Electronic Supplementary Material (ESI) for Lab on a Chip

Supporting Information

Constant-rate perfused array chip for high-throughput screening of drug permeability through brain endothelium

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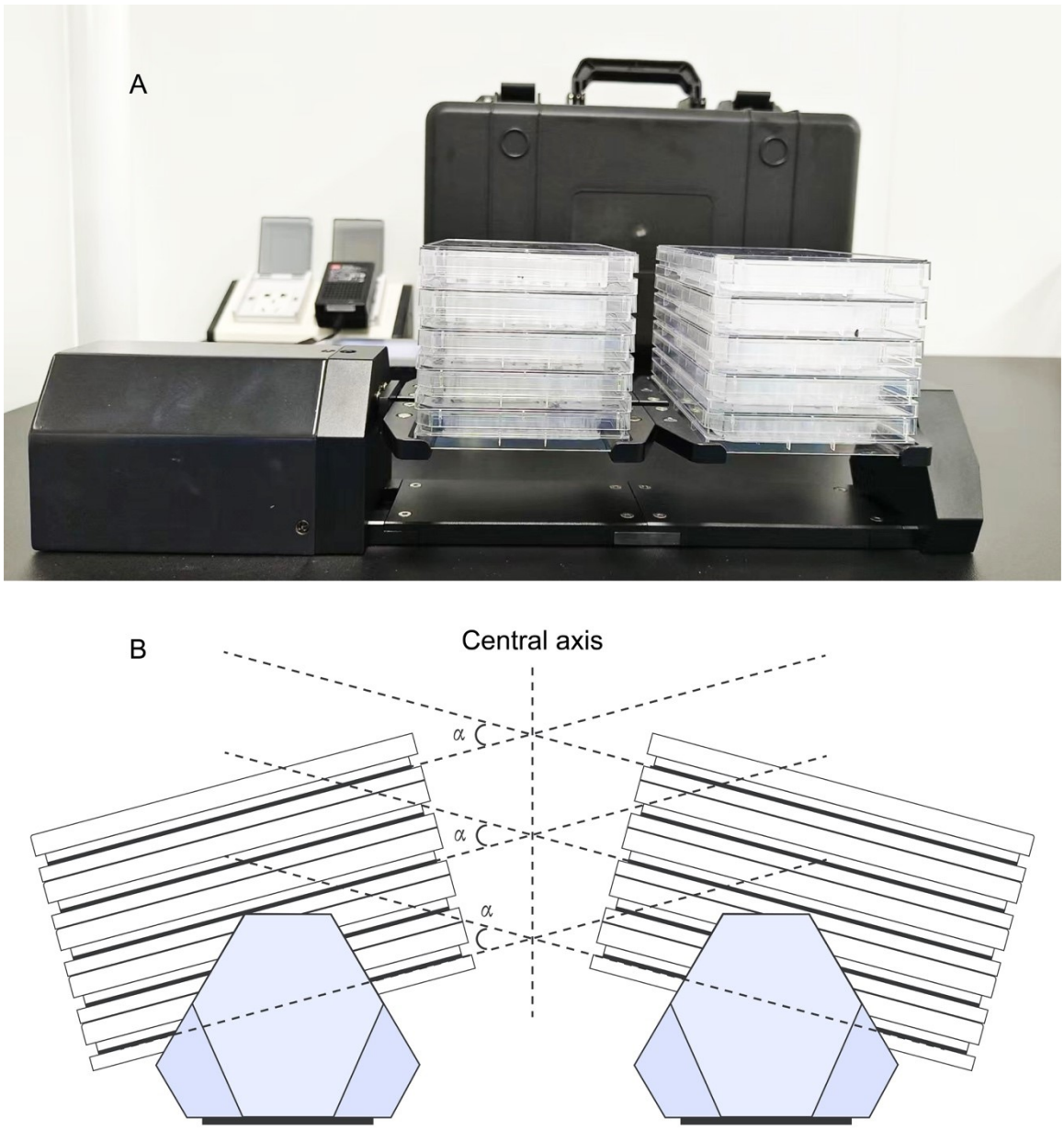

Fig. S1. Photograph and schematic diagram of the constant-rate flow system with 10 layers of the cPACs stacked onto a rocker. (A) Phtograpgh of the flow system with 10 layers of the chips. (B) All the chips rotate along the central axis with the same tilting angle (α) and frequency.

