# $A\beta_{1-42}$ (Amyloid-beta 1–42)

**Name**: Amyloid-beta (1–42) **Abbreviation**: $A\beta_{1-42}$ **Type**: Peptide fragment **Length**: 42 amino acids **Molecular weight**: ~4.5 kDa **Encoded by**: **APP** (Amyloid precursor protein) gene

## Origin and Structure

- $A\beta_{1-42}$ is generated from the **proteolytic cleavage** of amyloid precursor protein (APP) by **β-secretase (BACE1)** and **γ-secretase**
- Exists in multiple conformations: **monomers, oligomers, fibrils**
- $A\beta_{1-42}$ is more **hydrophobic** and prone to aggregation than $A\beta_{1-40}$

## Biological and Clinical Significance

- Major component of **amyloid plaques** found in **Alzheimer's disease (AD)** brain tissue
- **Neurotoxic**, especially in its **soluble oligomeric** forms
- Impairs synaptic plasticity, induces oxidative stress, disrupts calcium homeostasis
- Oligomers may inhibit long-term potentiation (LTP) and memory formation

## Diagnostic and Research Use

- **Cerebrospinal fluid (CSF)** $A\beta_{1-42}$ levels are **decreased** in Alzheimer's disease due to plaque deposition
- Used in **CSF biomarker panels**:
  - ↓ $A\beta_{1-42}$
  - ↑ Total tau (t-tau)
  - ↑ Phosphorylated tau (p-tau)
- Investigated in **PET imaging** (e.g., with radiotracers like Pittsburgh compound B)
- Animal models of AD often use **intraventricular or hippocampal injection** of synthetic $A\beta_{1-42}$

## Therapeutic Implications

- Target of **anti-amyloid therapies**, including:
  - **Monoclonal antibodies** (e.g., aducanumab, lecanemab)
  - **Secretase inhibitors** (limited success)
  - **Aβ-clearance enhancers**
- Immunotherapy against $A\beta_{1-42}$ aims to prevent plaque formation and toxicity

## ⚠ Pathophysiological Notes

- **$A\beta_{1-42}/A\beta_{1-40}$ ratio** is often more informative than absolute levels

- Accumulation precedes clinical symptoms by years or decades
- Ongoing debate: **Amyloid hypothesis** vs **tau-first hypothesis** in AD pathogenesis

## References


- PubChem: $A\beta_{1-42}$
- AlzForum: Aβ42 Biomarker
- NCBI: APP gene