Product Datasheet

Biological Description

Specificity	Phospho-Tau (Ser262) Antibody [N15P23] detects endogenous levels of total Tau protein only when it is phosphorylated at Ser262.
Background	Phospho-Tau (Ser262) refers to the microtubule-associated protein tau phosphorylated at serine 262 within its proline-rich microtubule-binding repeat domain (R1/R2 junction), existing as natively unstructured isoform (0N, 1N, 2N variants) that contains four imperfect microtubule-binding repeats (MTBRs) with 275-VQIVYK283 KXGS motifs; phosphorylation at Ser262, often accompanied by pSer356, disrupts the KXGS epitope primed by MARK2/Par-1 kinase and drastically reduces tau's affinity for β-tubulin (Kd shifts >10-fold) by sterically interfering with the microtubule lattice. Initiated by amyloid-β oligomers activating MARK2 via calpain cleavage or CDK5/p25 hyperactivation, this phosphorylation event triggers rapid microtubule depolymerization through conformational unbinding, as pSer262 locks the R1/R2 inter-repeat loop in a disordered state, thereby exposing distal phosphorylation sites (Ser202/Thr205, Ser396/Ser404) for priming by GSK3β/Fyn. This sequential phosphorylation promotes tau oligomerization into toxic 4R-prefibrillar seeds capable of trans-synaptic propagation via neuronal uptake and exocytosis, while causing tau mislocalization from axons to somatodendritic compartments. Physiologically, transient cycling of pSer262 via PP2A-mediated dephosphorylation regulates microtubule dynamics during neuronal plasticity, but chronic hyperphosphorylation, elevated in Alzheimer's disease (Braak I-II), precedes neurofibrillary tangle (NFT) formation by years, establishing pSer262 as an "early gatekeeper" biomarker detectable in cerebrospinal fluid (pTau262/tau ratio) that mediates Aβ42 synaptotoxicity, synaptic loss, and cognitive decline with specificity for granular pre-tangles over mature paired helical filaments (PHFs).

Usage Information

Application	IHC, ELISA	Dilution	IHC 1:100-1:200
Reactivity	Human		
Source	Mouse Monoclonal Antibody	MW	33-79 kDa
Storage Buffer	PBS, pH 7.2+50% Glycerol+0.05% BSA+0.01% NaN3		
Storage (from the date of receipt)	-20°C (avoid freeze-thaw cycles), 2 years		

Experimental Methods

IHC

Experimental Protocol:

Deparaffinization/Rehydration
1. Deparaffinize/hydrate sections:
2. Incubate sections in three washes of xylene for 5 min each.
3. Incubate sections in two washes of 100% ethanol for 10 min each.
4. Incubate sections in two washes of 95% ethanol for 10 min each.
5. Wash sections two times in dH2O for 5 min each.
6.Antigen retrieval: For Citrate: Heat slides in a microwave submersed in 1X citrate unmasking solution until boiling is initiated; continue with 10 min at a sub-boiling temperature (95°-98°C). Cool slides on bench top for 30 min.

Staining
1. Wash sections in dH2O three times for 5 min each.
2. Incubate sections in 3% hydrogen peroxide for 10 min.
3. Wash sections in dH2O two times for 5 min each.
4. Wash sections in wash buffer for 5 min.
5. Block each section with 100–400 µl of blocking solution for 1 hr at room temperature.
6. Remove blocking solution and add 100–400 µl primary antibody diluent in to each section. Incubate overnight at 4°C.
7. Remove antibody solution and wash sections with wash buffer three times for 5 min each.
8. Cover section with 1–3 drops HRPas needed. Incubate in a humidified chamber for 30 min at room temperature.
9. Wash sections three times with wash buffer for 5 min each.
10. Add DAB Chromogen Concentrate to DAB Diluent and mix well before use.
11. Apply 100–400 µl DAB to each section and monitor closely. 1–10 min generally provides an acceptable staining intensity.
12. Immerse slides in dH2O.
13. If desired, counterstain sections with hematoxylin.
14. Wash sections in dH2O two times for 5 min each.
15. Dehydrate sections: Incubate sections in 95% ethanol two times for 10 sec each; Repeat in 100% ethanol, incubating sections two times for 10 sec each; Repeat in xylene, incubating sections two times for 10 sec each.
16. Mount sections with coverslips and mounting medium.

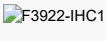
References

https://pubmed.ncbi.nlm.nih.gov/39930142/ https://pubmed.ncbi.nlm.nih.gov/20466736/

Application Data

IHC

Validated by Capsid Bio



Immunohistochemical analysis of formalin fixed paraffin embedded mouse brain tissue with F3922 at 1:50 dilution.