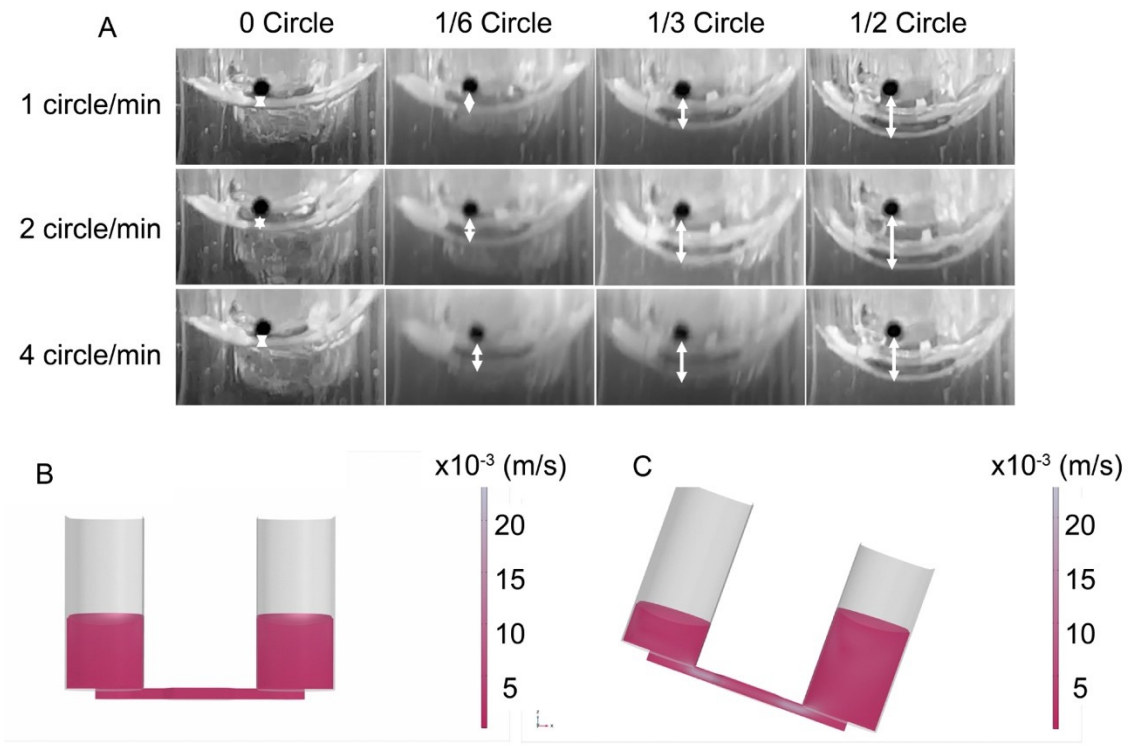

Fig. S2. The height of the medium in the reservoir changed with the tilting angle. (A) The photographs showing the height of the medium in the reservoir changed with the tilting angle under different tilting frequencies. (B-C) Simulation of flow rates in the flow channel under the tilting angle of 0 degree (B) and 20 degrees (C), respectively.

