Amyloid beta (Aβ) in Alzheimer's disease (AD)

AD AND Aβ

AD is characterized by dense accumulation of proteins—called Aβ plaques and tau tangles—in the brain.

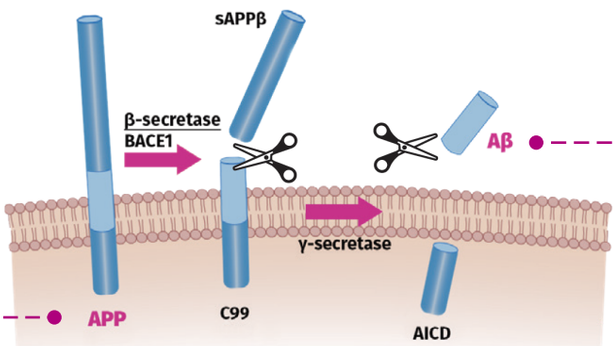
Aβ builds up decades **before symptoms** begin and is one of the earliest detectable biological markers that can indicate AD.

Aβ occurs in different forms, some of which are **toxic to brain** cells.

An **imbalance** between the production of Aβ in the brain and its removal from the brain is associated with protein misfolding, aggregation, and accumulation in plaques.

WHAT IS Aβ AND HOW IS IT MADE?

Aβ is a fragment of a larger protein called amyloid precursor protein **(APP)**, which is found in many types of brain cells.



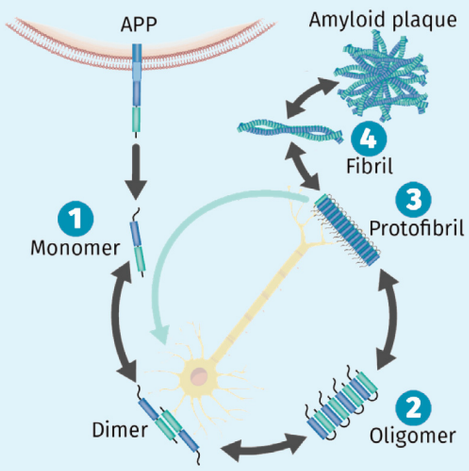
APP is **cleaved** twice by different enzymes to create Aβ.

Once cleaved, **Aβ is released from the cell**. Outside the cell, Aβ can exist in several forms that are either soluble or insoluble.

AICD, APP intracellular domain; APP, amyloid precursor protein; BACE 1, β-APP-cleaving enzyme-1; C99, C-terminal fragment; sAPPβ, soluble N-terminus of APP; Figure from Hampel H., et al. Mol Psychiatry 26, 5481–5503 (2021). This article is licensed under a Creative Commons Attribution 4.0 International License.

WHAT ARE THE DIFFERENT FORMS (SPECIES) OF Aβ?

Aβ species and reversible states: Aβ cycle



1 Aβ is first produced as a soluble, one-protein fragment called a **monomer**.

2 A handful of Aβ monomers can bind together to form soluble **oligomers** of different sizes, from dimers to dodecamers.

3 Aβ can also gather into larger, soluble clumps called **protofibrils**, which may be the most toxic Aβ species.

4 **Fibrils and amyloid plaques are clumps** of Aβ that are insoluble and associated with toxicity.

APP, amyloid precursor protein; Figure from Hampel H., et al. Mol Psychiatry 26, 5481–5503 (2021).

KEY TAKEAWAYS

Aβ is an early and key contributor to AD.

There is an important balance between Aβ production and clearance in the brain.

Monoclonal antibodies that remove different forms of Aβ have been developed and are under investigation, aiming to slow disease progression in early clinical stages of AD.

REFERENCES:

1. Hampel H., et al. Mol Psychiatry. 2021;26(10):5481-5503.

ABBREVIATIONS:

Aβ, amyloid beta; AD, Alzheimer's disease; AICD, APP intracellular domain; APP, amyloid precursor protein; BACE 1, β-APP-cleaving enzyme-1; C99, C-terminal fragment; sAPPβ, soluble N-terminus of APP.