

## **Supplementary information**

### **Traction force transmission via bioactive matrix hydrogel promotes epithelial collective migration mediated by integrin**

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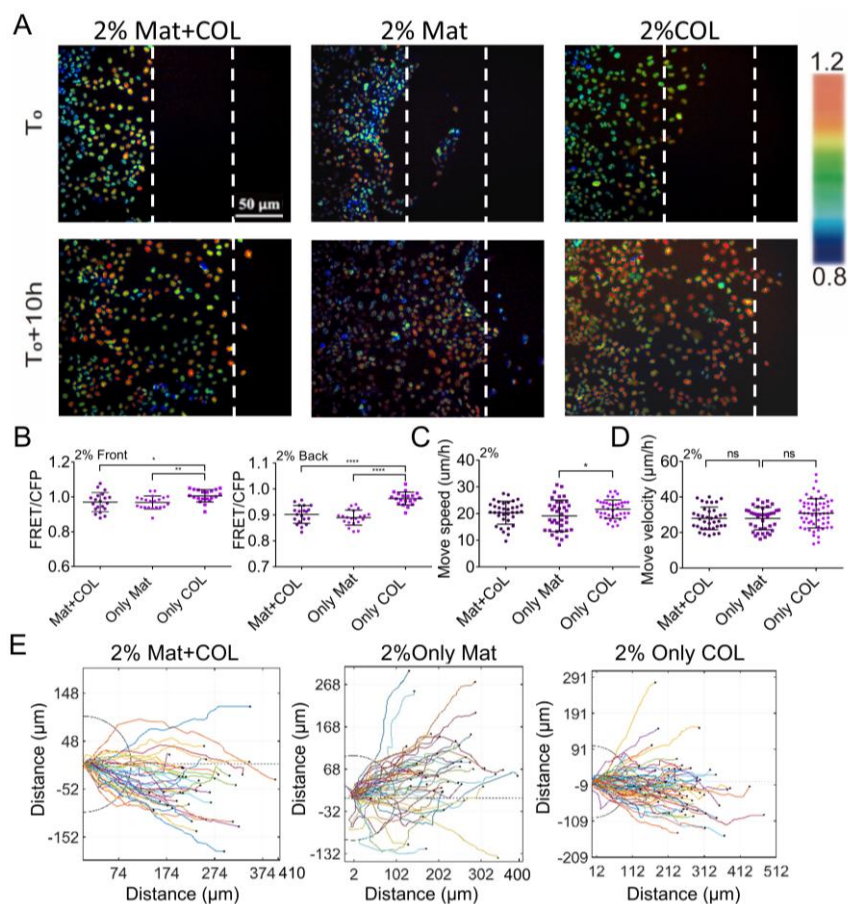
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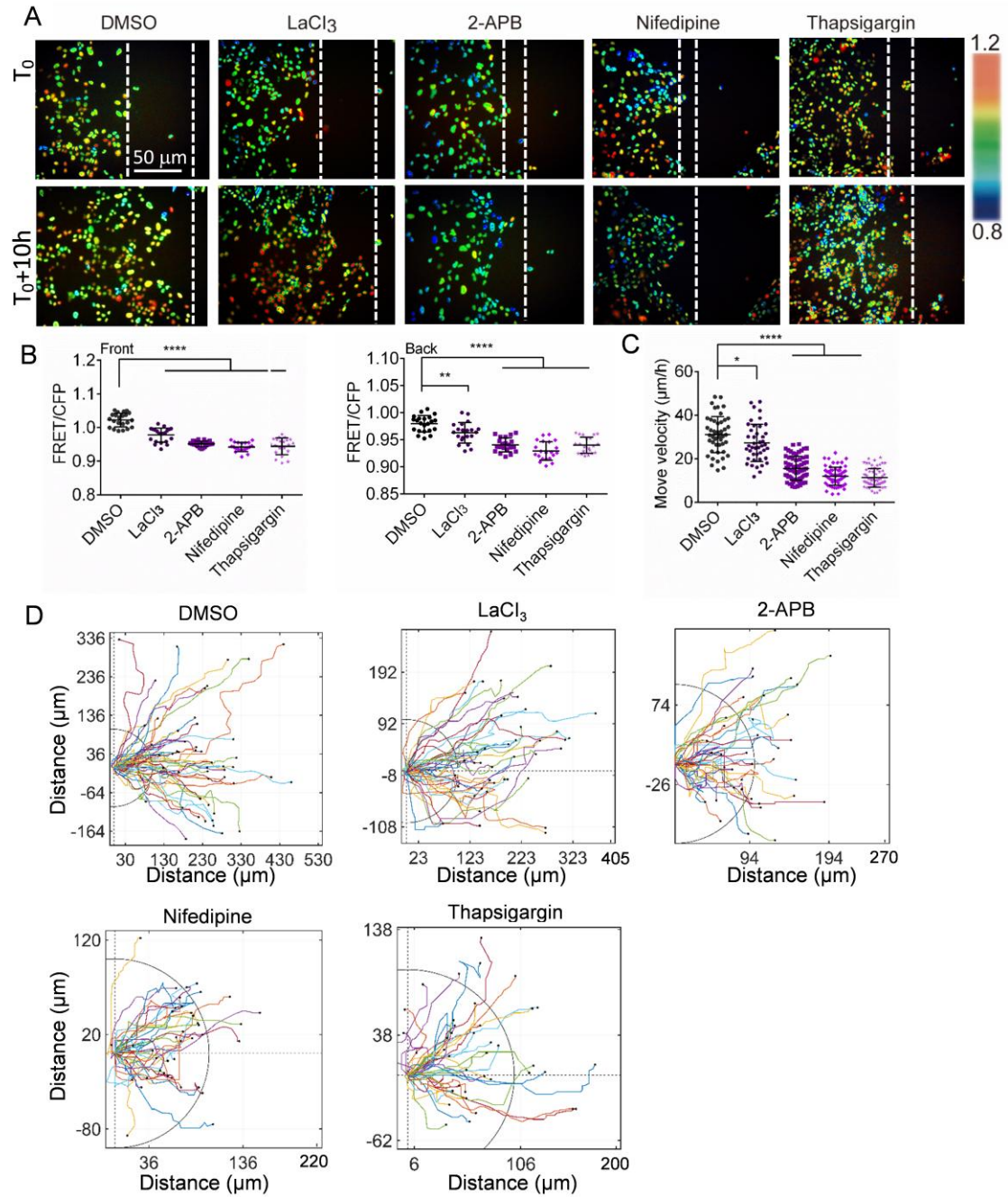
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The Supporting information contains two supplementary figures, and two movies.

