

CRYOEM STRUCTURE OF GAMMA SECRETASE: A KEY COMPONENT IN ALZHEIMER
NEURODEGENERATIVE DISEASE (Renzi_FP7_IOF2007)

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Figures

Fig.1

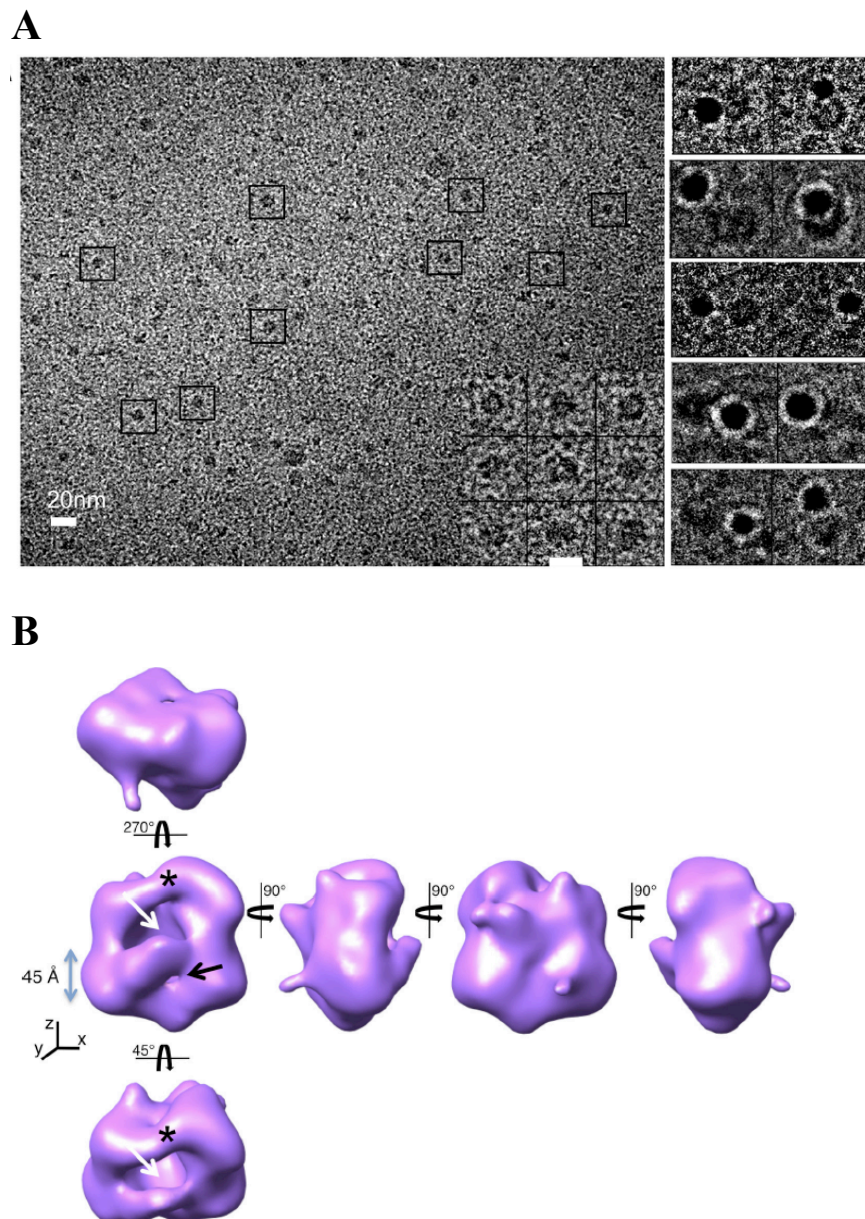


FIGURE 1. Single-particle electron microscopy of gamma-secretase. *A*, representative CCD image of in vitreous ice tetrameric gamma-secretase (left) and gold labeling with antibodies against each subunit and with a substrate analog (right). *B*, **Three-dimensional reconstruction of γ -secretase.** Shown are views of the final three-dimensional volume of γ -secretase filtered at 18 Å and set to a threshold equivalent to a molecular mass of ~200 kDa. The *double-headed arrow* delimits the proposed location of the transmembrane region of the complex. The *asterisks* depict the proposed location of the ectodomain of NCT. The *arrows* mark a cavity (*white arrows*) in the extracellular region that extends to the transmembrane region ending in a lateral opening (*black arrows*)

