

SUPPORTING INFORMATION

N-Terminal Lipid Conjugation Leads to the Formation of N-Terminally Extended Fibrils

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Table S1. Isotropic ^{13}C and ^{15}N chemical shifts (δ , relative to TMS) and order parameters (S) for fibrils of the investigated lipidated A β (1-40) hybrids and A β (1-40) wildtype¹ determined by ^{13}C and ^{15}N CP MAS NMR spectroscopy at 30°C

Residue		octanoyl-A β (1-40)		palmitoyl-A β (1-40)		A β (1-40) wildtype ¹	
		δ / ppm	S	δ / ppm	S	δ / ppm	S
Ala ₂	C α	48.0	0.91 \pm 0.09	48.5	0.90 \pm 0.09	50.6	0.65 \pm 0.06
	C β	20.0	0.47 \pm 0.05	20.9	0.21 \pm 0.02	17.1	0.21 \pm 0.02
	CO	173.6		173.4		173.1	
	N	125.4	0.24 \pm 0.02	122.93			
Phe ₄	C α			54.6	0.85 \pm 0.09	55.6	0.61 \pm 0.1
	C β			39.4	0.76 \pm 0.08	37.8	0.84 \pm 0.1
	C1			136.7			
	C2 - C6			129.0			
	C4						
	CO			172.5			
	N						
Ser ₈	C α			56.8	0.81 \pm 0.08	56.7	0.74 \pm 0.06
	C β			62.0	0.54 \pm 0.05	61.7	0.42 \pm 0.04
	CO			172.5			
	N						
Gly ₉	C α			43.4	0.86 \pm 0.09	43.3	0.84 \pm 0.06
	CO			171.6		170	
	N						
Val ₁₂	C α			58.8	0.85 \pm 0.09	58.3	0.94 \pm 0.12
	C β			32.7	0.74 \pm 0.07	32.5	0.59 \pm 0.05
	C γ			19.4	0.22 \pm 0.01		
	CO			172.5			
	N						
Phe ₁₉	C α	54.0	0.89 \pm 0.09	53.6	0.89 \pm 0.09	54.1	0.82 \pm 0.06
	C β	39.3	0.91 \pm 0.09	40.8	0.90 \pm 0.09	40.3	0.75 \pm 0.05
	C1	136.6		136.8			
	C2 - C6	128.5		129.2		129.0	
	C4	125.1		126.4			
	CO	171.2		170.6		171.8	
	N	125.4		125.3			
Gly ₂₅	C α	44.7	0.96 \pm 0.1	43.2	0.91 \pm 0.09	45.1	1.00 \pm 0.15
	CO	169.4		170.1		170.0	
	N	110.81		111.41			
		116.1		113.4			
Val ₃₉	C α	58.7	0.90 \pm 0.09	58.8	0.89 \pm 0.09	59.2	0.84 \pm 0.06
	C β	33.0	0.80 \pm 0.08	33.1	0.72 \pm 0.07	33.3	0.72 \pm 0.05
	C γ	19.3	0.24 \pm 0.02	19.5	0.21 \pm 0.02	19.6	0.21 \pm 0.02
	CO	171.9		172.7		172.3	
	N	118.4		120.3			