## Supplementary figures



**Figure S1. MDCK cell collective migrations on ECM-coated glass surfaces.** Glass-bottom surfaces of confocal dishes were coated with adhesive ECM solution containing 2% Matrigel+collagen, 2% Matrigel only, or 2% collagen, followed by the procedures for MDCK cells seeding and FRET imaging process similar to the hydrogel one. **(A)** ERK FRET (YPet/ECFP) ratiometric images for cell collective migrations under the indicated coating conditions. **(B)** ERK FRET comparisons of the front or rear cell groups on the three types of hydrogel conditions (mean $\pm$ S.D., n=30). **(C, D)** Quantitative comparisons for moving speed (C) or velocity (D) of individual cells at migration front groups ( $\mu m/h$ , mean $\pm$ S.D.) within 10 h. The sample size n=35, 37, 39, respectively. **(E)** Trajectory analysis of individual cells from the migration front groups in 10 h (n=37, 40, 58, respectively). The diameter of the shown trajectory circles is 100  $\mu m$ . In statistical T-test analysis, \*, \*\*, \*\*\*, \*\*\*\* indicate  $P < 0.05$ , 0.01, 0.001, 0.0001 for significant differences, respectively.



**Figure S2. Calcium channels in regulating epithelial cell migration.** MDCK cells were seeded on Mat+COL hydrogel cocultured with DMSO or calcium channel inhibitors. **(A)** Representative ERK FRET images during cell collective migrations with or without the indicated inhibitor (LaCl<sub>3</sub>, 2-APB, Nifedipine, Thapsigargin). **(B)** FRET level comparisons of the front or rear cell groups (mean±S.D., n=30) between control (DMSO) and inhibitor treatments at the 10<sup>th</sup> hour timepoint. **(C)** Quantitative comparisons of cell moving velocities (mean ± S.D.) between control (DMSO) and calcium channel inhibitor treatments. **(D)** Trajectory analysis of individual cells from

the migration front groups in 10 h under the indicated conditions. The sample size  $n = 48, 43, 63, 65, 65$ , respectively. \*, \*\*, \*\*\*, \*\*\*\* indicate  $P < 0.05, 0.01, 0.001, 0.0001$  for significant differences by T-test analysis, respectively.

### **Supplementary movies**

**Movie 1.** ERK FRET imaging of MDCK epithelial collective migrations on the indicated three types of matrix hydrogels in 10 hours. Interval time was 15 min.

**Movie 2.** ERK FRET imaging of MDCK epithelial collective migrations without or with integrin inhibitory AIIB2 antibody ( $2 \mu\text{g/mL}$ ) on 50% Matrigel hydrogel containing 1 mg/ml type I collagen in 10 hours. Interval time was 15 min.