Fig.2

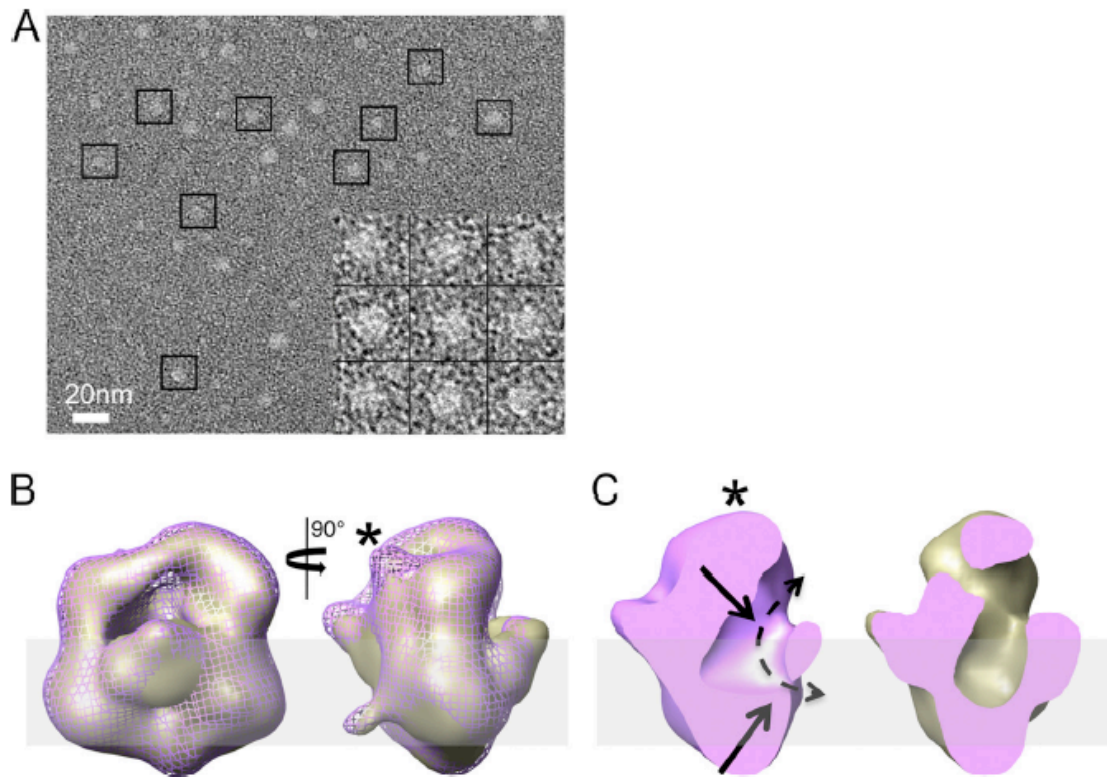


FIGURE 2. Comparison of gamma-secretase with a trimeric pre-activation intermediate lacking PEN-2. *A*, representative CCD image of the trimeric preactivation intermediate under negative stain. *B*, for comparison, the three-dimensional reconstruction of the pre-activation intermediate (yellow) was docked manually in the envelope corresponding to gamma-secretase (magenta mesh). An asterisk marks differences in density between the two reconstructions. *C*, cut-through views of gamma-secretase (magenta) and the pre-activation intermediate (yellow). The black arrows mark the widening of the mouth and the lateral opening. The double-headed arrow depicts the putative path of substrate/product release/entry. The proposed location of the lipid membrane is depicted as a slab.