

Cell interactions with protein micropatterns: a way to unravel cell adhesion dynamics and signaling



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Mechanical constraint  $\Rightarrow$  Control of cell architecture

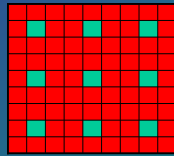
Mechanical constraint  $\Rightarrow$  Control of cell physiology

Stem cell fate  
Cell death  
Proliferation  
Differentiation

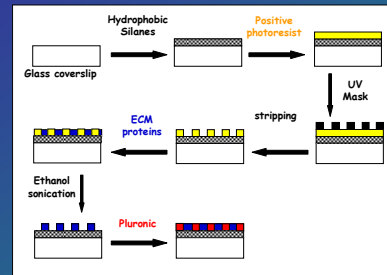
Microstructuration of extracellular matrix

Adhesive square of  $4 \times 4 \mu\text{m}$  (made of fibronectin, vitronectin...)

anti adhesive surfaces (Pluronic)

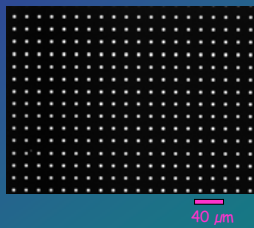


Micro fabrication based on "Lift off" technology  
And non specific hydrophobic interactions

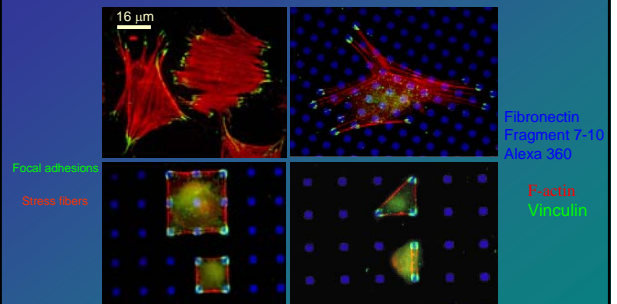


Characterization of the surfaces

Square Plots  $4 \times 4 \mu\text{m}$  distance between patches: 4 to  $18 \mu\text{m}$



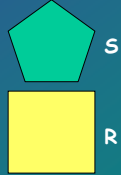
Simplification of cell architecture on micro-patterned protein arrays



Quantitative cell shape analyses on structured surface

Cell compactness coefficient:

$$C = S/R$$



$$C = 0.78$$



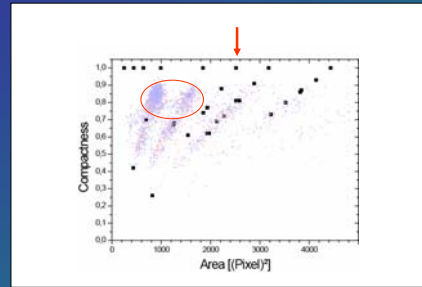
$$C = 0.5$$



$$C = 1$$

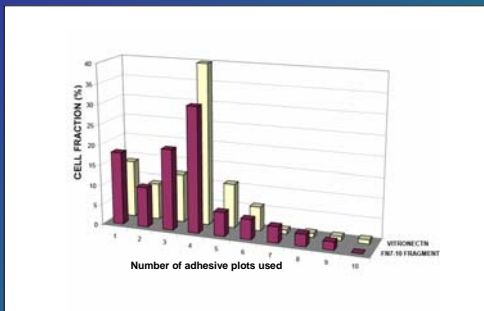


Preferential cell distribution

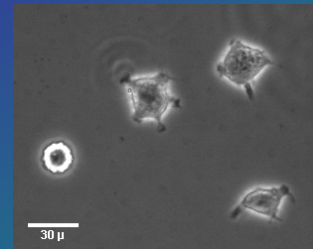


Black squares: Diffusion Limited Agregation model

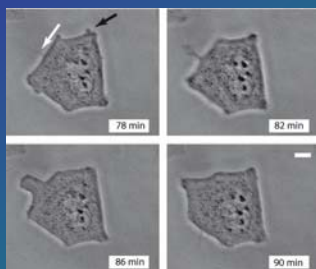
Preferential rectangular shapes do not depend on extracellular matrix protein



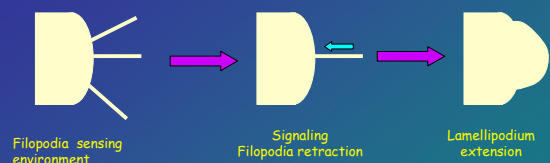
Video microscopy of cell spreading on structured matrix



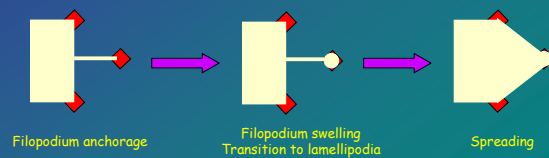
Video microscopy of cell spreading on structured matrix



