SynCAMs: From Synaptic Adhesion to Synapse Formation

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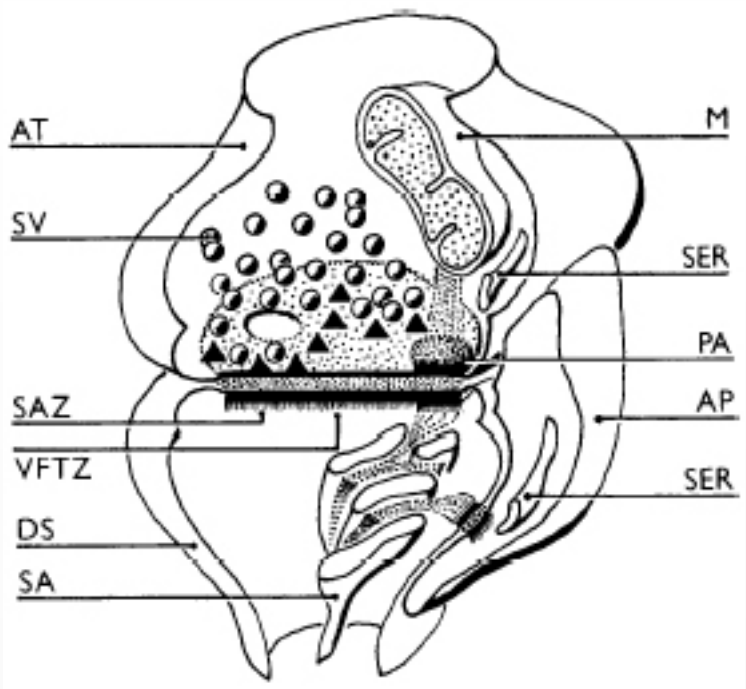
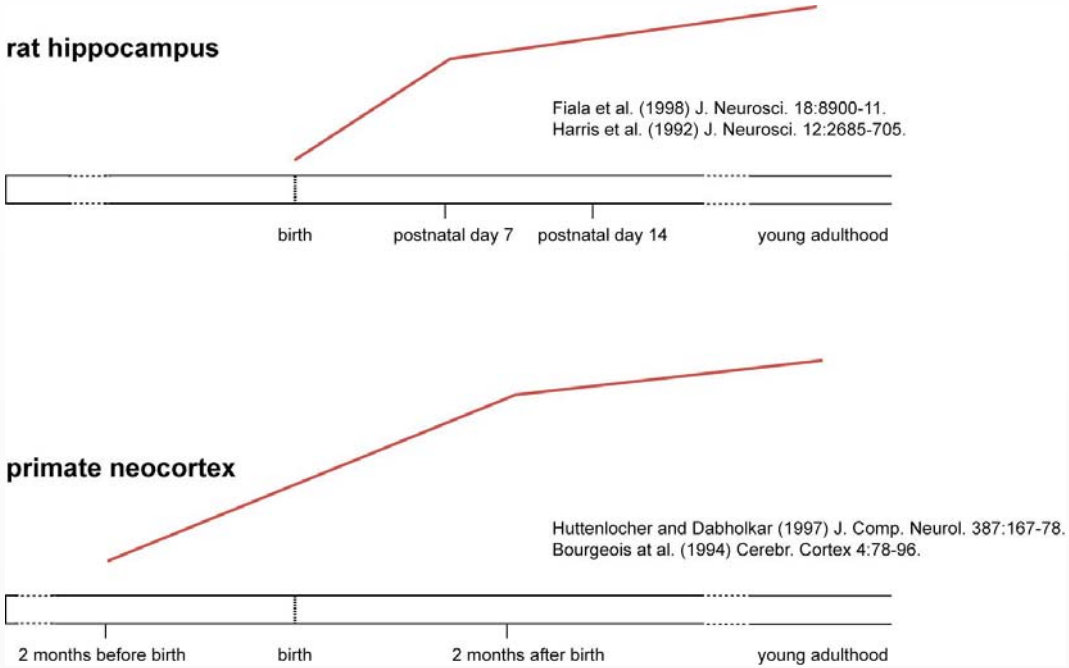
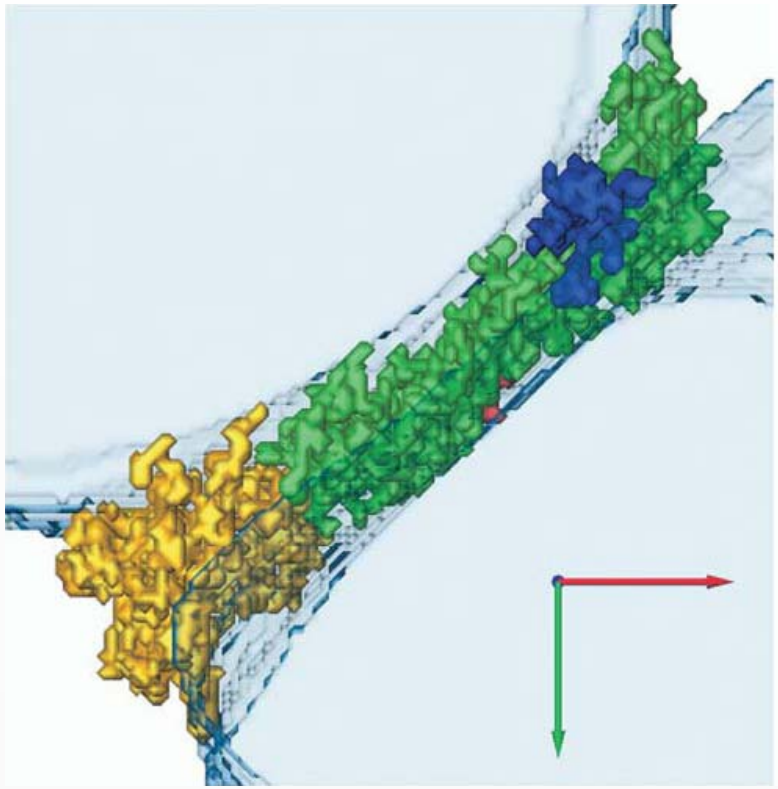
Synaptogenesis is Key to the Developing Brain

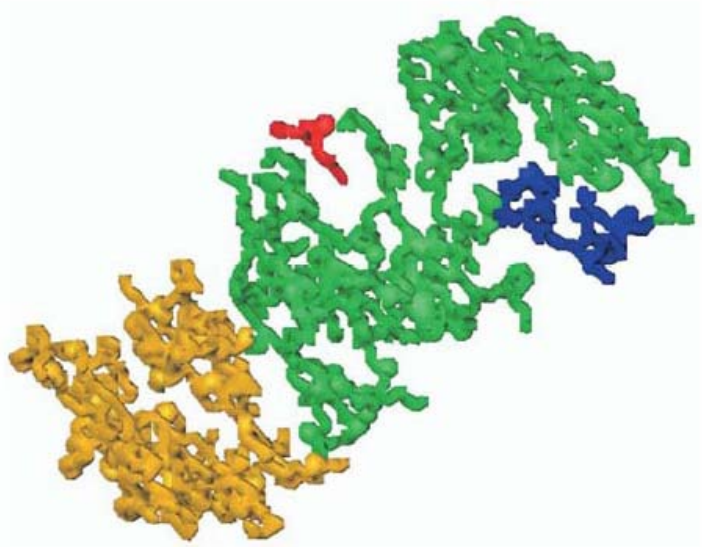


Spacek and Harris (1998)
J Comp Neurol. 393:58-68.



Molecular Complexes of the Synaptic Cleft

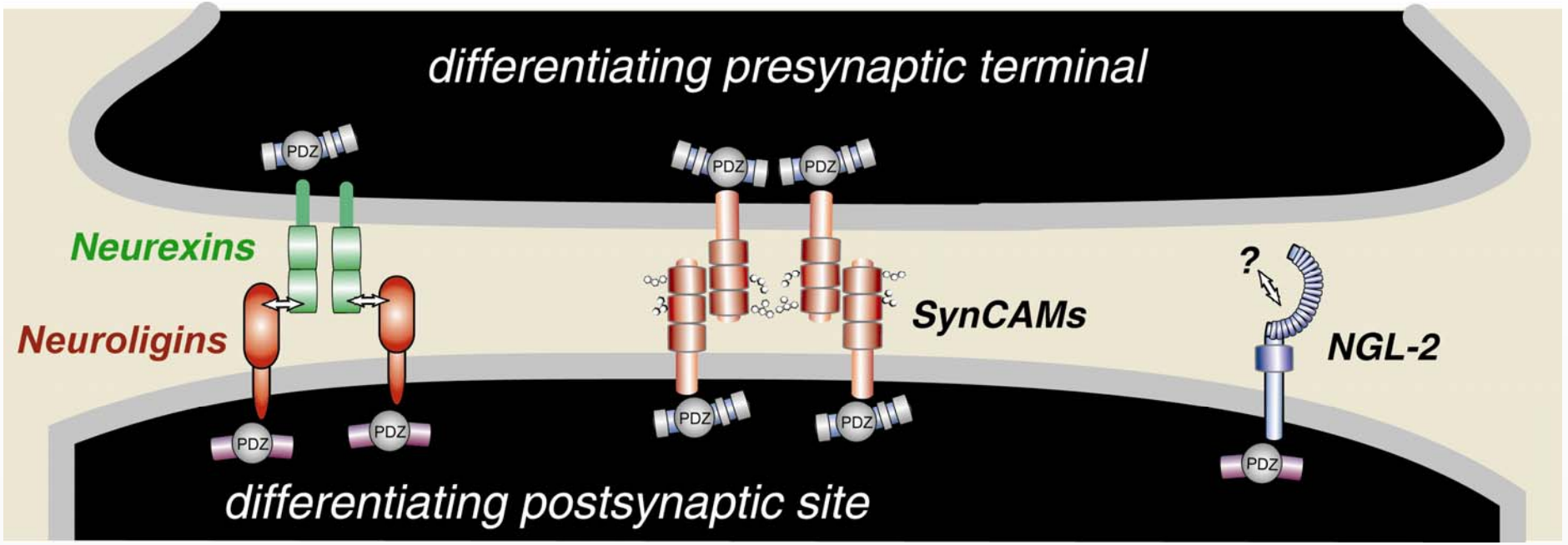




Lucic et al. (2005) Structure 13:423-34.

