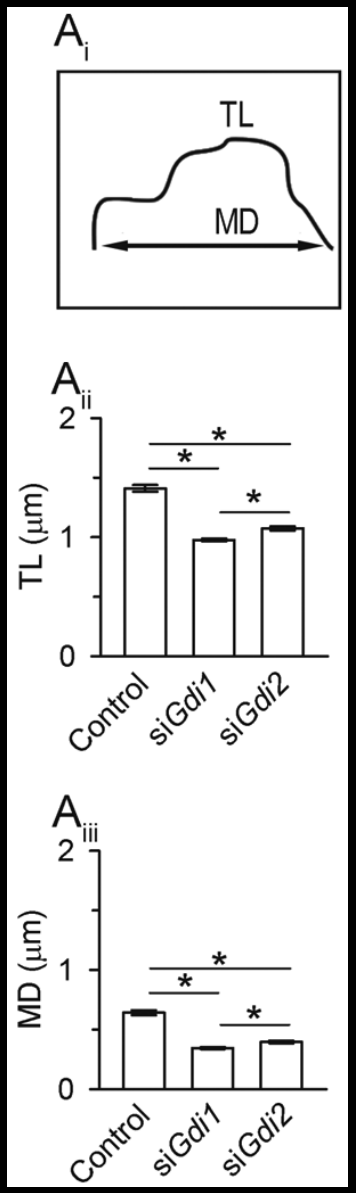

GDF
GDI
Rab
GEF
b Uncoating
a Sorting
c Motility
d Tethering
e Fusion
GAP
Donor membrane
Acceptor membrane
Ligand
Receptor
Sorting adaptor
PI kinase or phosphatase
Motor adaptor
Tether
Cytoskeletal track
Motor
PI-binding coat protein
GDP-bound inactive Rab
GTP-bound active Rab
t- and v-SNAREs
PI-x
PI-y
Nature Reviews | Molecular Cell Biology

Rat astrocytes express αGDI and βGDI.

