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### **Elucidating the in vivo Role of BACE2**

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Alzheimer's disease (AD), the most common cause of dementia in the elderly, is characterized by the presence of neurofibrillary tangles along with senile plaques composed primarily of amyloid-beta peptides ( $A\beta$ ). Endoproteolytic cleavages of amyloid- $\beta$  precursor protein (APP) by  $\beta$ -secretase (BACE1) and  $\gamma$ -secretase result in the generation of  $A\beta$ . Amyloid formation may be precluded through the action of  $\alpha$ -secretase, which cleaves within the  $A\beta$  region to generate an APP c-terminal fragment, C83 which is then cleaved by  $\gamma$ -secretase to generate p3. A homologue of BACE1, termed BACE2, has been found to cleave APP within the  $A\beta$  region, similar to the action of  $\alpha$ -secretase. To evaluate the in vivo role of BACE2, we began by generating a BACE2 knockout mouse. The lack of BACE2 mRNA validated the deletion of BACE2 in mice. These knockout mice will be useful for examining the impact of the lack of BACE2 during development and in aging.