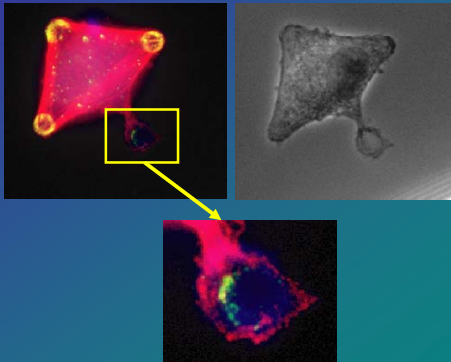
Classical Model



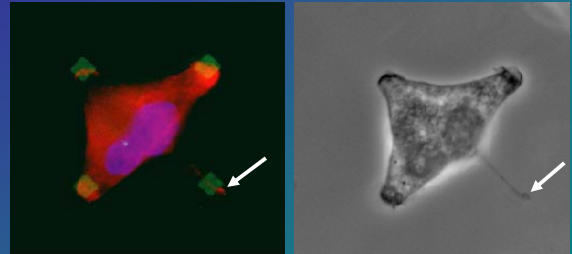
Observations on structured matrix



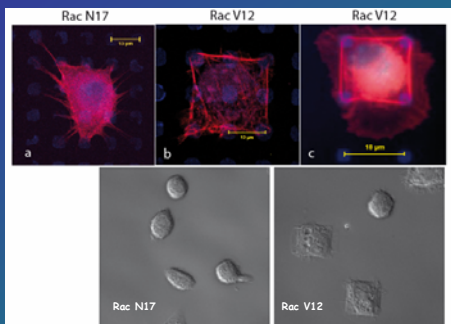
### F-actin Localization



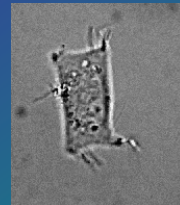
### Rac-1 Localization



### Filopodia transition depends on Rac1 signalling



### Why spreading does not occurs at the angles?



### Spreading on homogenous support

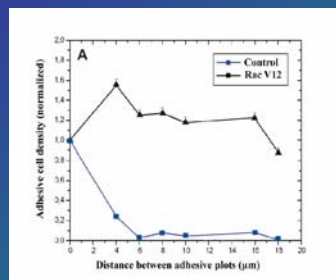


Swelling from filopodium basis

#### Hypothesis :

Integrins engagement is required for filopodia to lamellipodia transition

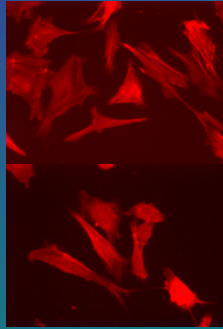
### Spreading on patterned anti integrin antibodies



Patterned surfaces and cellular diagnosis

MEF *Icap* +/+

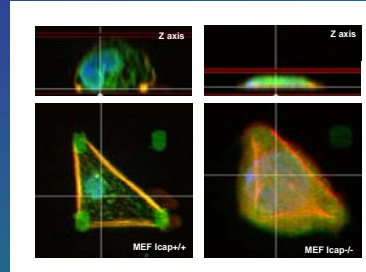
MEF *Icap* -/-



Patterned surfaces and cellular diagnosis

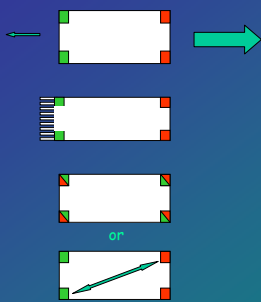
MEF *Icap* +/+

MEF *Icap* -/-



Adhesive microarrays with multiple proteins

What for?

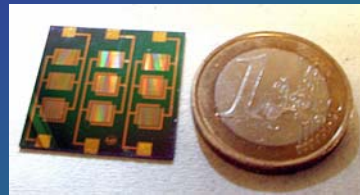


Unidirectional movement

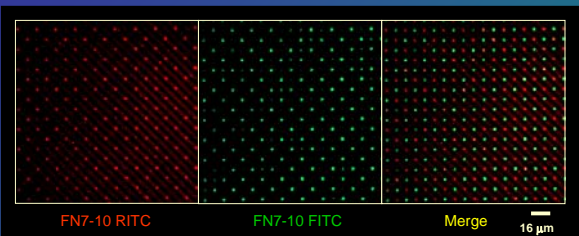
Polarization, differentiation

Cross talk between receptors  
Integrins/syndecans  
Integrins/cadherins  
Integrins/growth factors

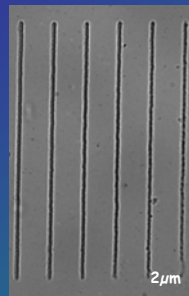
Making a microarray with two proteins



Preliminary results of micro-patterning



Alternative strategies (suitable for small areas)  
Multiphoton excited polymerization



Suitable for 3D patterning





CRTBT UPR 5001

- Hervé Guillou



LEDAC UMR 5538

- Marc Block
- Adeline Depraz  
Depland
- Emmanuelle Planus



CEA LETI

- Frédérique Revol-  
Cavallier
- Patrice Caillat