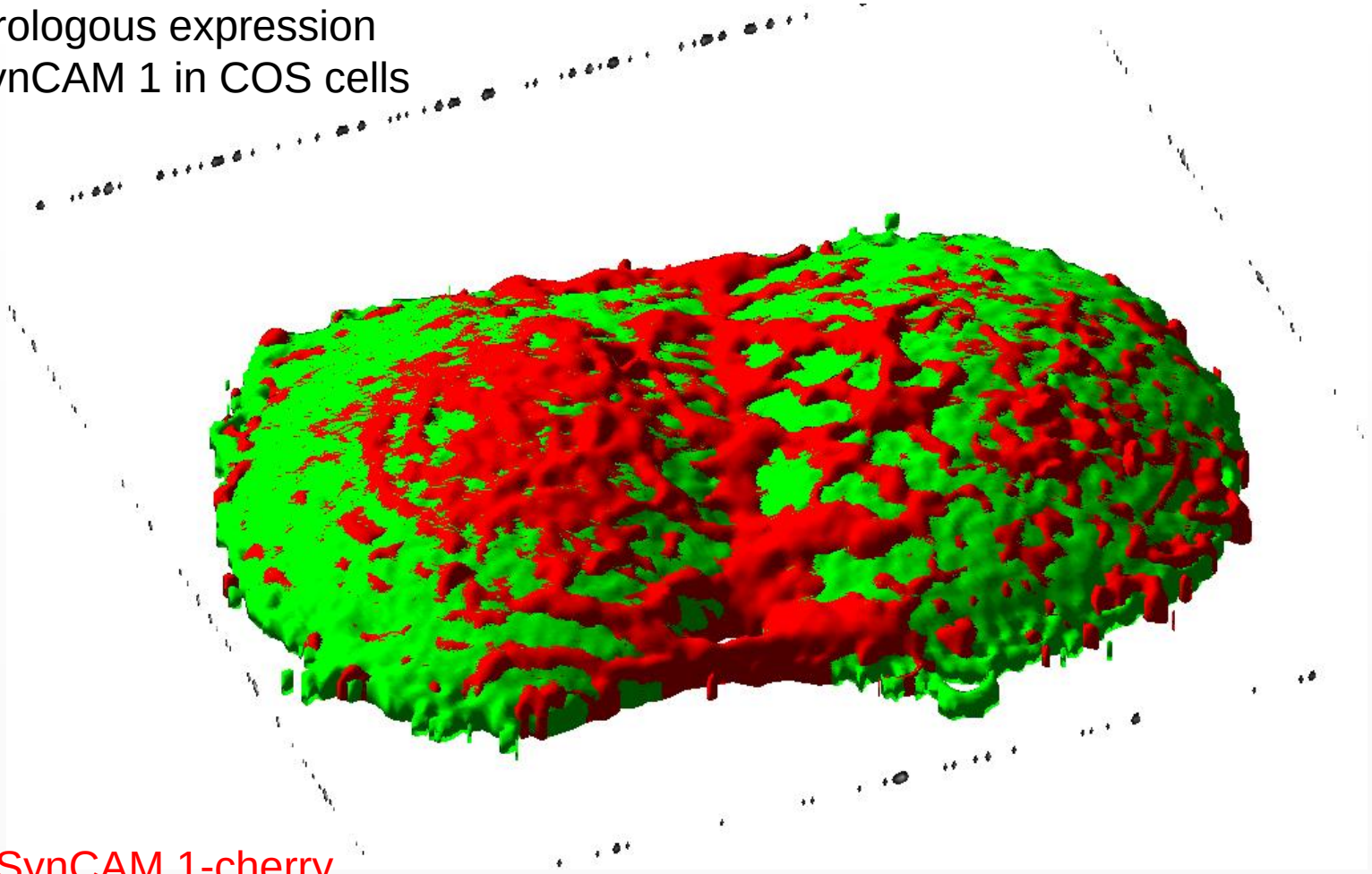
- extensive connections along the cleft form a highly connected structure
- dimensions of pre- and postsynaptic specialization are tightly correlated
- width of synaptic cleft is even

Adhesion Systems at the Developing Synaptic Cleft



SynCAM 1 Mediates Homophilic Adhesion

heterologous expression
of SynCAM 1 in COS cells



red: SynCAM 1-cherry
green: soluble GFP

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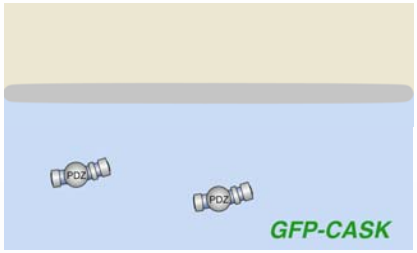
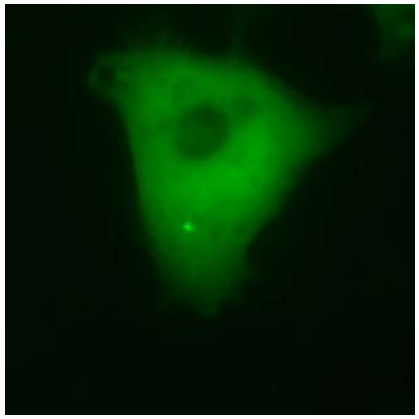
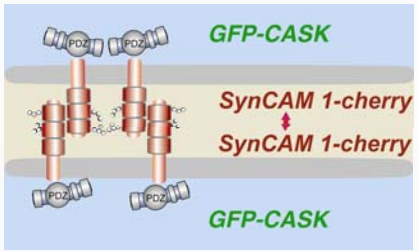
SynCAM 1 Recruits Scaffolding Molecules to Sites of Homophilic Adhesion

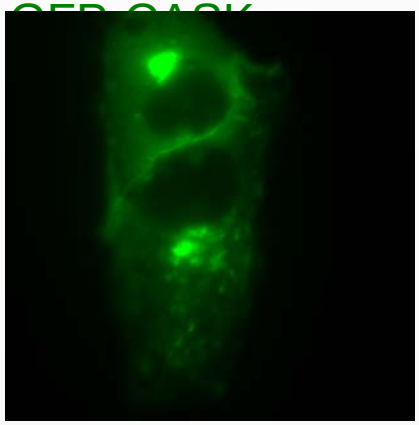


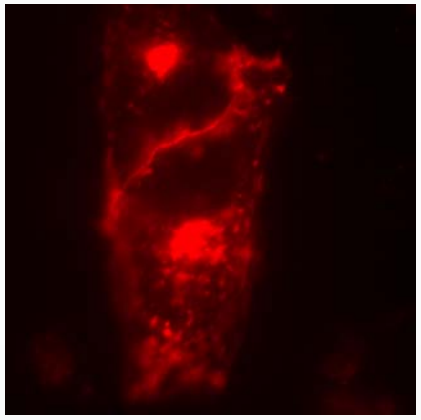


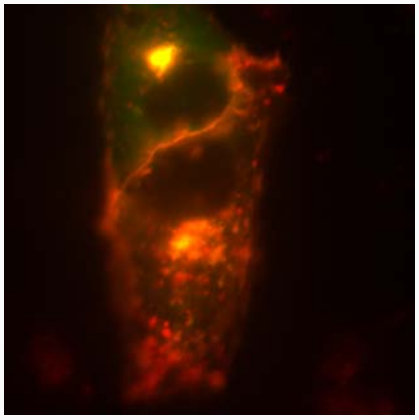
heterologous expression in COS cells

green:









green:
GFP-CASK

red:
SynCAM 1-cherry

overlay

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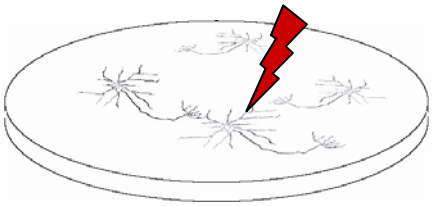
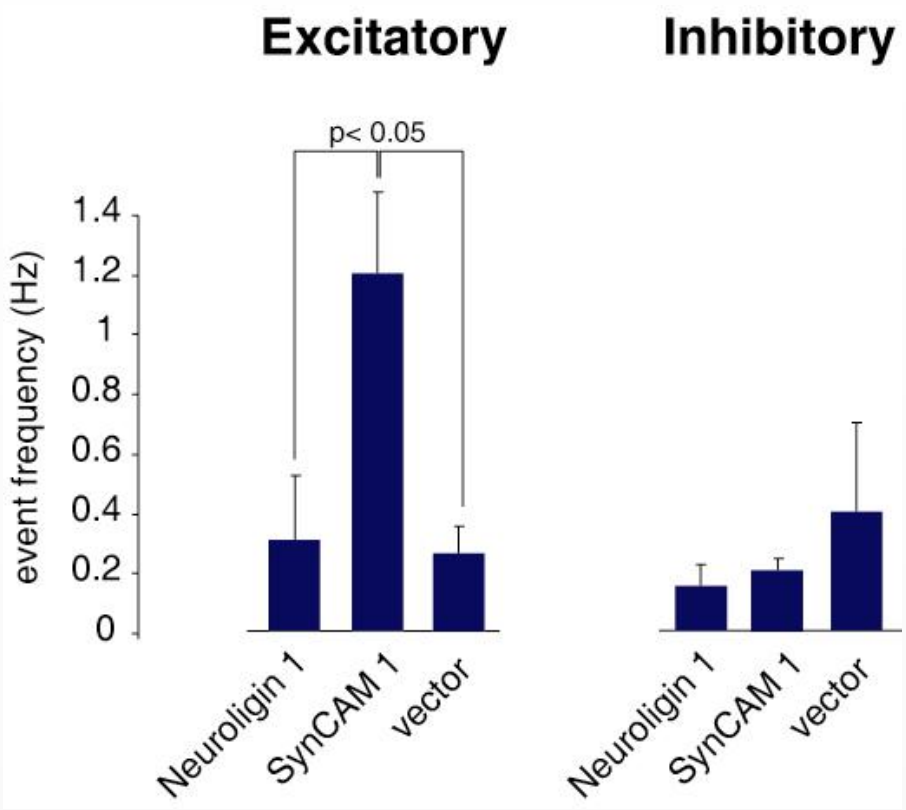
SynCAM 1 Potentiates Excitatory Transmission in Hippocampal Neurons





