Investigation on the potential application of kaemperide in hyperuricemia based on kidney-on-a-chip

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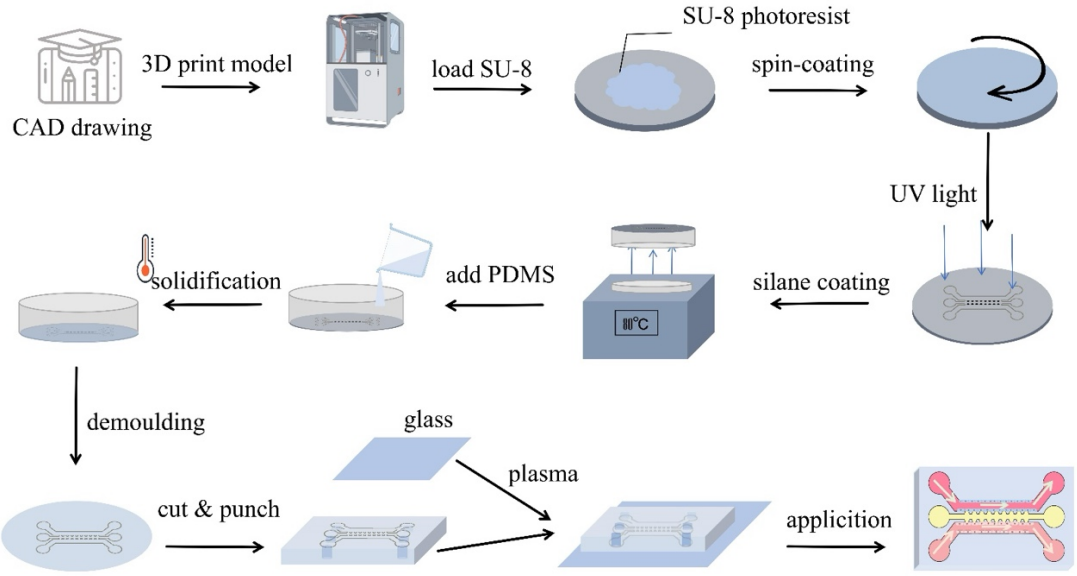

Figure S1. The production flow chart of microfluidic chip

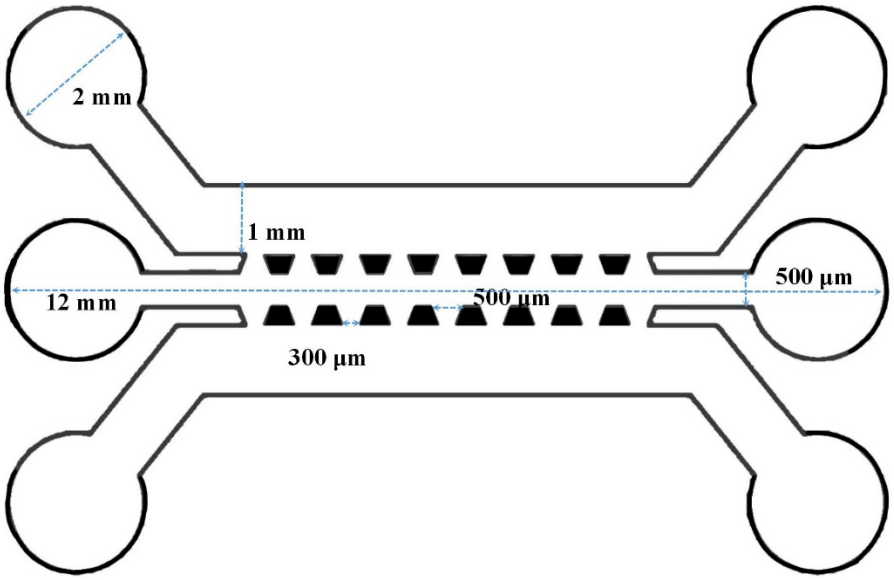

Figure S2. The size diagram of the chip.

