Enhanced validation data

Anti-APOE4 recombinant antibody – ab279714
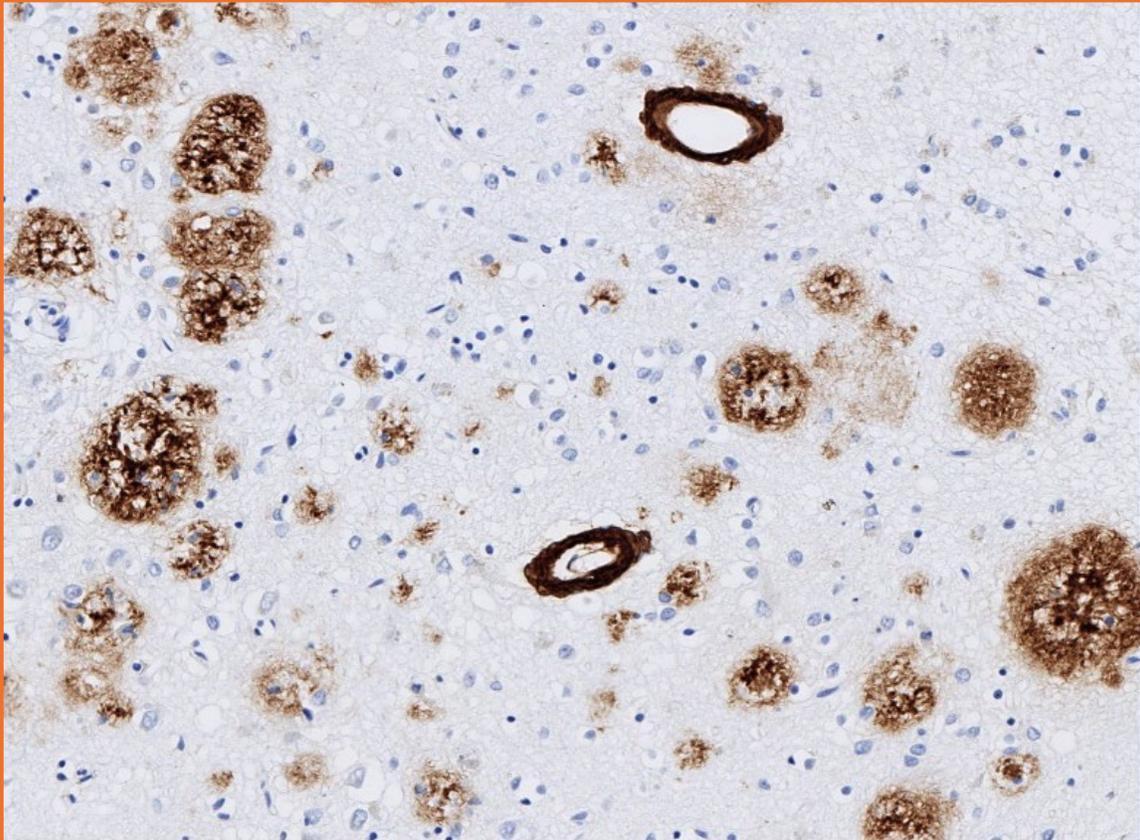
APOE4 expression in Alzheimer's tissue

progress happens together

abcam

Table of contents

Enhanced validation of Anti-Apolipoprotein E4 antibody [EPR24181-64] – ab279714

Enhanced validation designed for your needs

We understand the challenge of finding the right antibody clone – highly specific and sensitive to your intended target – at early selection stages of your development program. To de-risk this clone selection process for you, we generated enhanced validation data for our best recombinant antibody clones to some of the most promising targets.

Our enhanced validation gives you an extra level of confidence in an antibody clone

— Provides additional data on the specificity and sensitivity of our recombinant antibodies in immunohistochemistry (IHC) and other relevant techniques

— Carried out in a custom manner, specific both to the target and the relevant research and clinical settings

— Builds upon our high-quality standard validation

Our framework for enhanced validation

— Our enhanced validation focuses on generating detailed IHC expression profiles for promising neuroscience targets in selected formalin-fixed paraffin-embedded (FFPE) human tissue microarrays (TMAs).

— In this study, we demonstrate the sensitivity and specificity of Anti-APOE4 antibody (ab279714) in IHC in selected tissues and TMAs using a BOND™ RX Research Stainer (Leica®) and DISCOVERY ULTRA system (Roche Diagnostics).

Target overview

HGNC symbol
APOE

Approved name
Apolipoprotein E isoform 4

Chromosomal location
19q13.32

Function

- Apolipoprotein E (APOE) encodes a lipid-carrier protein crucial for lipoprotein particles and receptor-mediated uptake[1]. APOE has three common isoforms: ε2, ε3, and ε4. ε2 is rare and reduces Alzheimer's disease (AD) risk, ε4 is common and increases risk, while ε3, the most prevalent, poses no risk[2].

- APOE ε4 (APOE4) enhances amyloid beta (Aβ) plaque formation, impairs Aβ clearance through the blood-brain barrier (BBB), and reduces Aβ phagocytosis by glia[3]. It also increases tau phosphorylation (p-Tau)[4], leading to neurofibrillary tangle (NFT) formation[5], and promotes reactive gliosis and neuroinflammation[6], potentially disrupting the BBB[7].

Tissue specificity

- ApoE is expressed in peripheral tissues and the central nervous system, mainly produced by the liver in the periphery. In the brain, it's found in astrocytes and upregulated in activated microglia and stressed neurons during pathological conditions and injury[8].

- APOE4 promotes the aggregation and deposition of amyloid-beta (Aβ) peptides into plaques in AD[9]. APOE4 is less efficient at clearing Aβ from the brain than other APOE isoforms[10].

Cellular localization

- Secreted; organelles

Database links (APOE)

Entrez Gene: 348
OMIM®: 107741
Uniprot: P02649

Materials and methods

Human tissues were selected based on the target's expression and its current relevance to ongoing research and clinical trials.

Tissue microarray (TMA)	Cores	Cases	Normal/ Benign cases	Cancer cases	Source (#catalog number)
Multi-normal [a]	15	15	15	0	In-house TMA
Multi-cancer [b]	35	35	1	34	In-house TMA
Nervous system tumor	96	48	3	45	Quick arrays (# NGL961)
Nervous system tumor	102	102	5	97	Quick arrays (# NST1021)

Table 1. List of human TMAs used in the enhanced validation. All tissues were sourced from Abcam-approved tissue suppliers.

a) The multi-normal TMA consists of the following tissues from one donor: colon, cerebrum, tonsil, stomach, testis, prostate, lung, skeletal muscle, heart, skin, spleen, pancreas, kidney, placenta, and liver.

b) The multi-cancer TMA consists of the following tissues from two donors: seminoma, prostate adenocarcinoma, bladder carcinoma, renal cell carcinoma, melanoma, stomach adenocarcinoma, pancreatic adenocarcinoma, hepatocellular carcinoma, ovarian carcinoma, cervical cancer, head and neck carcinoma, and endometrial cancer. The following issues were from single donors: lung (squamous cell carcinoma (SCLC) and non-squamous cell carcinoma (NSCLC)), colon (adenocarcinoma and invasive adenocarcinoma), breast (ductal carcinoma and invasive lobular carcinoma), B-cell lymphoma, T-cell lymphoma, gliomas (grade II and IV), and placenta.

Anatomic site	Cases	Disease
Brain	11	Alzheimer's disease
Brain (Thalamus)	1	Normal
Brain (Cortex)	2	Normal
Brain (Hippocampus)	2	Normal

Table 2. List of human FFPE tissues used in the enhanced validation. All tissues were sourced from Abcam approved tissue suppliers.

Enhanced validation data

Step	Reagents	Method
Deparaffinization	DISCOVERY Wash (RUO)	Standard
Cell conditioning	ULTRA Cell Conditioning Solution (ULTRA CC1)	32 min, 100 °C
Pre-primary peroxidase inhibitor	OptiView Peroxidase Inhibitor	4 min
Primary antibody	Anti-Apolipoprotein E4 antibody [EPR24181-64] - ab279714 diluted in VENTANA Antibody Diluent with Casein (#760-219) to final concentration of 0.25 µg/mL	16 min, 37 °C
Counterstain	Hematoxylin II	8 min
Post counterstain	Bluing Reagent	4 min

Table 3. IHC staining protocol on the DISCOVERY ULTRA (Roche Diagnostics) instrument. Staining was performed using standard conditions with OptiView DAB IHC Detection kit (#760-700).

Step	Reagents	Method
Dewax	Bond™ dewax solution (AR922), alcohol, BOND wash solution (AR9590)	Dewax
Antigen retrieval	Bond™ epitope retrieval ER2 solution (AR9640)	HIER with ER2 (pH 9.0), 20 min, 100°C

Step	Reagents	Number of washes	Time (minutes)
Peroxide block	3-4% (v/v) Hydrogen peroxide	-	5
Wash	Bond™ wash solution	3x	0
Primary antibody	Anti-Apolipoprotein E4 antibody [EPR24181-64] - ab279714 diluted in Bond™ primary antibody diluent (#AR9352) to final concentration of 0.25 µg/mL	-	15
Wash	Bond™ wash solution	4x	0
Secondary antibody	Bond™ polymer refine detection (DS9800)	-	8
Wash	Bond™ wash solution	2x	4
	Deionized water	1x	0
Visualization	Mixed DAB refine (DS9800)	1x	0
	Mixed DAB refine (DS9800)	-	10

Enhanced validation data

Wash	Deionized water	3x	0
Counterstain	Hematoxylin (DS9800)	-	5
Wash	Deionized water	1x	0
	Bond™ wash solution	1x	0
	Deionized water	1x	0

Table 4. IHC staining protocol on BOND™ RX Research Stainer (Leica®). The protocol used is the same as the default IHC protocol F on BOND™ RX Research Stainer (Leica®), apart from the standard post-primary step, which has been excluded from our protocol. All steps were performed at room temperature.

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BOND™ is a trademark of Leica Biosystems Melbourne Pty. Ltd.

APOE4 expression in FFPE cell pellets (BOND™ RX)

Below are representative images of APOE2, APOE3, and APOE4 overexpression in FFPE 293T (human embryonic kidney epithelial) cells. APOE4 expression was detected in the APOE4-overexpressing cell line and absent in the APOE2 and APOE3-expressing cell lines.

Formalin fixed paraffin-embedded 293T cells

APOE4

Human APOE2 overexpression   Human APOE3 overexpression
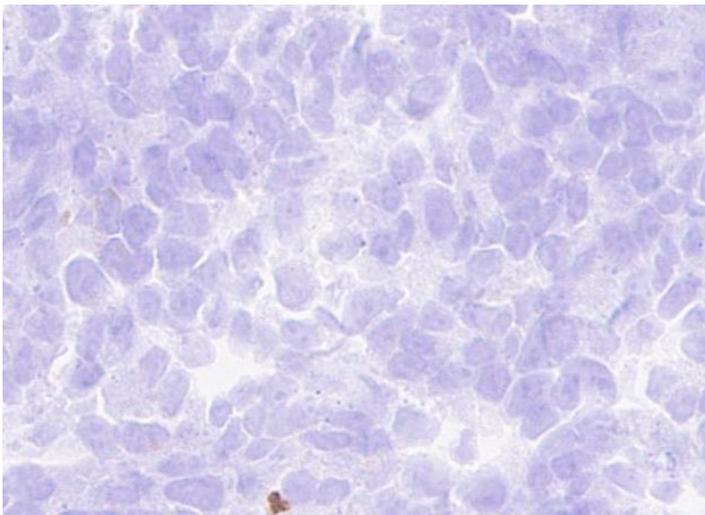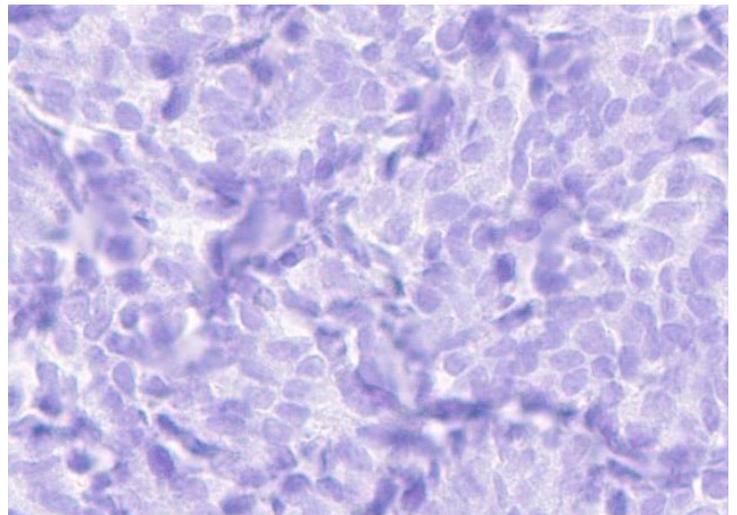
APOE4   **Secondary antibody only control**

Human APOE4 overexpression
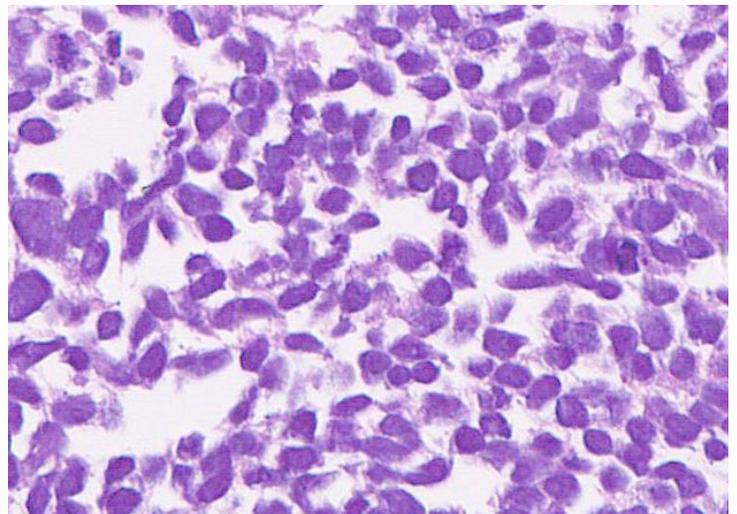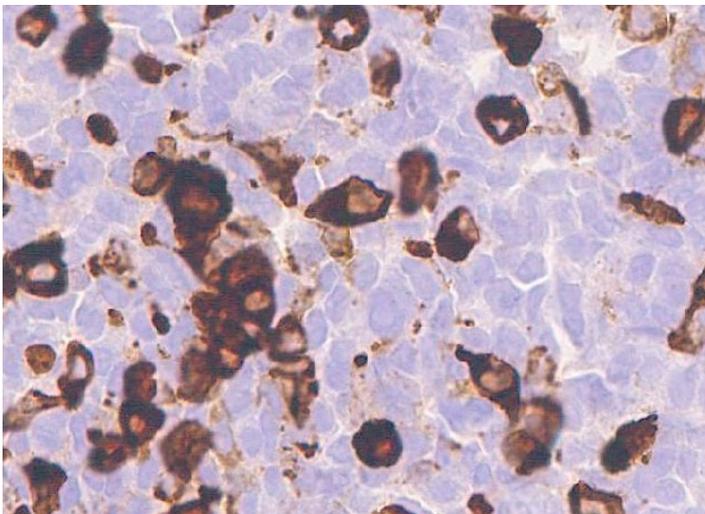
Figure 1. Immunohistochemical analysis of APOE4 expression in FFPE 293T (human embryonic kidney epithelial) cells transfected with overexpression vectors (APOE2, APOE3, and APOE4). IHC images show APOE4 detection using Anti-Apolipoprotein E4 antibody ab279714 at a concentration of 1/1000 or secondary only antibody control. Positive staining in brown; nuclear hematoxylin counterstain in blue.

APOE4 expression in Alzheimer's disease and normal brain

APOE4 increases amyloid beta (Aβ) plaque formation, reduces Aβ clearance through the blood-brain barrier (BBB), and reduces Aβ phagocytosis by glia. It also increases reactive gliosis and neuroinflammation, which can lead to a disrupted BBB.

We have shown representative images of varied APOE4 expression in the Aβ plaques and neurovascular compartments of the analyzed tissues.

Donor	Diagnosis	APOE4 expression		
		Aβ plaques	**Vasculature**	**Neuron**
#1	Alzheimer's	+	+	-
#2	Alzheimer's	+	+	+
#3	Alzheimer's	+	-	-
#4	Alzheimer's	-	-	-
#5	Alzheimer's	+	+	-
#6	Alzheimer's	+	-	+
#7	Alzheimer's	+	+	+
#8	Alzheimer's	-	-	-
#9	Alzheimer's	+	+	+
#10	Alzheimer's	-	+	-
#11	Alzheimer's	-	-	-
#12	Thalamus	-	-	-
#13	Normal Cortex	+	+	+
#14	Normal Cortex	+	+	+
#15	Normal Hippocampus	-	-	-
#16	Normal Hippocampus	+	+	+

Table 5. Summary of APOE4 expression in the Alzheimer's disease and normal brain. The IHC images corresponding to orange donor numbers are shown in Figures 2-6 (BOND™ RX) and Figures 7-11 (DISCOVERY ULTRA). Expression is shown as either positive (+), or negative (-).