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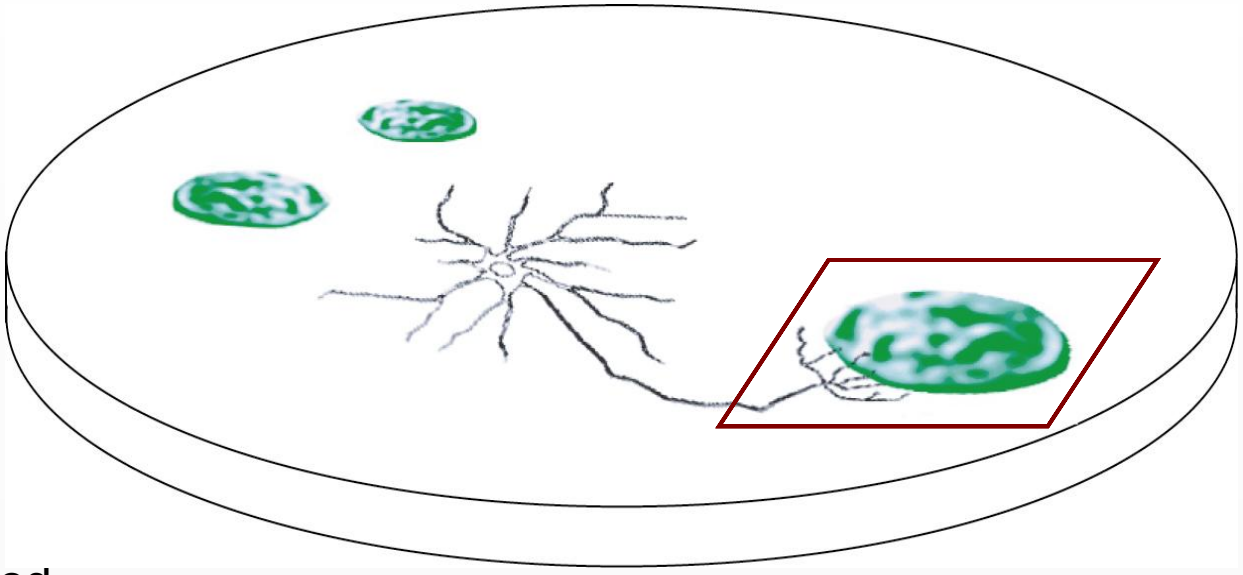
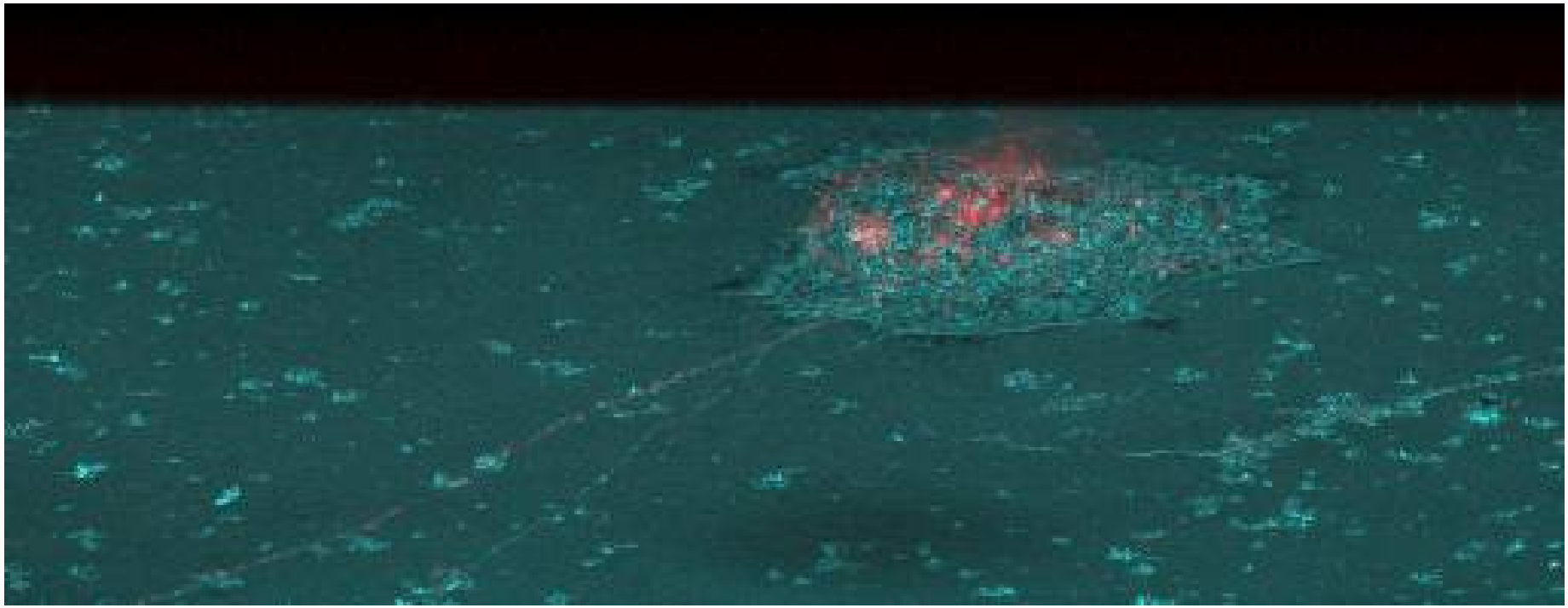
Induction of Synaptic Specializations in Co-Cultures

epithelial-like HEK293 cells expressing both SynCAM 1 and ECFP are seeded atop hippocampal neurons



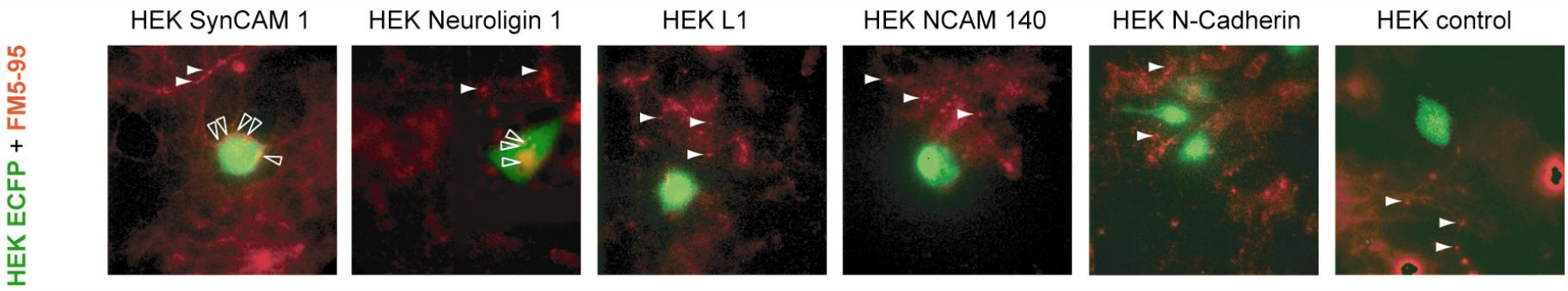
after 1-2 days *in vitro*, the co-cultures are analyzed for the formation of specializations containing presynaptic markers on the surface of the HEK293 cells

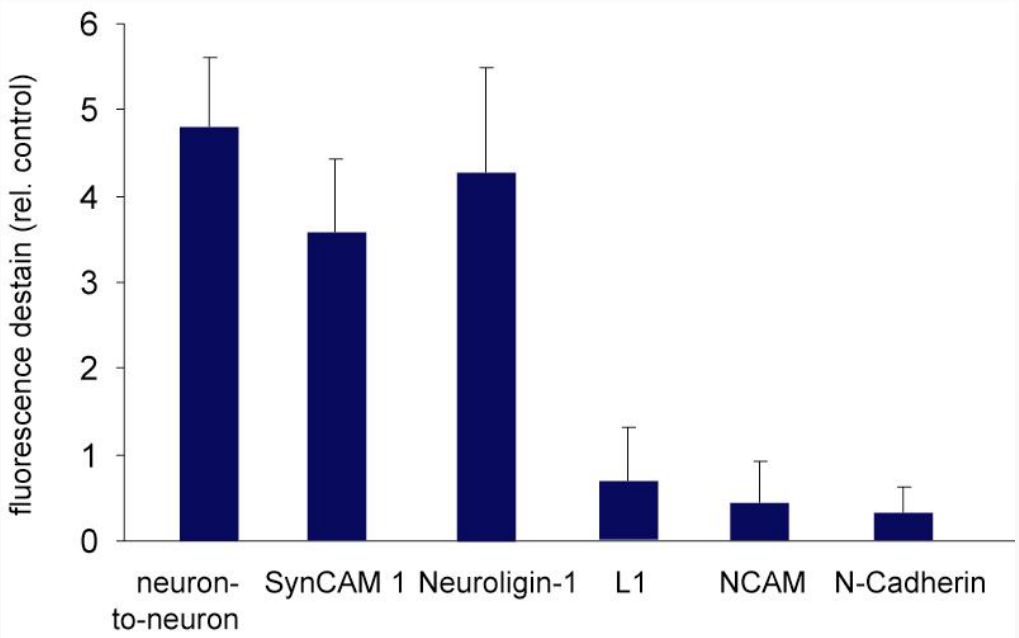
SynCAM 1 Induces Presynaptic Specializations



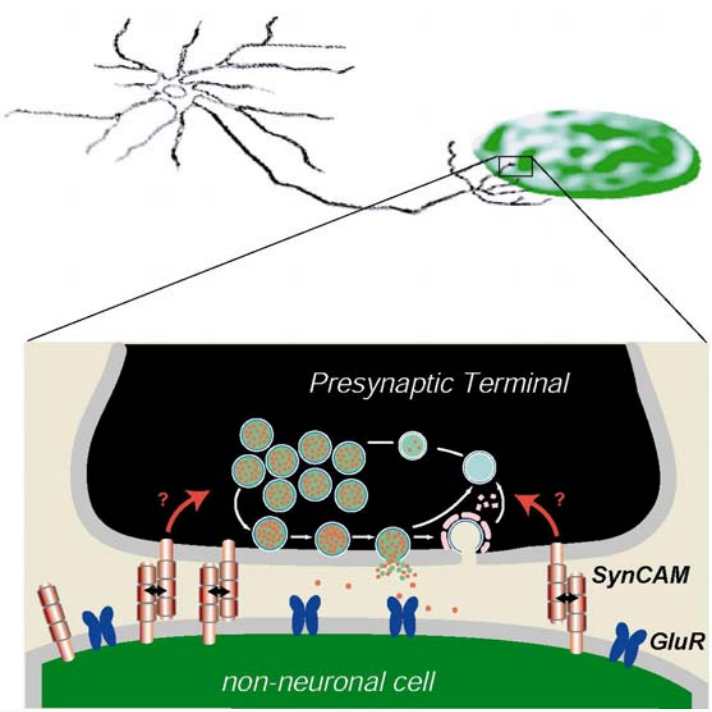
red synaptophysin

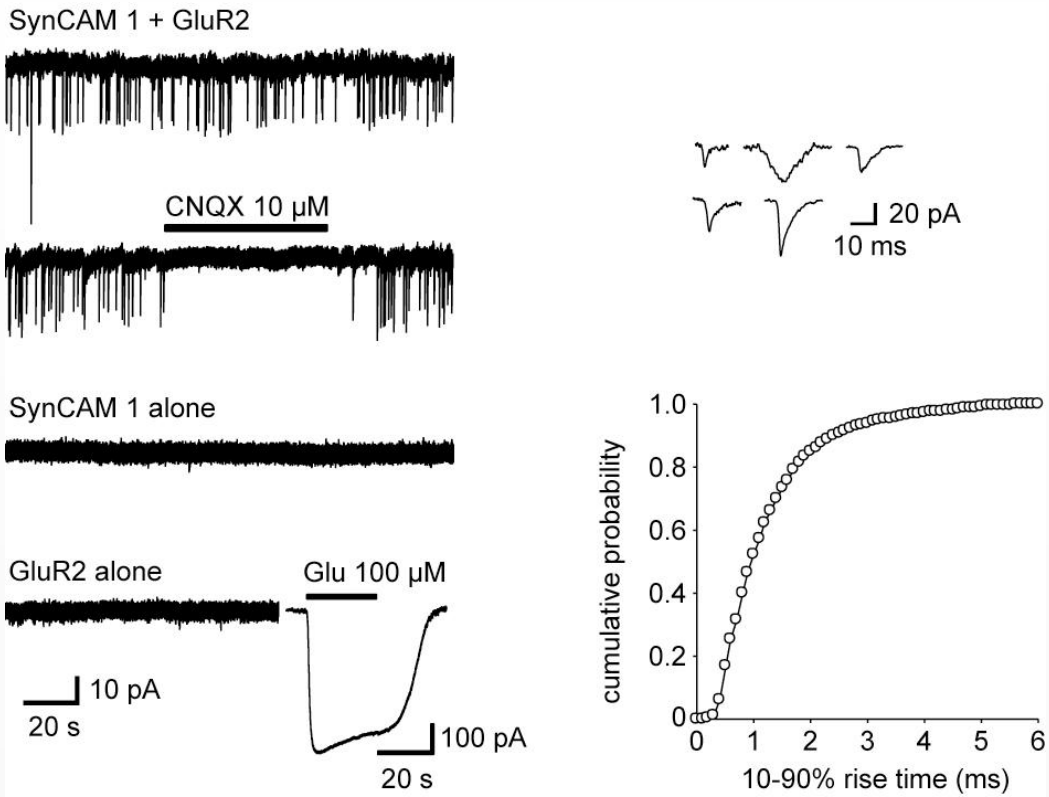
SynCAM 1 and Neuroligin Induce Presynaptic Terminals with Functional SV Recycling





