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Protocol

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Three-dimensional human neural culture on a chip recapitulating neuroinflammation and neurodegeneration

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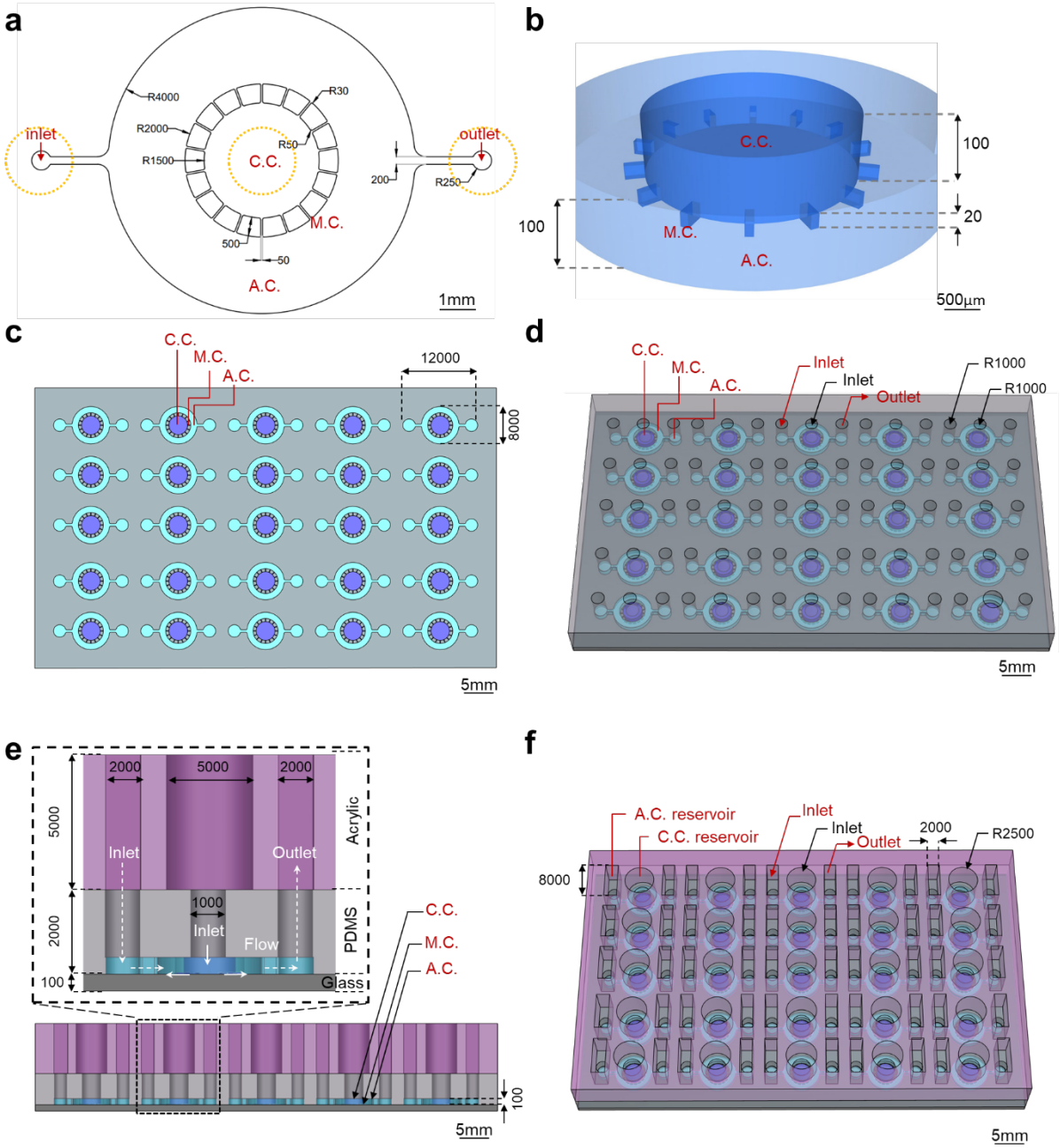
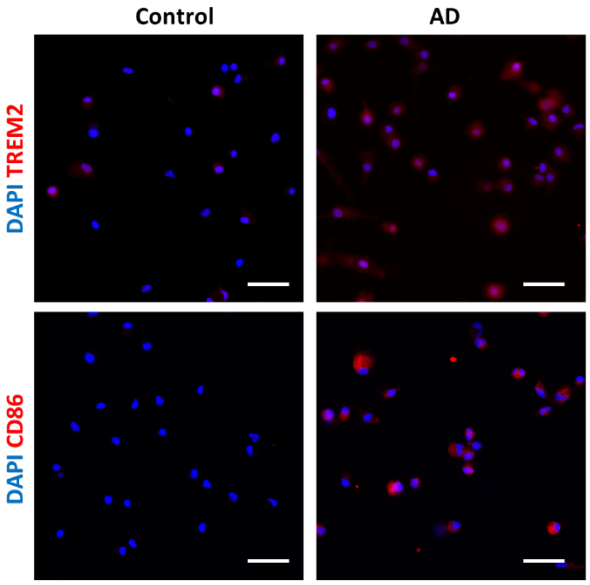
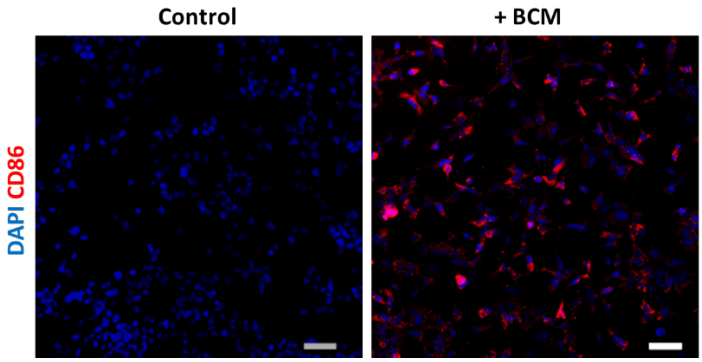