APOE4 expression in Alzheimer's disease (BOND™ RX)

Below are representative images of an individual case of Alzheimer's disease showing APOE4 expression.
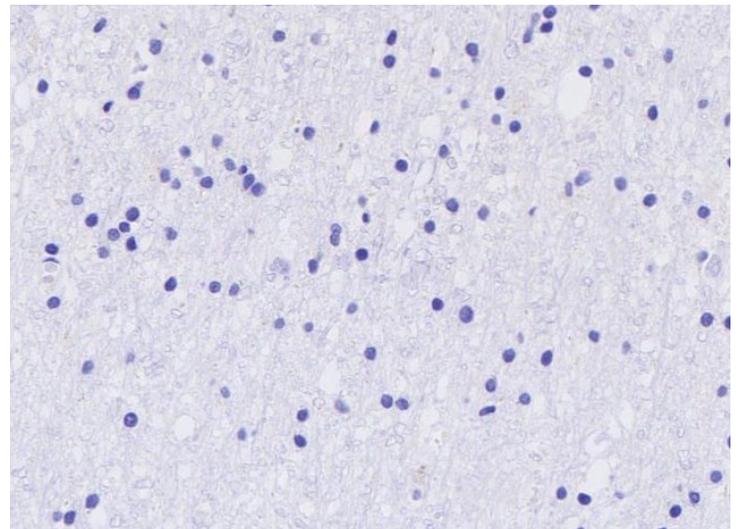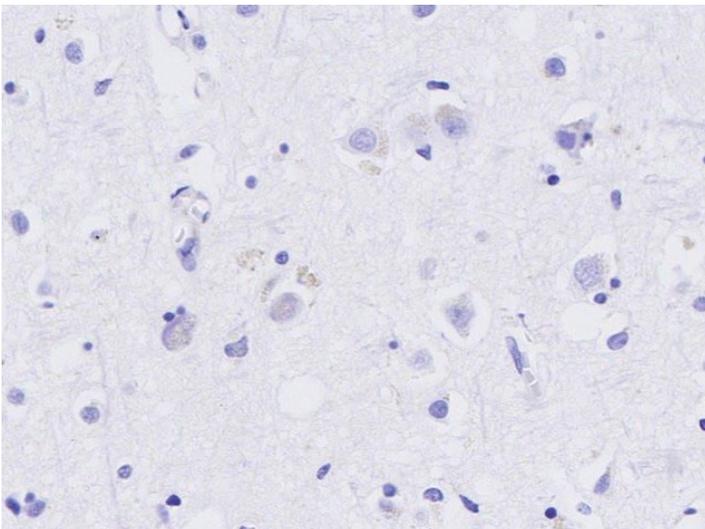
APOE4 expression in donor #1 (a)
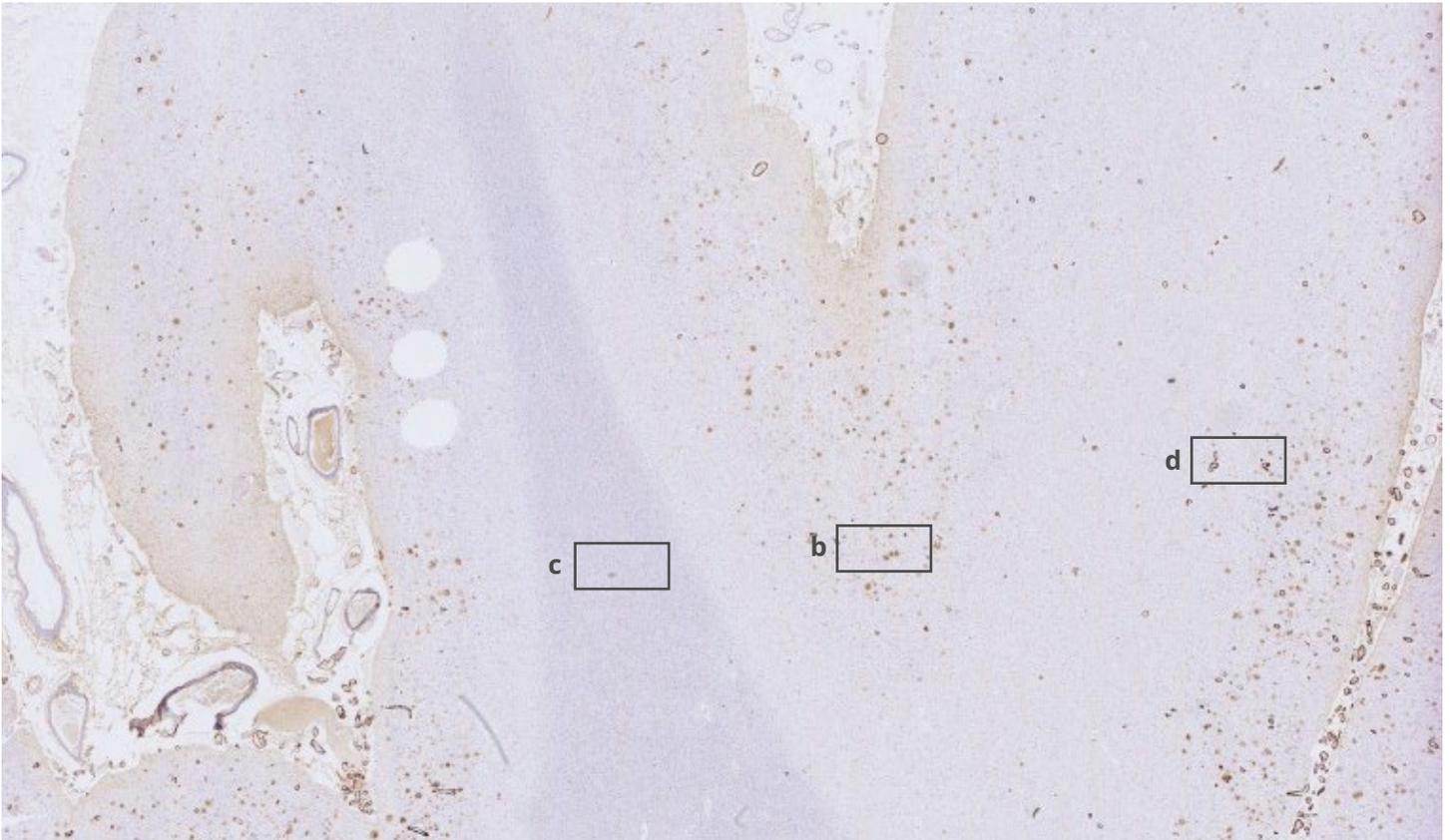
Aβ plaques in grey matter (b)   White matter (c)
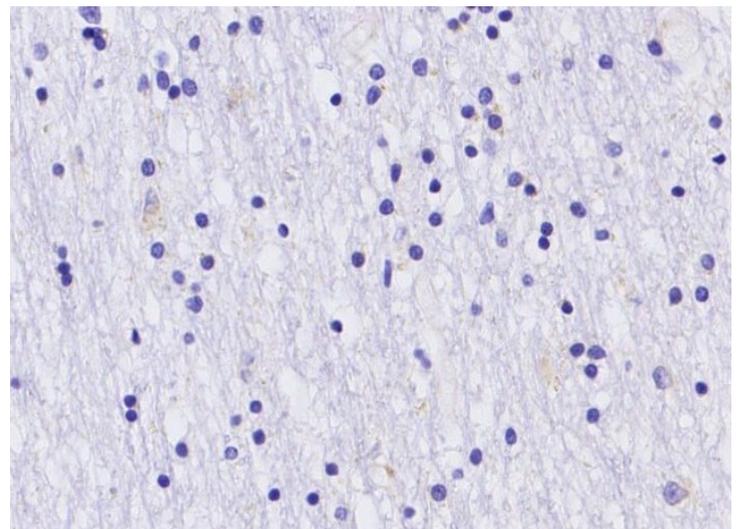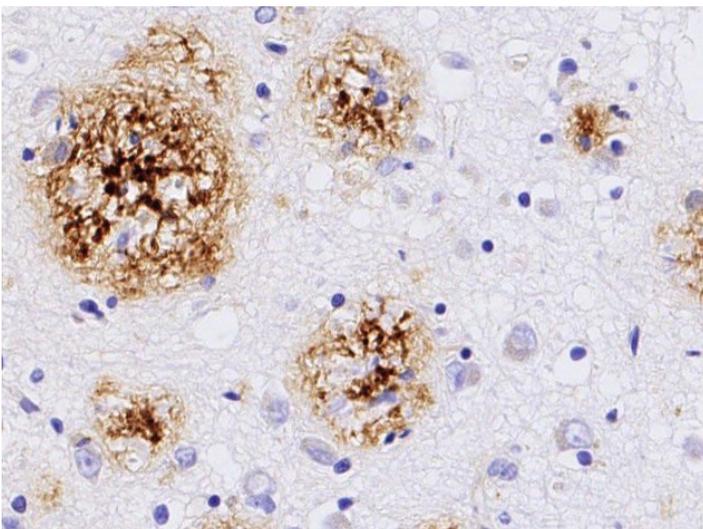
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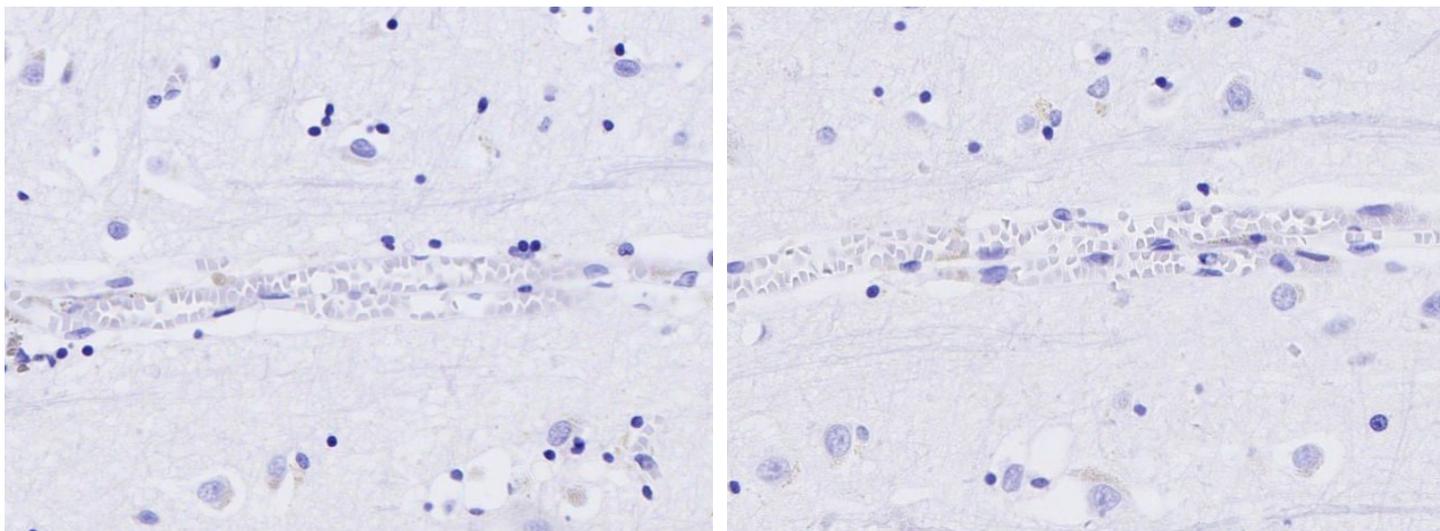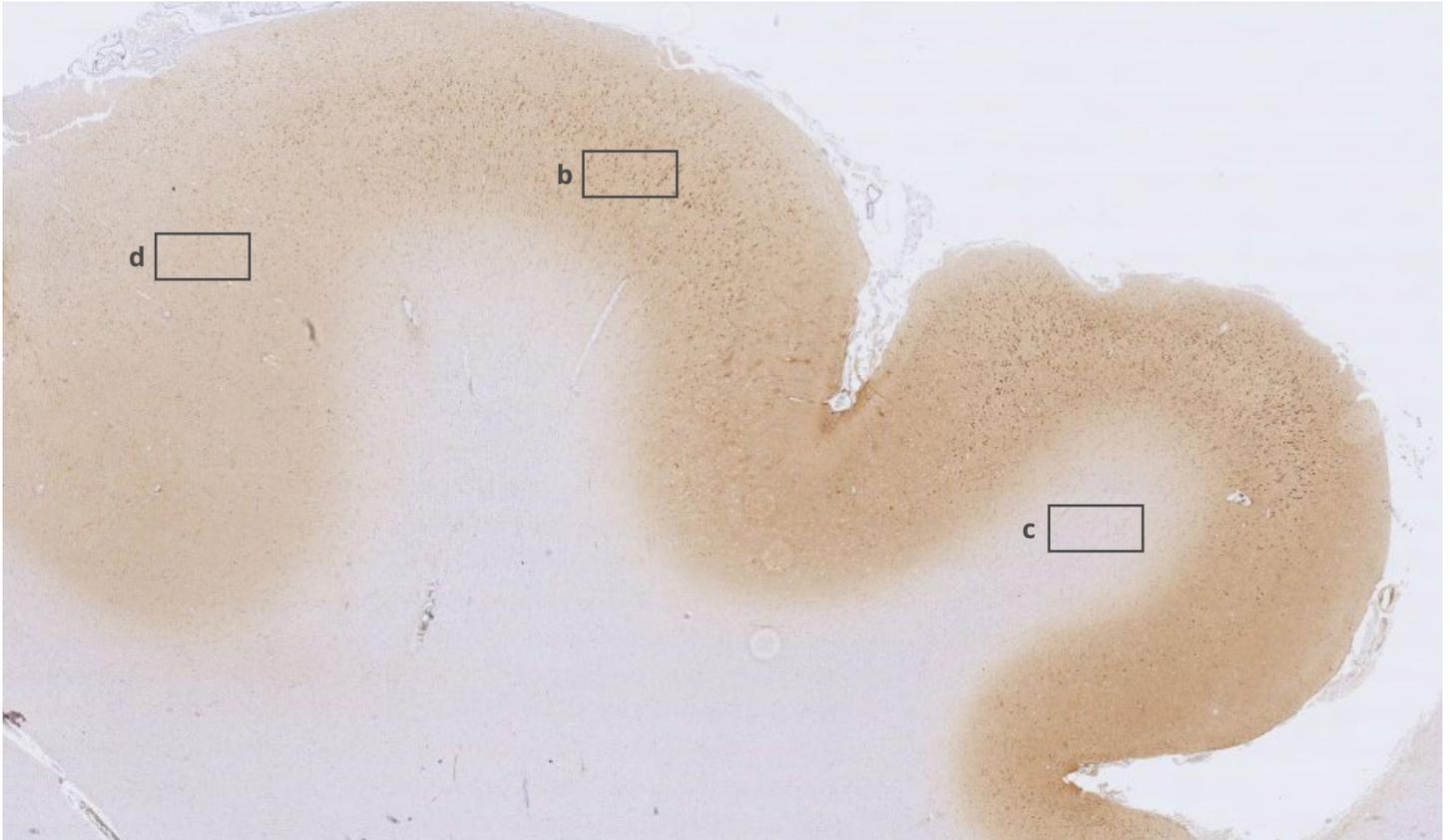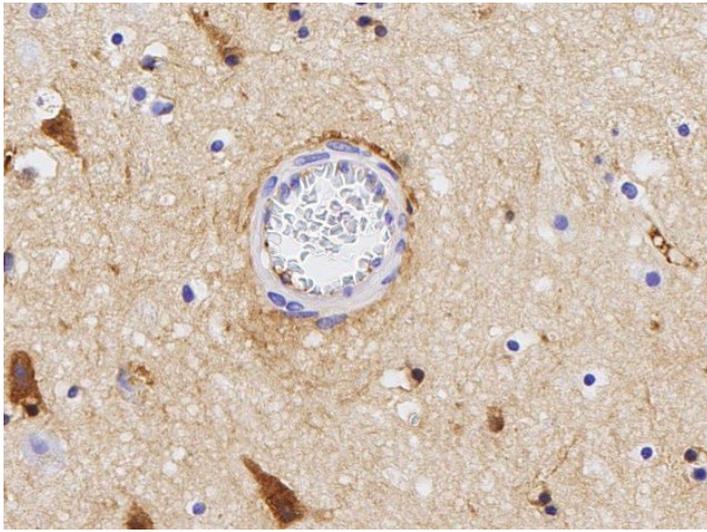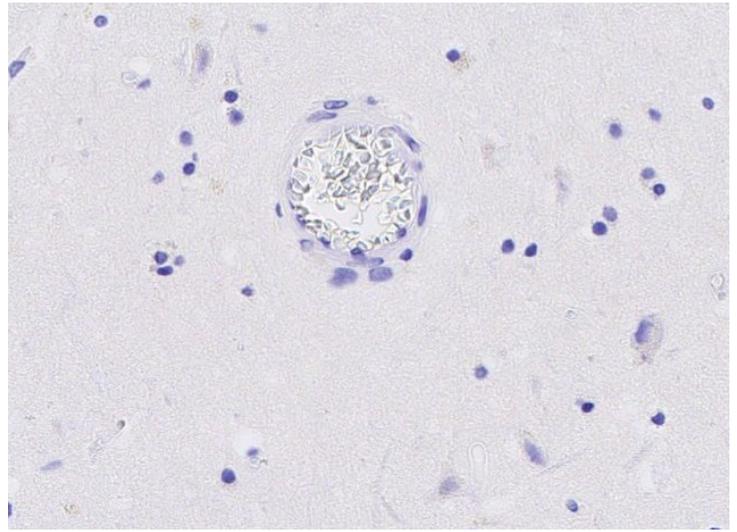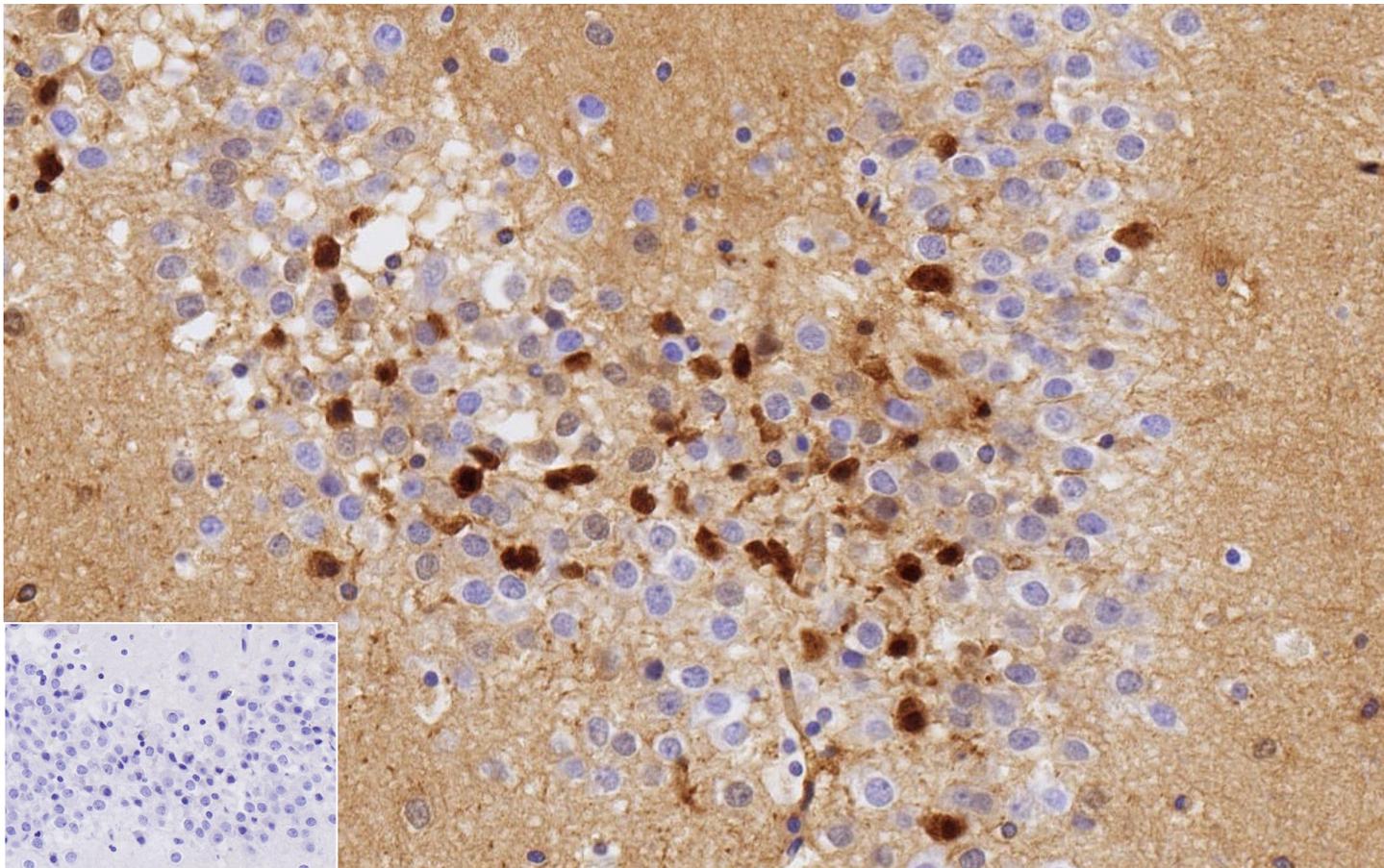
Blood vessel (d) | Isotype control (e)
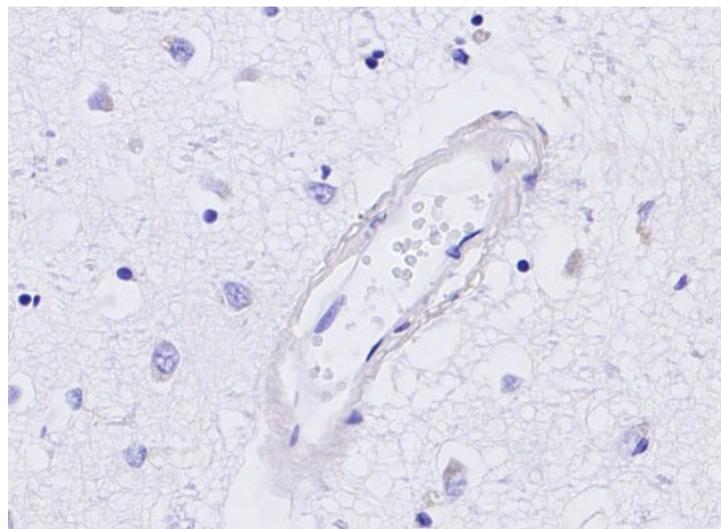
Figure 2. APOE4 expression in Alzheimer's disease. IHC staining of Alzheimer's brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 μg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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APOE4 expression in donor #2 (a)