Reconstitution of Synaptic Transmission with SynCAM 1 and GluR2





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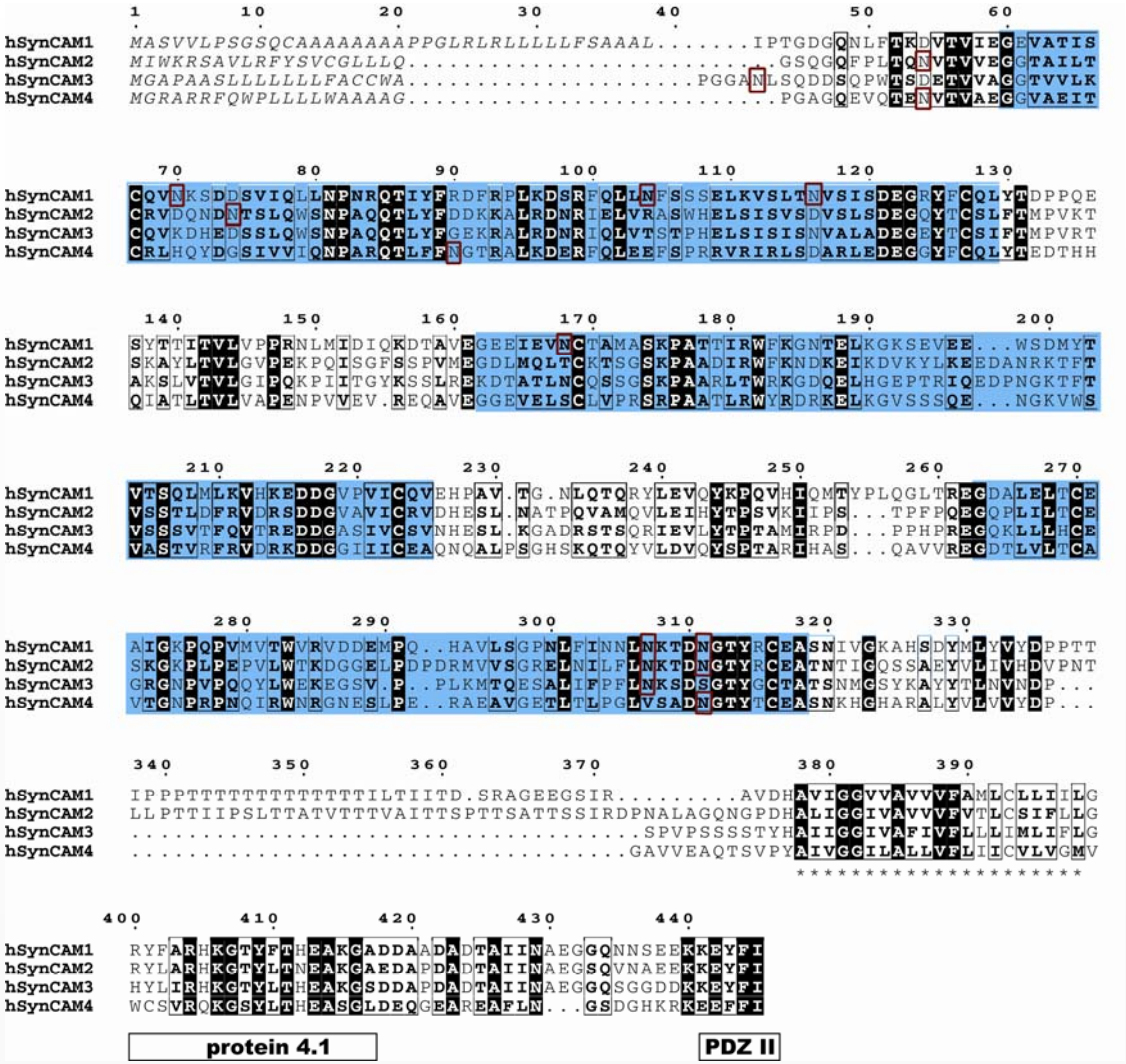
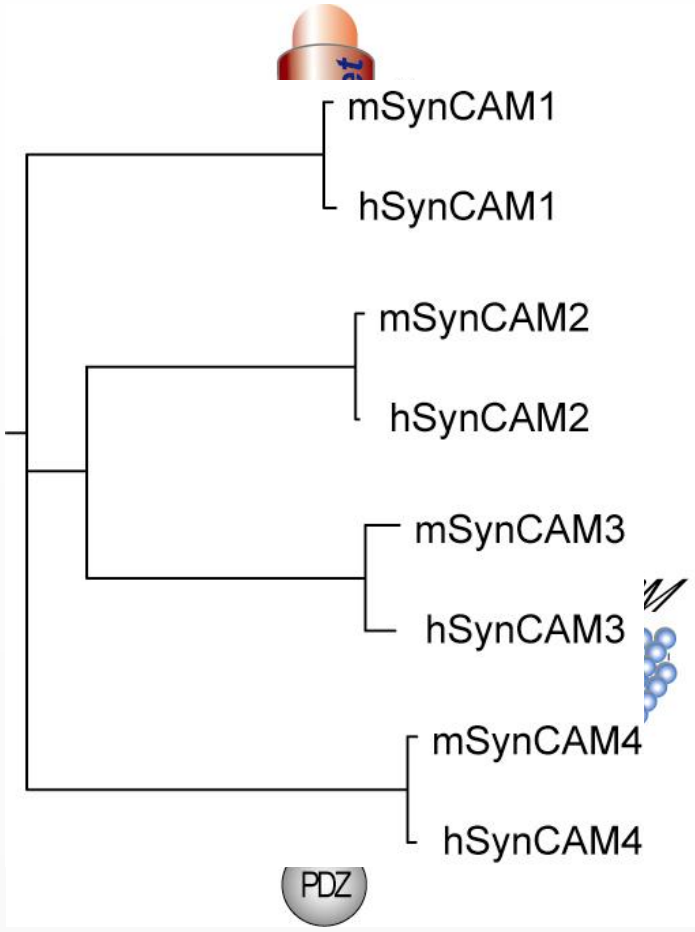
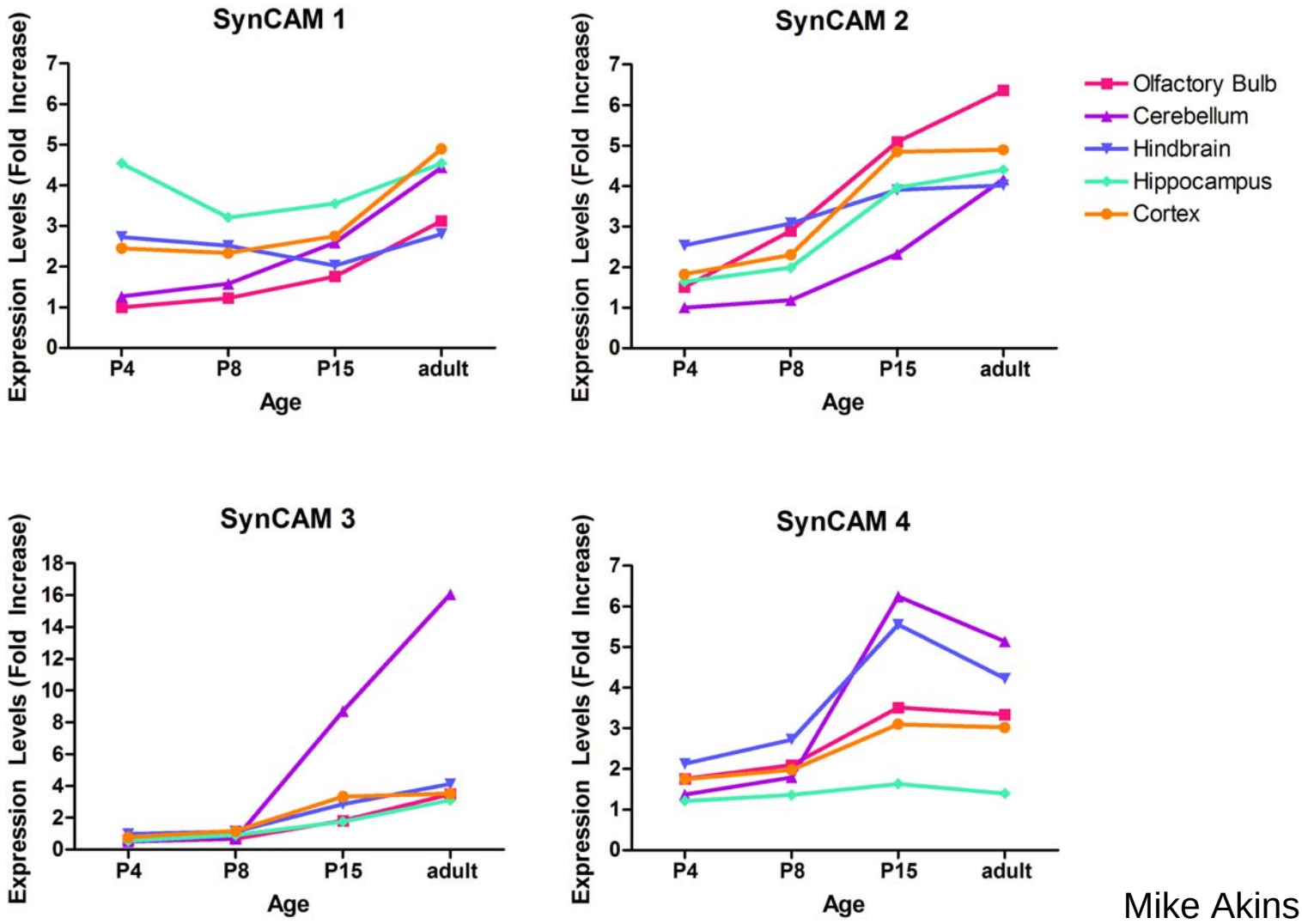
Sequence Alignment of SynCAM Family Members