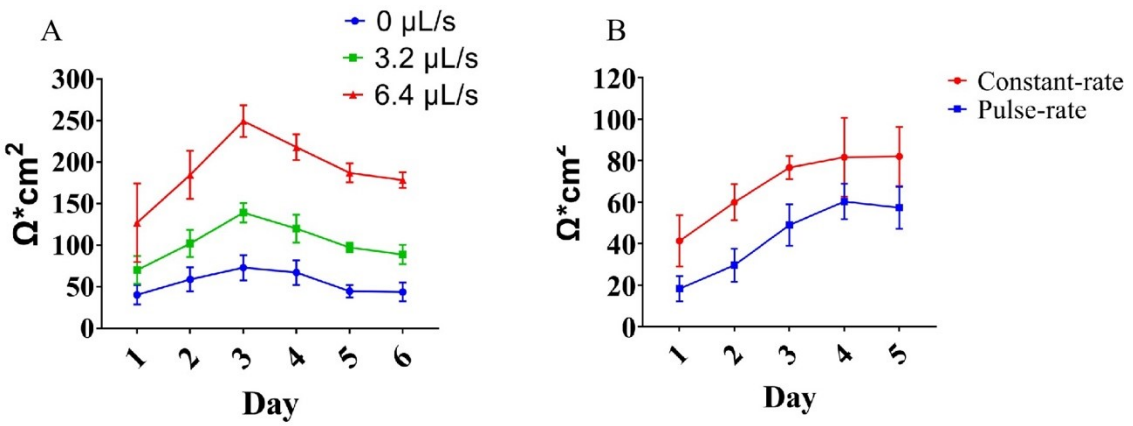

Fig. S3. TEER values of the hBMECs under different flow rates (A) and flow modes (B) on the cPAC. The pulse-rate flow was achieved by keeping the rocker at the maximum angle that the flow rate decreased over time. The pulse-rate led to the unstable shear stress.

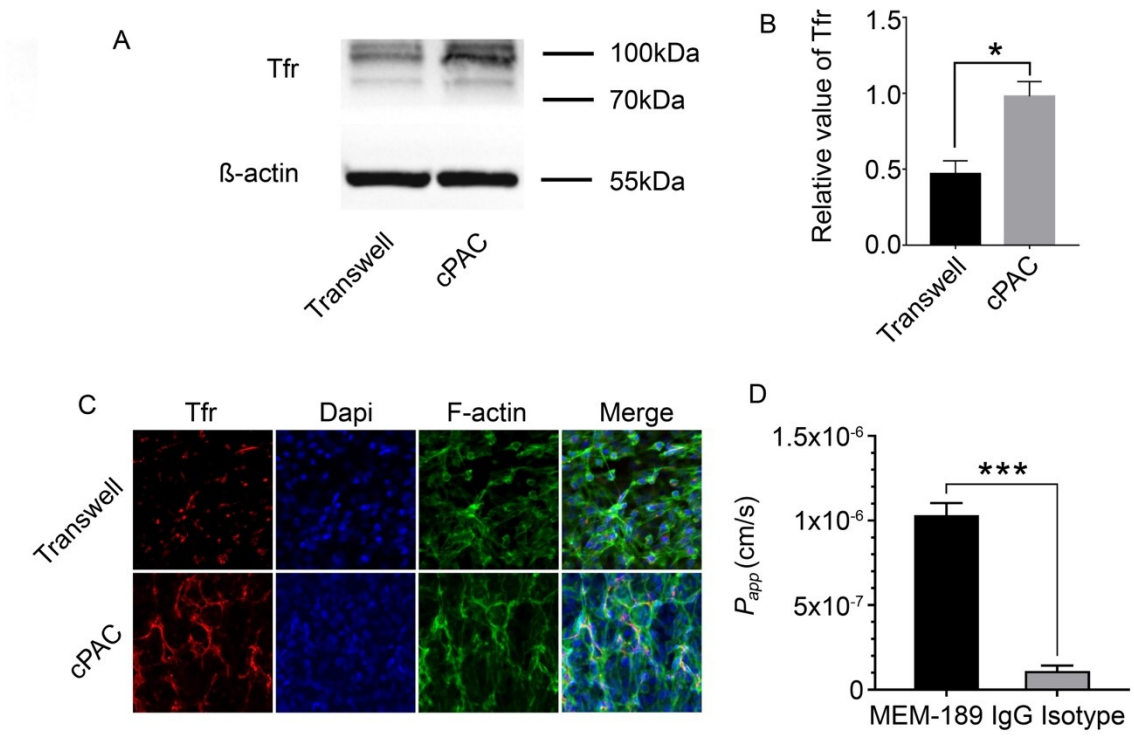

Fig. S4. The expression of transferrin receptor (Tfr) and brain penetration of antibodies through the hBMECs cultured on the cPAC. (A-B) Western Blot of the Tfr protein expressed in the hBMECs cultured on the cPAC and transwell. (C) Immunofluorescence staining against the Tfr (Red) of the hBMECs cultured on the cPAC and transwell. (D) the P_{app} values of the antibody MEM-189 (positive) and antibody IgG Isotype (negative) through the brain endothelium model. *$p < 0.05$, ***$p < 0.001$.