Aβ plaques in grey matter (b)   White matter (c)
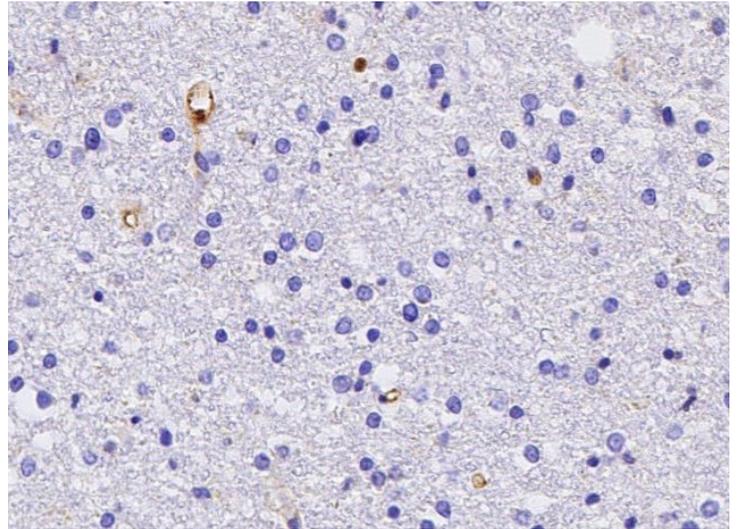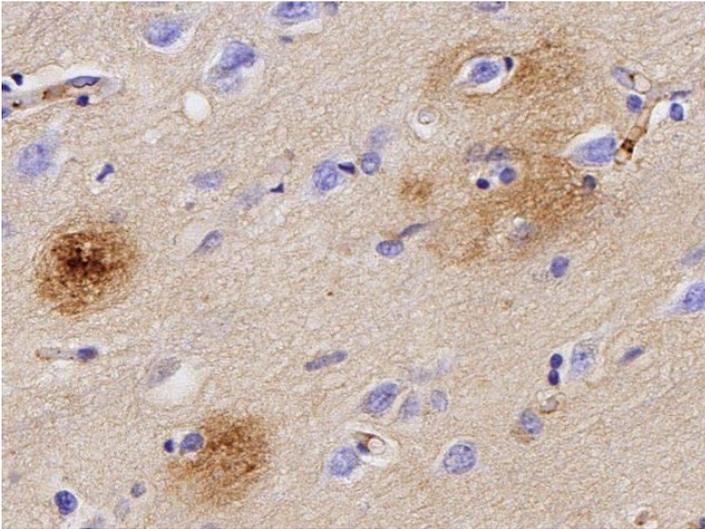
Enhanced validation data

Blood vessel (d)   Isotype control (e)
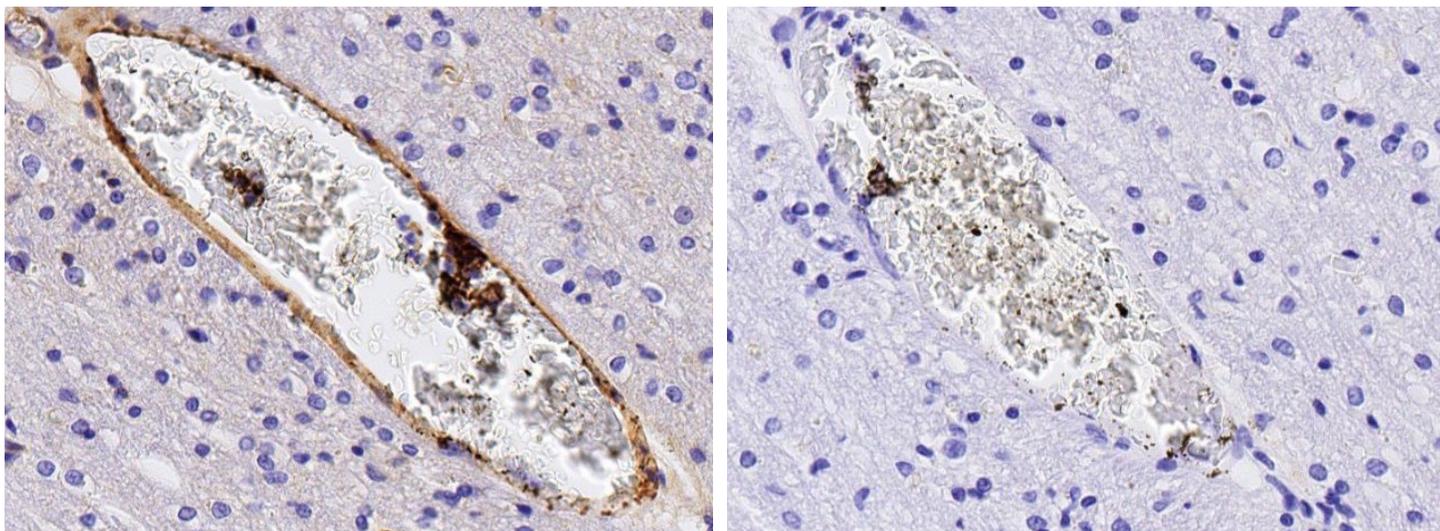
Figure 3. APOE4 expression in Alzheimer's disease. IHC staining of Alzheimer's brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on the NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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Enhanced validation data

APOE4 expression in donor #8 (a)
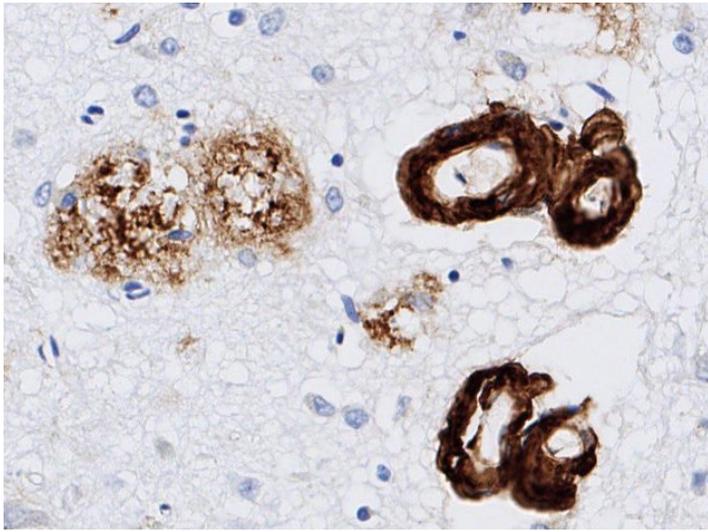

Grey matter (b)

White matter (c)

Enhanced validation data

Blood vessel (d)   Isotype control (e)
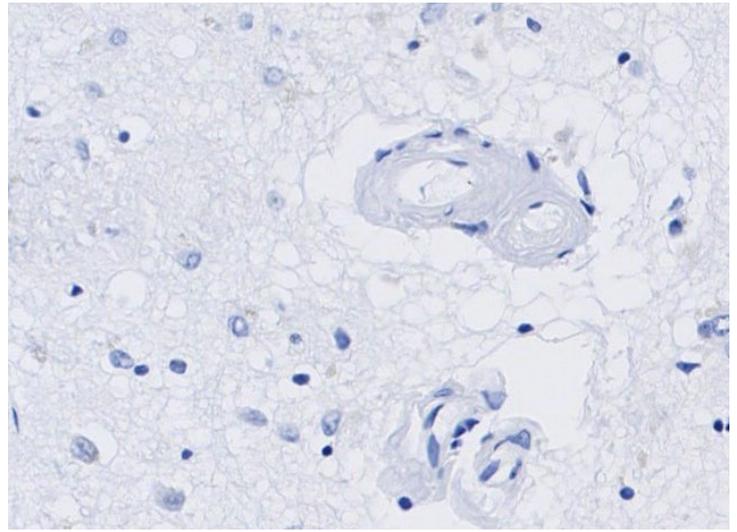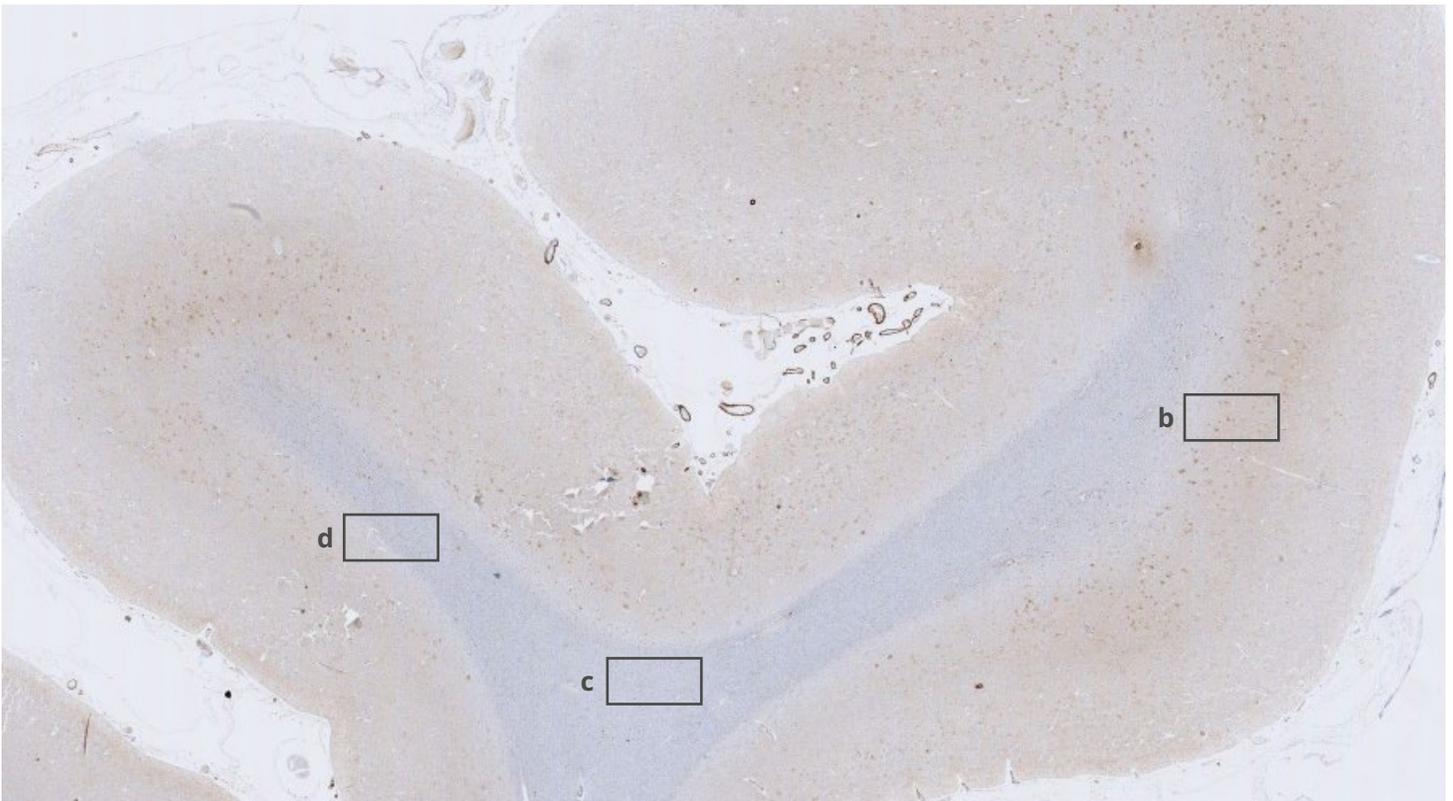

Figure 4. APOE4 expression in Alzheimer's disease. IHC staining of Alzheimer's brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on the NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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APOE4 expression in normal brain (BOND™ RX)

Below are representative images of an individual donor of normal brain showing APOE4 expression in the cortex.

APOE4 expression in donor #13 (a)

Grey matter (b)

White matter (c)

AB0440_v2.0_100325
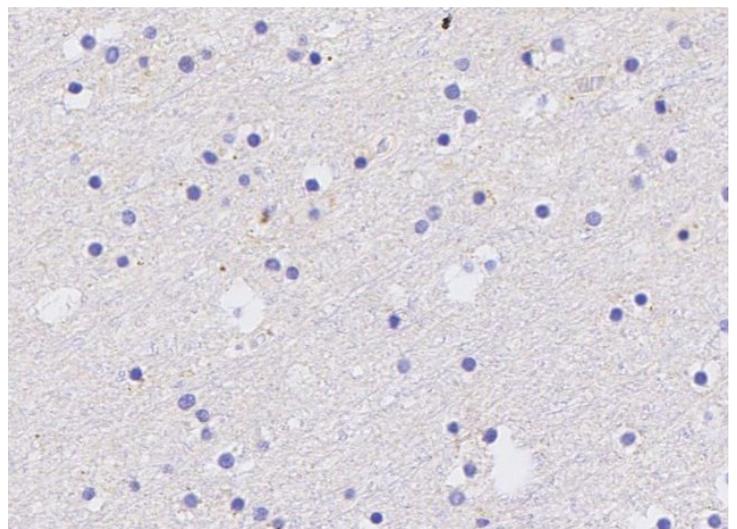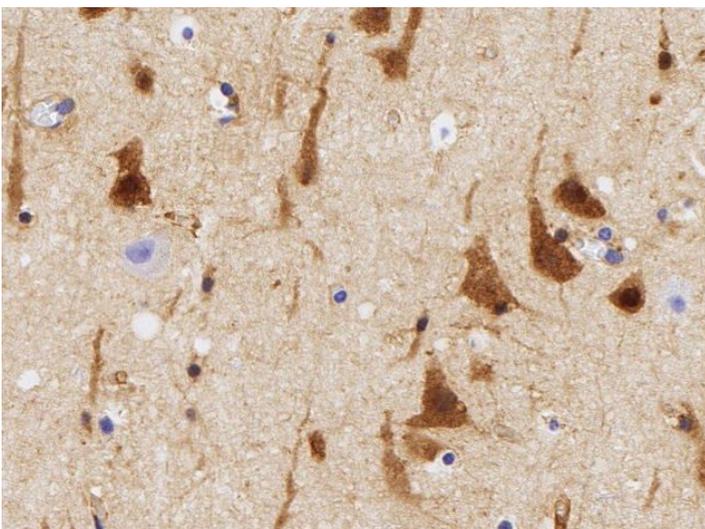
Enhanced validation data

Blood vessel (d)   Isotype control (e)

Figure 5. APOE4 expression in normal brain. IHC staining of normal brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 μg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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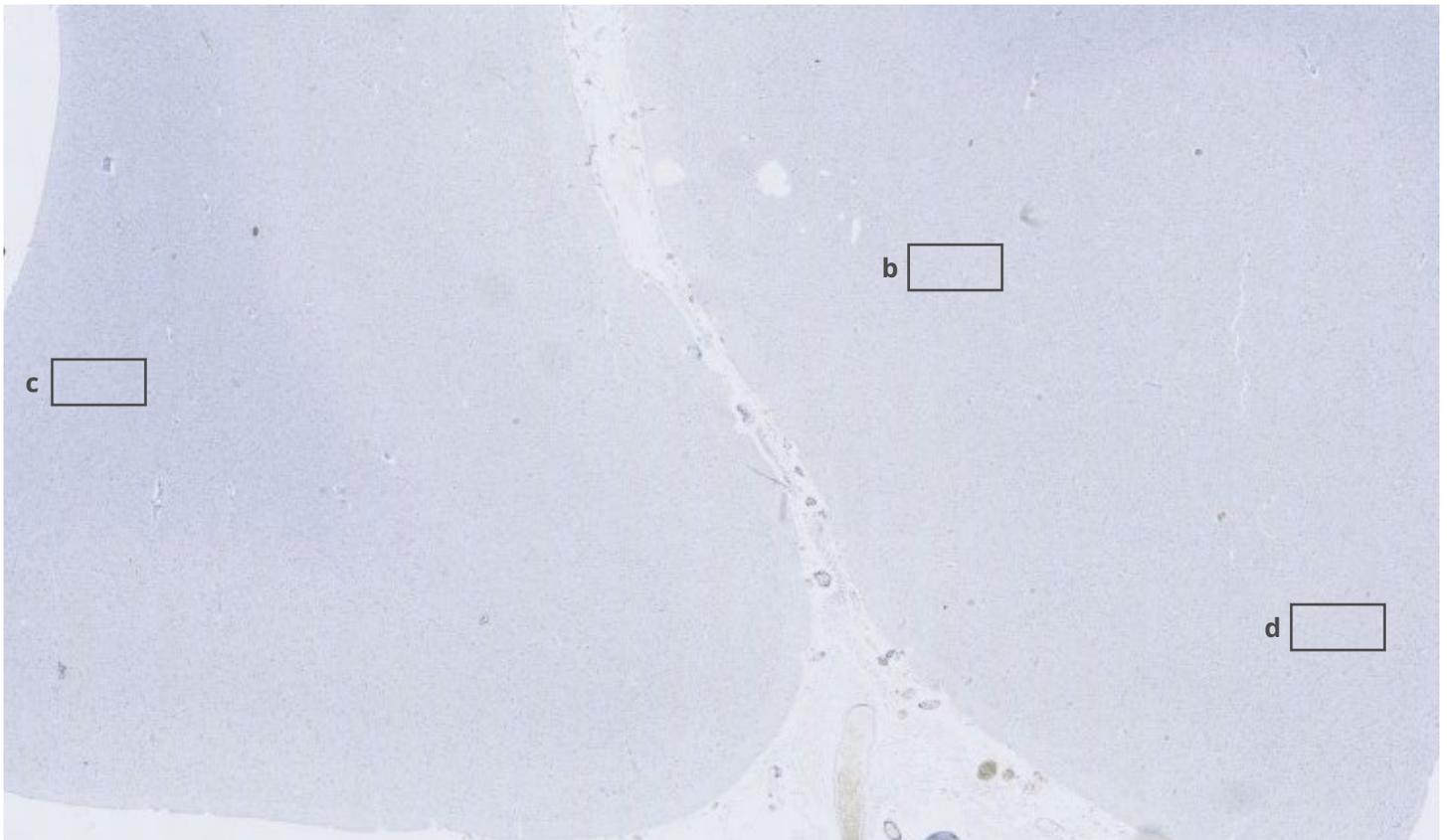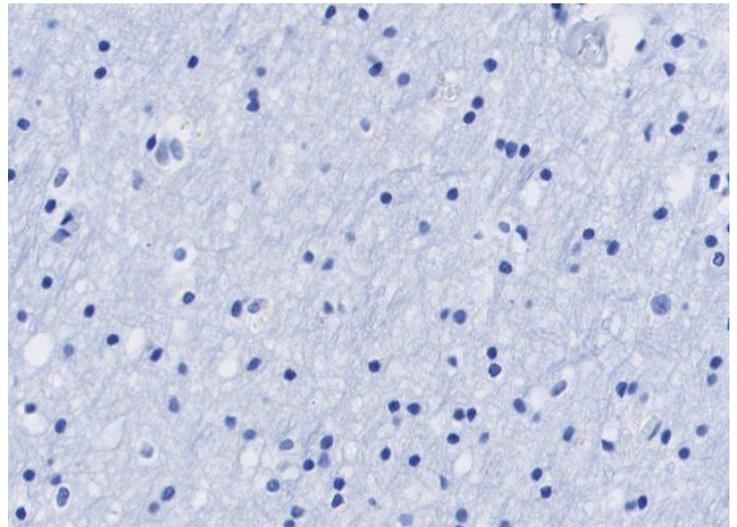
Enhanced validation data

Below are representative images of an individual donor of normal brain showing APOE4 expression in the hippocampus.

