Expanded View Figures

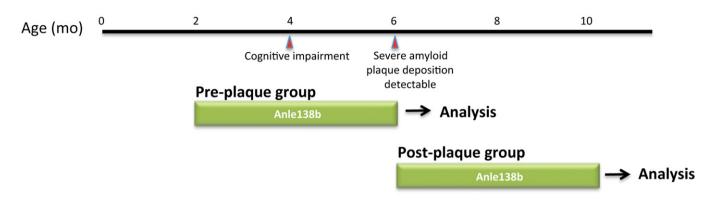


Figure EV1. Experimental design.

Overview of the experimental approach employed for the pre-plaque and the post-plaque group. Red arrows underneath the time line indicate onset of pathology in APPPS1 $\triangle 9$ mice.

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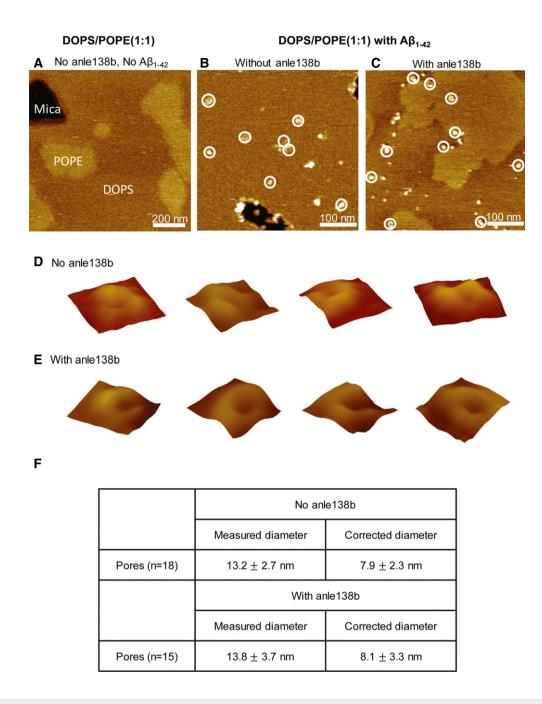


Figure EV2. Observation of Aβ pores by AFM in anle138b-doped membranes.

EV2

AFM tapping mode images showing similar pore structures in membranes with and without anle138b.

- POPE/DOPS (1:1) membranes without compound and not exposed to $A\beta_{1-42}$ showing lateral phase separation. Scale bar is as indicated and z scale is 5 nm.
- $Membrane \ with \ the \ same \ lipid \ composition \ as \ in \ (A) \ without \ compound \ reconstituted \ with \ A\beta_{1-42} \ at \ a \ 1:60 \ peptide/lipid \ molar \ ratio. White \ circles \ represent \ the$ position of pore-like structures. Scale bar is 100 nm and z scale is 5 nm.
- Membrane with the same lipid composition as above with anle138b (10 mM with respect to lipid volume) and reconstituted with $A\beta_{1.-42}$ (1:60 peptide/lipid molar ratio). White circles represent the position of pore-like structures. Scale bar is 100 nm and z scale is 5 nm.
- D, E Four representative pores extracted from (B) and (C), respectively. Image size is $23.4 \text{ nm} \times 23.4 \text{ nm}$.
- Table summarizing that A β pores show the same dimension in the presence or absence of anle138b. Values are represented as average \pm SD.

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