An example of mechanical cell competition

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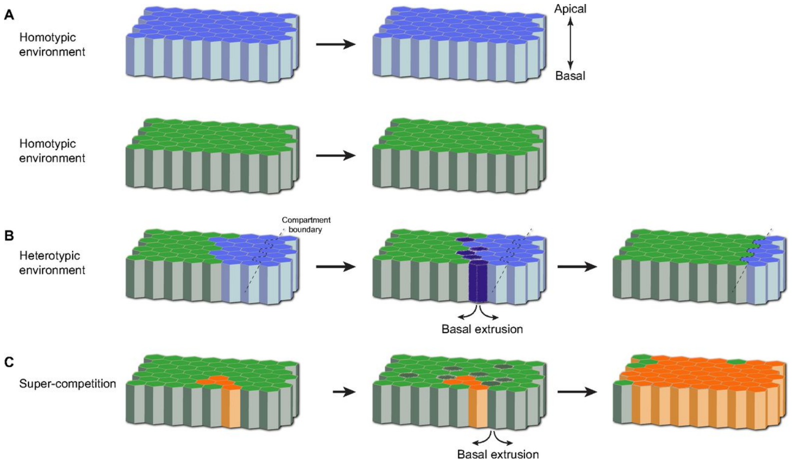
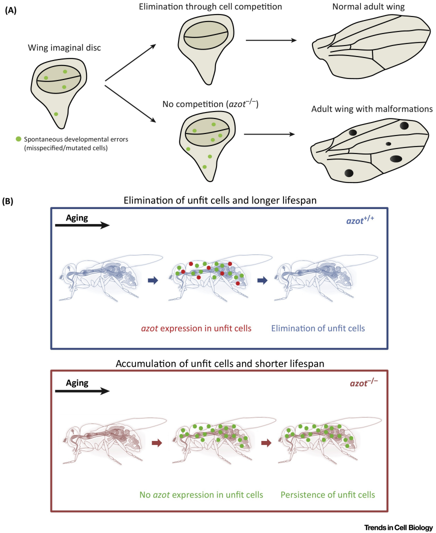
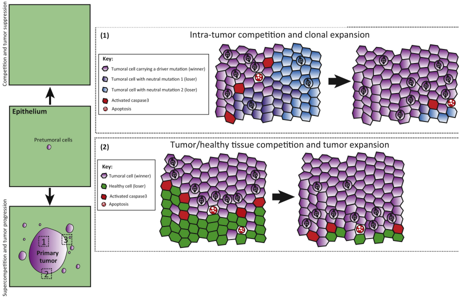
Cell competition: how to eliminate your neighbours



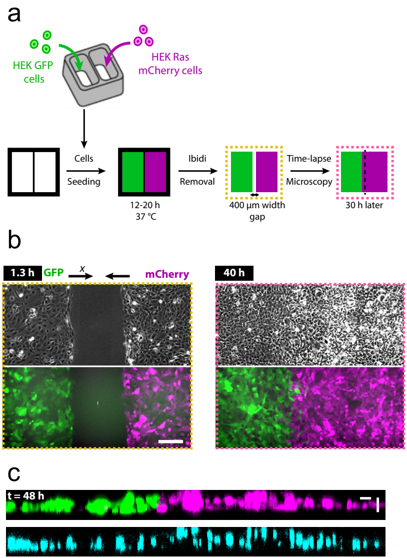
Amoyel *et al.*, Development (2014)

