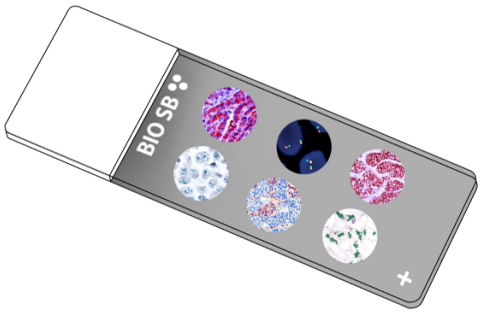
APOE4 Control Slides

CE IVD



Intended Use
For In Vitro Diagnostic Use.

Summary and Explanation
Apolipoprotein E4 (APOE4) is a protein known to contribute to the onset of Alzheimer's disease. While it is expressed in many organs, in the brain APOE4 has been associated with deposition of insoluble Aβ40 and Aβ42 in the cortex and hippocampus. APOE isoforms are produced by astrocyte cells, and assist in the delivery of lipids such as cholesterol to the neurons. LDL receptor-related protein 1 (LRP1) metabolizes APOE4 and Aβ plaques, and the presence of APOE4 decreases the clearance or solubility of Aβ40 and Aβ42.
In knockout mice models, APOE4 isoform was shown to be correlated with increased insoluble Aβ in the presence of LRP1. APOE4 has been found to be a genetic factor in the pathology of Alzheimer's disease, Lewy Body Dementia, and Parkinson's Disease. Overproduction of plaques and interference in clearing the insoluble peptides results in the accumulation of Aβ42. The Aβ plaque burden in the brains of Alzheimer's patients with APOE4 isoform is around 2.7 times that of patients with APOE3 isoform, indicating a role of APOE4 in Aβ metabolism. Accumulated Aβ oligomers have been shown to disrupt synaptic function- the loss of dendritic spines contributes to the loss of cognitive function.

Presentation
Five slides of APOE4 positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

Catalog No.	*Quantity*
BSB-9436-CS	5 slides

Storage Store at 20-25°C

Precautions
1. For professional users only. Results should be interpreted by a qualified medical professional.
2. Ensure proper handling procedures are used with this reagent.
3. Always wear personal protective equipment such as a laboratory coat, goggles, and gloves when handling reagents.
4. Dispose of unused solution with copious amounts of water.
5. Follow safety precautions of the heating device used for epitope retrieval (TintoRetriever Pressure Cooker or similar).
8. For additional safety information, refer to the Safety Data Sheet for this product.
9. For complete recommendations for handling biological specimens, please refer to the CDC document, "Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories" (see References in this document).

Stability
This product is stable up to the expiration date on the product label.
Do not use the after expiration date listed on the package label.

IHC Protocol
1. Subject tissues to heat induced epitope retrieval (HIER) using a suitable retrieval solution such as ImmunoDNA Retriever with Citrate (BSB 0020-BSB 0023) or EDTA (BSB 0030-BSB 0033).
2. Any of three heating methods may be used:
a. TintoRetriever Pressure Cooker or Equivalent
Place tissues/slides in a staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA and place on trivet in the pressure cooker. Add 1-2 inches of distilled water to the pressure cooker and turn heat to high. Incubate for 15 minutes. Open and immediately transfer slides to room temperature.
b. TintoRetriever PT Module or Water Bath Method
Place tissues/slides in a pre-warmed staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA at 95°-99° C. Incubate for 30-60 minutes.
c. Conventional Steamer Method
Place tissues/slides in a pre-warmed staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA in a steamer, cover and steam for 30-60 minutes.
3. After heat treatment, transfer slides in ImmunoDNA Retriever with Citrate or EDTA to room temperature and let stand for 15-20 minutes.
4. For manual staining, perform antibody incubation at ambient temperature. For automated staining methods, perform antibody incubation according to instrument manufacturer's instructions.
5. Wash slides with ImmunoDNA washer or DI water.
6. Continue IHC staining protocol. Wash slides between each step with ImmunoDNA washer solution.

Abbreviated Immunohistochemical Protocol

Step	ImmunoDetector AP/HRP	PolyDetector AP/HRP	PolyDetector Plus HRP
Peroxidase/AP Blocker	5 min.	5 min.	5 min
Primary Antibody	30-60 min.	30-60 min.	30-60 min.
1st Step Detection	10 min.	30-45 min.	15 min.
2nd Step Detection	10 min.	Not Applicable	15 min.
Substrate- Chromogen	5-10 min.	5-10 min.	5-10 min.
Counterstain/Coverslip	Varies	Varies	Varies

Abbreviated IF Protocol

Step	Incubation Time
Rinse slides in IF wash buffer	5 minutes
Drain and wipe excess IF wash buffer off slide	
Conduct remaining steps in the dark	
Apply Antibody	30-60 minutes
Rinse with 3 changes of IF wash buffer	3x15 minutes each
Coverslip with IF mounting medium	

Mounting Protocols

For detailed instructions using biodegradable permanent mounting media such as XyGreen PermaMounter (BSB 0169-0174) or organic solvent based resin such as PermaMounter (BSB 0094-0097), refer to PI0174 or PI0097.

Product Limitations

Due to inherent variability present in immunohistochemical procedures (including fixation time of tissues, dilution factor of antibody, retrieval method utilized, and incubation time), optimal performance should be established through the use of positive and negative controls. Results should be interpreted by a qualified medical professional.

References

1. Zhao N, et al. APOE4 exacerbates α-synuclein pathology and related toxicity independent of amyloid. Sci Transl Med. 2020;12(529):1809
2. Tachibana M, et al. APOE4-mediated amyloid-β pathology depends on its neuronal receptor LRP1. J Clin Invest. 2019;129(3):1272-1277
3. Koren-Iton A, et al. Central and Peripheral Mechanisms in ApoE4-Driven Diabetic Pathology. Int J Mol Sci. 2020;21(4):1289.
4. Hashimoto T, et al. Apolipoprotein E, especially apolipoprotein E4, increases the oligomerization of amyloid β peptide. J Neurosci. 2012;32(43):15181-92.
5. Castellano J, et al. Human apoE isoforms differentially regulate brain amyloid-β peptide clearance. Sci Transl Med. 2011;3(89):89ra57.
6. Martin L, et al. VEGF counteracts amyloid-b-induced synaptic dysfunction. Cell Reports. 2021;35: 109121.
7. Bittner T, et al. Multiple Events Lead to Dendritic Spine Loss in Triple Transgenic Alzheimer's Disease Mice. PLoS ONE. 2010;5(11): e15477.

Symbol Key / Légende des symboles/Erläuterung der Symbole

EC REP QAdvis EAR AB Ideon Science Park Scheelevägen 17 SE-223 70 Lund, Sweden	Storage Temperature Limites de température Zulässiger Temperaturbereich	Manufacturer Fabricant Hersteller	REF Catalog Number Référence du catalogue Bestellnummer
IVD In Vitro Diagnostic Medical Device Dispositif médical de diagnostic in vitro In-Vitro-Diagnostikum	Read Instructions for Use Consulter les instructions d'utilisation Gebrauchsanweisung beachten	Expiration Date Utiliser jusque Verwendbar bis	LOT Lot Number Code du lot Chargenbezeichnung

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