APOE4 expression in donor #15 (Normal brain-Hippocampus)

Enhanced validation data

APOE4 expression in donor #16 (Normal brain-Hippocampus)
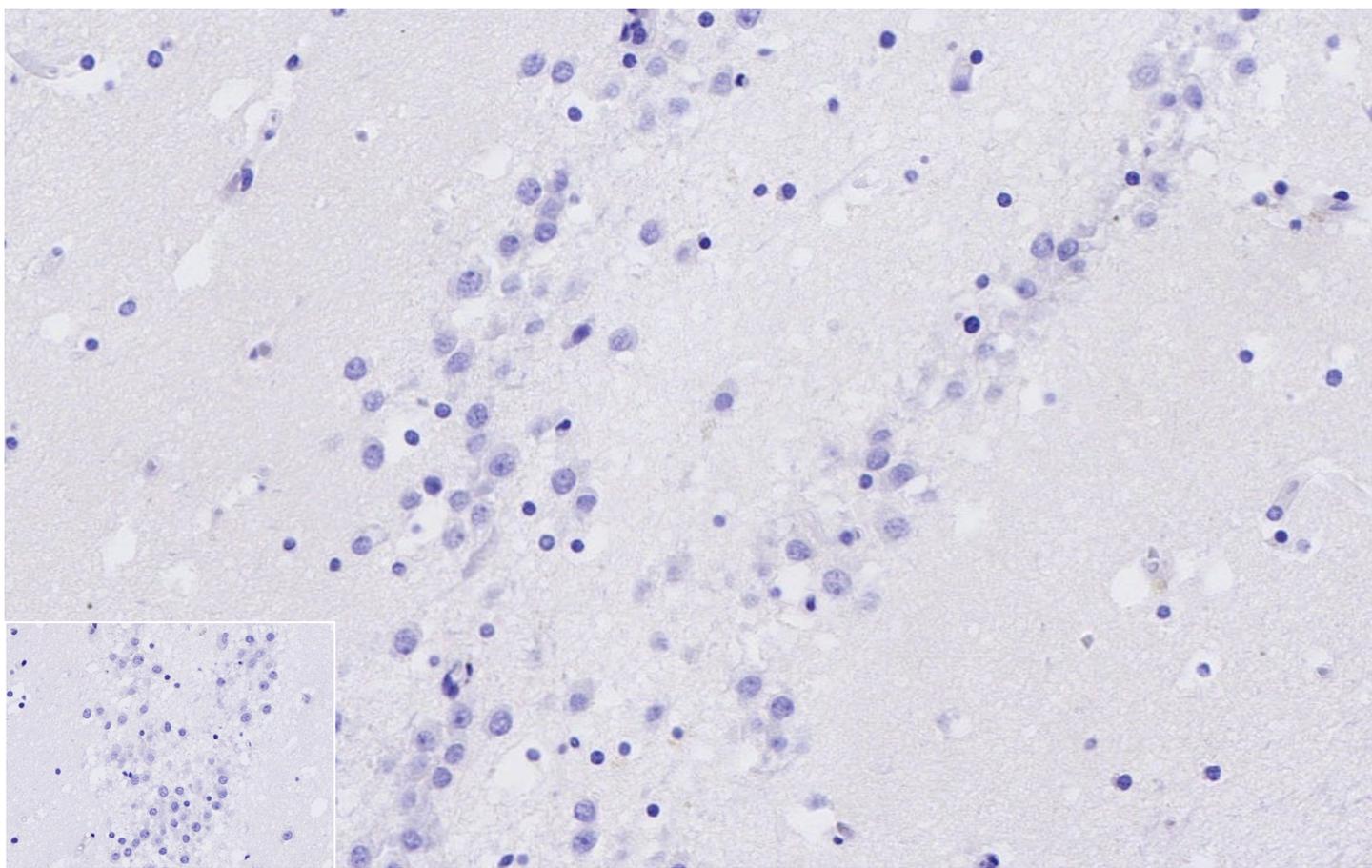
Figure 6. APOE4 expression in normal brain. IHC staining of normal brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

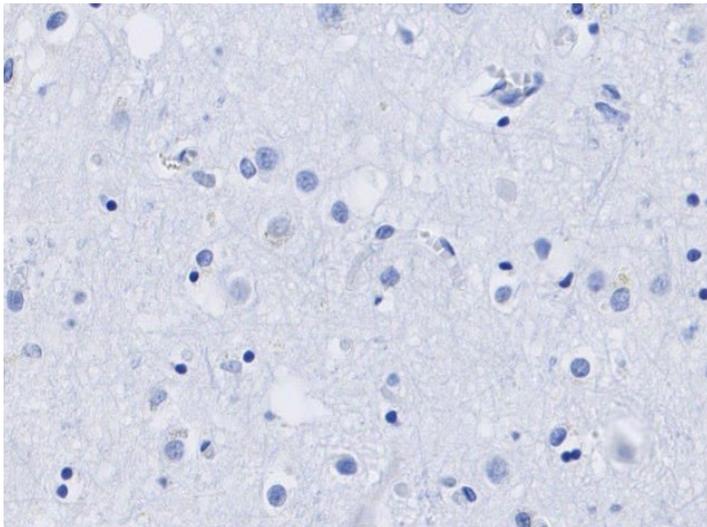NanoZoomer® is a registered trademark of Hamamatsu Photonics K.K.

APOE4 expression in Alzheimer's disease (DISCOVERY ULTRA)

Below are representative images of an individual case of Alzheimer's disease showing APOE4 expression.

APOE4 expression in donor #1 (a)
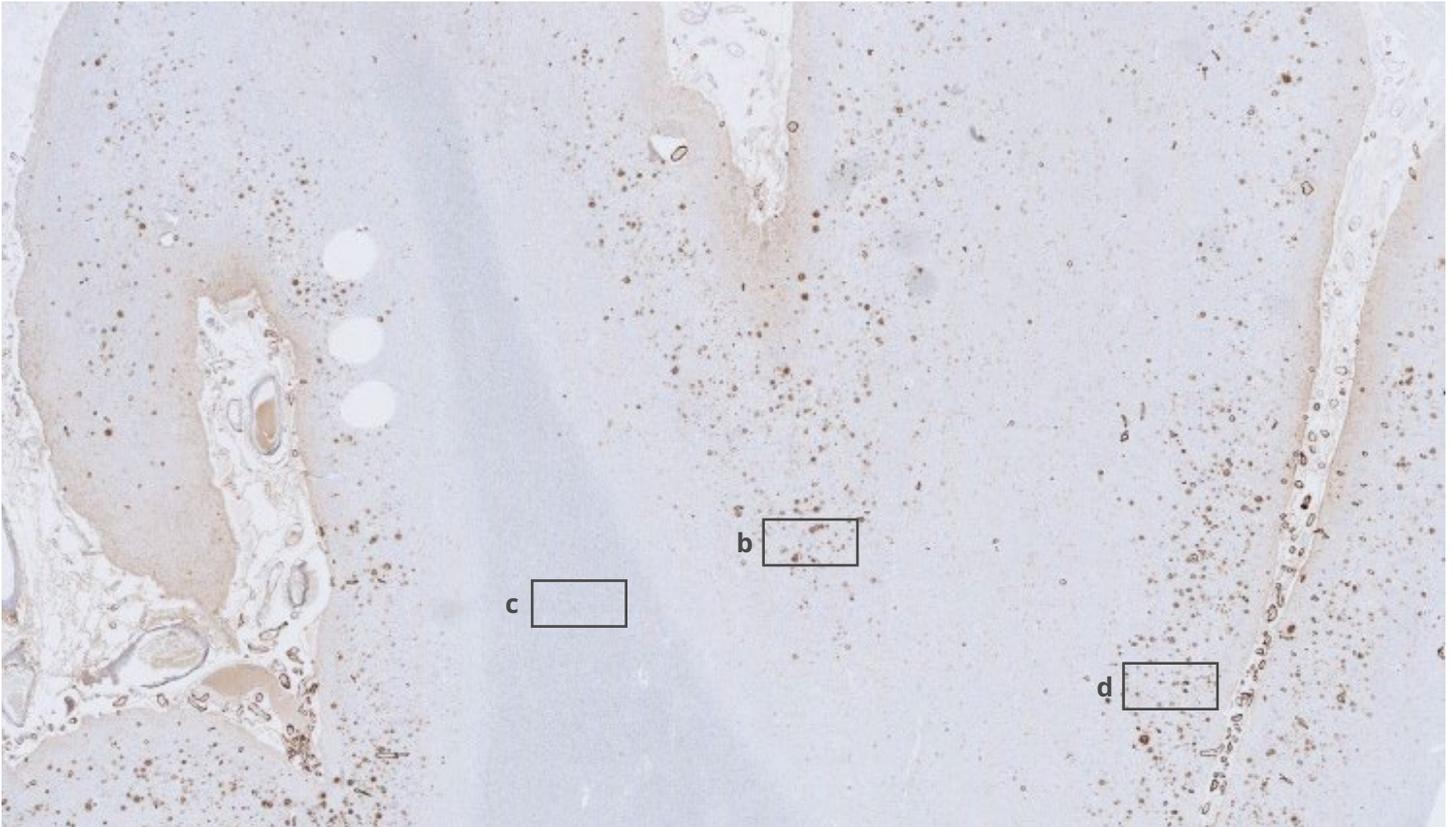
Aβ plaques in grey matter (b)

White matter (c)
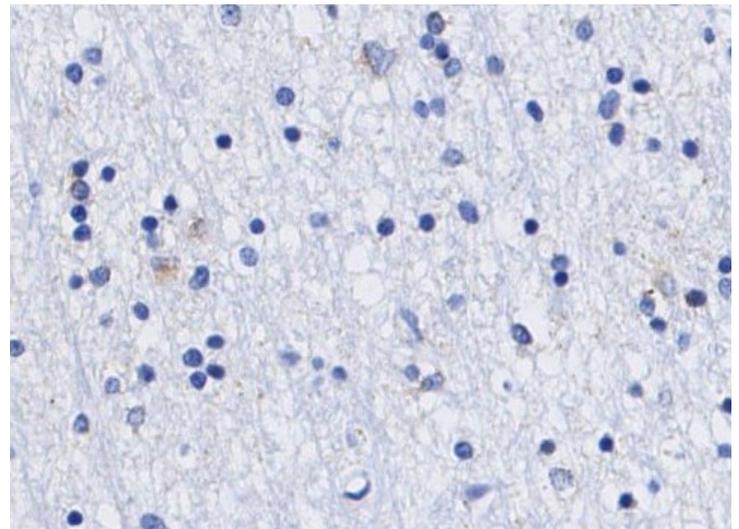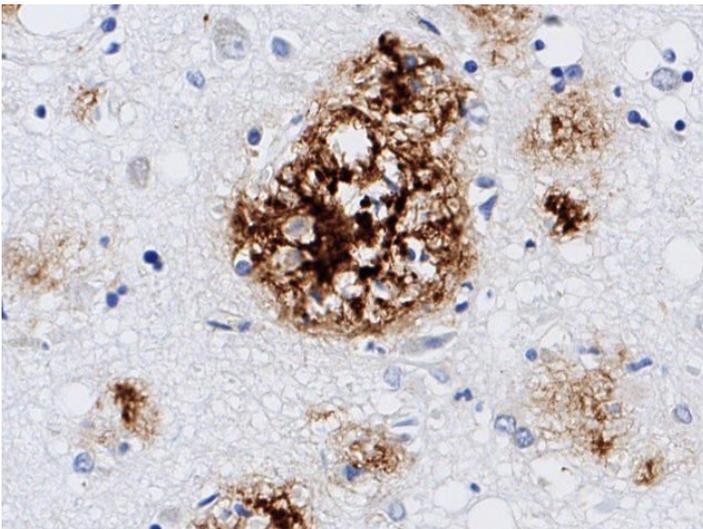
Enhanced validation data

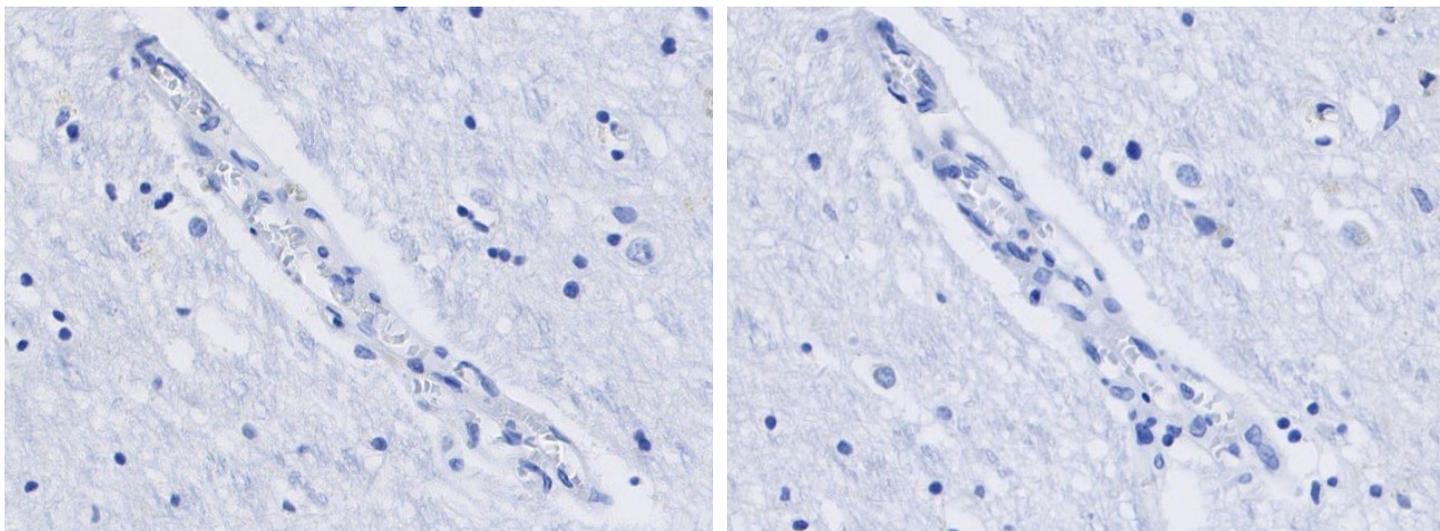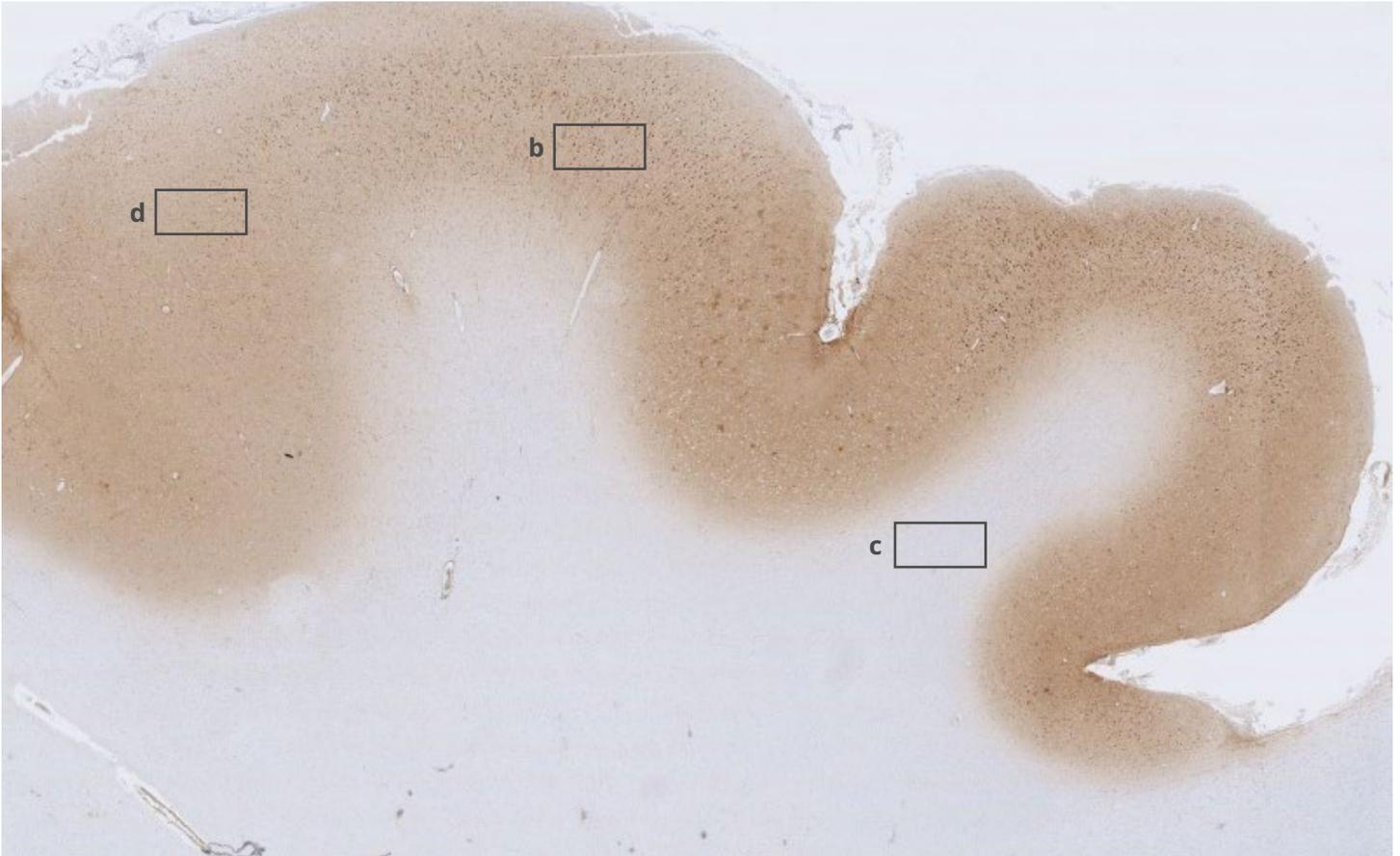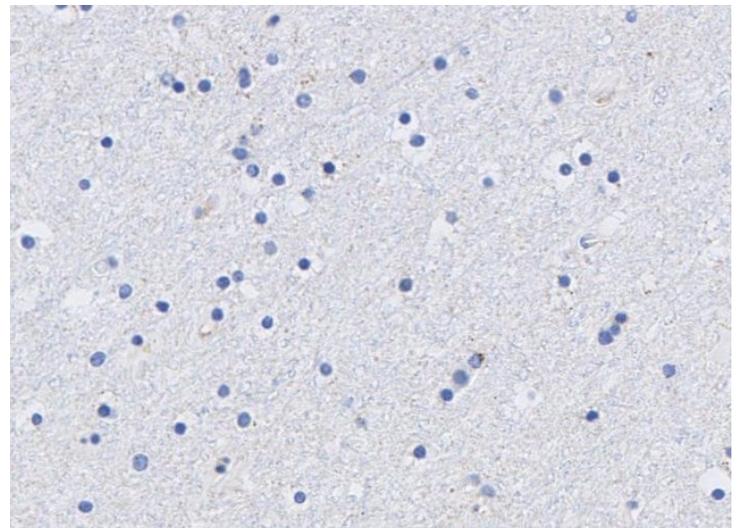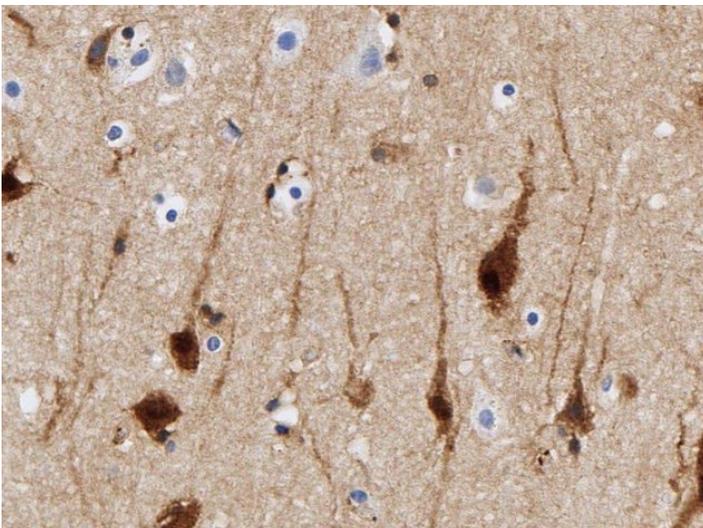Blood vessel (d)   Isotype control (e)