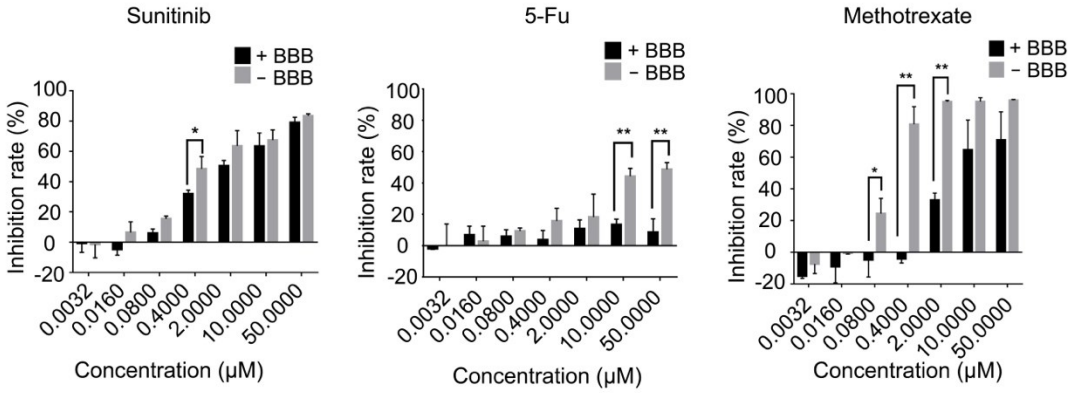

Fig. S5. Simultaneous evaluation of permeability and anti-glioma efficacy of model drugs (sunitinib, 5-Fu, and methotrexate) on the cPAC.

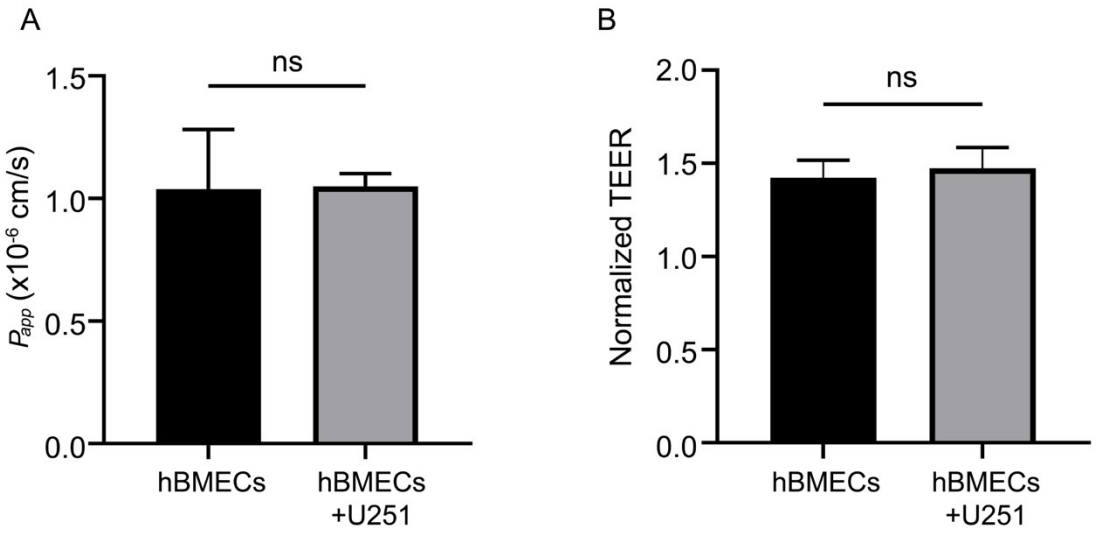

Fig. S6. The barrir function of the brain endothelium with or without the U251 cancer cells coculture for 2 days. (A) The permeability (P_{app}) of the FITC-dextran (4 kDa) on day 3. (B) The normalized TEER values of the hBMECs on day 3. The TEER values of the hBMECs on day 3 were normalized by those on day 1 before adding the U251 cells for coculture.