All Four SynCAM Family Members are Transcribed in the Developing and Adult Brain

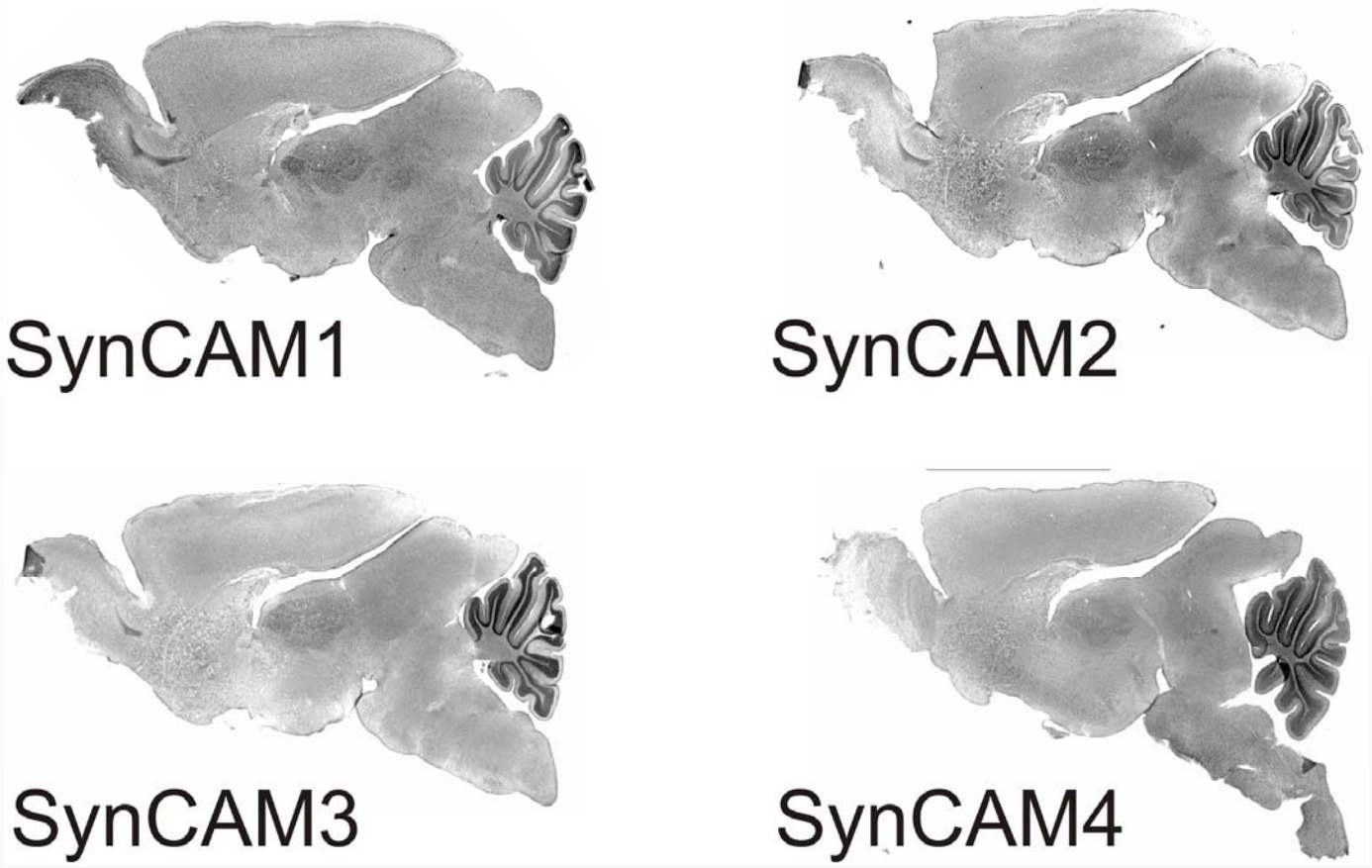
real-time RT-PCR standardized to actin



Mike Akins

SynCAM Family Expression in Brain

in situ hybridizations at P15:



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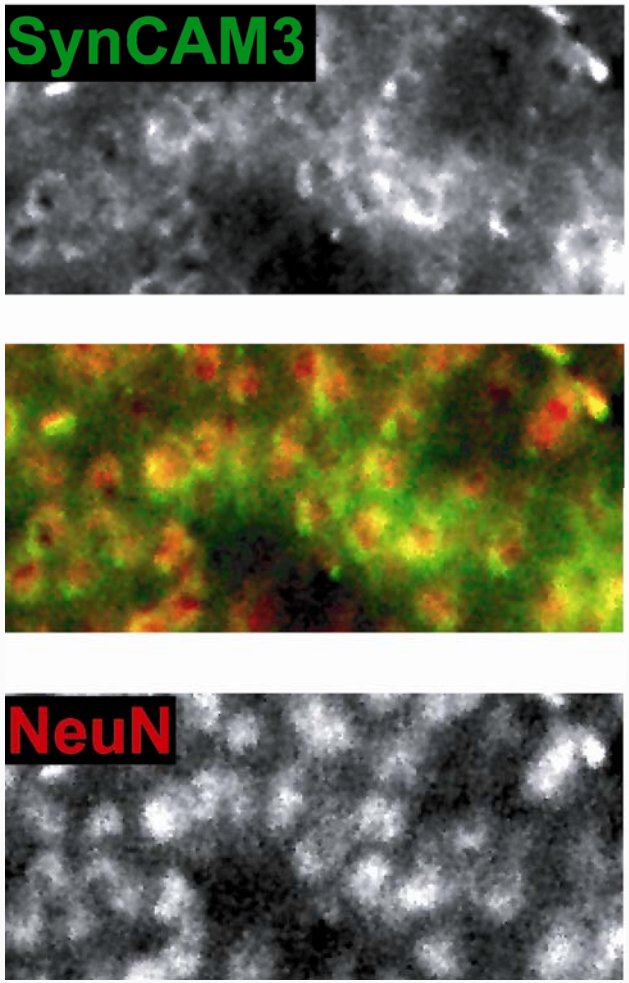
SynCAM Family Members are Expressed in Neurons

rat cortex



SynCAM 3 *in situ* hybridization

NeuN immunostaining

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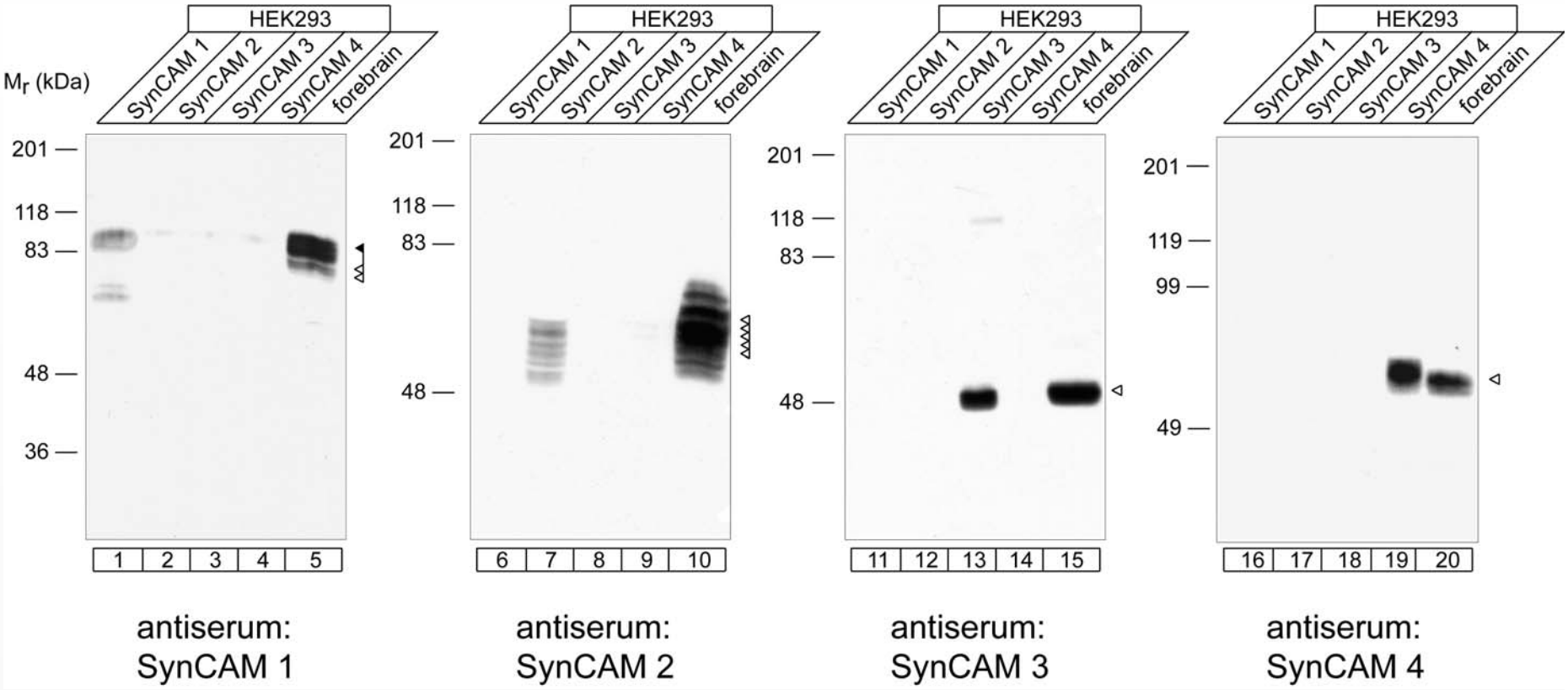
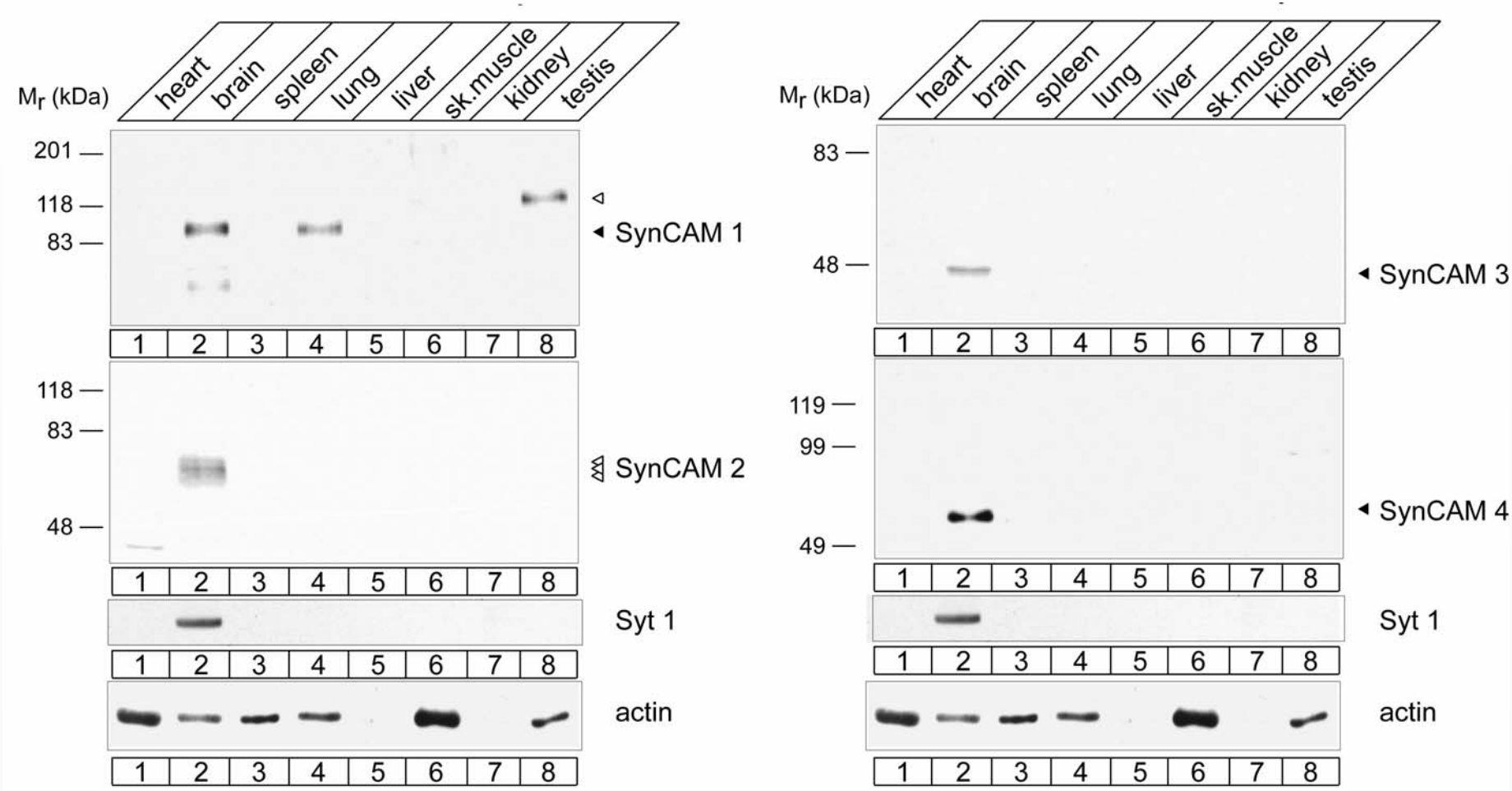
SynCAM Antibody Specificity