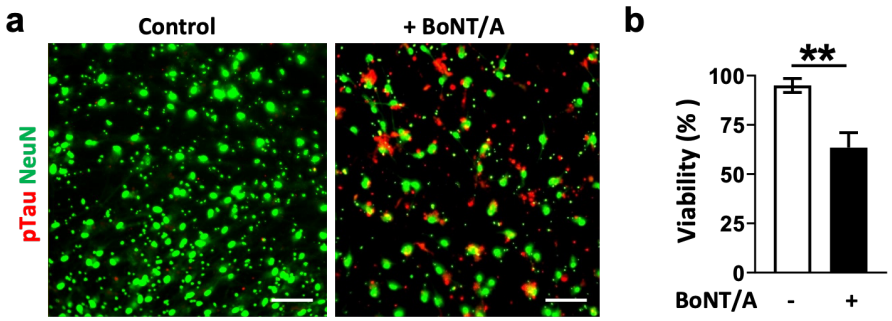
Supplementary Fig. 1 | Dimensions of the human BoC model. a-b, Dimensions of the chip design for a single model platform in top view and 3D view. C.C.: central chamber; A.C.: annular chamber; M.C.: migration channel. A 2-mm puncher will be used to make a hole in the C.C. and two holes in the A.C. for fluid inlet (marked yellow, see Step 5). **c-d,** Dimensions of arrayed platforms in top view and 3D view. **e.** Dimensions of the assembled BoC for a single model platform and arrayed platforms in side view. **f.** Dimensions of arrayed BoCs in 3D view.



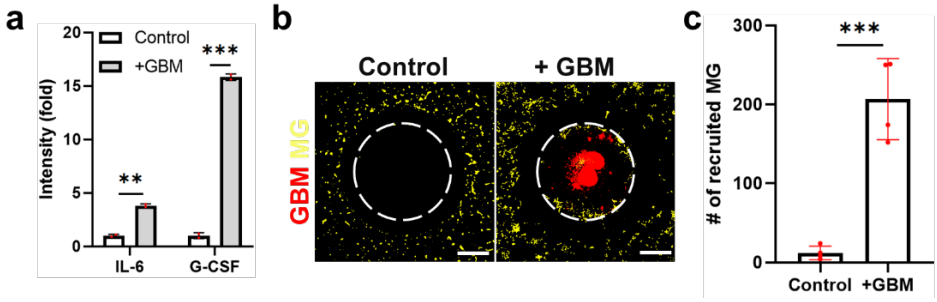
Supplementary Fig. 2 | Induction of DAM and M1 types of microglia in "human AD BoC". iMG cells exposed to conditioned media from AD BoCs retained DAM (TREM2-positive) and M1 (CD86-positive) phenotypes. Scale bars represent 50 μm.