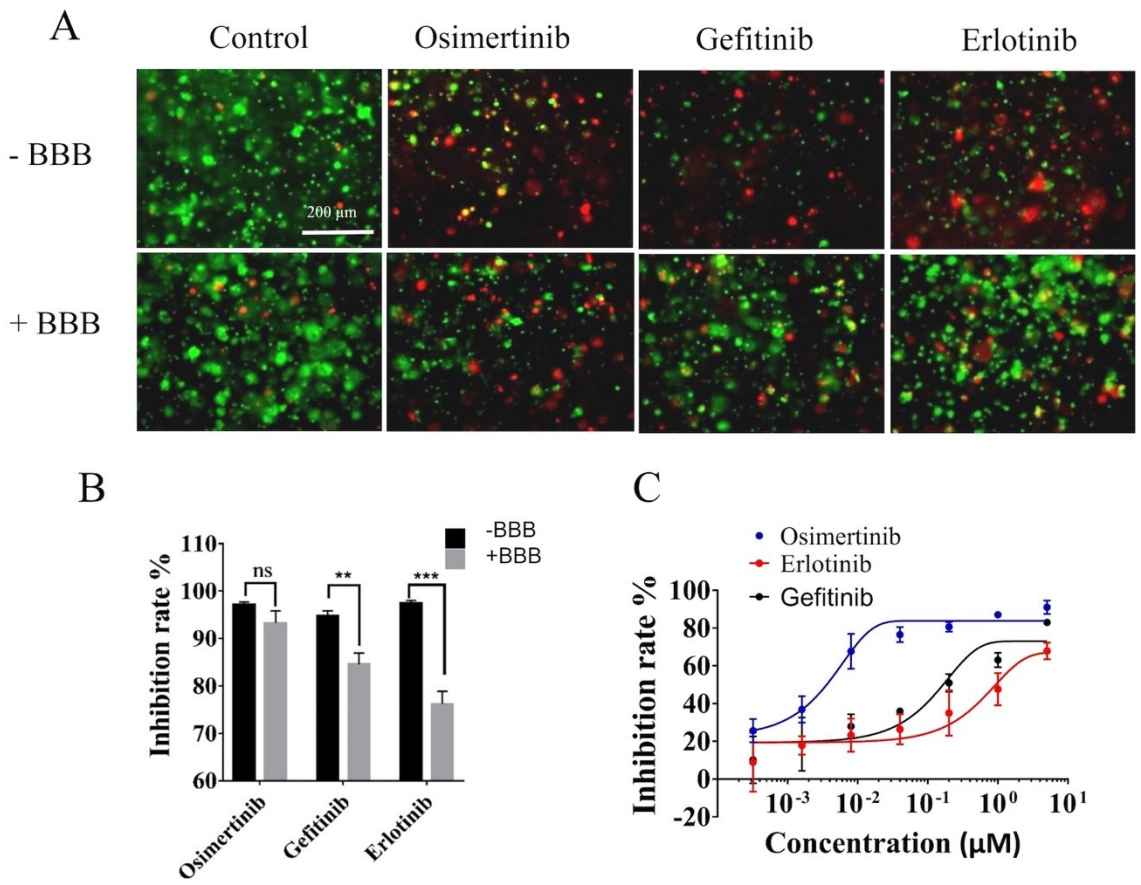

Fig. S7. Simultaneous evaluation of permeability and brain metastases therapy of osimertinib, gefitinib, and erlotinib on the cPAC. (A-B) Live-dead staining and ATP activity detection of the non-small cell lung cancer PC-9 cells in the presence and absence of the brain endothelium. Scale bar, 200 μm. The live cells were stained in green, whereas the dead cells were stained in red. (C) Dose-dependent drug responses against the 3D lung cancer cells on the cPAC in the presence of the brain endothelium.