Figure 7. APOE4 expression in Alzheimer's disease. IHC staining of Alzheimer's brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 μg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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Enhanced validation data

APOE4 expression in donor #2 (a)


Aβ plaques in grey matter (b)   White matter (c)
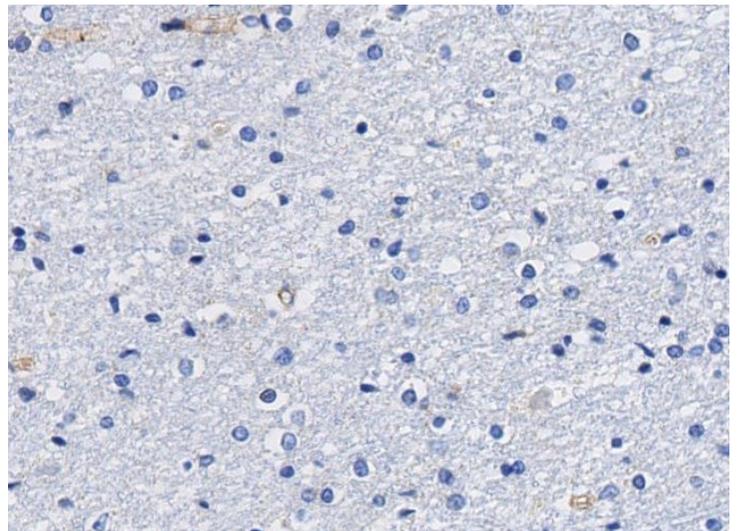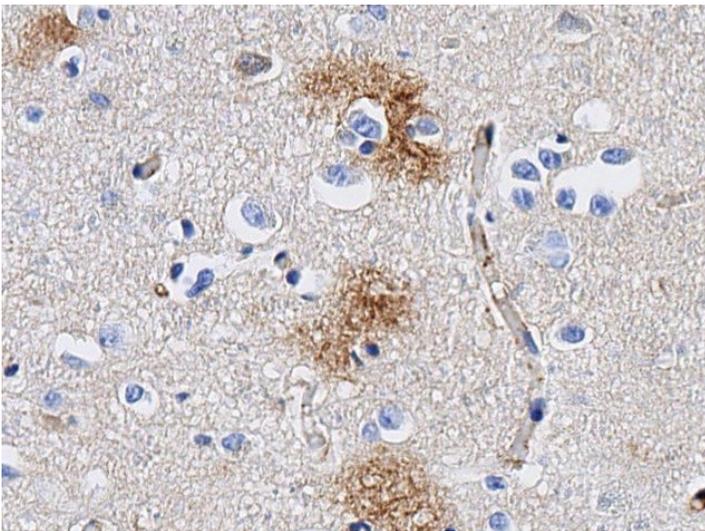
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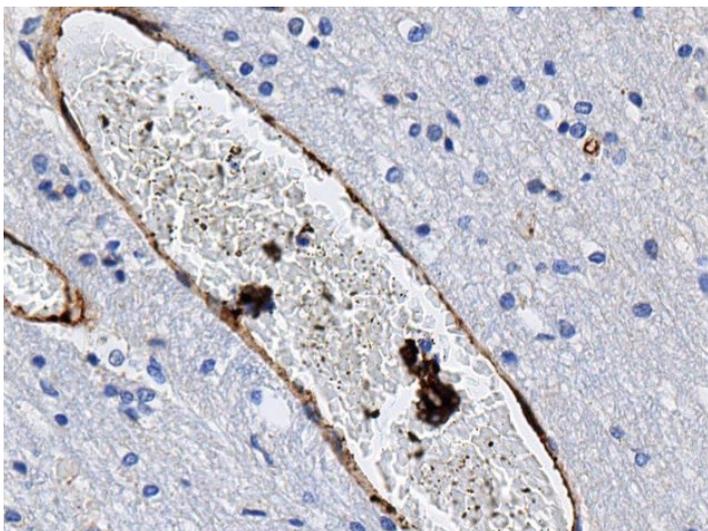
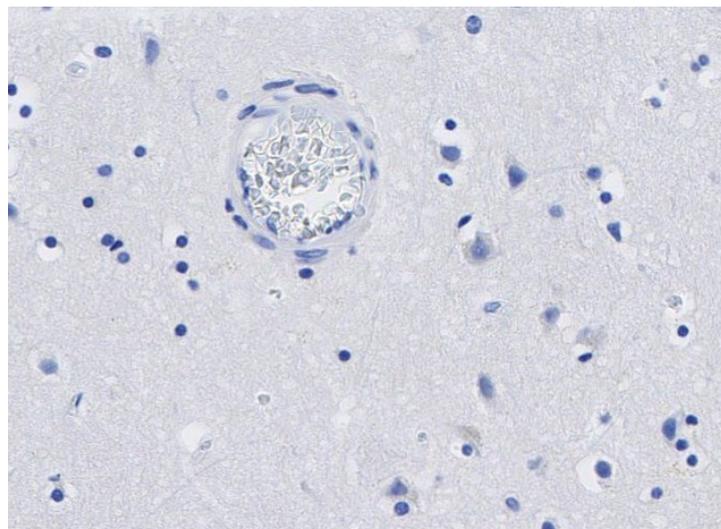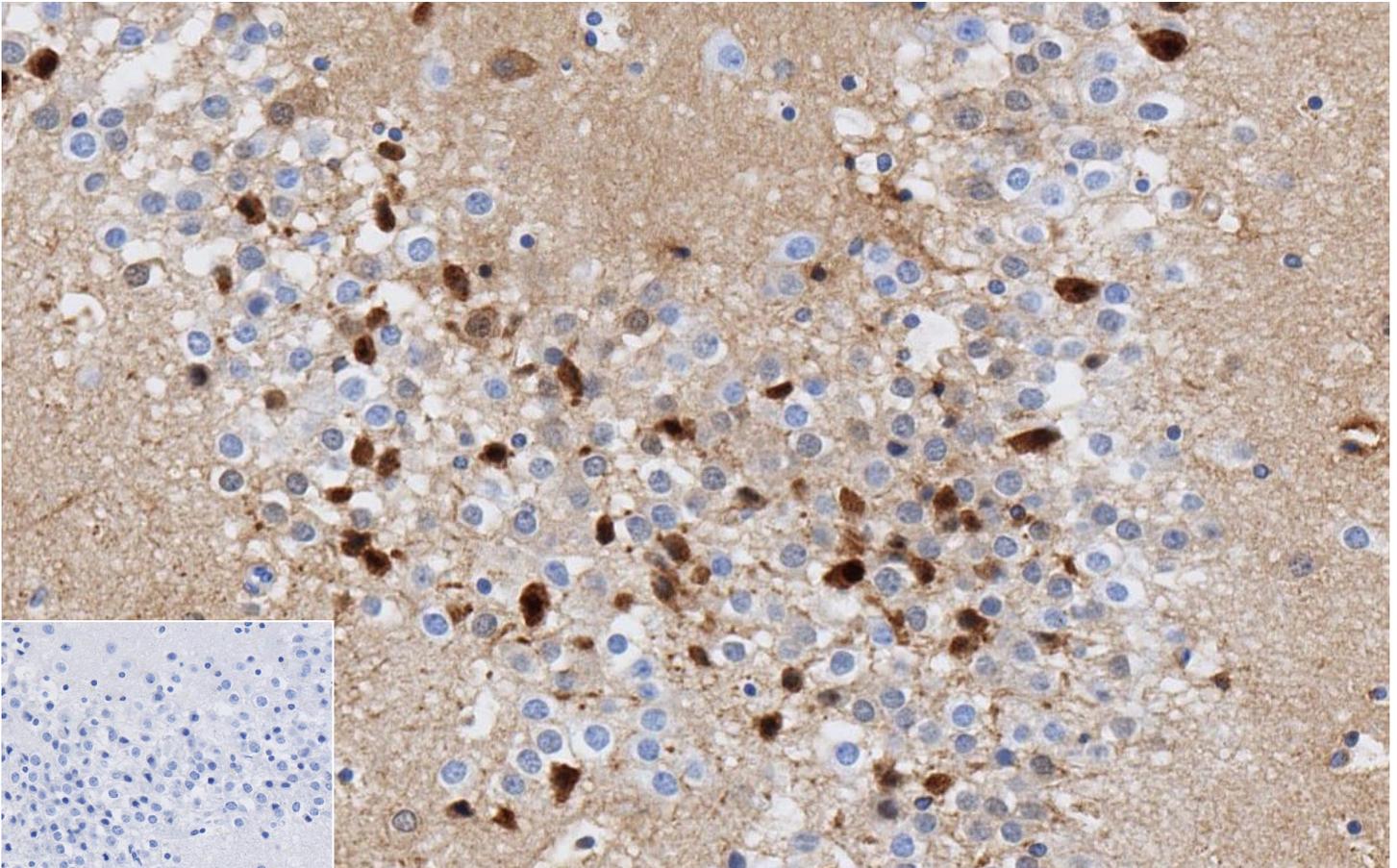Blood vessel (d)   Isotype control (e)
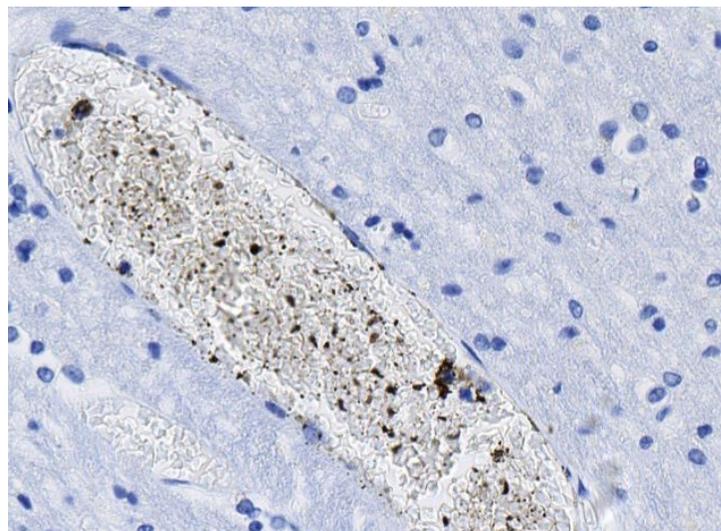
Figure 8. APOE4 expression in Alzheimer's disease. IHC staining of Alzheimer's brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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Enhanced validation data

APOE4 expression in donor #8 (a)

Grey matter (b)   White matter (c)

Enhanced validation data

Blood vessel (d)   Isotype control (e)

Figure 9. APOE4 expression in Alzheimer's disease. IHC staining of Alzheimer's brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.
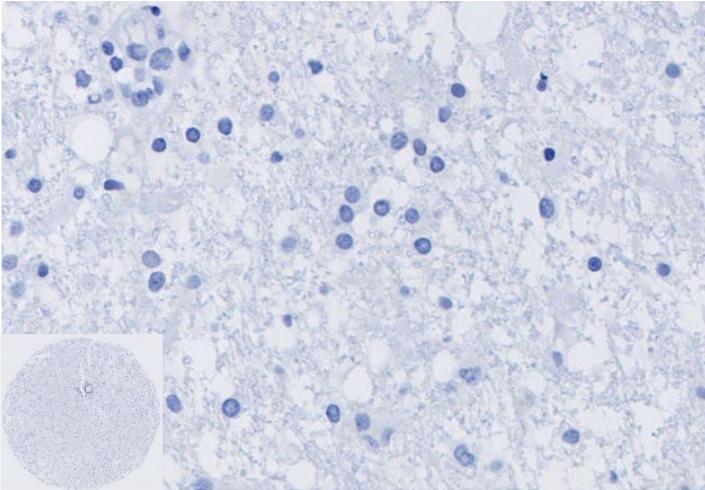
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# APOE4 expression in normal brain (DISCOVERY ULTRA)

Below are representative images of an individual donor of normal brain showing APOE4 expression.

APOE4 expression in donor #13 (a)

Grey matter (b)

White matter (c)

Enhanced validation data
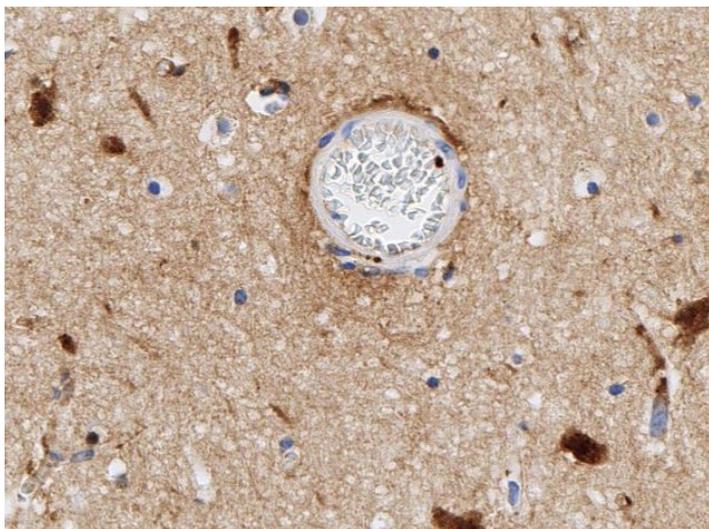
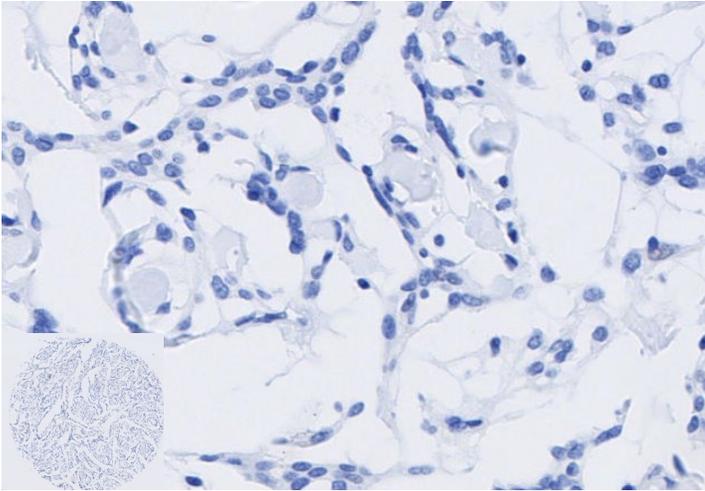Blood vessel (d)   Isotype control (e)

Figure 10. APOE4 expression in normal brain. IHC staining of normal brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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Below are representative images of an individual donor of normal brain showing APOE4 expression.

APOE4 expression in donor #15 (Normal brain-Hippocampus)

Enhanced validation data

APOE4 expression in donor #16 (Normal brain-Hippocampus)

Figure 11. APOE4 expression in normal brain. IHC staining of normal brain tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and and imaged at 0.4 x (a) and 20X (b-d) on Aperio® ImageScope.

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APOE4 expression in glioma TMA (DISCOVERY ULTRA)

Below are the representative images of human glioma TMA consisting of various grades of gliomas.

APOE4

| Pilocytic astrocytoma (Grade I)	Diffuse astrocytoma (Grade II)
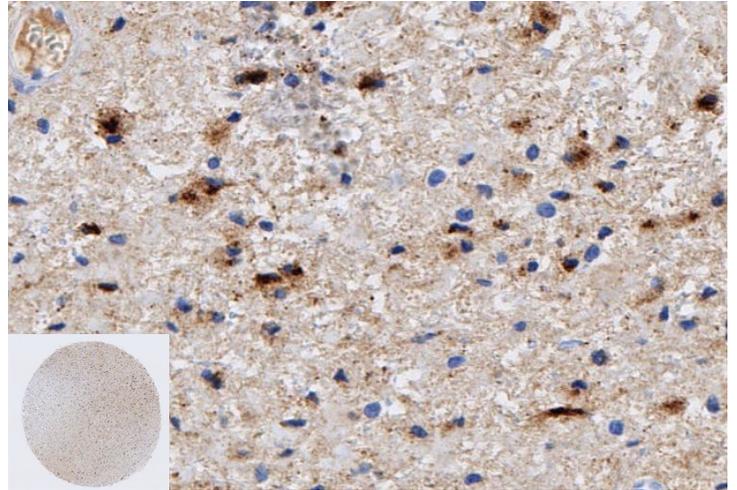
Anaplastic astrocytoma (Grade III)	Anaplastic astrocytoma (Grade III~IV)

Enhanced validation data
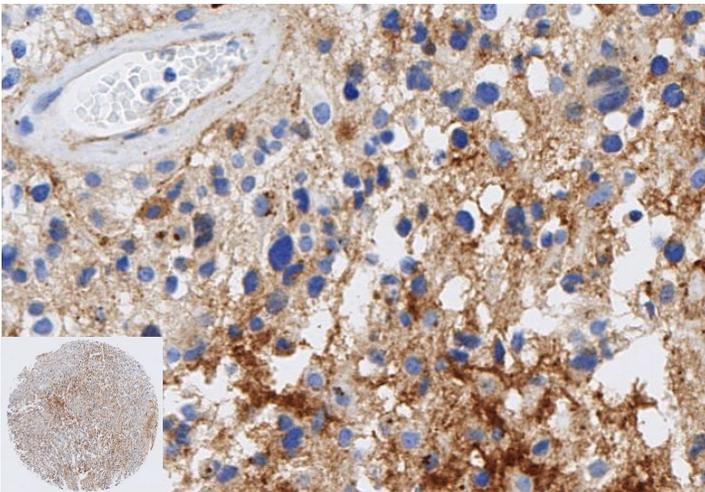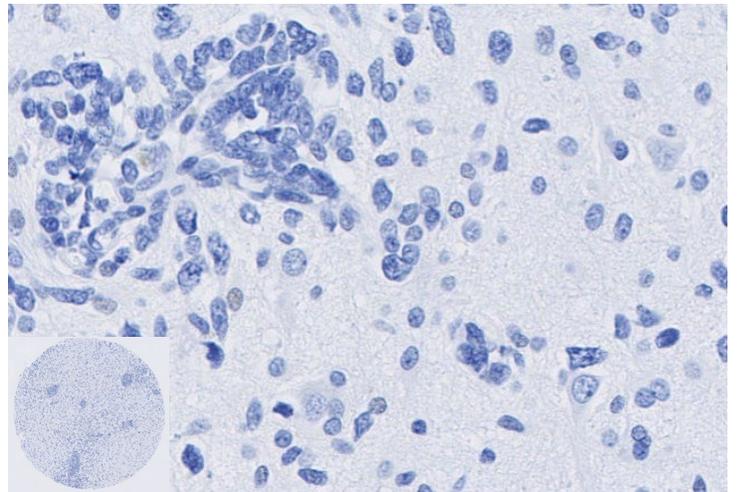
APOE4

Glioblastoma	Ependymoma
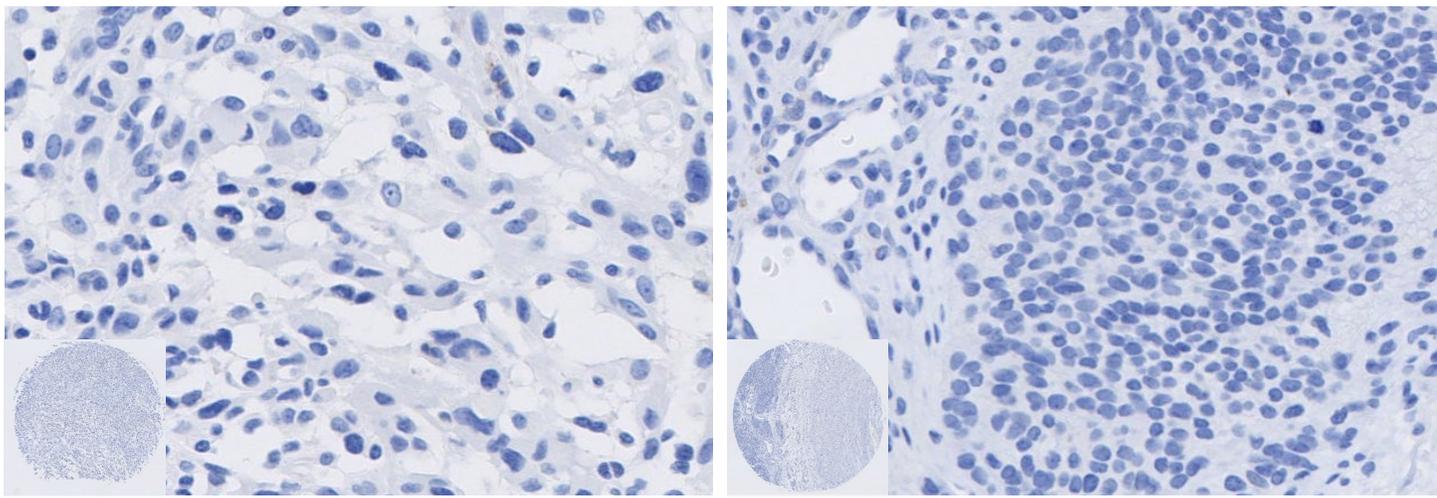
Figure 12. APOE4 expression in glioma TMA. IHC staining of human glioma TMA using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 20X (whole core insets at 5x) inset on Aperio® ImageScope.

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APOE4 expression in nervous system tumor TMA (DISCOVERY ULTRA)

Below are the representative images of the human nervous system TMA, consisting of various nervous system tumors.

APOE4

Fibroblastic meningioma

Atypical meningioma
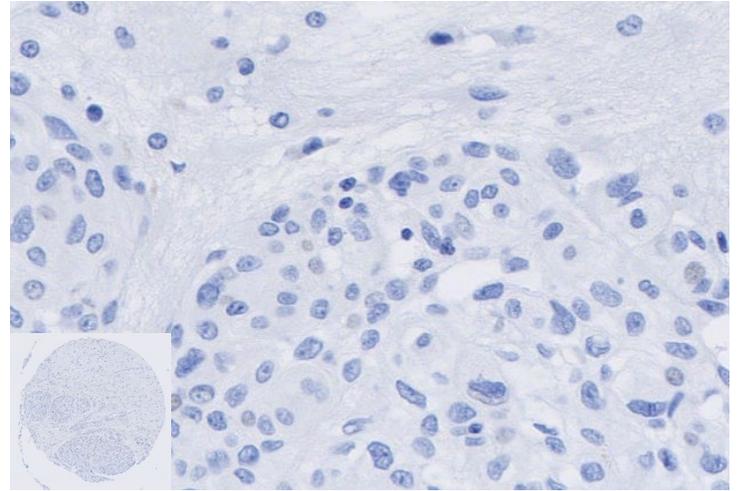
Oligodendroglioma

Schwannoma
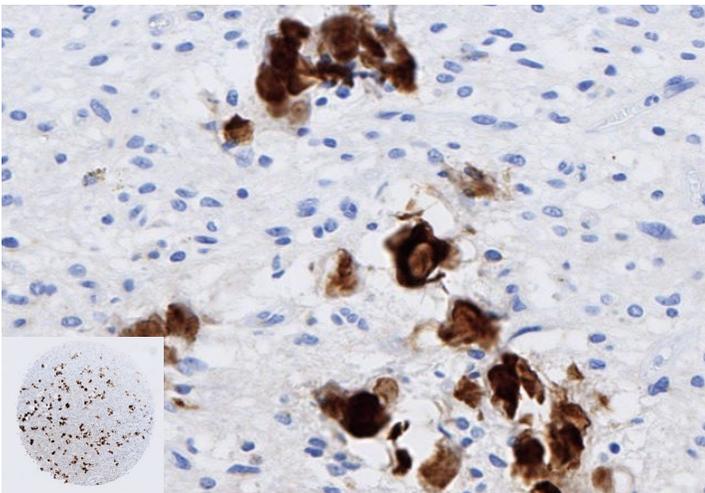
Enhanced validation data
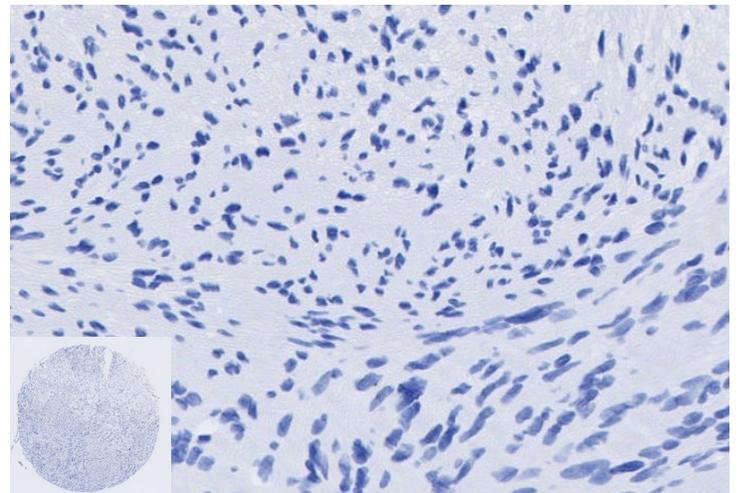
APOE4

| Neuroblastoma | Hemangioblastoma |
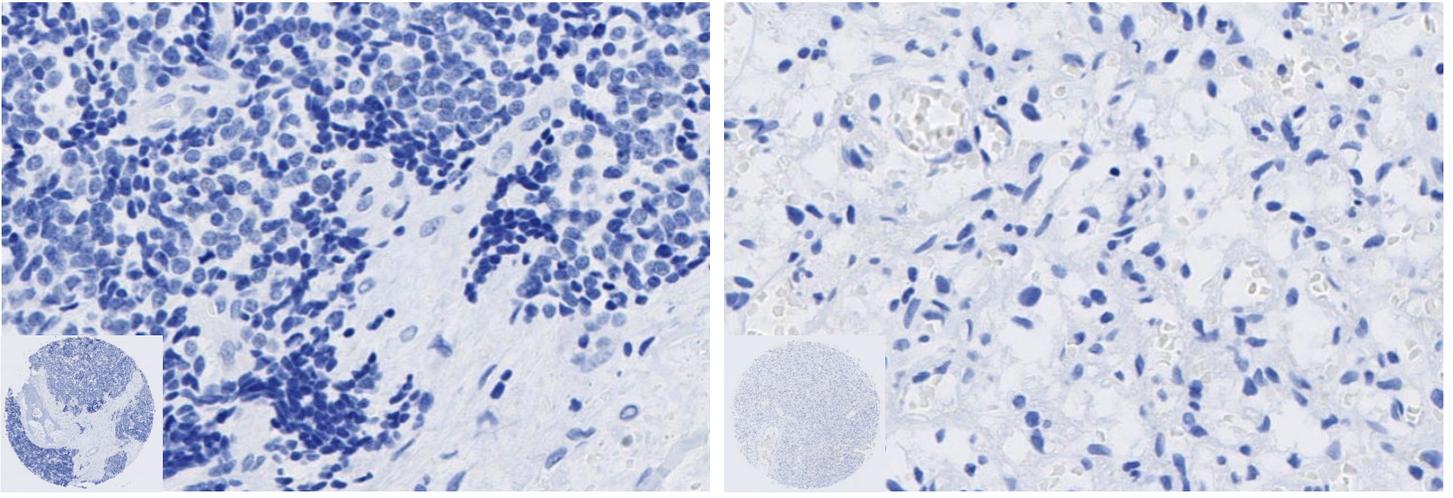
Figure 13. APOE4 expression in nervous system TMA. IHC staining of human glioma TMA using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 μg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 20X (whole core insets at 5x) on Aperio® ImageScope.

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Appendix

Enhanced validation data

APOE4 expression in multi-normal TMA (BOND™ RX)

Below are the representative images of selected tissues from multi-normal TMA. APOE4 expression was detected in the skin and kidney. Expression was absent from the placenta, spleen, pancreas, prostate, heart, liver, brain and kidney.

APOE4

Placenta

Skin

Spleen

Pancreas

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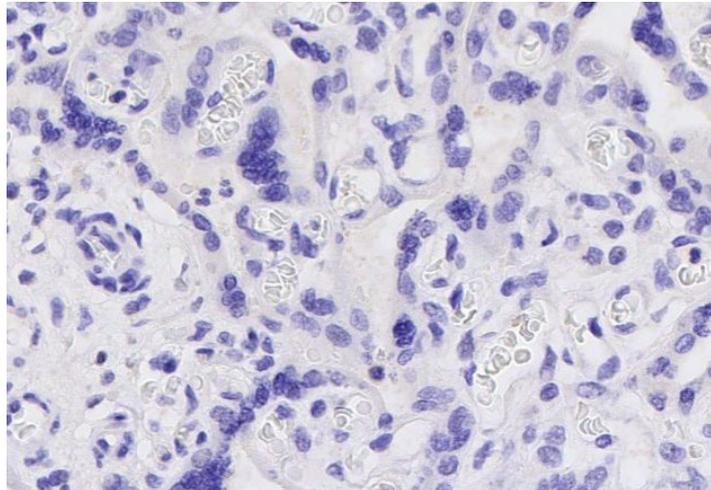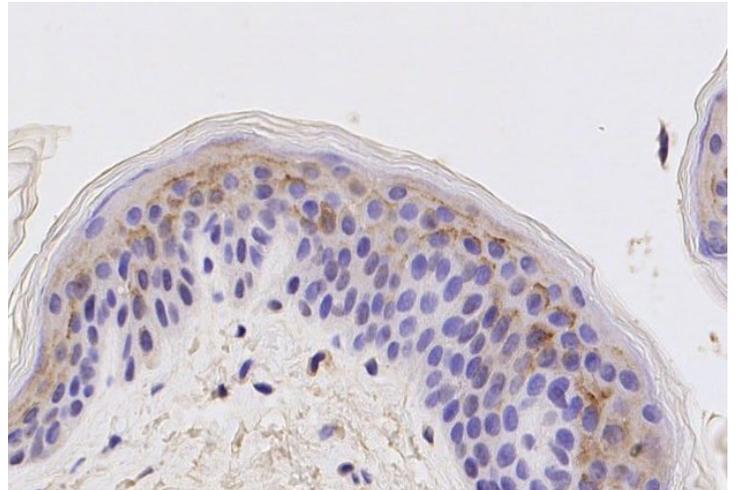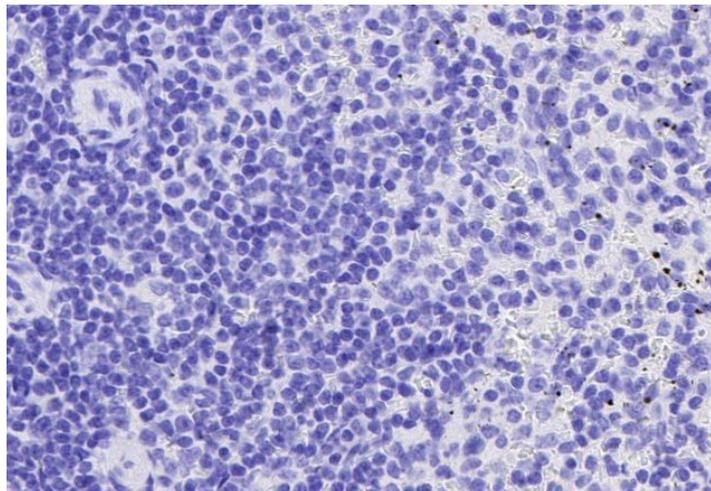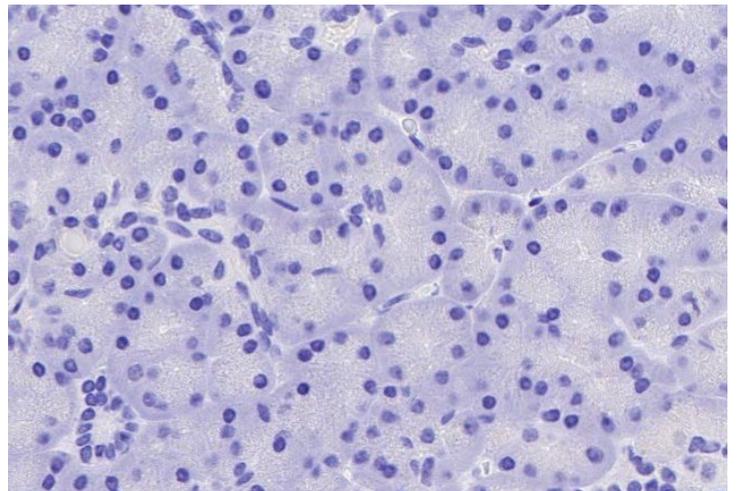
Enhanced validation data

APOE4

Prostate
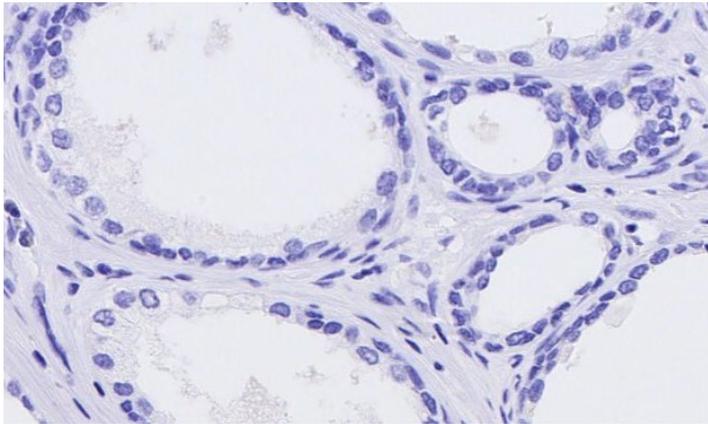
Heart
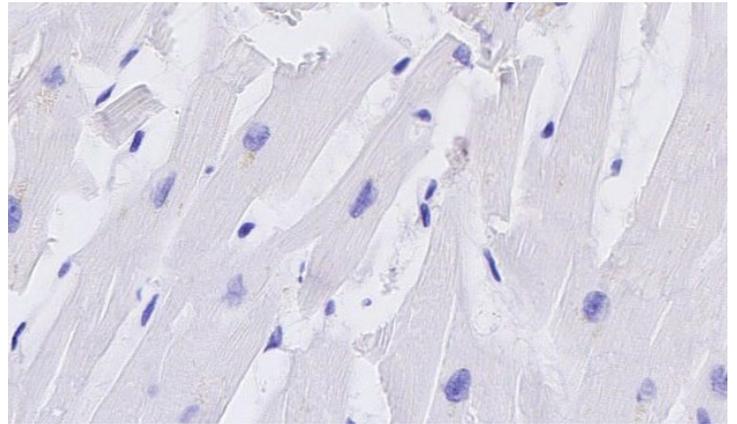
Liver
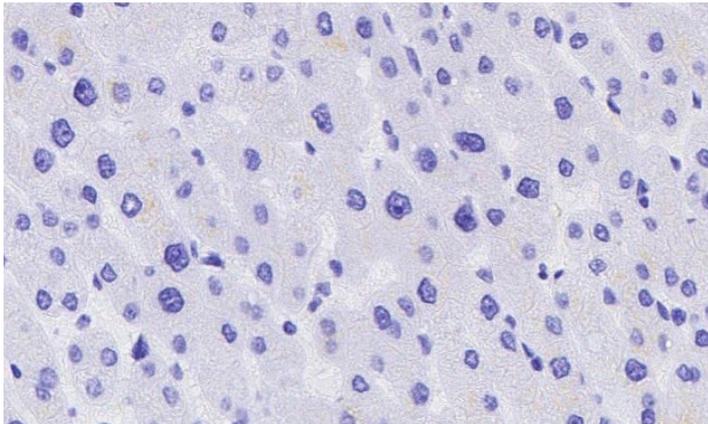
Cerebrum
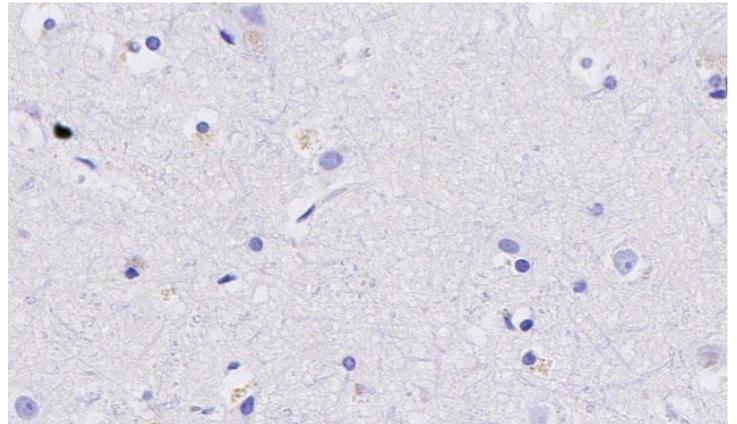
Kidney
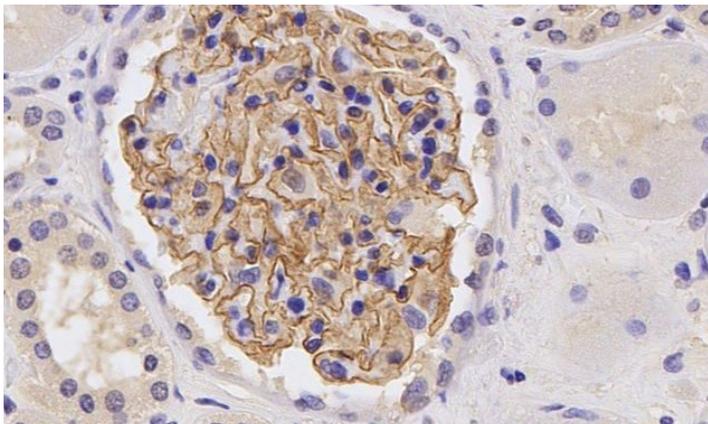
Kidney-Isotype control
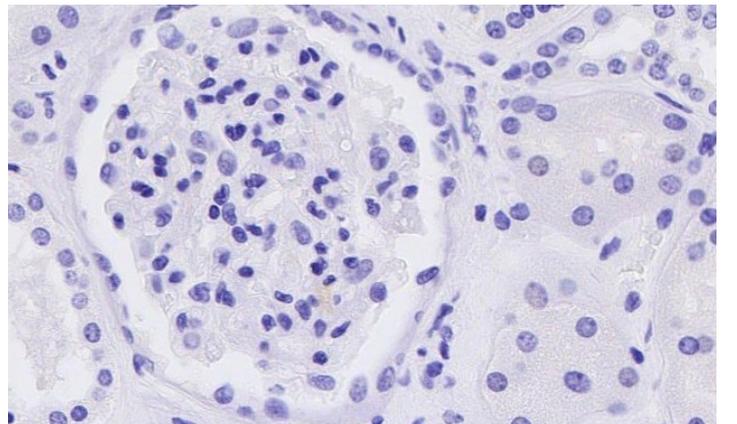
Figure 14. APOE4 expression in normal tissues. IHC staining of multi-normal human tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 20X on Aperio® ImageScope.

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APOE4 expression in multi-cancer TMA (BOND™ RX)

Below are the representative images of selected tissues from the multi-cancer TMA. APOE4 expression was absent in head and neck cancer, ovarian cancer, stomach adenocarcinoma, T cell lymphoma, liver carcinoma, breast ductal carcinoma, renal cell carcinoma, glioblastoma, pancreatic cancer, seminoma, and bladder carcinoma.
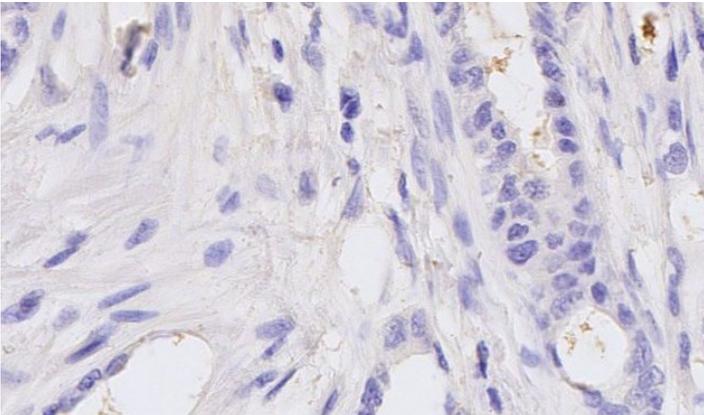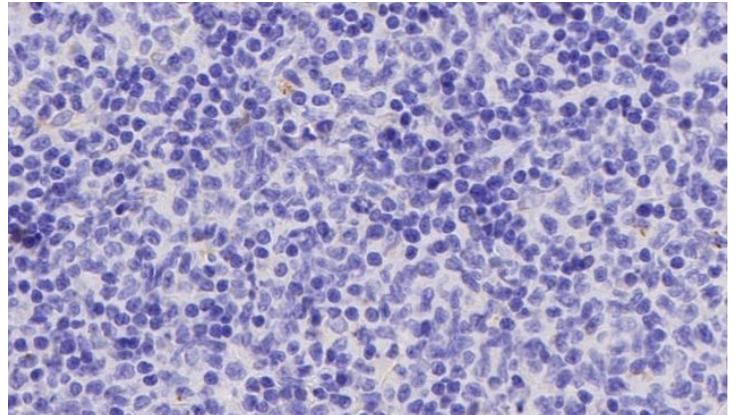
APOE4

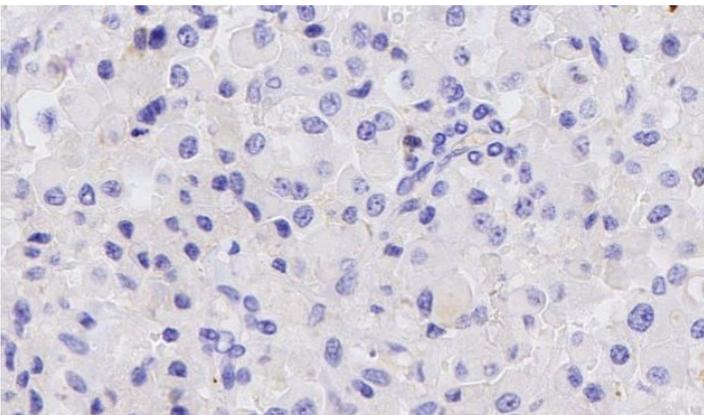Head and Neck cancer
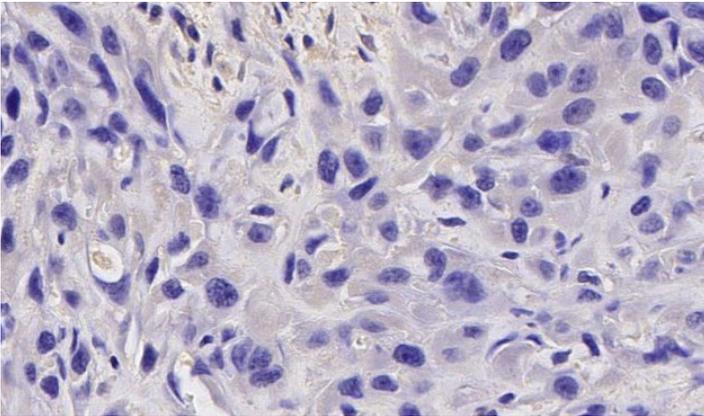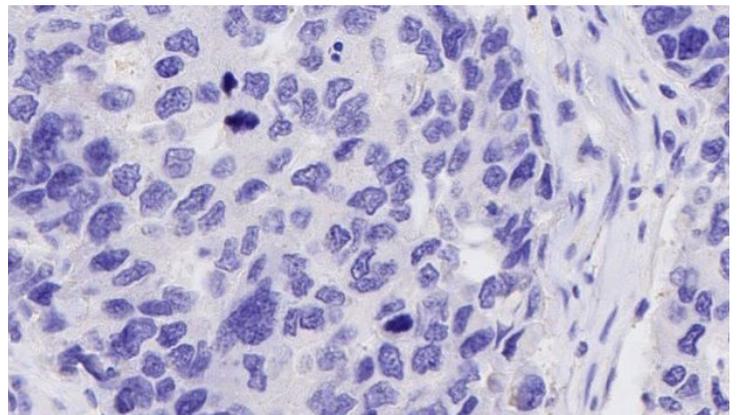

Ovarian cancer
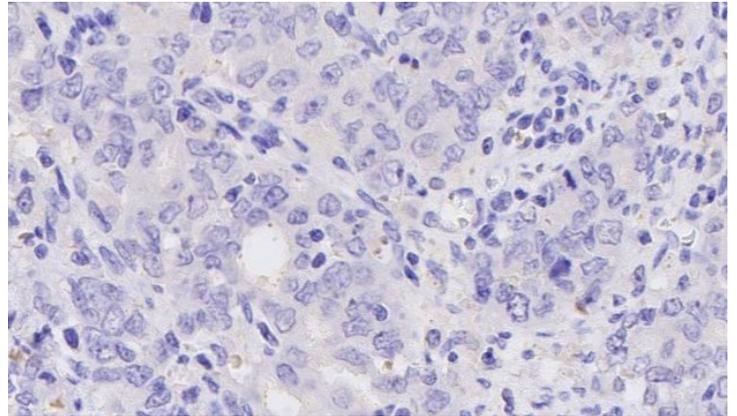
Stomach adenocarcinoma
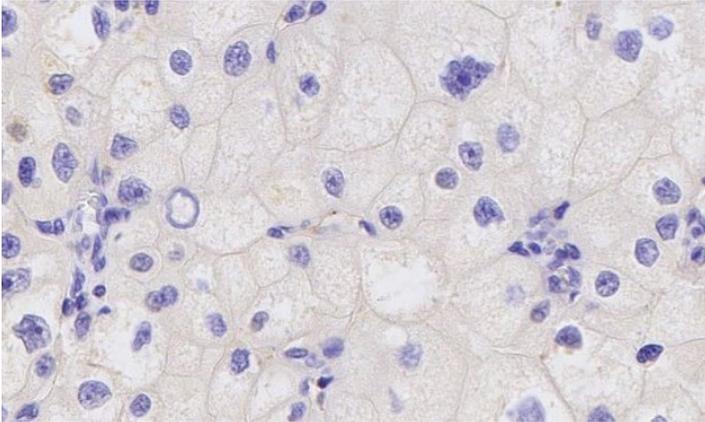

T cell lymphoma

Liver carcinoma

Breast ductal carcinoma

Enhanced validation data

APOE4

Renal cell carcinoma	Glioblastoma
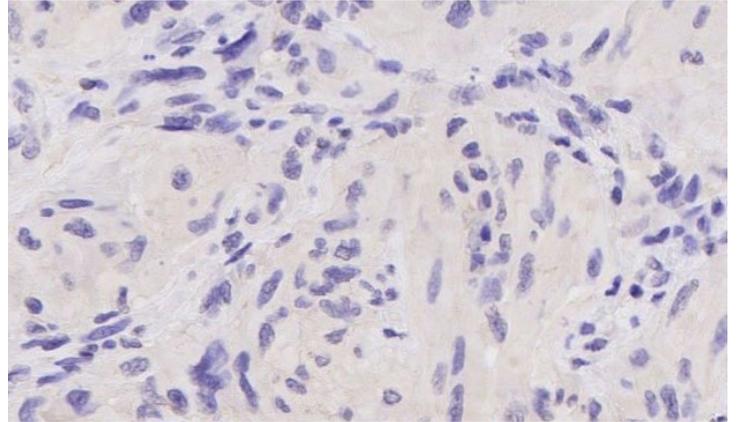
Pancreatic cancer	Seminoma
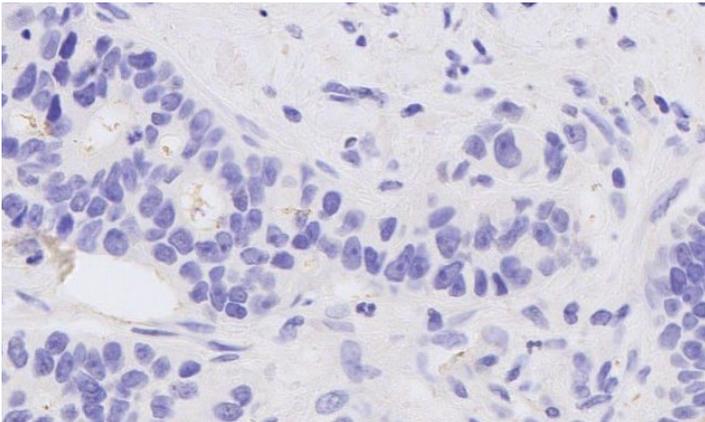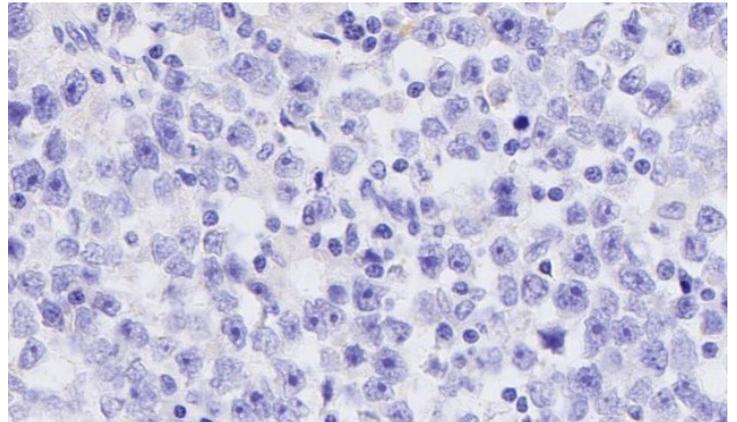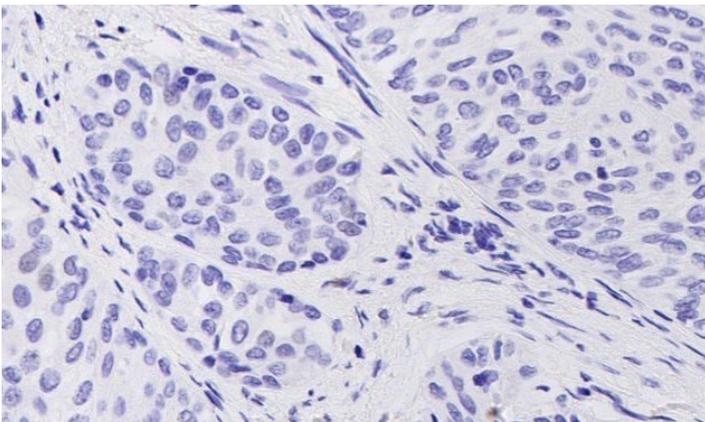
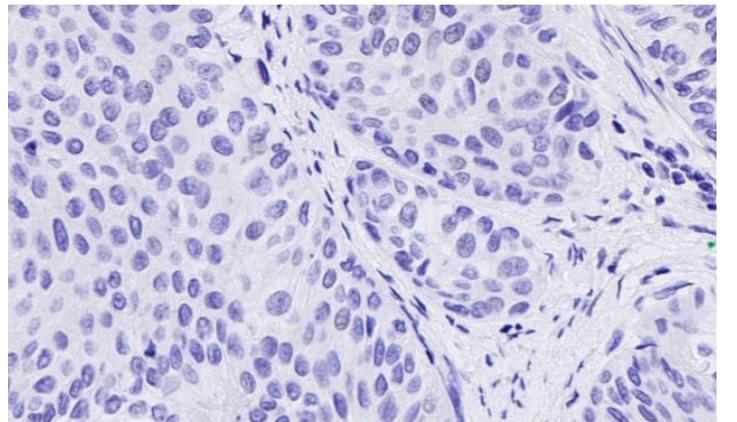| Bladder Carcinoma	Bladder Carcinoma-Isotype control

Figure 15. APOE4 expression in human cancer tissue. IHC staining of multi-cancer human tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 20X on Aperio® ImageScope.

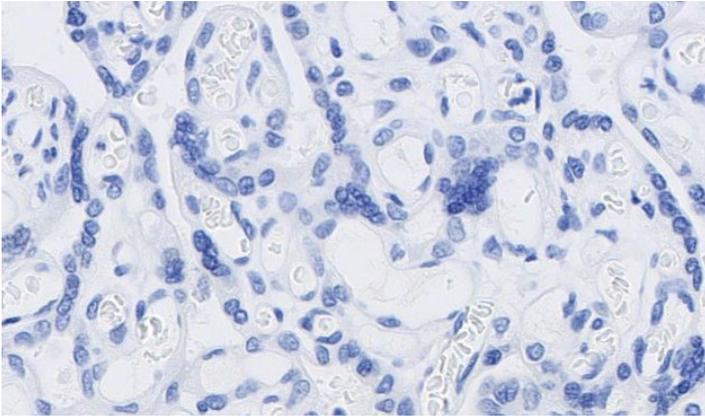NanoZoomer® is a registered trademark of Hamamatsu Photonics K.K.

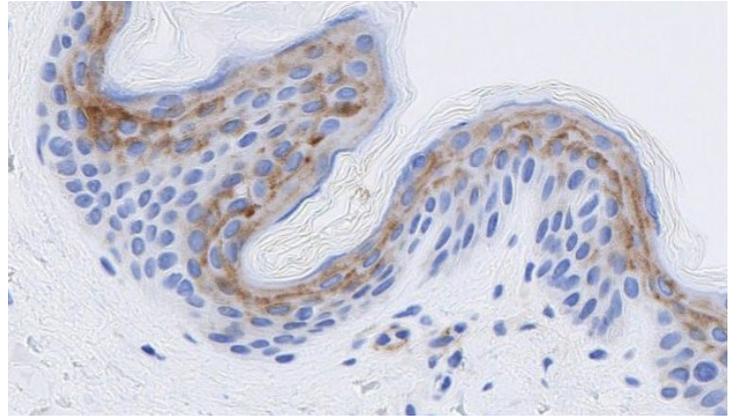# APOE4 expression in multi-normal TMA (DISCOVERY ULTRA)

Below are the representative images of selected tissues from multi-normal TMA. APOE4 expression was detected in the skin and kidney. Expression was absent from the placenta, testis, pancreas, prostate, heart, liver, colon, spleen, cerebrum, brain and kidney.
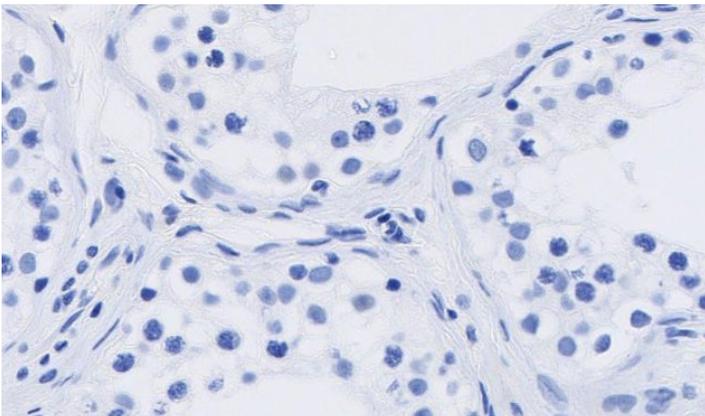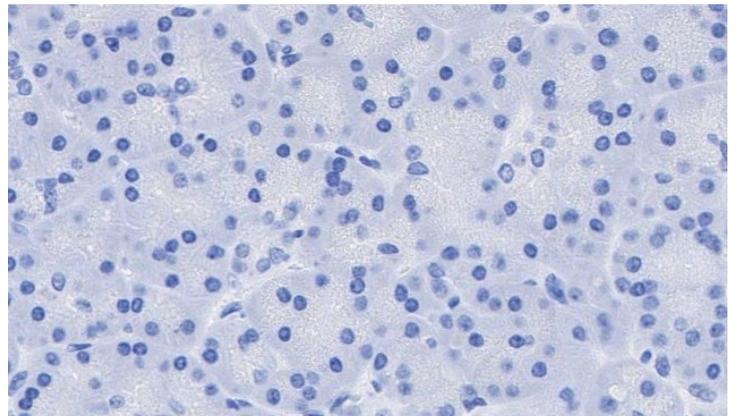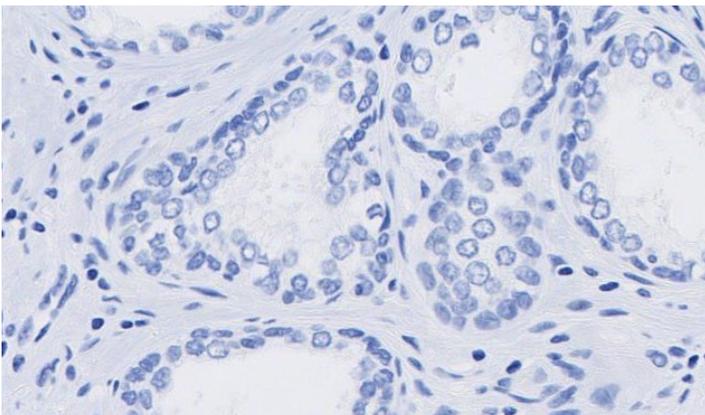
APOE4

Placenta	Skin

Testis	Pancreas

Prostrate	Heart

Enhanced validation data

APOE4

Liver	Colon

Spleen	Cerebrum

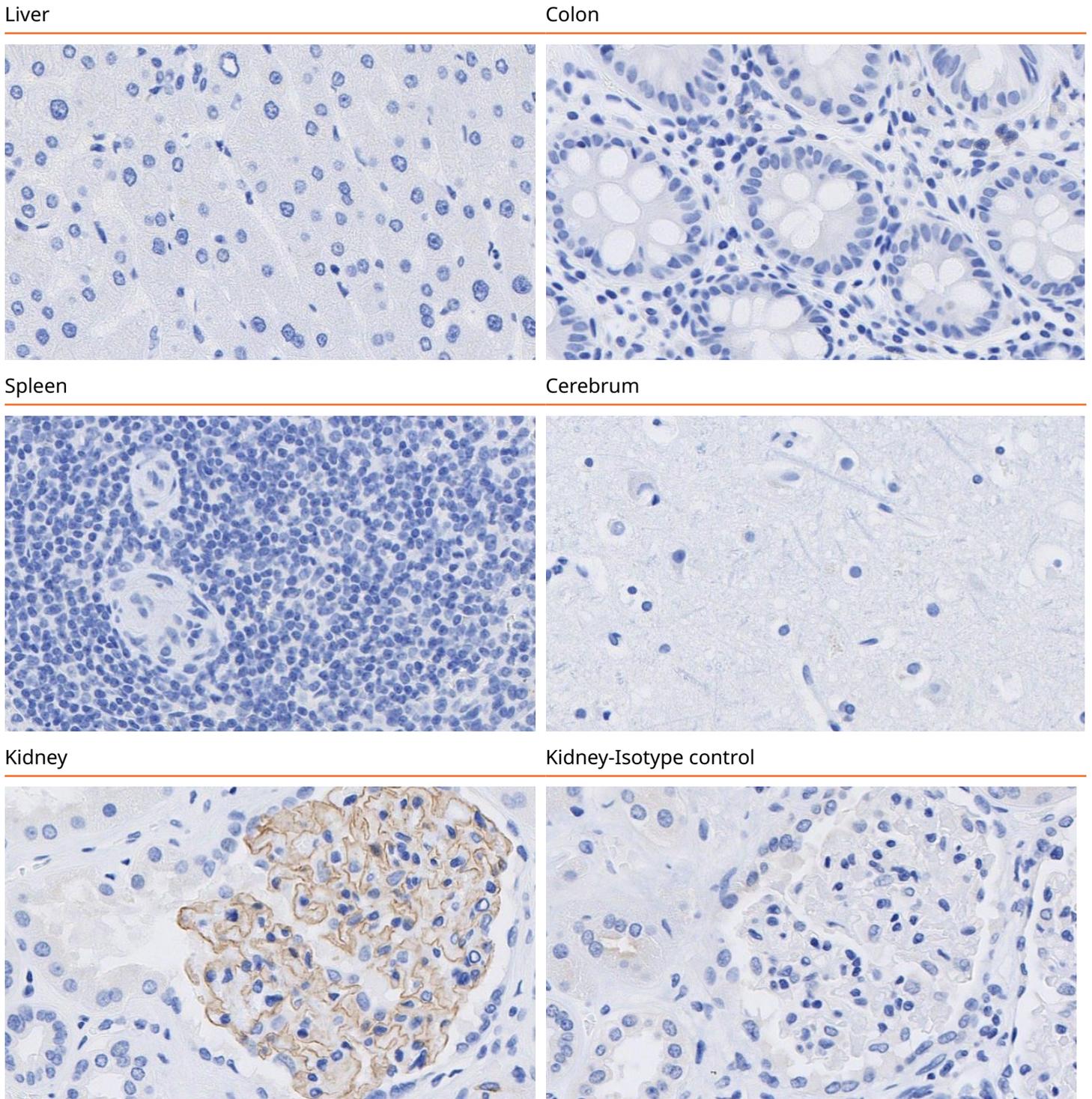| Kidney	Kidney-Isotype control
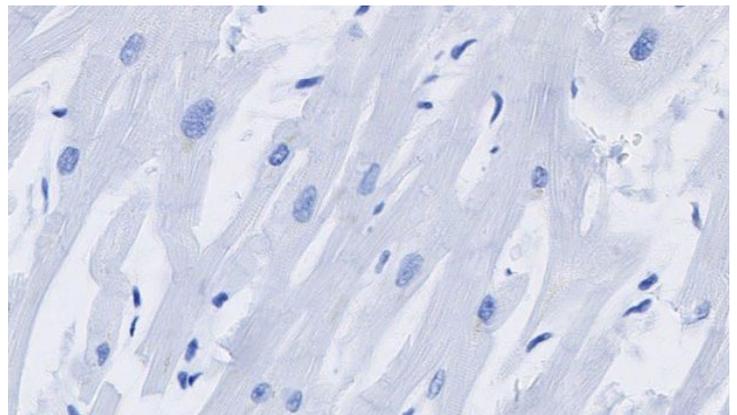
Figure 16. APOE4 expression in normal tissues. IHC staining of multi-normal human tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 µg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 20X on Aperio® ImageScope.

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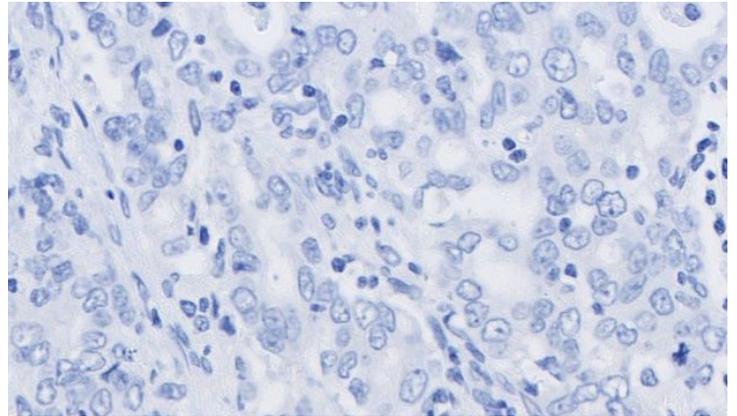# APOE4 expression in multi-cancer TMA (DISCOVERY ULTRA)

Below are the representative images of selected tissues from the multi-cancer TMA. APOE4 expression was absent in head and neck cancer, ovarian cancer, stomach adenocarcinoma, T cell lymphoma, liver carcinoma, breast ductal carcinoma, renal cell carcinoma, glioblastoma, pancreatic cancer, seminoma, and bladder carcinoma.
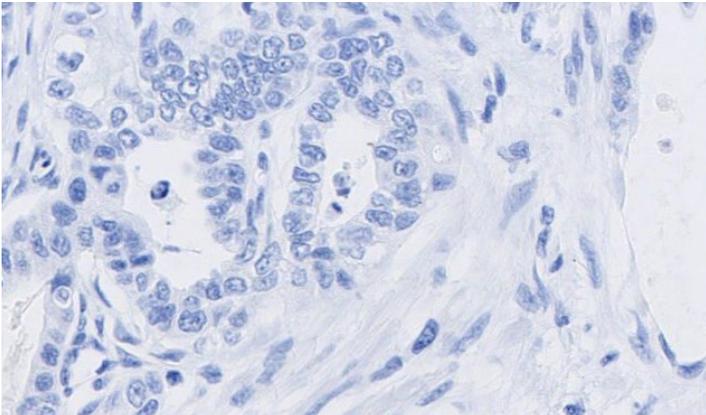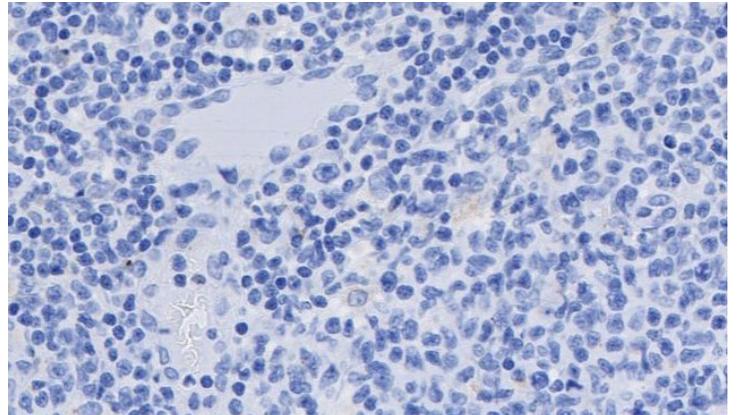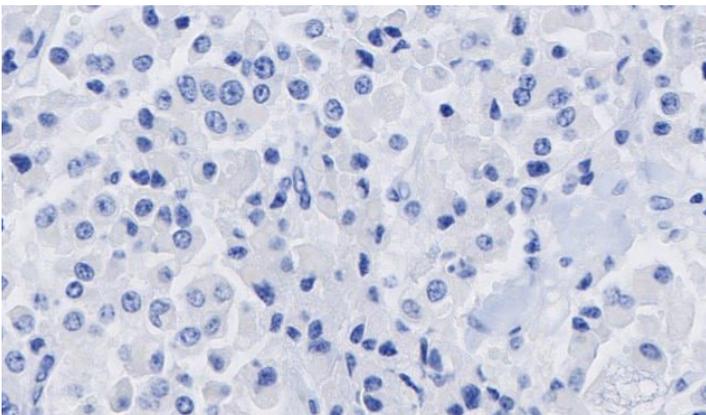
APOE4

Head and Neck cancer	Ovarian cancer
Stomach adenocarcinoma	T cell lymphoma
Liver carcinoma	Breast ductal carcinoma
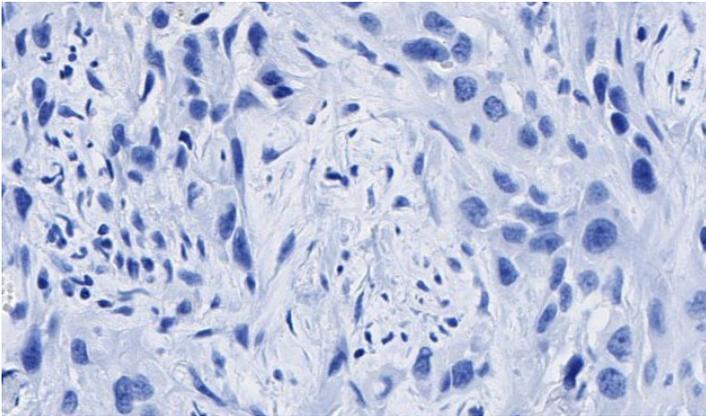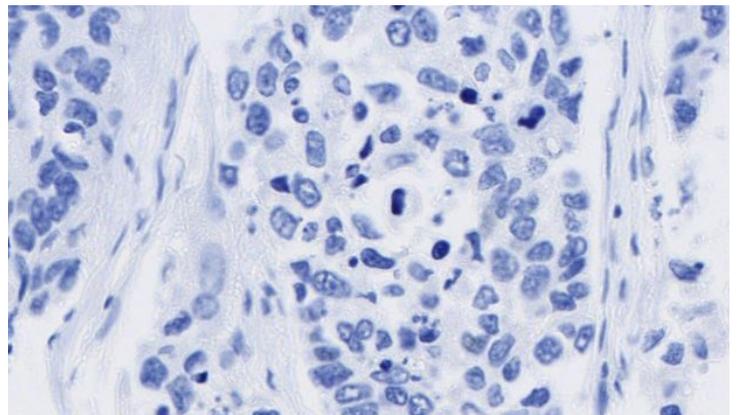
Enhanced validation data

APOE4
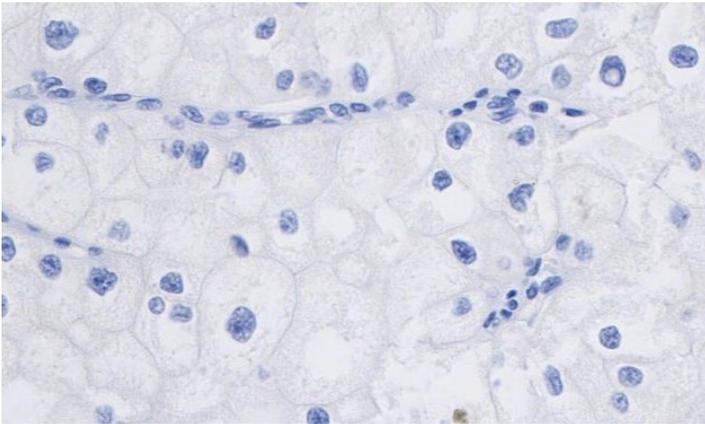
Renal cell carcinoma	Glioblastoma
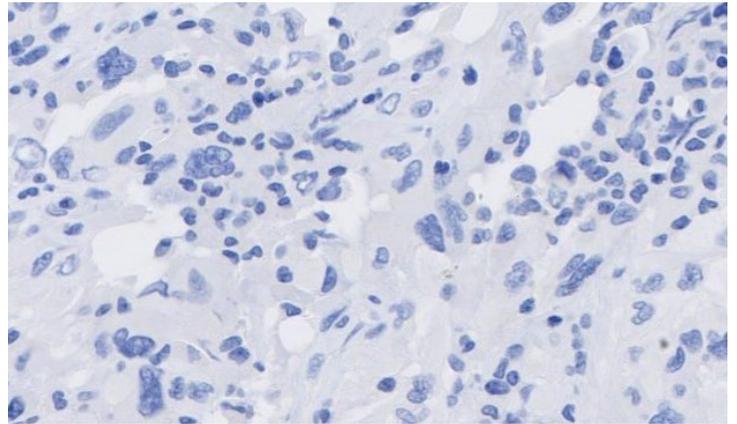
Pancreas adenocarcinoma	Seminoma
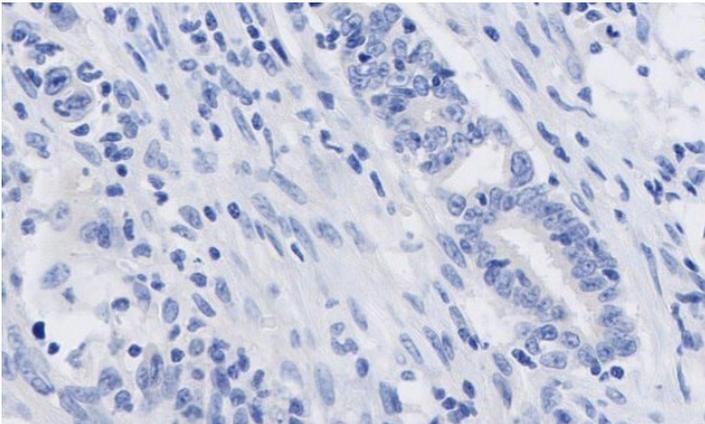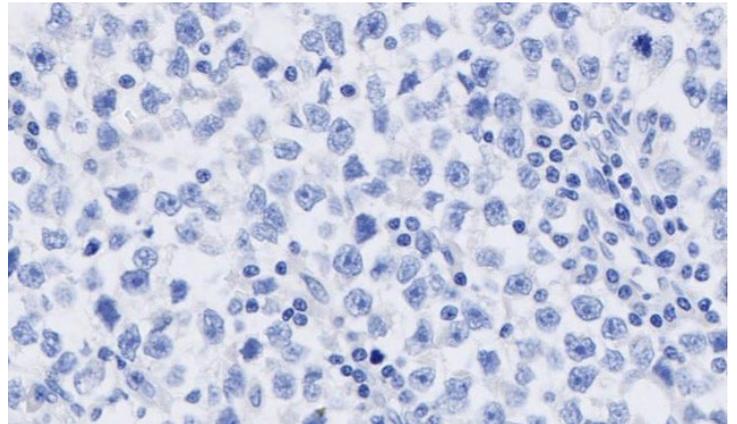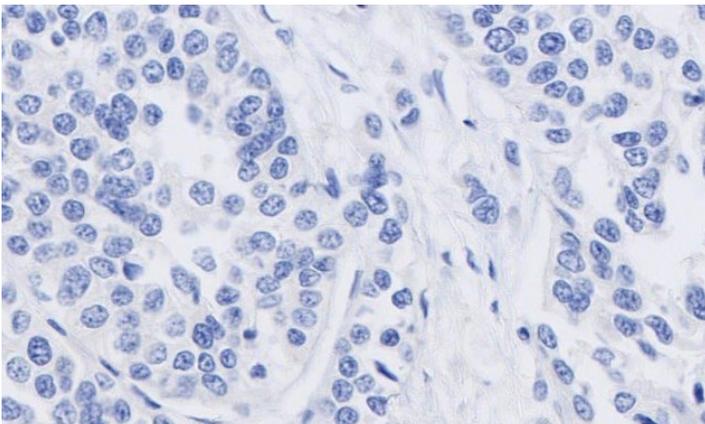
Bladder Carcinoma	Breast ductal carcinoma-Isotype control
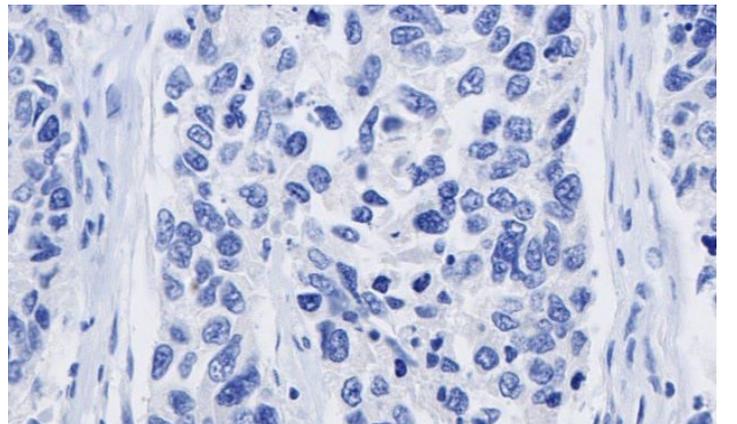
Figure 17. APOE4 expression in cancer tissues. IHC staining of multi-cancer human tissues using Anti-Apolipoprotein E4 antibody ab279714 or anti-rabbit IgG-isotype control antibody (1.0 μg/mL) (ab172730). Positive staining in brown; nuclear hematoxylin counterstain in blue. Slides were scanned at 20x on NanoZoomer S360 (Hamamatsu Photonics K.K.) and imaged at 20X on Aperio® ImageScope.

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Enhanced validation data

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