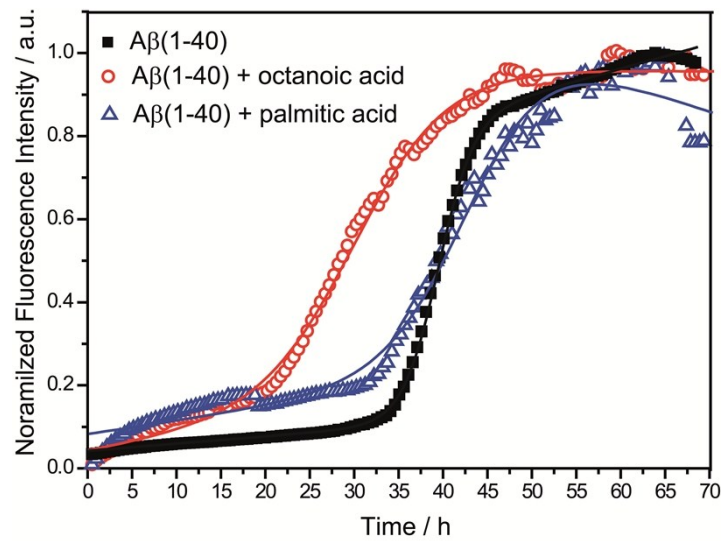


Figure S1. Thioflavin T (ThT) fluorescence intensity of wildtype A β (1-40) (black) and A β (1-40) in the presence of octanoic acid (red) and palmitic acid (blue) as a function of time. Peptide and free fatty acid concentrations were 230 μ M each. Data were fitted using functions discussed in the literature.² Measurements were performed in a 96 well plate and the following shaking protocol was used: 30 min cycles (2 s of shaking (at 2 mm shaking amplitude), 5 min waiting, 2 s shaking, 5 min waiting, 2 s shaking) followed by the measurement. For WT A β (1-40), a $t_{\text{lag}} = 35.0$ h and a $t_{\text{char}} = 39.2$ h was determined under these conditions. In the presence of octanoic acid, these time constants were reduced to $t_{\text{lag}} = 19.9$ h and a $t_{\text{char}} = 30.3$ h. In the presence of palmitic acid, the time constants were $t_{\text{lag}} = 34.0$ h and a $t_{\text{char}} = 43.1$ h.

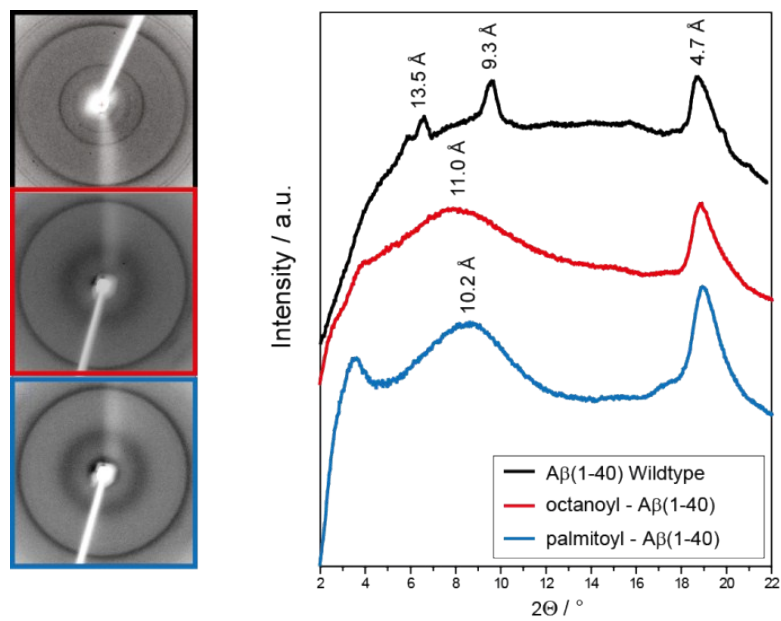


Figure S2. X-ray diffraction patterns of fibrils of Aβ(1-40) (black), octanoyl-Aβ(1-40) (red) and palmitoyl-Aβ(1-40) (blue). The typical cross-β intersheet distances are indicated.

