



*Add a new dimension*

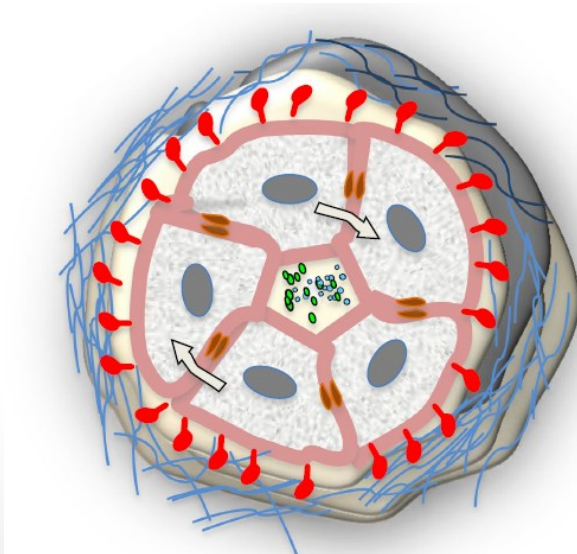
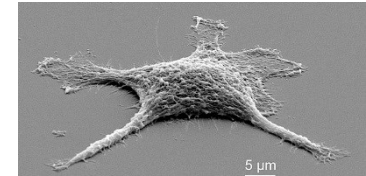
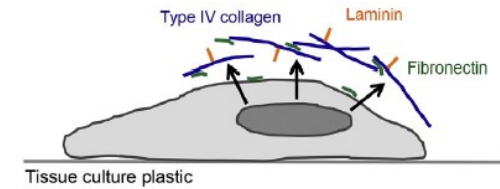
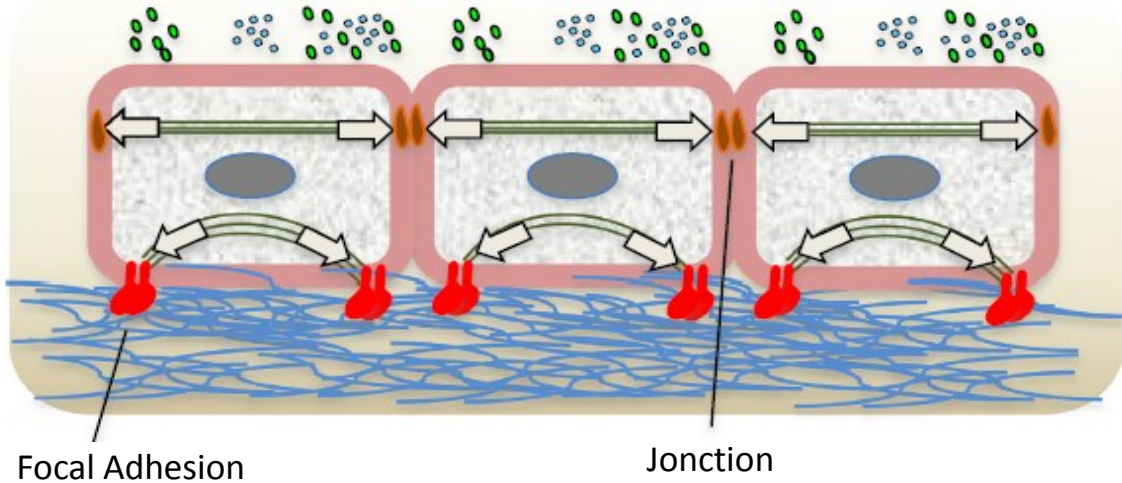
Comparison of a conventional 2D culture of colorectal cancer cells to a new physiological model : Biomimesys®