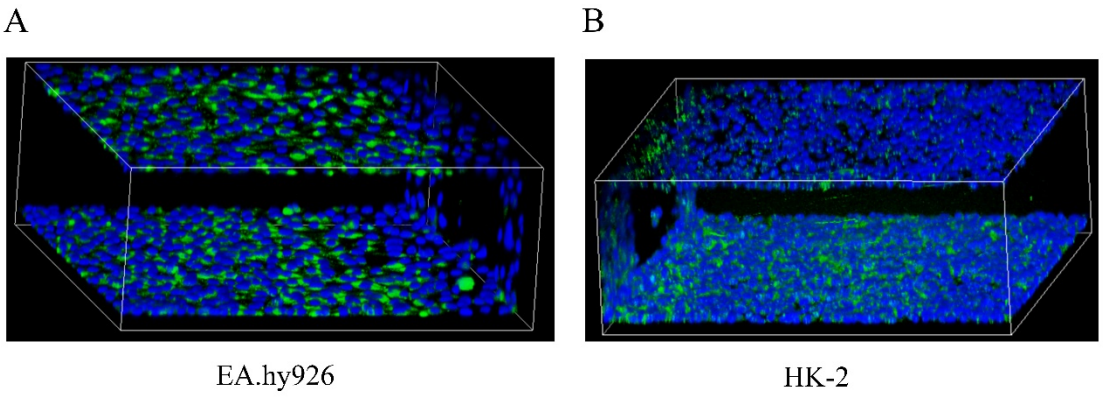

Figure S3. The 3D cell structure in the kidney-on-a-chip: (A) endothelial cell channel mimicking blood vessel and (B) epithelial cell channel mimicking the renal tubule. Green, E-Cadherin (HK-2), VE-cadherin (EA.hy926) ; blue, DAPI.

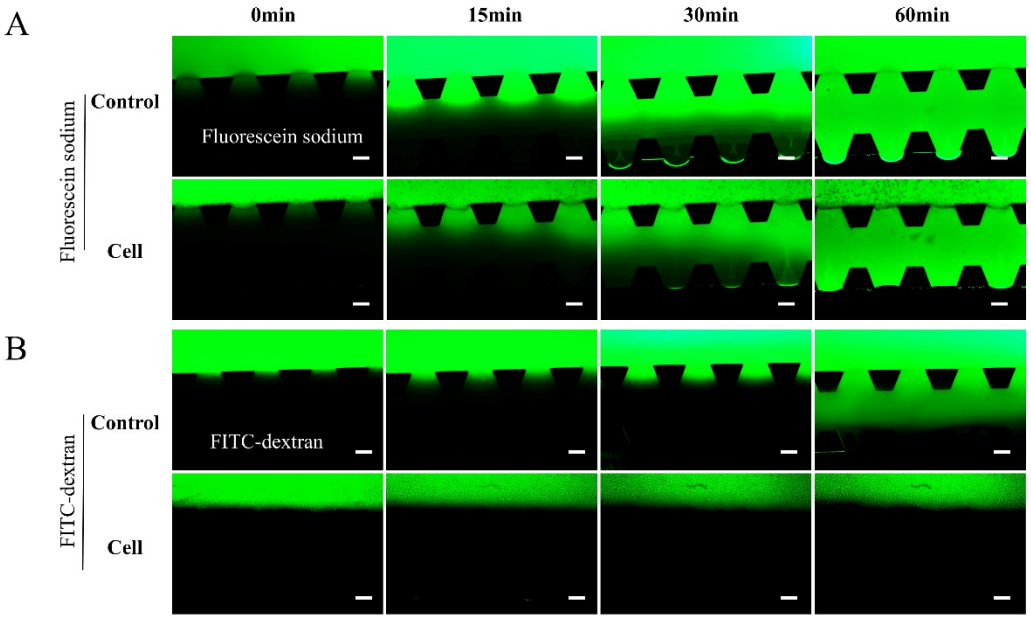

Figure S4. Characterization of barrier permeability in HK-2 cell layer. Scale bar is 100 μm.

