Supplementary materials

COMSOL simulations have been performed to obtain the minimum fluid stress. As shown in Fig. S1A, in the two-compartment chamber, only a small portion of the perfused medium diffused through the porous membrane into the bottom culture chamber to replenish nutrients. Thus, the two-compartment chamber can significantly reduce the fluid shear stress τ. The flow characteristics of the two-compartment chamber are determined by the culture chamber height *h,* as well as the pore diameter *d* and opening ratio *γ* of the membrane. To find the optimal parameters, a series of models with different *h*, *d* and *γ* were simulated. Fig. S1B-D shows the relationship of τ with respect to *h*, *d* and *γ*. It can be seen from Figure S1C that, τ decreased with increasing *h*, and the decrease slowed down noticeably when *h* > 1 mm; thus, the culture chamber height *h* was defined as 1.0 mm. Figure S1D shows that τ increased with *d*, and the increase became pronounced when *d* > 0.2 mm; thus the pore diameter *d* was defined as 0.2 mm. In this case, the surface area to volume (SA/V) of the two-compartment chamber is nearly 2.3 times larger than that of the 90 mm Petri dish, in which the medium is typically replaced every 2 days. Thus, the medium exchange rate for the two-compartment chamber should be no slower than 0.048 h^{-1}. Thus, the opening ratio *γ* was defined as 2%. Thus, parameters of the two-compartment chamber were defined as h_c = 1 mm, *d* = 0.2 mm and *γ* = 2%. In this case, the average shear stress τ was 1.5×10^{-6} dynes/cm^2.

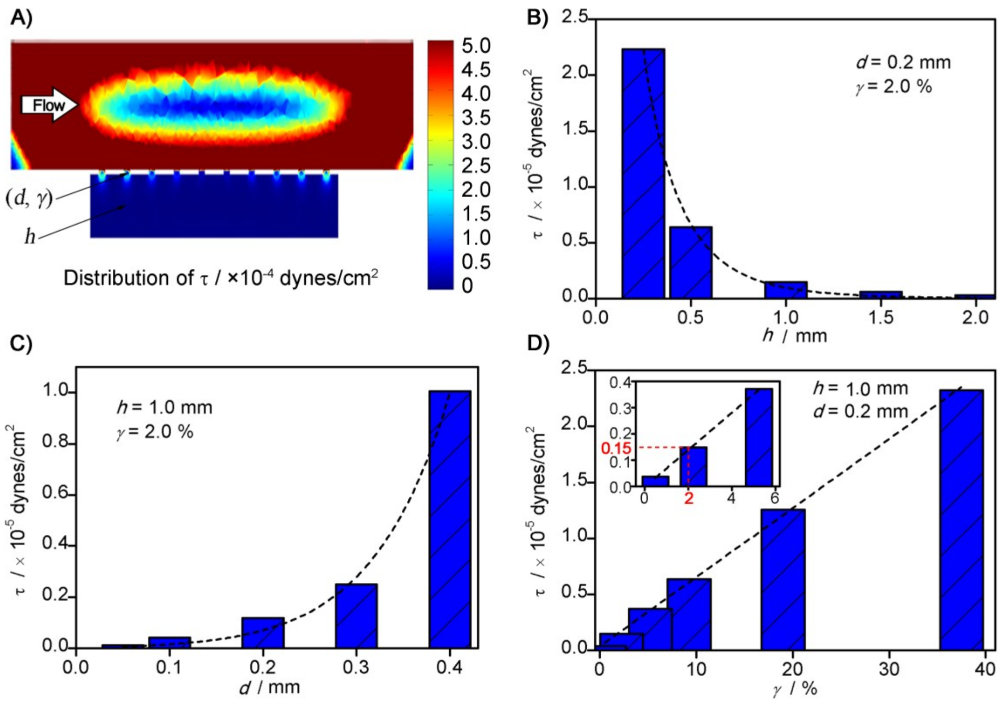

Fig. S1. A) The distribution of shear stress τ in the two-compartment culture chamber simulated using COMSOL. The relationship of the average shear stress τ with respect to the culture chamber height *h* (B), the porous membrane thickness *d* (B) and the porous membrane opening ratio *γ* (D).

The schematic illustrations of the microfluidic device assembly are shown in Fig. S2A. It was composed of a PDMS two-compartment cell culture chamber and a PMMA thermal isolation shell. A PT100 resistance thermometer detector (RTD) and two copper sheets sandwiched with a polyimide heating film were embedded in the PMMA shell, and a PID temperature controller (TC200, Thorlabs) was used to control the thermal support. The key dimensions of the assembly are shown in Fig. S2B.

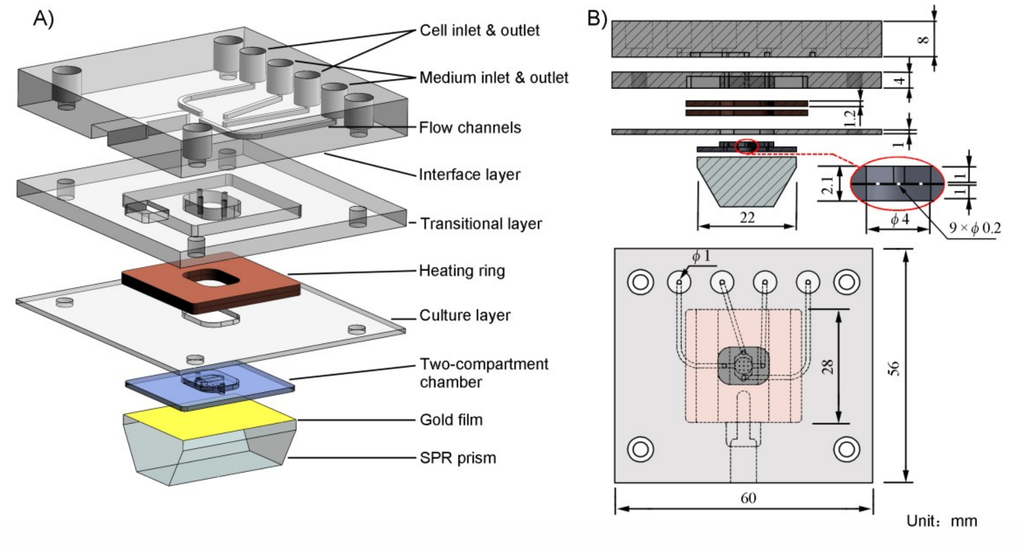

Fig. S2. A) The schematic illustrations of the microfluidic device assembly. B) The key dimensions of the assembly.