Anti-PSEN2 Rabbit Polyclonal Antibody

Presenilin-2, PS-2, EC 3.4.23.-, AD3LP, AD5, E5-1, STM-2, [Cleaved into: Presenilin-2 NTF subunit; Presenilin-2 CTF subunit

Gene: PSEN2 **UniProt:** P49810 **Host:** Rabbit **Clonality:** Polyclonal (pAb)

Product Image

Image placeholder — Western Blot

— Western Blot

Suggested image: Western blot of relevant cell or tissue lysates under reducing conditions, probed with the domain-specific antibody. Include a positive-control lane and empty-vector or knockout negative control. Loading: 10–20 µg/lane on 7.5–10% SDS-PAGE.

Key Product Facts

Supplier	Triple Point Biologics, Inc. (Sudbury, Ontario, Canada)
Product Name	Anti-PSEN2 Rabbit Polyclonal Antibody
Gene Symbol	PSEN2
Alternative Names	Presenilin-2, PS-2, EC 3.4.23.-, AD3LP, AD5, E5-1, STM-2, [Cleaved into: Presenilin-2 NTF subunit; Presenilin-2 CTF subunit
UniProt ID	P49810
Host Species	Rabbit
Clonality	Polyclonal (pAb)
Isotype	IgG
Concentration	1mg/ml
Purity	Affinity purified
Pack Size	100ug
Validated Application	WB
Recommended Dilution	WB-1/1000
Species Reactivity	Validated- Human Potential-
Immunogen Type	Synthetic Peptide from Uniprot Sequence
Conjugation	none
Buffer / Preservatives	Sodium Chloride 500 mM, Sodium Phosphate 10 mM, Potassium Phosphate 1.8 mM, Potassium Chloride 2.7 mM, Glycerol 50% (v/v)
Website	triplepointbiologics.com/anti-presenilin-2-rabbit-polyclonal-antibody

Available Domain-Specific Variants

Triple Point Biologics produces antibodies to defined structural domains of PSEN2. Each variant is directed at a specific structural region of the protein. Exact peptide sequences are proprietary; each variant is validated for the applications listed.

Domain / Variant	Epitope Region (approx. residues)	Cat. No.	Availability

N-terminal Fragment	**1–51** Region within the cytoplasmic N-terminal domain of human PSEN2, upstream of the first transmembrane helix (TM1, approximately residues 88–108 per UniProt P49810), encompassing the hydrophilic cytoplasmic head of the holoprotein prior to membrane insertion	RP1Presenilin2	In catalog
C-terminal Fragment	**247–297** Region within the cytoplasmic C-terminal tail of human PSEN2, downstream of the ninth transmembrane helix (TM9, ending approximately residue 369 per UniProt P49810), encompassing the hydrophilic C-terminal domain of the CTF subunit that is exposed to the cytosol within the gamma-secretase complex	RP2Presenilin2	In catalog
—	**1–297** Broad representation spanning multiple structural domains of human PSEN2, including the N-terminal cytoplasmic head, the nine transmembrane helices, the large cytoplasmic loop (approximately residues 263–378) that harbours the endoproteolytic cleavage site, and the C-terminal cytoplasmic tail, providing reactivity against both the NTF and CTF subunits	RP-Presenilin2	In catalog

Applications & Recommended Dilutions

App.	Species	Dilution Range	Notes
WB	Validated-Human Potential-	1:1000	Optimal dilution should be determined per laboratory and lot.

Optimal dilutions should be determined by each laboratory for each application. Triple Point Biologics antibodies include a peptide-neutralized negative control aliquot for specific-signal confirmation.

Storage & Handling

Short-term Storage	+4°C (1–2 weeks)
Long-term Storage	Aliquot and store at -20°C
Shipping Conditions	Shipped in styrofoam cooler on blue ice
Hazard Warning	Product may contain Sodium Azide — POISONOUS AND HAZARDOUS. Handle by trained personnel only.
Shelf Life	12 months from date of receipt under recommended conditions

Target Background

Protein Family & General Biology

Presenilin-2 (PSEN2) is a 448-amino acid multipass transmembrane aspartyl protease and one of two mammalian presenilin paralogs, the other being Presenilin-1 (PSEN1). Both presenilins serve as the catalytic subunit of the gamma-secretase complex, a high-molecular-weight intramembrane endoprotease that also includes nicastrin, APH-1, and PEN-2. The two conserved aspartate residues within transmembrane domains 6 and 7 of PSEN2 constitute the active site, classifying gamma-secretase as an aspartyl protease that cleaves substrates within the lipid bilayer. PSEN2 spans the membrane nine times and is processed endoproteolytically into stable N-terminal (NTF) and C-terminal (CTF) fragments that co-assemble within the mature complex.

Expression & Subcellular Localisation

PSEN2 is broadly expressed in human tissues, with notable levels in neurons of the cerebral cortex, hippocampus, and cerebellum, as well as in cardiac muscle, skeletal muscle, and kidney. At the subcellular level, PSEN2 localises predominantly to the endoplasmic reticulum (ER) membrane and to late endosomes and lysosomes, a distribution that is distinct from PSEN1, which is enriched at the cell surface and trans-Golgi network. This preferential late endosomal/lysosomal positioning confers upon PSEN2-containing gamma-secretase a bias toward processing substrates in acidic intracellular compartments and contributes to the generation of longer, more aggregation-prone amyloid-beta peptide species.