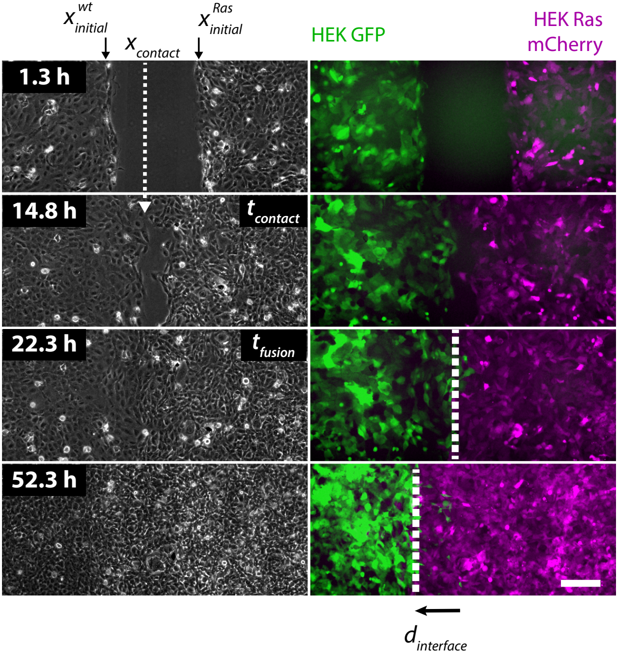




M.M. Merino *et al.*, Trends in Cell Biology (2016)

Human Embryonic Kidney cells – Wild Type *vs.* Ras

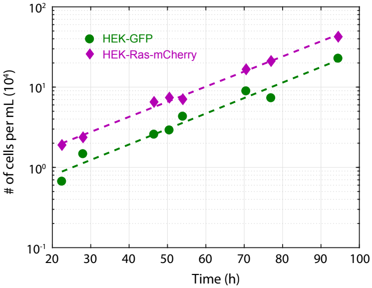




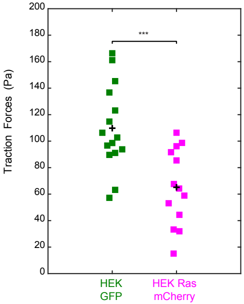
$x^{wt}_{initial}$
$x_{contact}$
$x^{Ras}_{initial}$
HEK GFP
HEK Ras mCherry
1.3 h
14.8 h
$t_{contact}$
22.3 h
t_{fusion}
52.3 h
$d_{interface}$

Experimental data

Same division rate

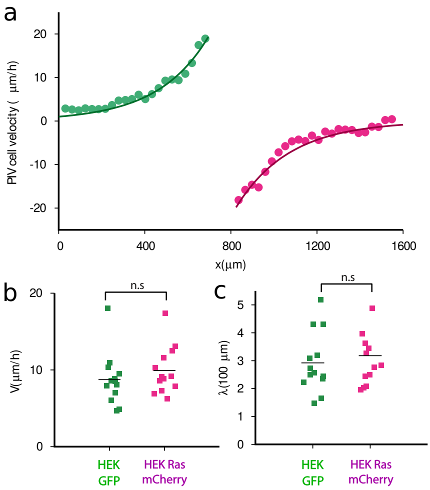


Different traction forces

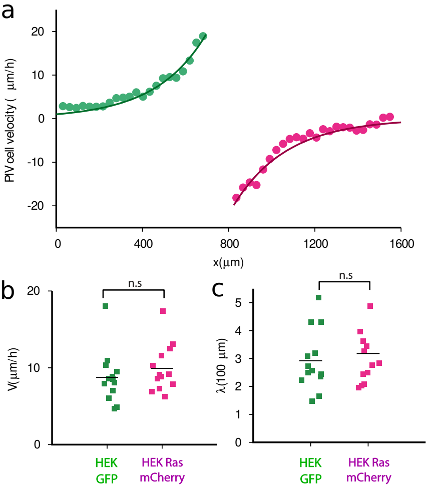


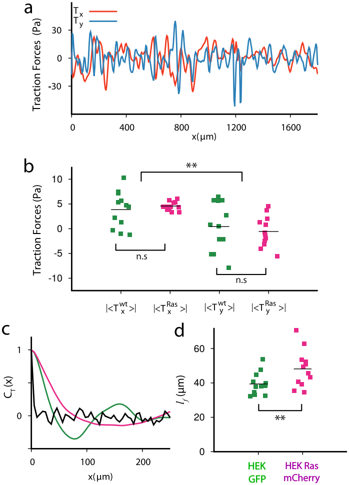
(single cell data)