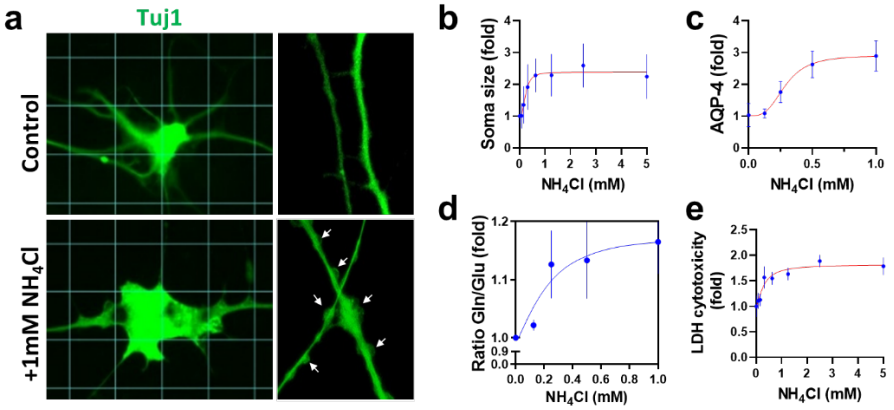
Supplementary Fig. 3 | Induction of M1 type microglia in "human infected BoC". SV40 microglia exposed to bacterial conditioned media (+BCM) retained M1 (CD86-positive) phenotype. Scale bars represent 100 μm.



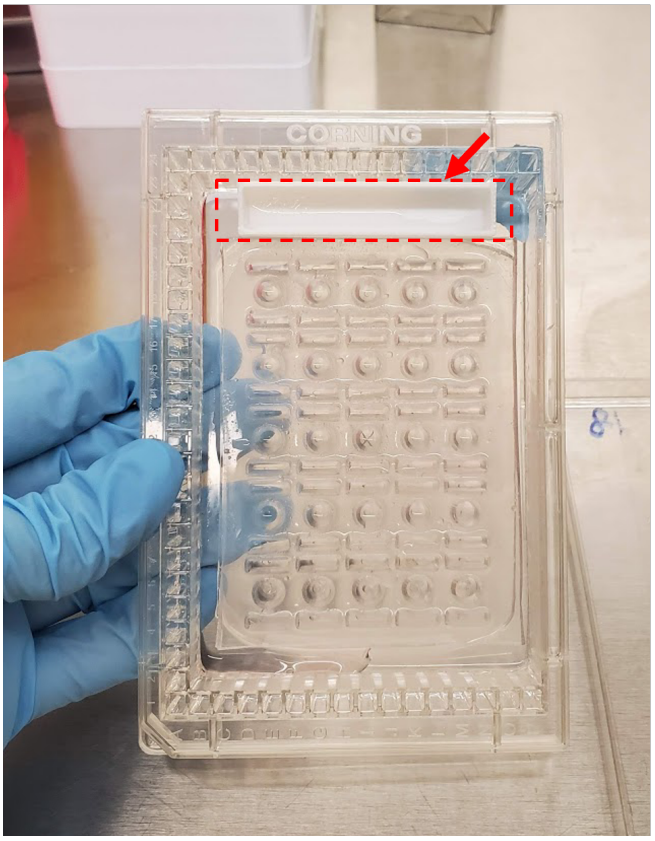
Supplementary Fig. 4 | Promotion of tau accumulation and neurodegeneration in "human infected BoC". a, Our BoCs exposed to bacteria-derived toxin (+BoNT/A) promoted hyperphosphorylated tau deposition (pTau-positive) near neuros (NeuN-positive). Scale bars represent 100 μm. **b,** Induction of neurodegeneration by BoNT/A treatment. Reduction of neural population was analyzed by counting NeuN-positive cells per unit area from fluorescent images (N=4).



Supplementary Fig. 5 |Validation of microglial recruitment and activation in response to "human tumor BoC". **a,** Multicytokine assay was performed with conditioned medium from central chambers to investigate any proinflammatory response in human tumor BoCs. The levels of cytokines such as IL-6 and G-CSF were significantly increased in human tumor BoCs (+GBM) compared to Control (N=2). **b,** Fluorescent images representing the microglial recruitment (MG, marked yellow) towards GBM spheroid (+GBM, marked red) in the central compartment (marked dash-line). Scale bars represent 1 mm. **c,** Quantification for recruited microglia found in the central chamber (N=4).



Supplementary Fig. 6 | Validation of "human edema BoC". a, Induction of neuronal swelling in edema BoCs. Each grid represents 10 μm. **b-e,** The soma size of neurons, expression level of AQP-4 in astrocytes, glutamine/glutamate ratio, and cytotoxicity were significantly increased in hyper-ammonia conditions, validating the induction of edema conditions (N=10).



Supplementary Fig. 7 | Additional humid chamber installed in the device.