GxxxG motifs within the amyloid precursor protein transmembrane sequence are critical for the etiology of $A\beta 42$

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f % -f 0%., f f f f . . ,





Aβ40 (%)







GxxxG mutations reduce Aβ42 levels and increase Aβ38 levels

b	•	,		f	ff	b f	b ff	,	b 0	I b
									,	

Aβ42 (%)

b 0 , b , 0 %, , -(00 %,).

b j f f. b 0 , b f b 0 f f -• Ι(b f).

f b f (), b f f b, b f f b **b**0. Ι f fb, b

(). I f b (00%) b b0. b

b , , , f f (). f ff b f f

f b f (). I

(b), f f f f b (I-). , f b f ff Ι f **b** 0 , b f Ι , I f ff **b** 0 , b ff f , 00 % f b0 (% f b f b).

ff b0 ff f , f b0 .

Effects of GxxxG mutants on A β production are independent of the APP ectodomain

f b- f b , b



GxxxG mutants increase *A*β37 and *A*β35/*A*β34 levels GxxxG mutants increas f f g f I . b f 0-, ((). f fb, . b f f b f f b f f b f b, Ι, f (). b f Ι Ι (). I ,

b , f b f (). I b b () 0 (f)

. g-, , b , , b , b b .

, I , I , , , Ι), (I (m) -) f f () f f .

ToxR assay

f f f lacZ f b f E. coli f , b--b- -(et al,).

Molecular modeling

ff , f , f f 000 000 0 0° +f ± 0 \pm 0 °. f 0 f f . f 0 f , 0. f f f

, 00). (

FRET f

et al, 00). (f f (f f). f , f . m f .

-f f - - . -

Sandwi	ch ELISA,	immunopred	pitation and	Western b	lots
× 0	0	f	× 0		f
× 0	0-	0 n	ı ff	-	•
	f.	b 0 -	b -	Ι,	0 m f
,			f	,	
(h).			
(D	a ,	,)	-	
()	•		, b
	f	(f		
	f	- (f	0).
f -	ı ,		ff	0	•
.,	0	,	, % - 0	%	- 00 .



(00) - - f f .EMBOJ25: , (000) f . f .Mol Cell 6: , , , , , , , , , I, , J , , , , , f () f

() f , , , , f in vivo. Neuron 17: 0 , , (00) Mol Cell Biol 23:

J Biol Chem 279: 0 0 , , , , (00) -

. J Biol Chem 281: 0

, (00) - f f . Mol Cell 15:

, J, , , , , , , , , , , , , , , , , (00) f I -414: