Supplementary Information

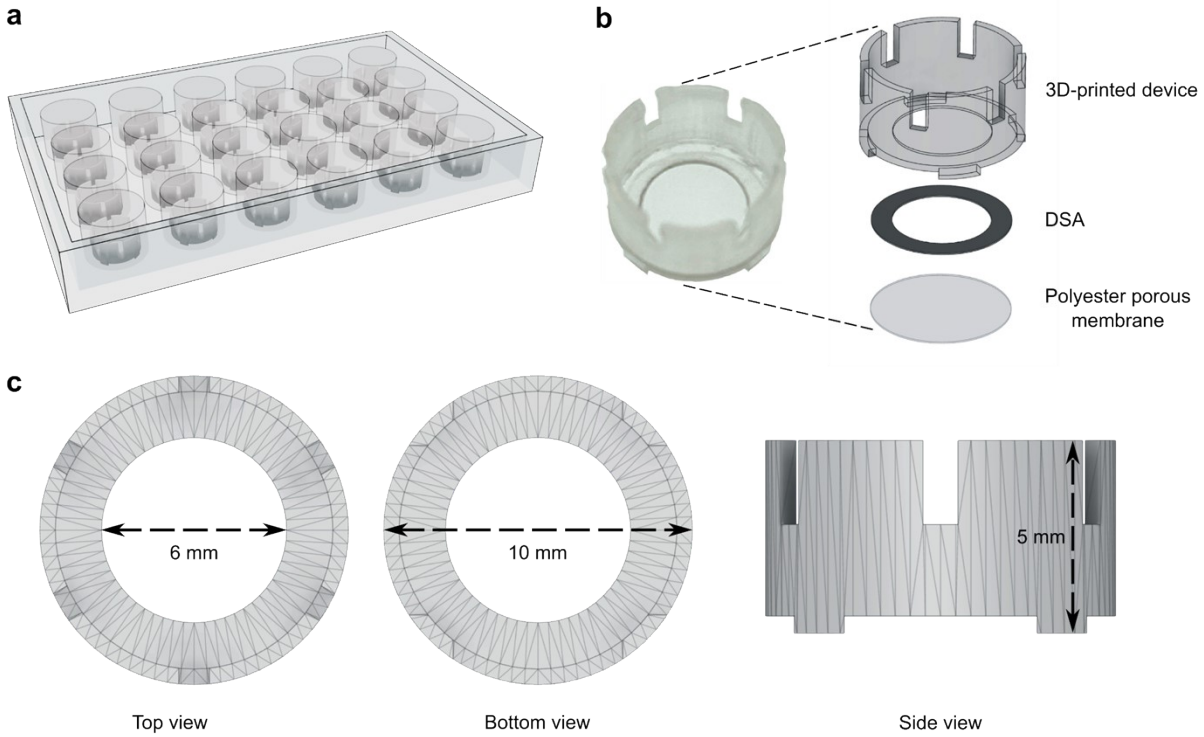

Figure S1. 3D-printed devices. a, 3D-printed holder devices are compatible with 24-well microtiter plates. **b,** The composition of 3D-printed holder devices. **c,** Detailed dimensions of 3D-printed holder device.

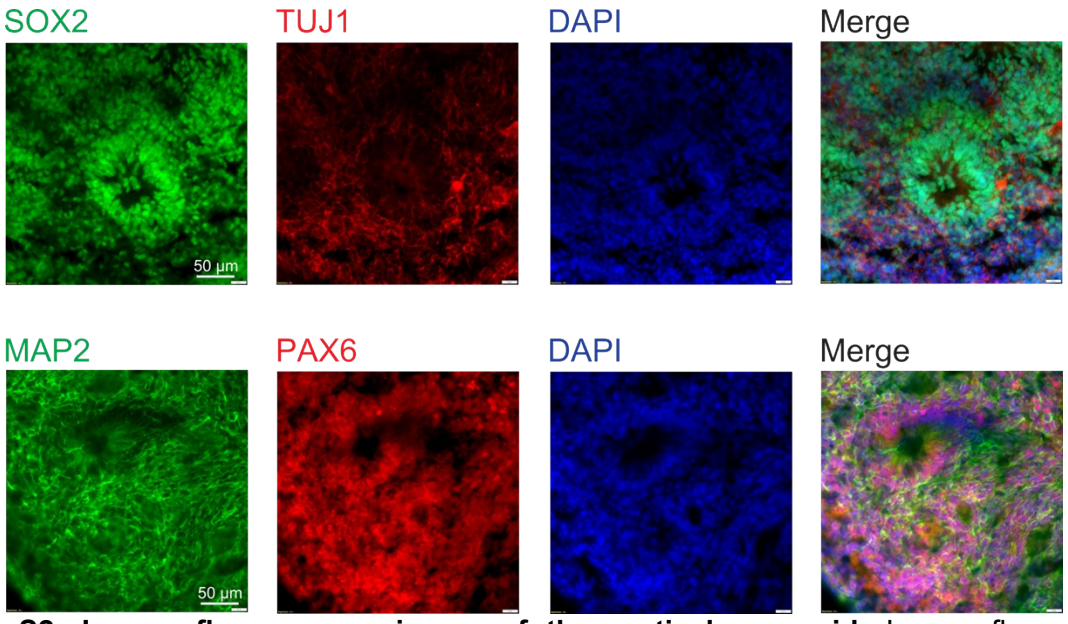

Figure S2. Immunofluorescence image of the cortical organoid. Immunofluorescence imaging shows the distribution of neural progenitor markers SOX2 and PAX6, neuronal markers TUJ1 and MAP2 in the cortical organoid. Scale bars: 50 μm.

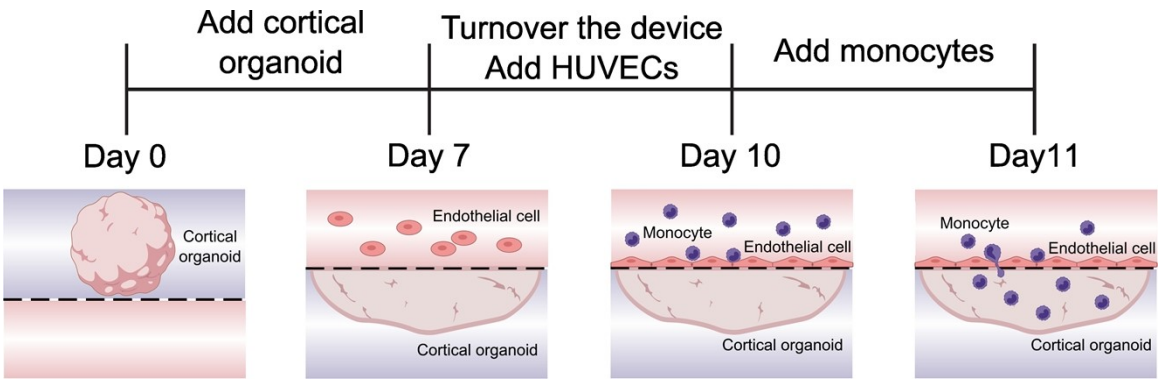

Figure S3. Schematic illustration of the establishment of BBB-MPS model.

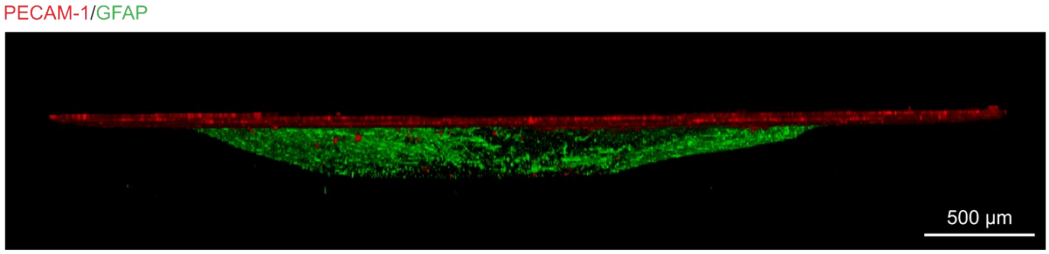

Figure S4. Immunofluorescent image of the BBB-MPS model. Identify the BBB-MPS by immunostaining of PECAM-1 (red, endothelial cell marker) and GFAP (green, astrocyte marker). Scale bar: 500 μm.

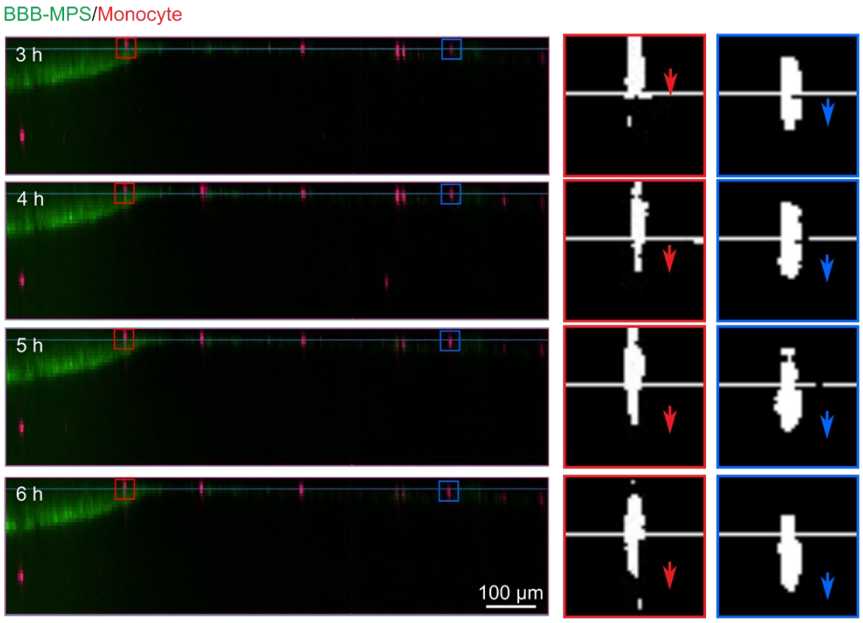

Figure S5. Dynamic penetration and infiltration of monocytes within the BBB-MPS model. The monocytes gradually penetrate BBB (both red and blue dash box) and infiltrate cortical organoids (red dash box). Scale bar: 100 μm.

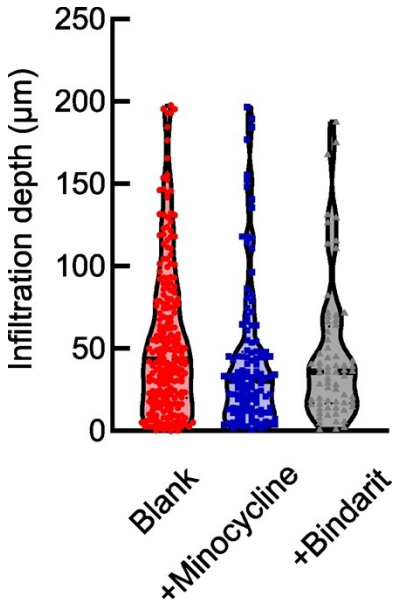

Figure S6. Comparison of infiltration depth of AD monocytes after the Minocycline (Minocycline+) and Bindarit (Bindarit+) treatments.

Table S1. Composition of human cortical organoid differentiation medium.

Medium name	Component	Final concentration	Vendor	Identifier
Cortical Organoid Medium 1 (COM I): EB Formation Medium	mTeSR1	1X	STEMCELL	100-0274
	SB431542	10 µM	STEMCELL	72234
	Dorsomorphin	1 µM	STEMCELL	72102
	Y-27632 (only for 24 h)	90 µM	STEMCELL	72304
Cortical Organoid Medium 2 (COM II): Proliferation Medium	Neurobasal	1X	Gibco	21103-409
	GlutaMAX	1X	Gibco	35050-061
	Gem21	1X	GeminiBio	400-160
	N2 NeuroPlex	1X	GeminiBio	400-163
	MEM-NEAA	1X	Gibco	11140-050
	Penn/Strep	1X	Gibco	15140122
	SB431542	10 µM	STEMCELL	72234
	Dorsomorphin	1 µM	STEMCELL	72102
Cortical Organoid Medium 3 (COM III): Expansion Medium	Neurobasal	1X	Gibco	21103-409
	GlutaMAX	1X	Gibco	35050-061
	Gem21	1X	GeminiBio	400-160
	N2 NeuroPlex	1X	GeminiBio	400-163
	MEM-NEAA	1X	Gibco	11140-050
	Penn/Strep	1X	Gibco	15140122
	FGF-2	20 ng/mL	Pepro Tech	100-18B
Cortical Organoid Medium 4 (COM IV): Differentiation Medium	Neurobasal	1X	Gibco	21103-409
	GlutaMAX	1X	Gibco	35050-061
	Gem21	1X	GeminiBio	400-160
	N2 NeuroPlex	1X	GeminiBio	400-163
	MEM-NEAA	1X	Gibco	11140-050
	Penn/Strep	1X	Gibco	15140122
	FGF-2	20 ng/mL	Pepro Tech	100-18B
	EGF	20 ng/mL	R&D Systems	236-EG

Medium name	Component	Final concentration	Vendor	Identifier
Cortical Organoid Medium 5 (COM V): Maintenance Medium	Neurobasal	1X	Gibco	21103-409
	GlutaMAX	1X	Gibco	35050-061
	Gem21	1X	GeminiBio	400-160
	N2 NeuroPlex	1X	GeminiBio	400-163
	MEM-NEAA	1X	Gibco	11140-050
	Penn/Strep	1X	Gibco	15140122
	BDNF	10 ng/mL	Pepro Tech	450-02
	GDNF	10 ng/mL	Pepro Tech	450-10

	NT3	10 ng/mL	Pepro Tech	450-03
	Ascorbic acid	0.2 mM	Sigma-Aldrich	A4403
	cAMP	100 µM	Sigma-Aldrich	A9501
Cortical Organoid Medium 6 (COM VI): Proliferation Medium	Neurobasal	1X	Gibco	21103-409
	GlutaMAX	1X	Gibco	35050-061
	Gem21	1X	GeminiBio	400-160
	N2 NeuroPlex	1X	GeminiBio	400-163
	MEM-NEAA	1X	Gibco	11140-050
	Penn/Strep	1X	Gibco	15140122

Table S2. Antibodies used for immunofluorescence staining.

Antibodies	Host	Dilution	Vendor	Identifier
PECAM-1	Sheep	1:40	R&D	AF806
ZO-1	Mouse	1:100	Thermo Fisher	33-9100
VE-cadherin	Rabbit	1:100	Cell Signaling	2158
GAFP	Rabbit	1:200	Agilent Dako	Z033429-2
SOX2	Goat	1:100	R&D	AF2018-SP
TUJ1	Rabbit	1:200	Cell Signaling	D71G9
PAX6	Rabbit	1:200	BioLegend	901301
MAP2	Chicken	1:500	Millipore	AB5543
NeuN	Mouse	1:400	Cell Signaling	94403
Cleaved caspase-3	Rabbit	1:100	Cell Signaling	9661S