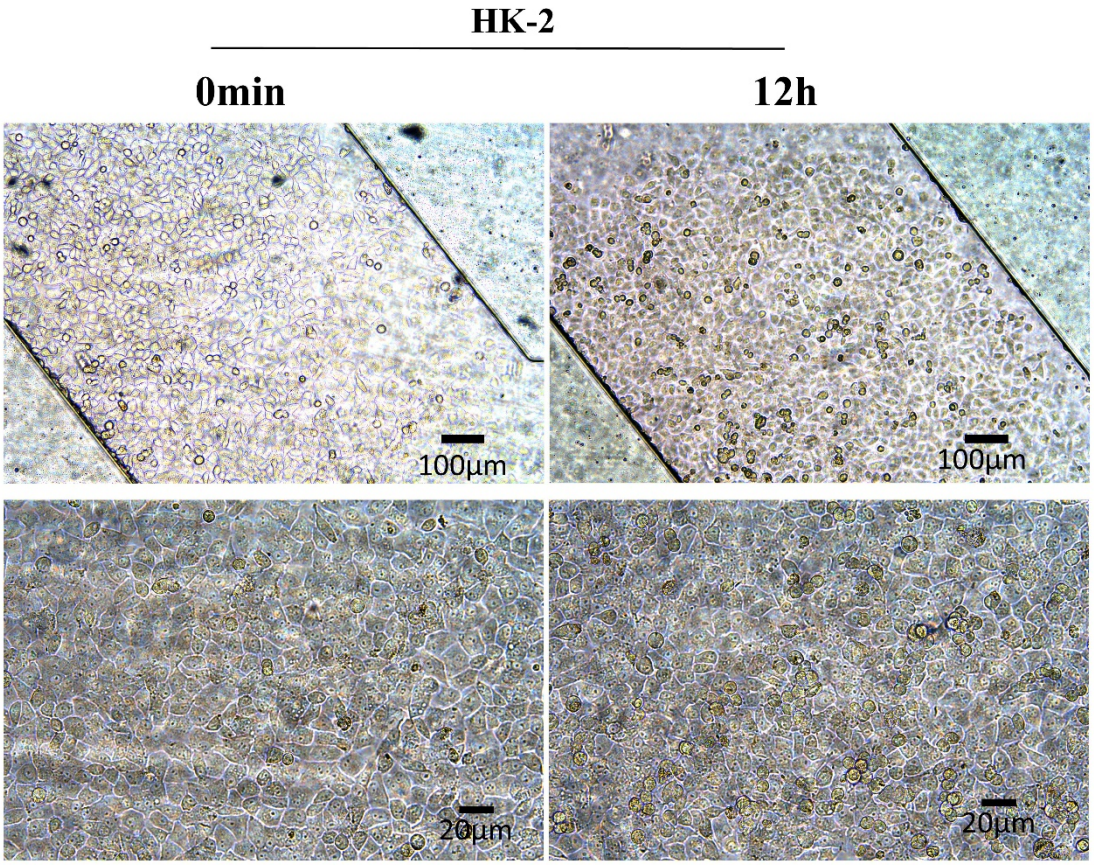

Figure S5. Trends in cell elongation and arrangement under dynamic and static culture conditions.

Figure S6. The amount of UA in EA.hy926 cell medium under dynamic culture. Data are mean ± SEM (n=3).

