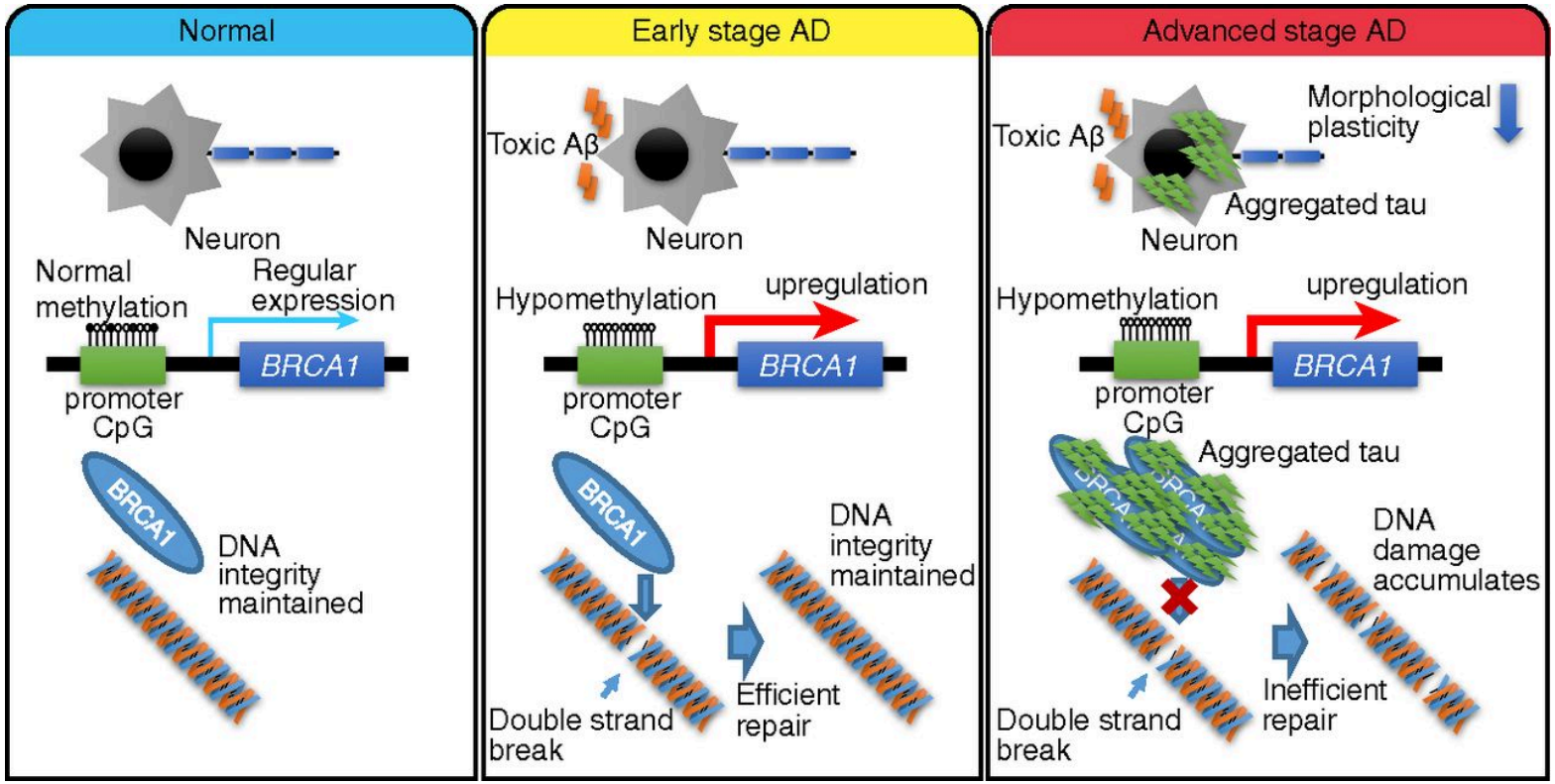
From Laboratory of Neurology

Neuron-specific methylome analysis reveals epigenetic regulation and tau-related dysfunction of BRCA1 in Alzheimer's disease.



Schematic illustration summarizing our current hypothesis regarding Aβ-induced DNA damage, tau, and epigenetic regulation of BRCA1 in AD. In normal brain without Aβ or tau accumulation, there is no need for BRCA1 up-regulation (*Left*). At an early stage of AD with no accumulated tau, BRCA1 efficiently repairs DNA DSBs induced by toxic Aβ (*Middle*). However, at an advanced stage of AD, cytoplasmic aggregated tau sequestrates BRCA1 to an insoluble fraction, resulting in its dysfunction (*Right*). While neurons try to cope with this situation by up-regulating expression of the *BRCA1* gene through epigenetic mechanisms, they are eventually overwhelmed by the accumulation of DNA damage.

Mano T et al Proc Natl Acad Sci U S A. 114(45): E9645-E9654, 2017 Nov 7

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