Adam Fogel

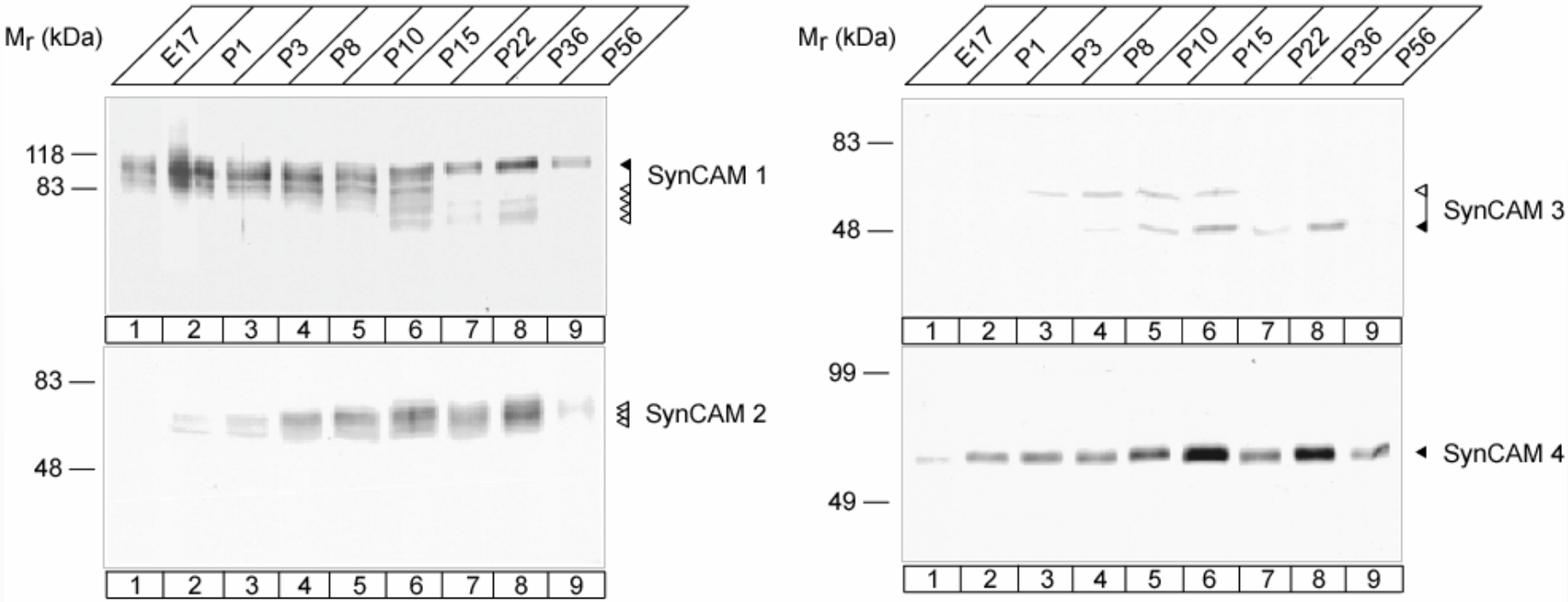
The Four SynCAM Proteins are Expressed in Adult Brain



Adam Fogel

The Developmental Profile of SynCAM Proteins Correlates with Synaptogenesis

rat brain preparations:



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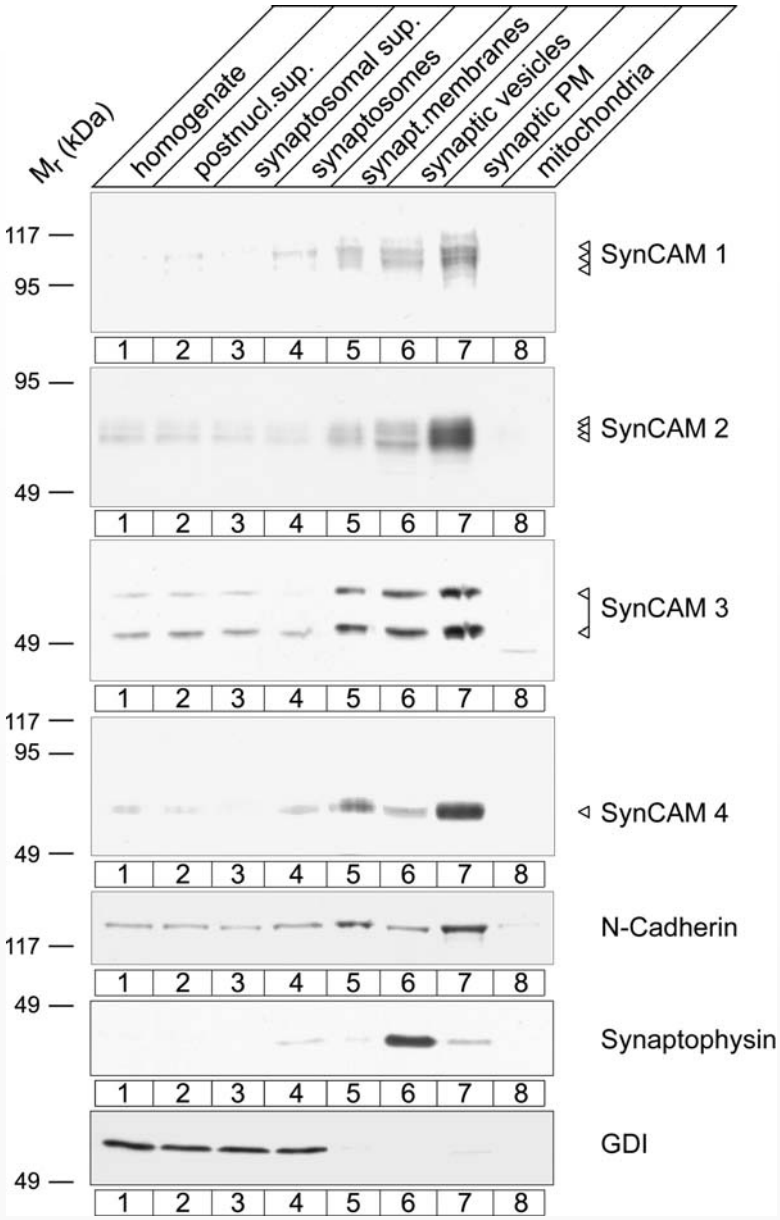
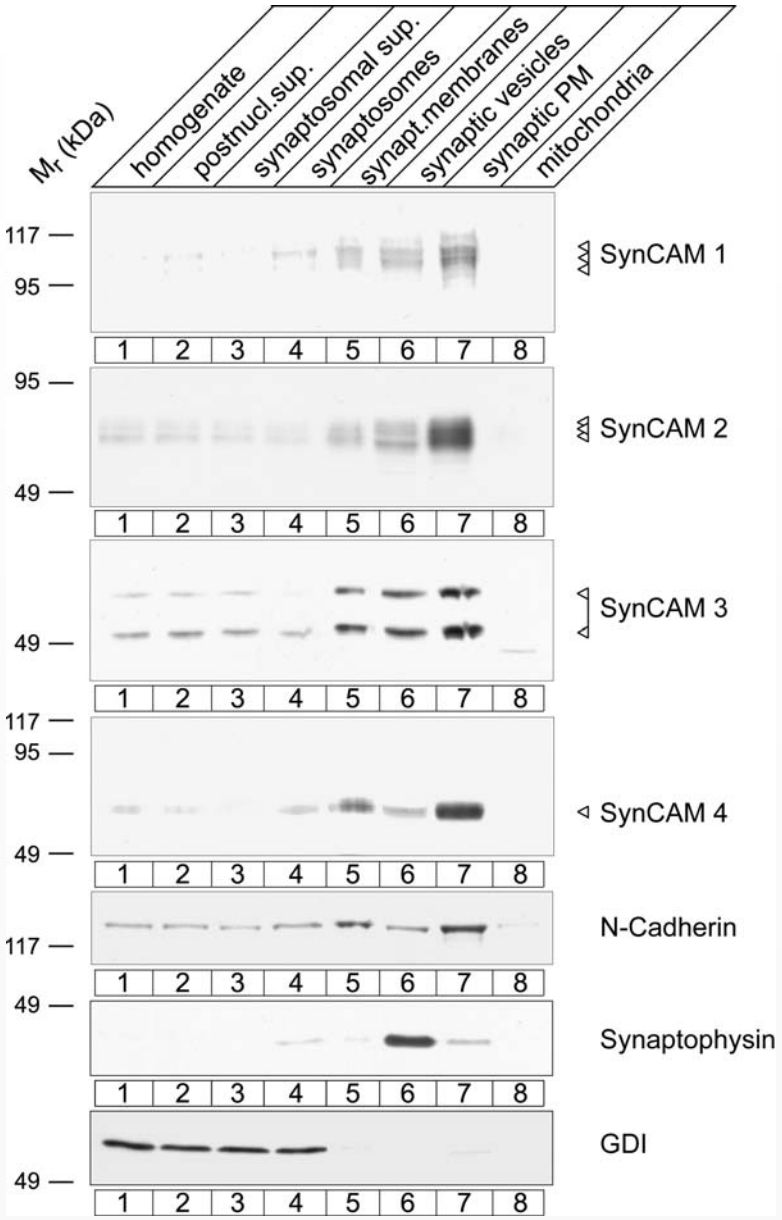
SynCAMs Fractionate as Synaptic Plasma Membrane Proteins



rat forebrain P9

SynCAM Proteins are Prominent Components of Synaptic Plasma Membranes



	fraction of total SPM protein in P15 forebrain
SynCAM 1	$^1/_{180}$
SynCAM 2	$^1/_{300}$
SynCAM 3	$^1/_{1200}$