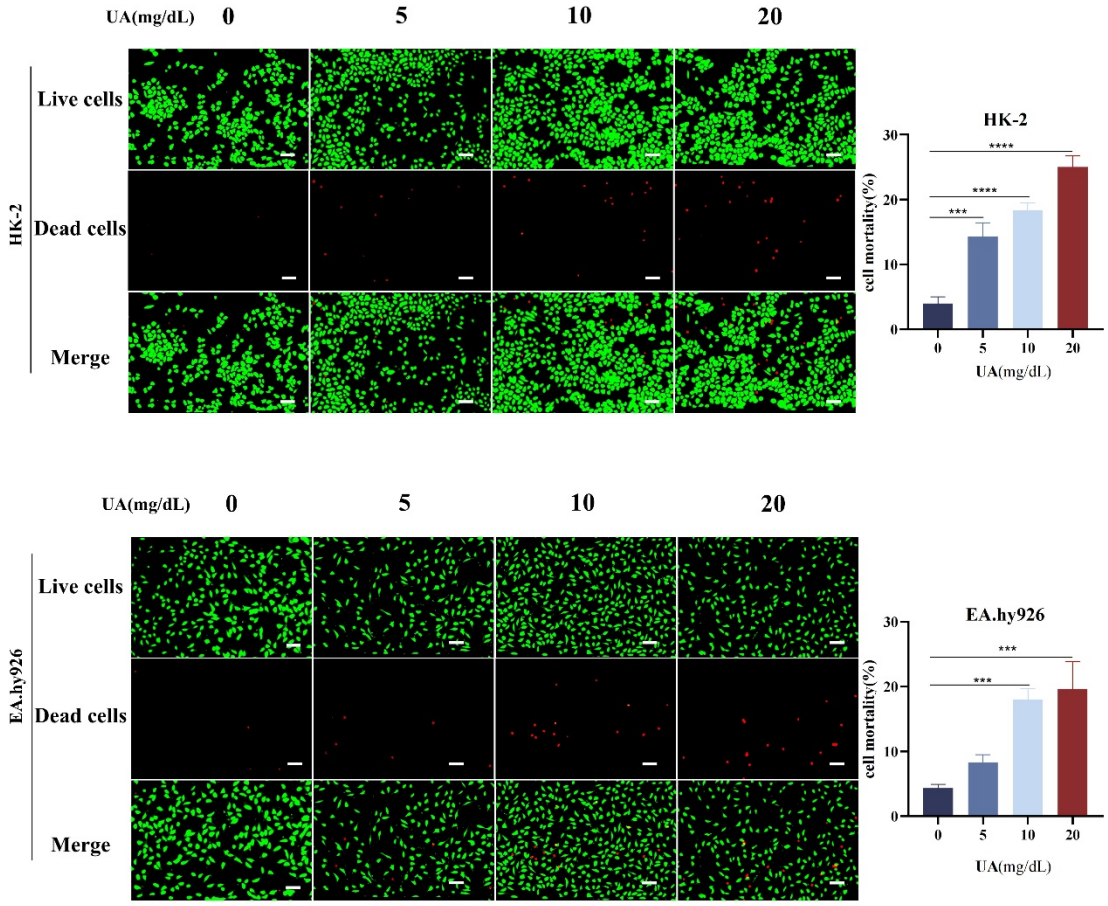

Figure S7. Cell viability was measured by calcein AM/PI within well plates. The data of bars are presented as mean ± SEM (n=3). *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001. Scale bar is 100 μm.

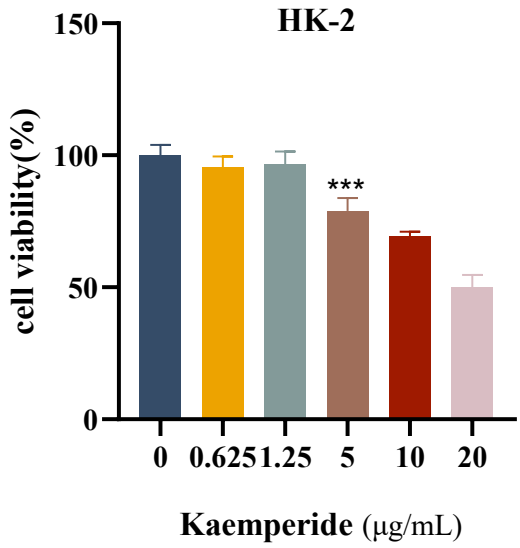

Figure S8. The effect of Kaemperide concentration on the HK-2 cell viability.