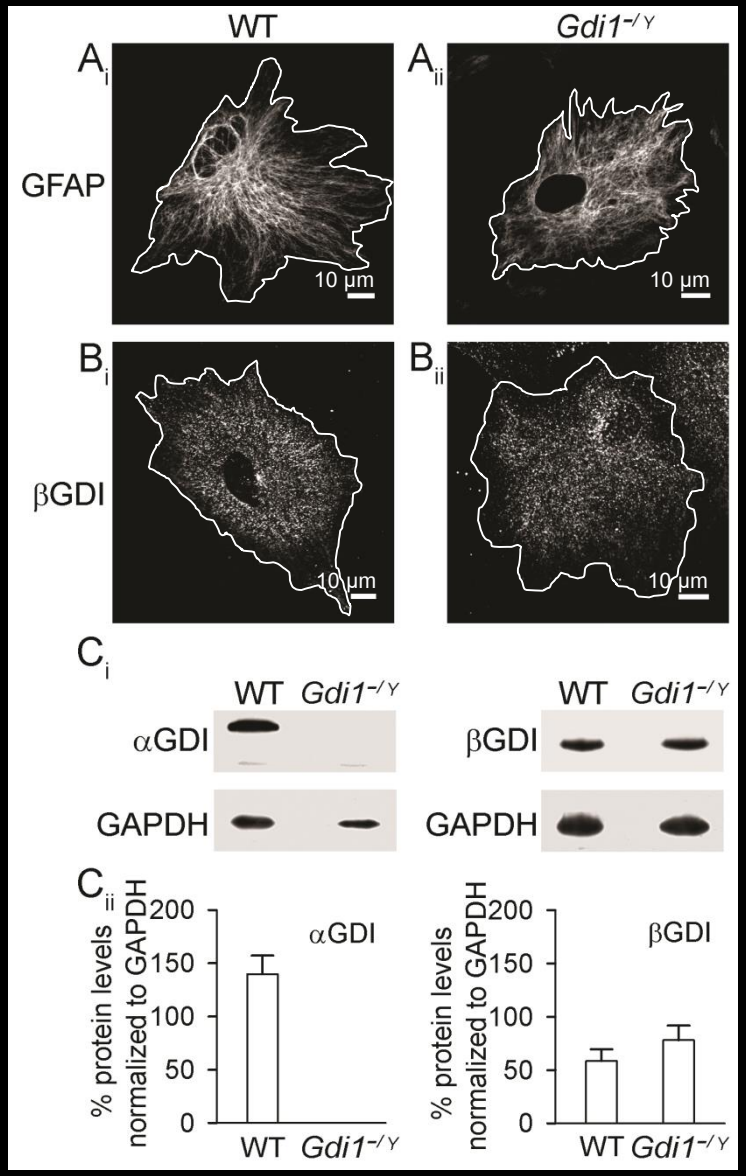


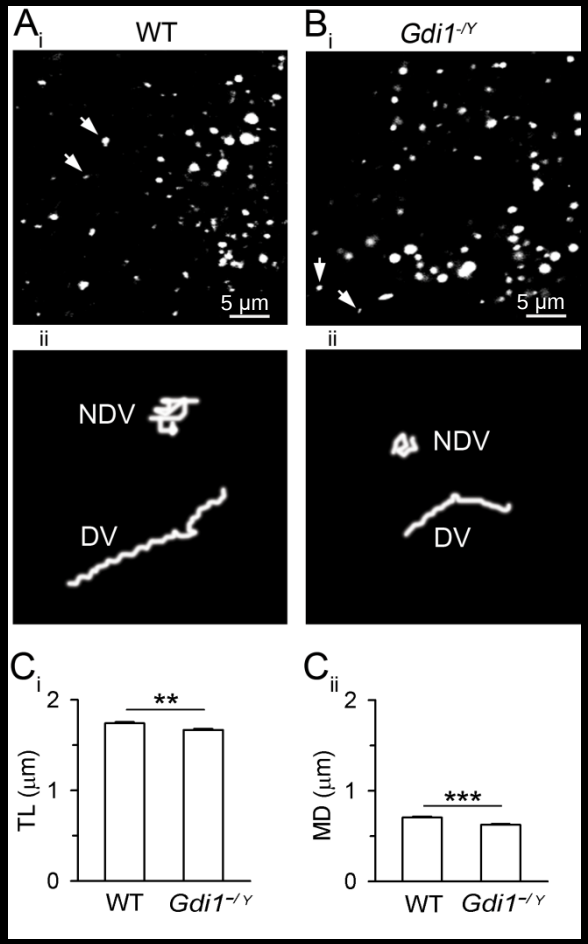
Vesicle mobility in astrocytes





αGDI absence in Gdi1$^{-/Y}$ mice attenuates vesicle mobility





Potokar et al., 2016

Conclusions

- Smaller, synaptic like, vesicles in astrocytes contain amino acid and peptidergic transmitters, while larger vesicles contain ATP.
- There are 15 to 25 Sb2 molecules per astrocytic vesicle.
- Regulated exocytosis is present in astrocytes.
- ATP stimulation triggers distinct response of two vesicle populations.
- Vesicle mobility in astrocytes is affected in pathological conditions.

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Single-vesicle architecture of synaptobrevin2 in astrocytes

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Cellular and Molecular Life Sciences

ORIGINAL ARTICLE

Dominant negative SNARE peptides stabilize the fusion pore in a narrow, release-unproductive state

Alenka Guček[1] · **Jernej Jorgačevski**[1,2] · **Priyanka Singh**[1] · **Claudia Geisler**[3] · **Marjeta Lisjak**[1] · **Nina Vardjan**[1,2] · **Marko Kreft**[1,2,4] · **Alexander Egner**[3] · **Robert Zorec**[1,2]

Mol Neurobiol
DOI 10.1007/s12035-016-9834-1

Impaired αGDI Function in the X-Linked Intellectual Disability: The Impact on Astroglia Vesicle Dynamics

Maja Potokar[1,2] · **Jernej Jorgačevski**[1,2] · **Valentina Lacovich**[1] · **Marko Kreft**[1,2,3] · **Nina Vardjan**[1,2] · **Veronica Bianchi**[4] · **Patrizia D'Adamo**[1,2,4] · **Robert Zorec**[1,2]