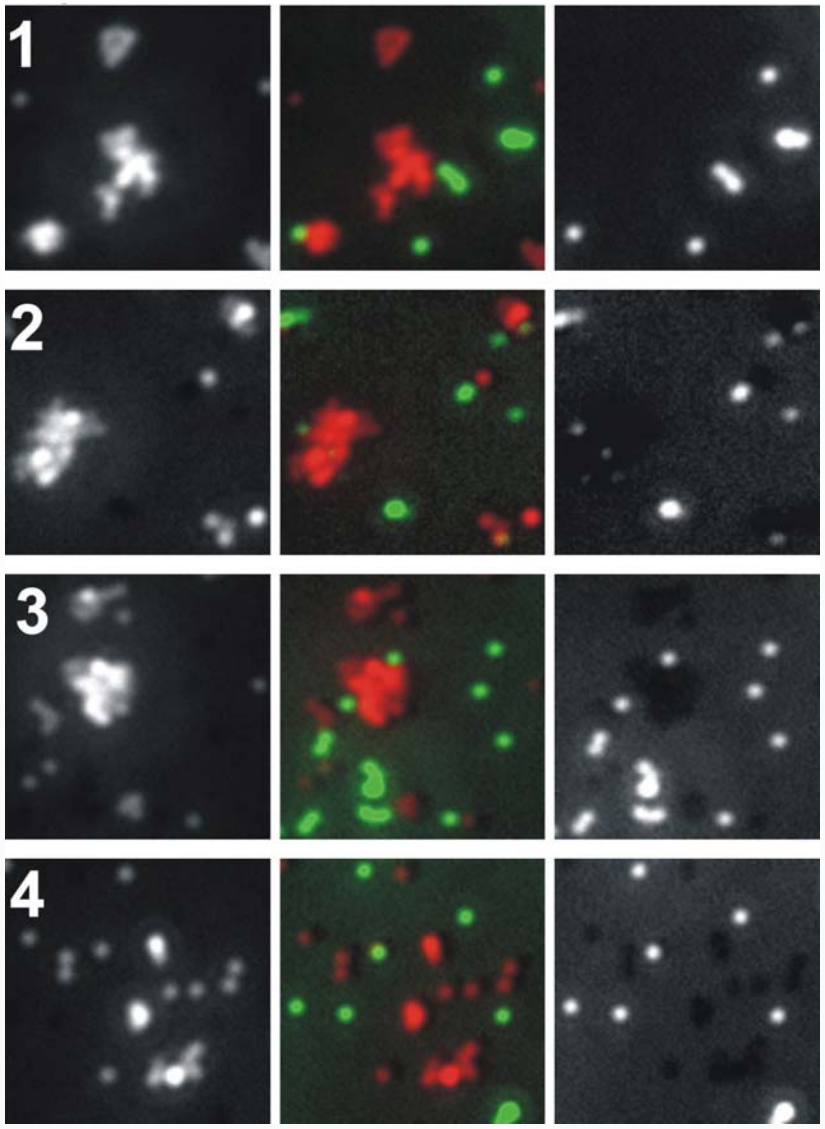
Adam Fogel

SynCAM Proteins Can Function as Homophilic Adhesion Molecules

SynCAM 1, 2 and 3 interact homophilically

no evidence for string homophilic SynCAM 4 interactions

- SynCAM-ECD coated beads
- control beads



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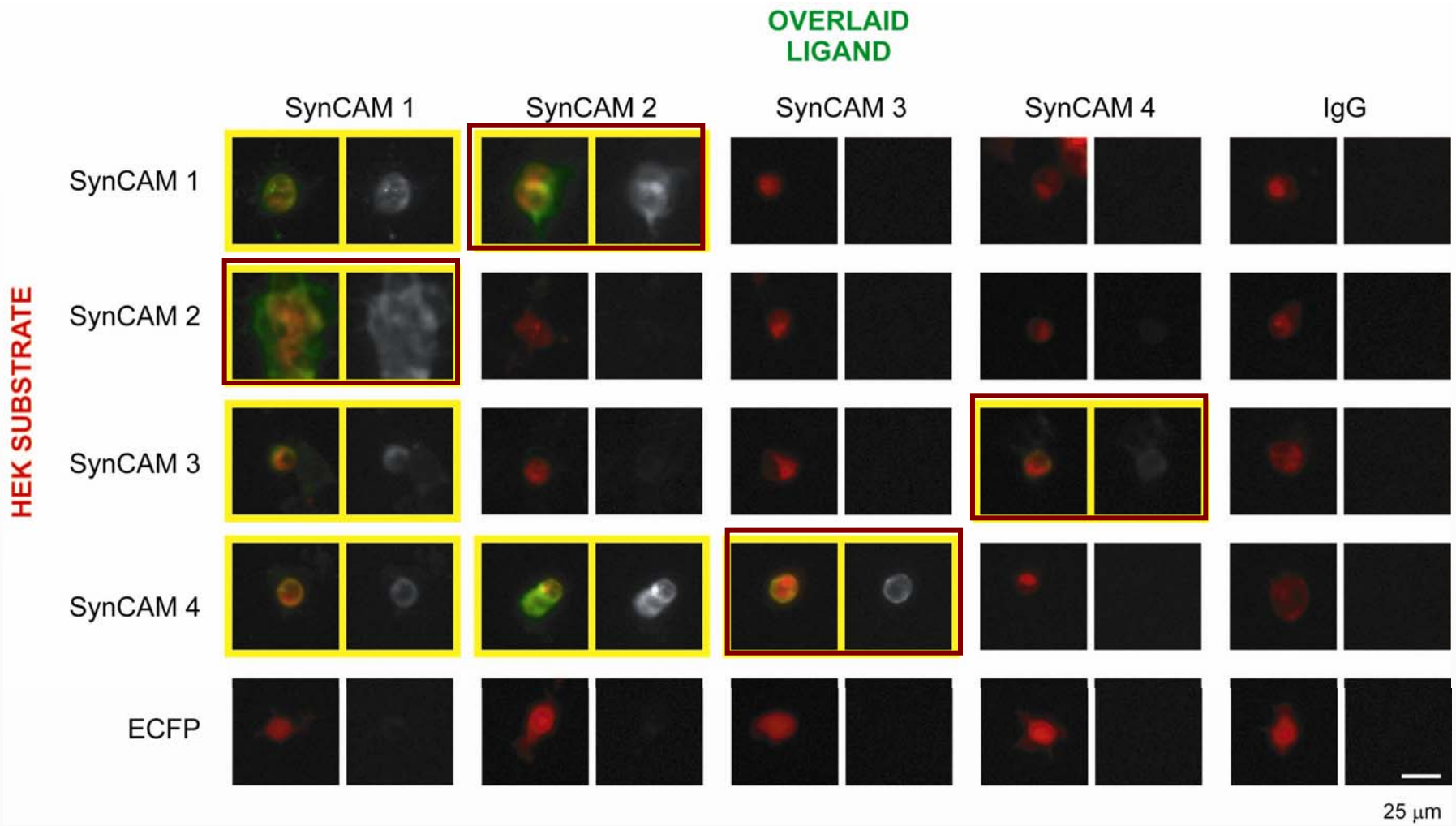
SynCAM Proteins Can Engage in Specific Heterophilic Interactions



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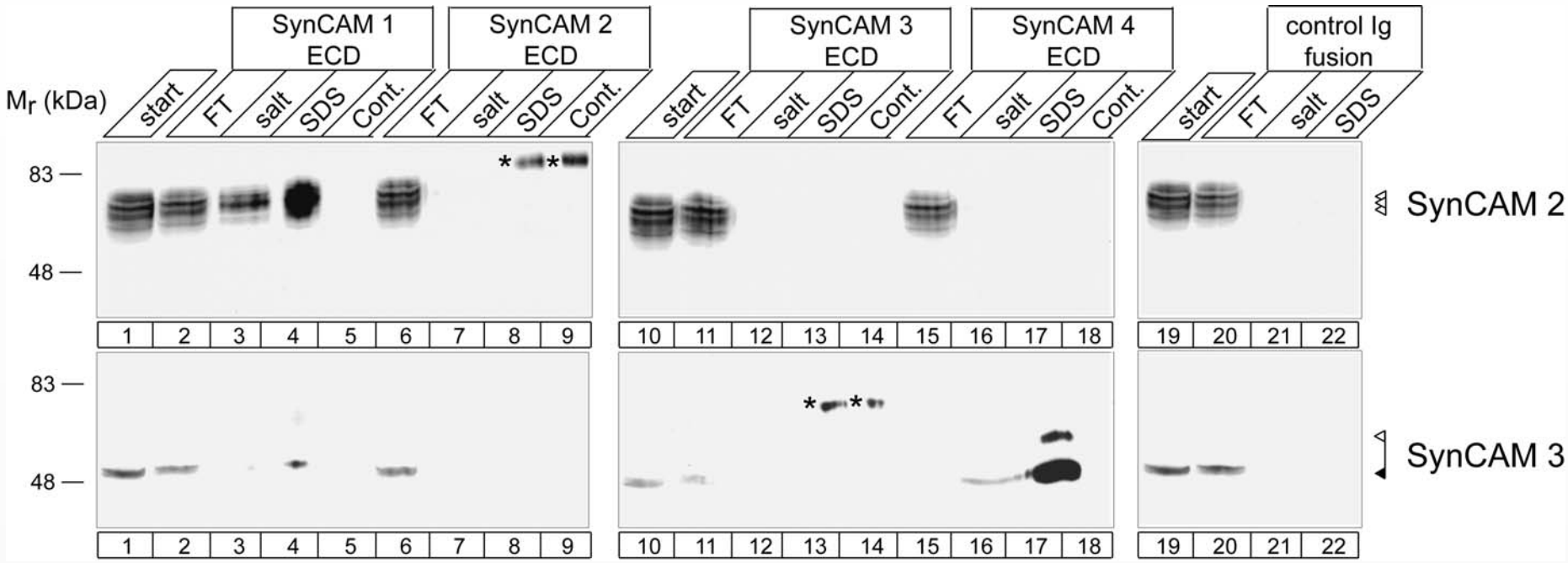
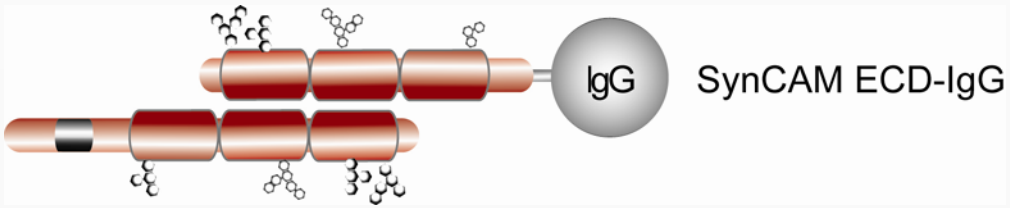
SynCAM Proteins Can Engage in Specific Heterophilic Interactions