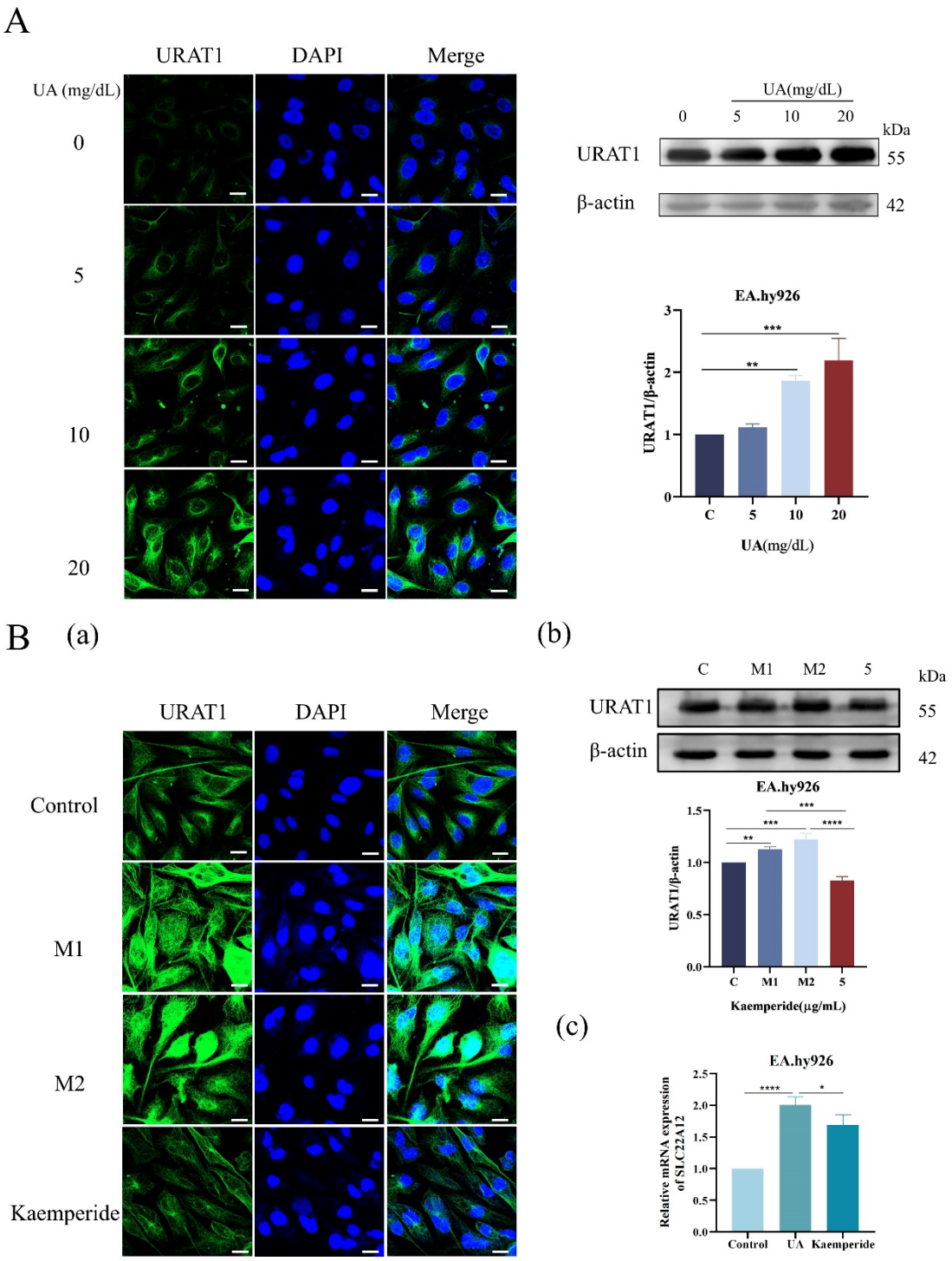

Figure S9. Effect of Kaemperide on the expression of URAT1. (A) The effect of different concentrations of UA on the expression of URAT1 inEA.hy926 cells. (B) The expression of URAT1 in EA.hy926 cells treated with Kaemperide. (a) Immunofluorescence assay was performed to detect the effect of kaemperide on URAT1 expression. (b) Western Blot was

performed to detect the effect of kaemperide on URAT1 expression. (c) RT-qPCR was performed to detect the effect of kaemperide on URAT1 expression. The data of bars are presented as mean ± SEM. *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$; ****, $p<0.0001$. Data are mean ± SEM (n=3). Scale bar is 20 μm.

Table S1. Key target information.

Target	Degree value	Function
ABCG2 (ATP binding cassette subfamily G member 2)	7	Mediating the export of protoporphyrin IX from both mitochondria to cytosol and cytosol to extracellular space, it also functions in the cellular export of heme.
AKR1B1 (Aldo-Keto Reductase Family 1 Member B)	6	Catalyzes the NADPH-dependent reduction of a wide variety of carbonyl-containing compounds to their corresponding alcohols.
MAOA (Monoamine Oxidase A)	5	Catalytic oxidative deamination of biogenic amines and exogenous amines.
PYGL (Glycogen Phosphorylase L)	5	Phosphorylase is an important allosteric enzyme in carbohydrate metabolism.
XDH (Xanthine Dehydrogenase)	4	Key enzyme in purine degradation. Catalyzes the oxidation of hypoxanthine to xanthine.
SLC22A12 (Solute Carrier Family 22 Member 12)	3	Regulates blood urate levels. Mediates saturable urate uptake by facilitating the exchange of urate against organic anions.