Tissue scale data

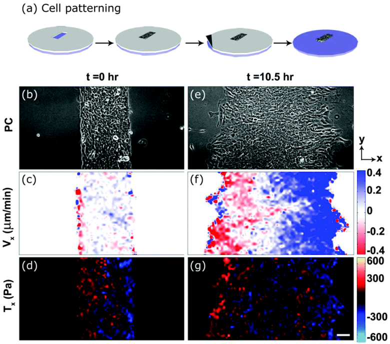


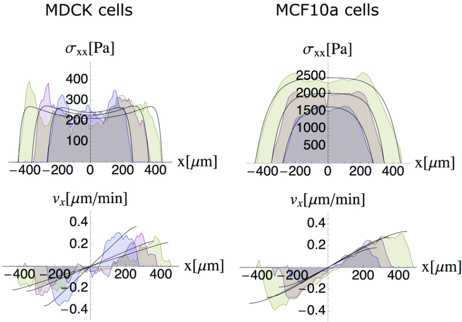
Tissue scale data





Epithelial spreading





C. Blanch-Mercader *et al.*, Soft Matter (2017)

Model (1)

One monolayer

Governing equations

$$\begin{aligned} \sigma &= \eta\, \partial_x v \\ \partial_x \sigma &= \xi v - T_0 p \\ 0 &= p - L_c^2\, \partial_x^2 p \end{aligned}$$

Boundary conditions

$$\begin{aligned} \sigma(x = L(t), t) &= 0 \\ p(x = L(t), t) &= +1 \end{aligned}$$

Hydrodynamic length $L_\eta = \sqrt{\eta/\xi}$

Front velocity $v_{\text{front}} = \frac{T_0 L_c}{\xi(L_c + L_\eta)}$

Model (2)

Two monolayers

Governing equations

$$
\begin{aligned}
\sigma^{l,r} &= \eta^{l,r}\,\partial_x v^{l,r}. \\
\partial_x \sigma^{l,r} &= \xi^{l,r} v^{l,r} - T_0^{l,r} p^{l,r} \\
0 &= p^{l,r} - (L_c^{l,r})^2\,\partial_x^2 p^{l,r}
\end{aligned}
$$

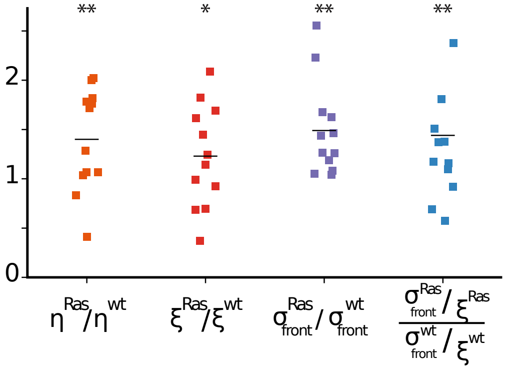
Boundary conditions

$$
\begin{aligned}
\sigma^l(x = L(t), t) &= \sigma^r(x = L(t), t) \\
v^l(x = L(t), t) &= v^r(x = L(t), t) \\
p^l(x = L(t), t) &= 1 \\
p^r(x = L(t), t) &= -1
\end{aligned}
$$

Interface velocity

$$
v_{\text{interface}} = \frac{L_\eta^r\,\eta^l\,v_{\text{front}}^l - L_\eta^l\,\eta^r\,v_{\text{front}}^r}{L_\eta^l\,\eta^r + L_\eta^r\,\eta^l}
$$