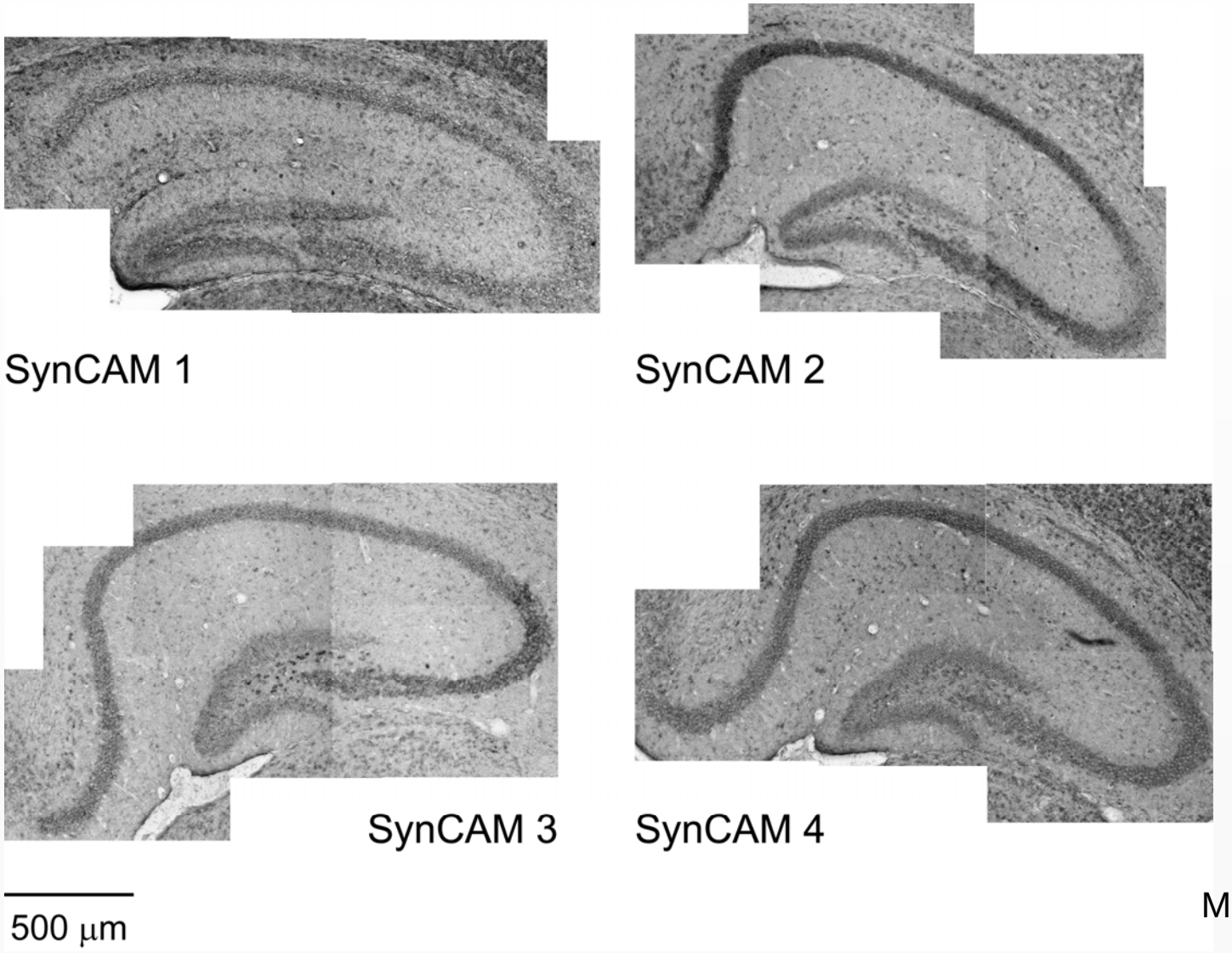




Adam Fogel

Distinct SynCAM Expression in Hippocampus

in situ hybridizations at P15:



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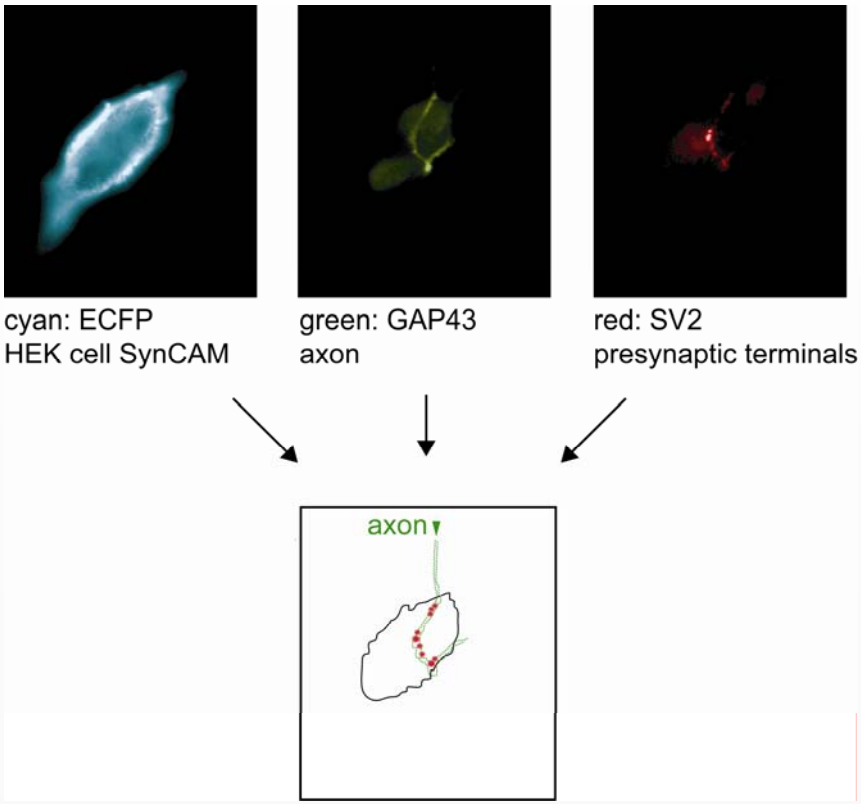
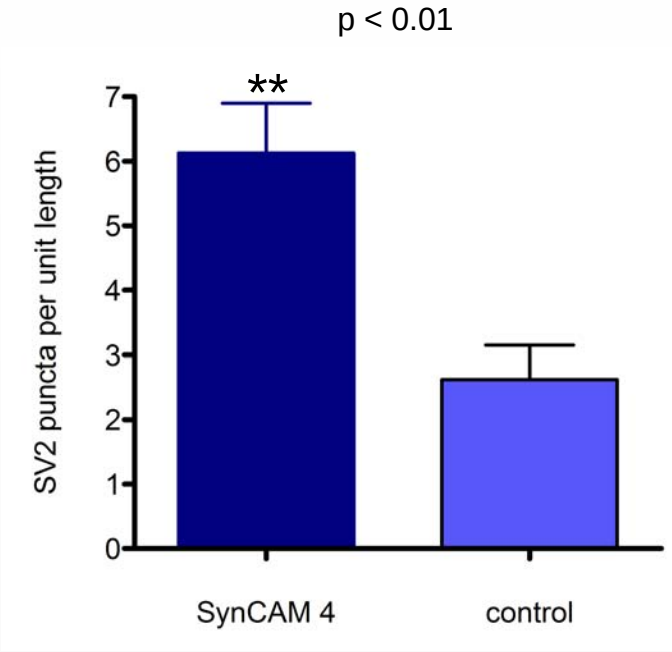
SynCAM 4 Induces Presynaptic Specializations





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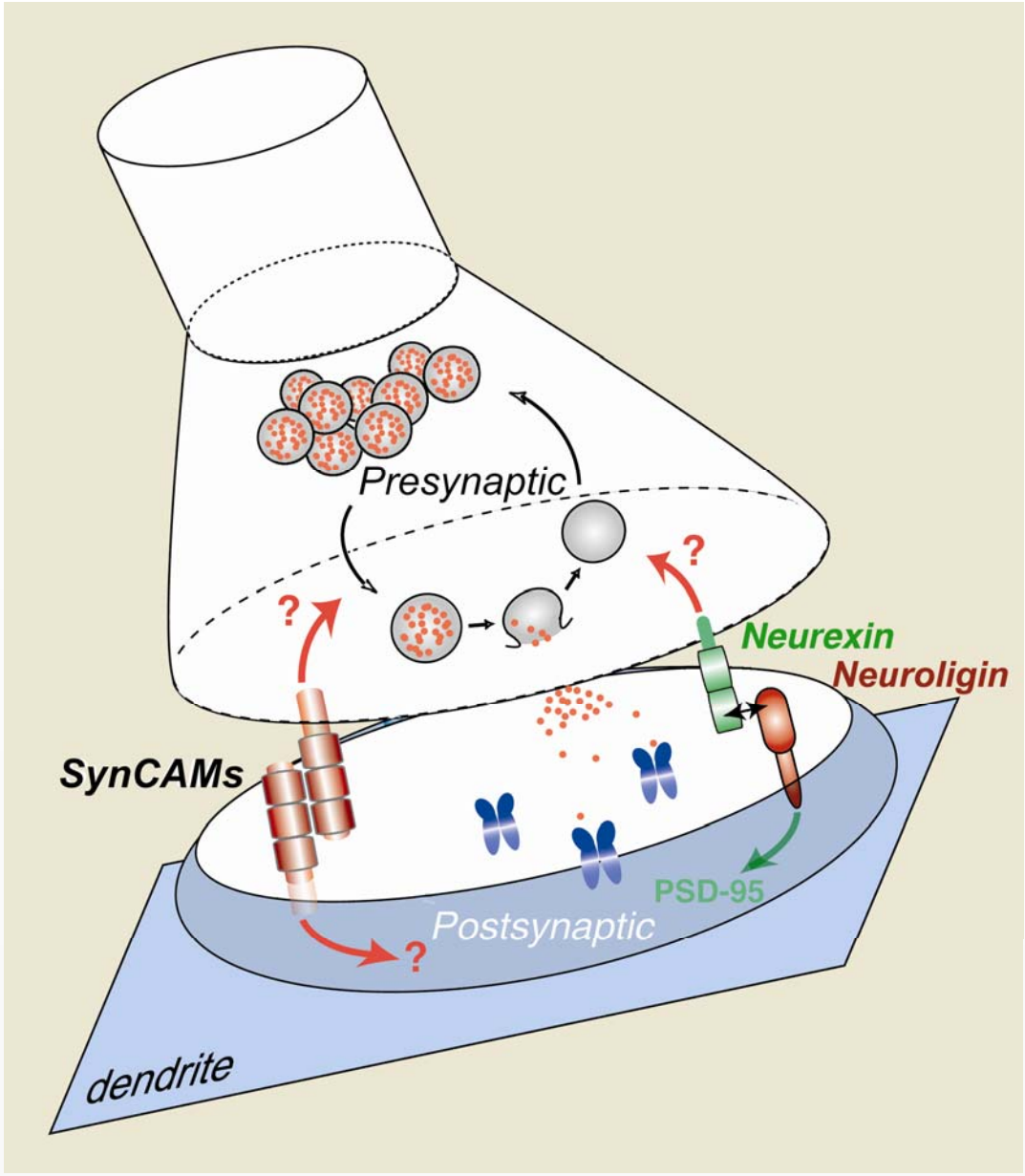
Synaptic Adhesion and Synaptogenesis: A Model



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Yildirim Sara

Thomas C. Südhof

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