Activation Mechanism & Complex Assembly

PSEN2 is synthesised as an inactive holoprotein that undergoes obligatory endoproteolytic cleavage within the large cytoplasmic loop (exon 10-encoded region, roughly residues 298–320) to produce the NTF (~35 kDa) and CTF (~20 kDa) heterodimer. This autoproteolytic event is facilitated within the assembled gamma-secretase complex and is required for catalytic competence. The stoichiometry of PSEN within the complex is one molecule per complex, meaning that PSEN2 and PSEN1 do not compete within the same complex but instead form two distinct gamma-secretase populations. Complex assembly is regulated by the availability of nicastrin, APH-1, and PEN-2 subunits, with PEN-2 incorporation triggering the final endoproteolytic maturation step.

Key Substrates & Catalytic Activity

The best-characterised substrates of PSEN2-containing gamma-secretase are amyloid precursor protein (APP) and the Notch receptor family. Sequential ectodomain shedding by alpha- or beta-secretase exposes APP for gamma-secretase cleavage at the epsilon, zeta, and gamma sites within the transmembrane domain, releasing the amyloid-beta peptide (predominantly Aβ40/Aβ42/Aβ43) and the APP intracellular domain (AICD). Notch processing releases the Notch intracellular domain (NICD), which translocates to the nucleus to drive transcriptional programmes governing cell fate. Additional validated substrates include ErbB4, N-cadherin, CD44, and Delta/Jagged ligands, underscoring the broad physiological reach of intramembrane proteolysis mediated by this complex.

Calcium Homeostasis & ER–Mitochondria Contacts

Independent of its protease function, the PSEN2 holoprotein acts as a passive, low-conductance calcium leak channel in the ER membrane, facilitating the slow efflux of luminal calcium into the cytosol. Loss-of-function mutations that impair this channel activity elevate ER calcium stores and alter cytosolic calcium transients. PSEN2 is also enriched at mitochondria-associated membranes (MAMs), where it modulates calcium transfer between the ER and mitochondria and influences mitochondrial metabolism and fission-fusion dynamics. These non-proteolytic functions are relevant to understanding how familial PSEN2 mutations contribute to cellular dysfunction beyond altered amyloid-beta production.

Disease Relevance

Missense mutations in PSEN2 are a cause of autosomal dominant early-onset familial Alzheimer disease (FAD). Pathogenic PSEN2 variants characteristically shift gamma-secretase cleavage toward longer Aβ42 and Aβ43 peptides, increasing the Aβ42/Aβ40 ratio, a metric strongly correlated with amyloid plaque formation. Unlike PSEN1 mutations, which typically cause

disease onset in the fourth to fifth decade, PSEN2 mutations are associated with a broader and later age-of-onset range (45–88 years) and incomplete penetrance in some kindreds. PSEN2 variants have additionally been implicated in familial dilated cardiomyopathy, consistent with its expression in cardiac tissue and its roles in calcium handling and Notch signalling in cardiomyocytes.

Gene & Protein Reference

Gene Symbol	PSEN2
HGNC	HGNC:9509
NCBI Gene ID (Human)	5664
NCBI Gene ID (Mouse)	19165
Ensembl	ENSG00000164362
OMIM	600759
UniProt (Human)	P49810
UniProt (Mouse)	P49023
Protein Family	Peptidase A22B family (presenilin-type aspartyl intramembrane protease)
Predicted MW	~54 kDa (holoprotein); NTF ~35 kDa, CTF ~20 kDa after endoproteolysis
Observed MW	Holoprotein ~54 kDa; NTF ~35 kDa; CTF ~20 kDa by SDS-PAGE
Chromosome	1q42.13
Paralogue	PSEN1 (Presenilin-1; HGNC:9508)
Key Substrates	APP (amyloid precursor protein), Notch1–4, ErbB4, N-cadherin, CD44, Delta/Jagged ligands
Activated by	Endoproteolytic cleavage within the assembled gamma-secretase complex (facilitated by PEN-2 incorporation); substrate engagement requires prior ectodomain shedding by alpha- or beta-secretase
Inhibited by	Gamma-secretase inhibitors (GSIs, e.g. DAPT, compound E, LY411575); transition-state analogue inhibitors (e.g. L-685,458); gamma-secretase modulators (GSMs) shift cleavage site selectivity without complete inhibition

About Triple Point Biologics

With over 30 years dedicated to antibody production, Triple Point Biologics is a Canadian company and the premier resource for proteinase and proteinase inhibitor research. Products have been cited in thousands of peer-reviewed publications.

The domain-specific antibody strategy — available in standard, ATK, SPA, and GSK kit formats — delivers predefined epitopes, built-in peptide-neutralized negative controls, and superior specificity for Western blot.

Website: www.triplepointbiologics.com

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