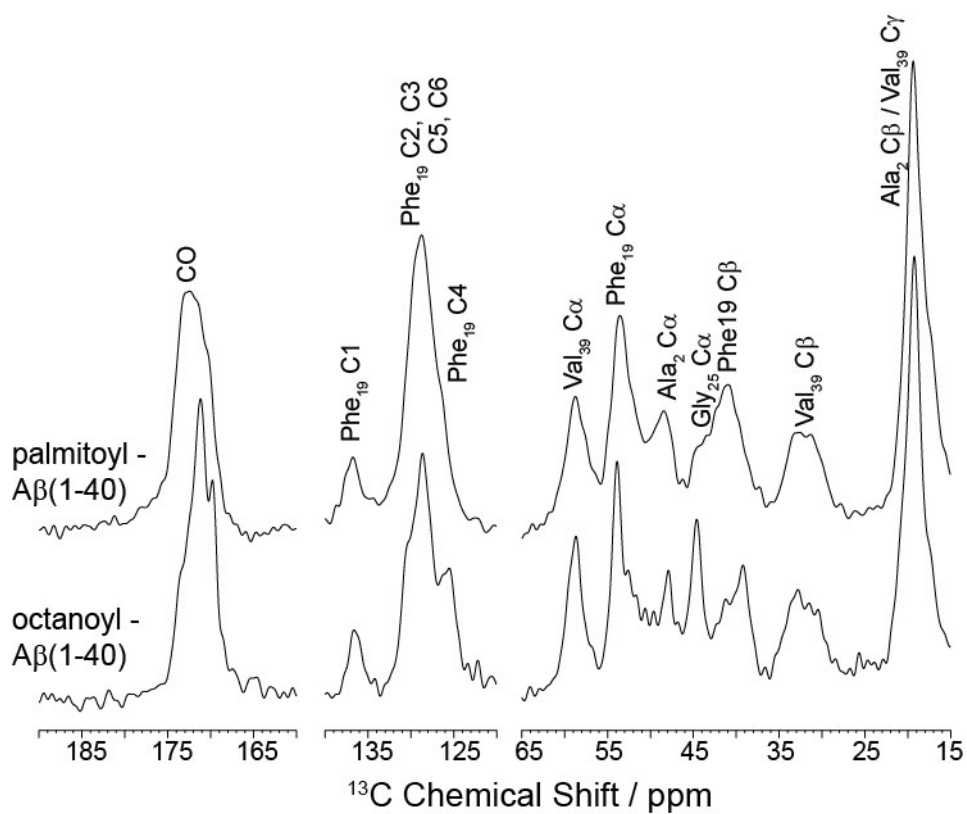


Figure S3. ^{13}C CP-MAS-NMR spectra of octanoyl-A β (1-40) and palmitoyl-A β (1-40) measured at 30°C using a MAS frequency of 11,777 Hz. Signal assignment for the labeled residues (Ala₂, Phe₁₉, Gly₂₅, Val₃₉) is given.

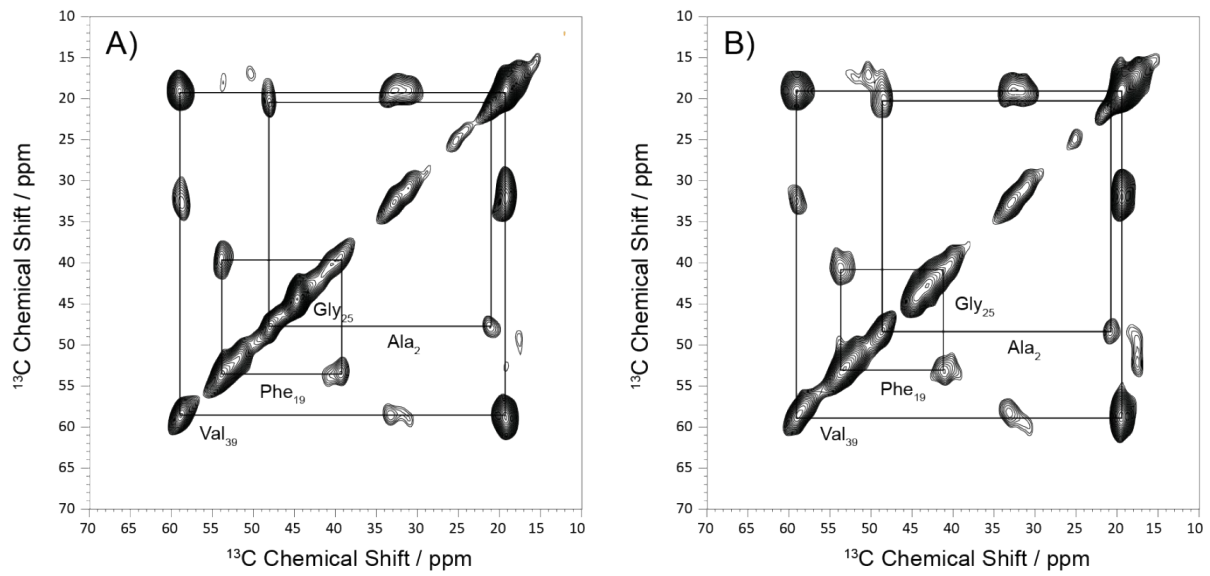


Figure S4. Contour plot of ^{13}C - ^{13}C DARR-NMR spectra of (A) octanoyl- $\text{A}\beta(1-40)$ and (B) palmitoyl- $\text{A}\beta(1-40)$ fibrils, measured at 30°C using a mixing time of 600 ms and an MAS frequency of 11,777 Hz.

Reference List

1. Scheidt, H. A.; Morgado, I.; Rothmund, S.; Huster, D. Dynamics of amyloid beta fibrils revealed by solid-state NMR. *J. Biol. Chem.* **2012**, *287*, 2017-2021.
2. Nielsen, L.; Khurana, R.; Coats, A.; Frokjaer, S.; Brange, J.; Vyas, S.; Uversky, V.N.; Fink, A.L. Effect of environmental factors on the kinetics of insulin fibril formation: Elucidation of the molecular mechanism. *Biochemistry* **2001**, *40*, 6036–6046.