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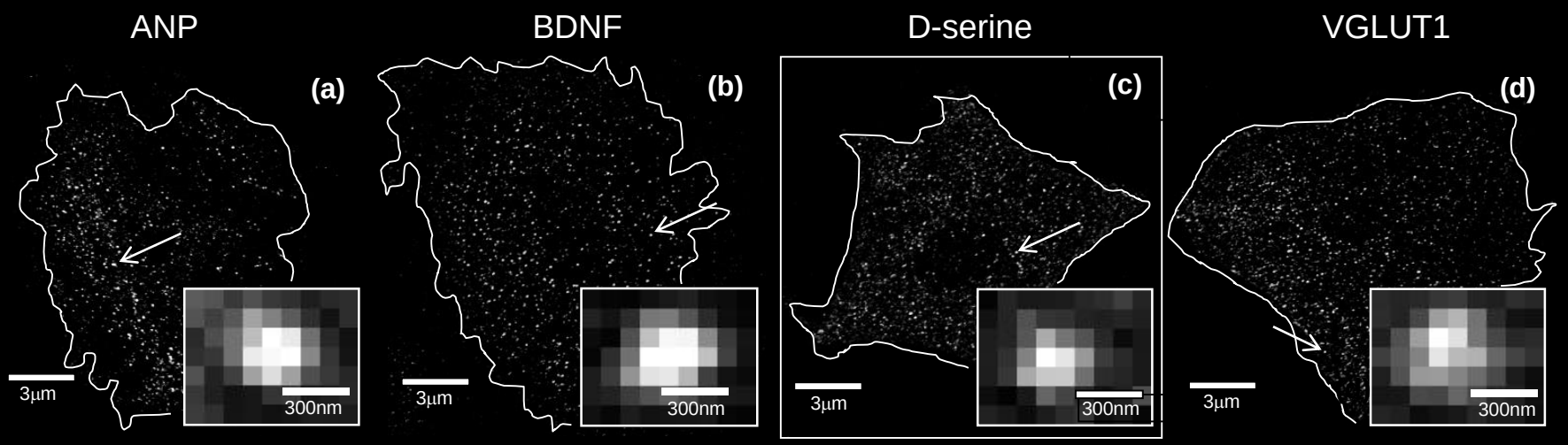
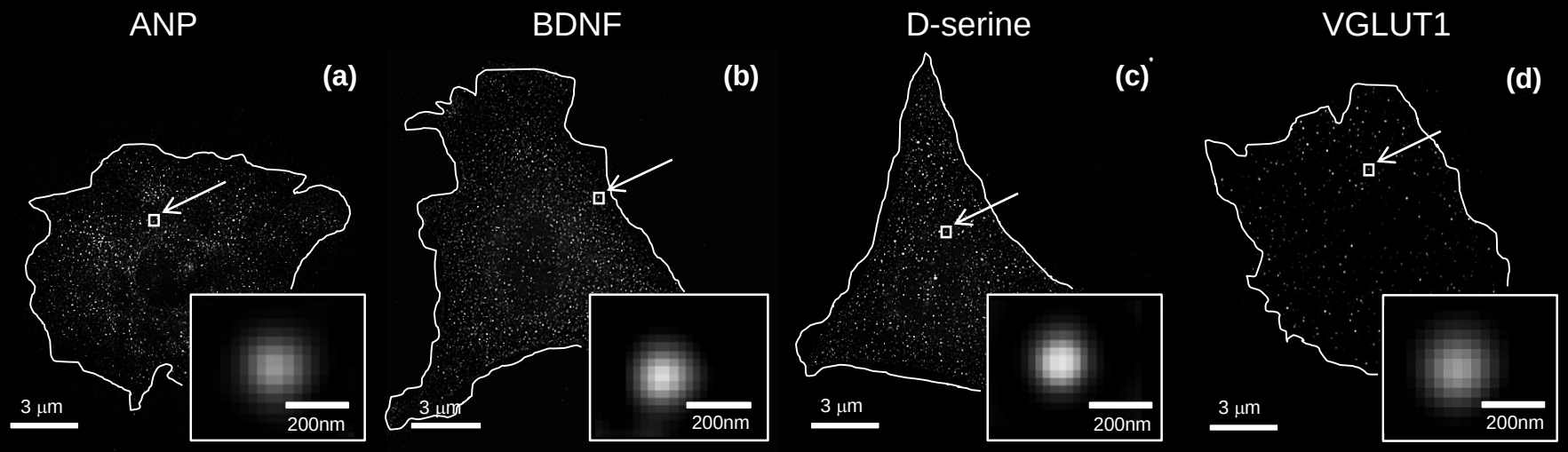
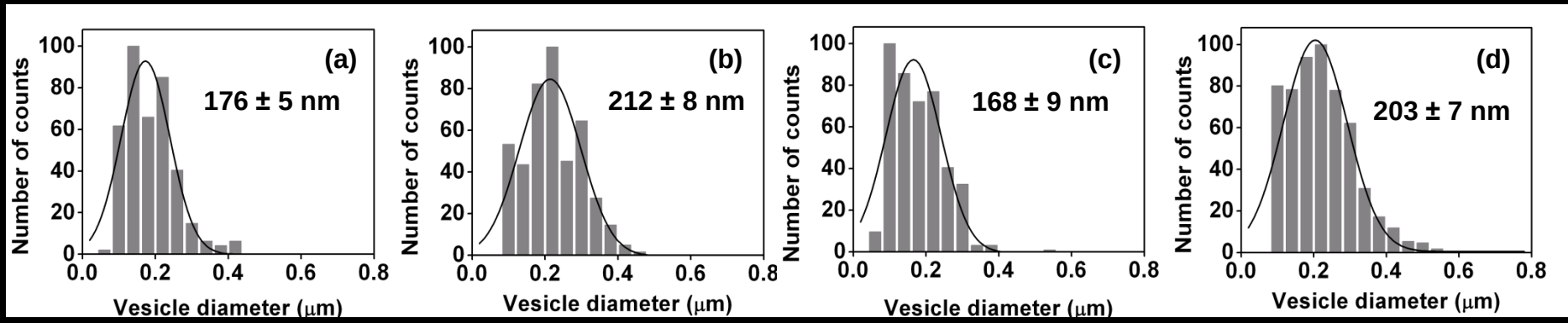
Astrocytic vesicles - CLSM



Astrocytic vesicles - SIM





XLID mutations of *αGDI* impair endolysosomal traffic in„ astrocytes