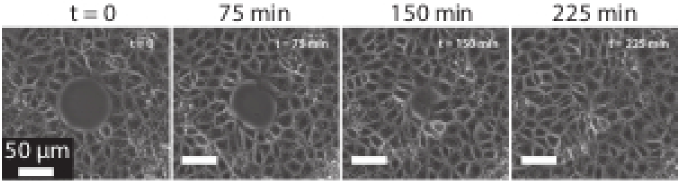
Model parameters

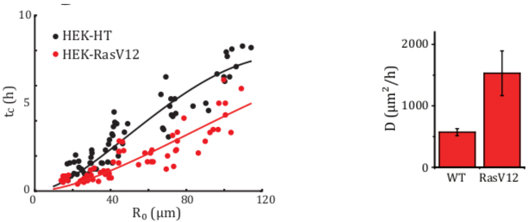


$$v_{\text{interface}} = \frac{\sigma^l_{\text{front}} - \sigma^r_{\text{front}}}{\eta^r/L^r_\eta + \eta^l/L^l_\eta} \quad \text{where} \quad \sigma_{\text{front}} = \frac{\eta\, v_{\text{front}}}{L_\eta} = \frac{T_0 L_c L_\eta}{L_c + L_\eta}$$

Consistent: $\sigma^{\text{Ras}}_{\text{front}} > \sigma^{\text{wt}}_{\text{front}}$

Wound healing assay: HEK wt and HEK Ras





Consistent: $\sigma_{\text{front}}^{\text{Ras}}/\xi^{\text{Ras}} > \sigma_{\text{front}}^{\text{wt}}/\xi^{\text{wt}}$ $(D = \sigma_{\text{front}}/\xi)$

O. Cochet-Escartin, J. Ranft *et al.*, Biophysical J. (2014)

Conclusion

- Good agreement with a model of the cell monolayers as compressible and active materials with different material parameters
- Collective stresses drive competition between monolayers of normal and Ras-transformed cells
- Velocity measurements yield (model-dependent) estimates of parameter ratios

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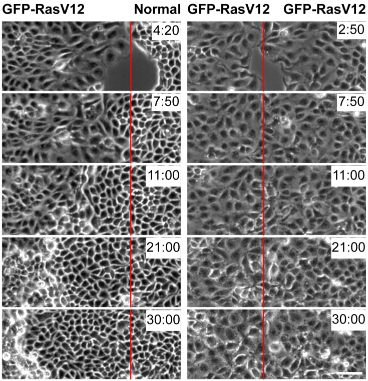
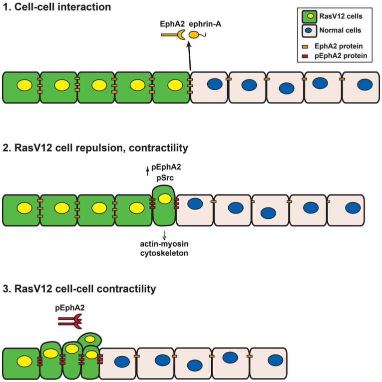
Some open questions

- How to relate single data traction forces and collective traction forces?
- How general are our results?

S. Moitrier, C. Blanch-Mercader *et al.*, Soft Matter (2019)

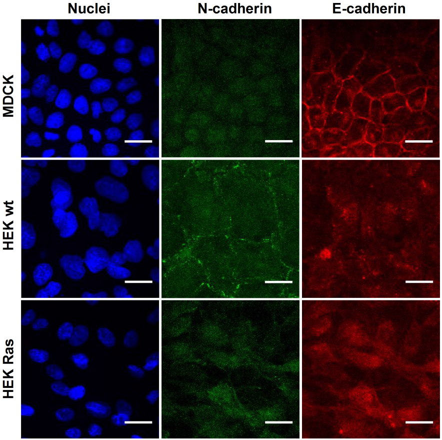
Madin-Darby Canine Kidney cells: Wild Type *vs.* Ras





S. Pozarinski *et al.*, Current Biology (2016)

Cadherin localization



Thank you!