Elise Demange

Workshop 3D model and applications in oncology

June 26, 2014

# 2D vs 3D

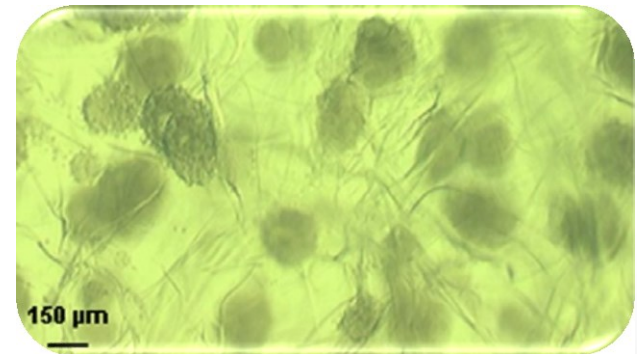
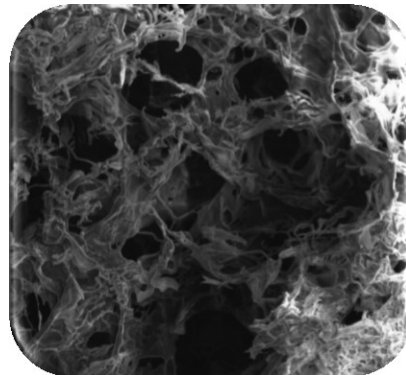
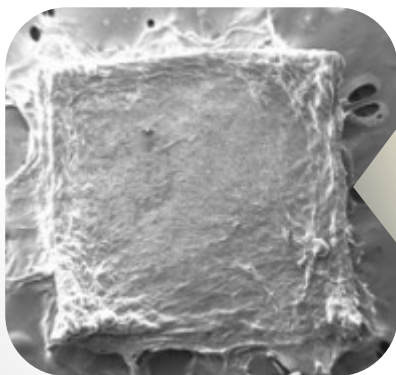
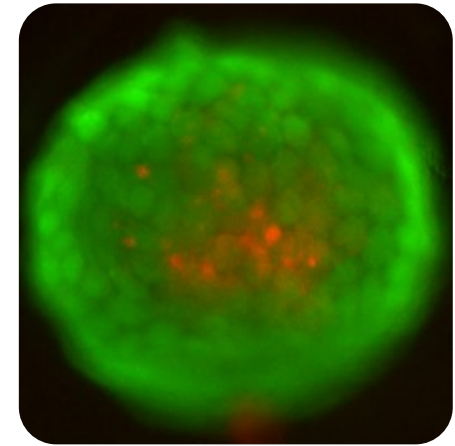


Cell-matrix interactions  
cell-cell adhesion  
Cellular signaling, gene and protein  
expression...

# Biomimesys®



Physiological and  
natural  
biodegradable  
scaffold :  
Hyaluronic Acid



David *et al.*, 2004  
David *et al.*, 2008  
Coquerel *et al.*, 2009  
Demange *et al.*, 2012  
Kassim *et al.*, under submission

# Biomimesys® : Application

➔ Tools for :

**Drug discovery (drug screening)**

**Cell based assay (toxicology)**

**Mechanistic studies (Pathways & gene activation)**

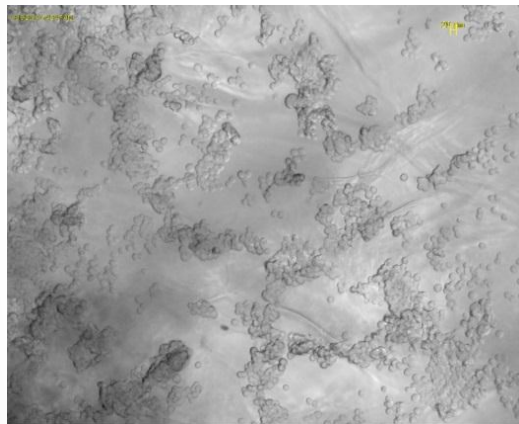
**Personalized medicine**

**More than 20 cell lines tested**

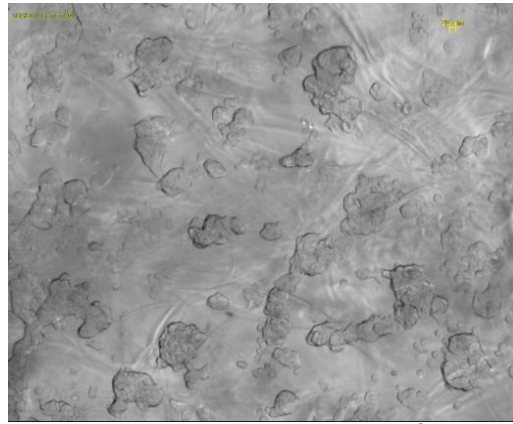
- |   |                                   |   |                                       |
|---|-----------------------------------|---|---------------------------------------|
| ✓ | <b>hepatoma</b>                   | ✓ | <b>metastatic breast cancer</b>       |
| ✓ | <b>human glioma or rat glioma</b> | ✓ | <b>glioblastoma</b>                   |
| ✓ | <b>prostate cancer</b>            | ✓ | <b>pancreatic cancer</b>              |
| ✓ | <b>colorectal cancer</b>          |   |                                       |
| ✓ | <b>lung cancer</b>                | ✓ | <b>human hematopoietic stem cells</b> |
| ✓ | <b>osteosarcoma</b>               |   |                                       |

Colorectal cancer cells

# Spheroid formation and proliferation analysis 1/2



15 min

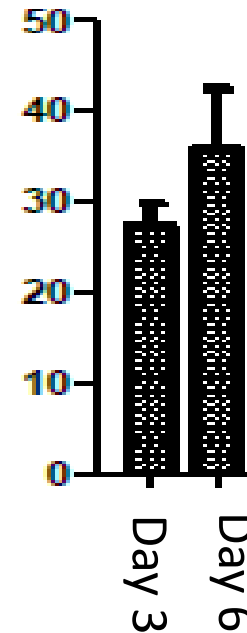


3 hrs

HT29 cells migrate inside Biomimesys®, aggregate and form Spheroid after 3hrs

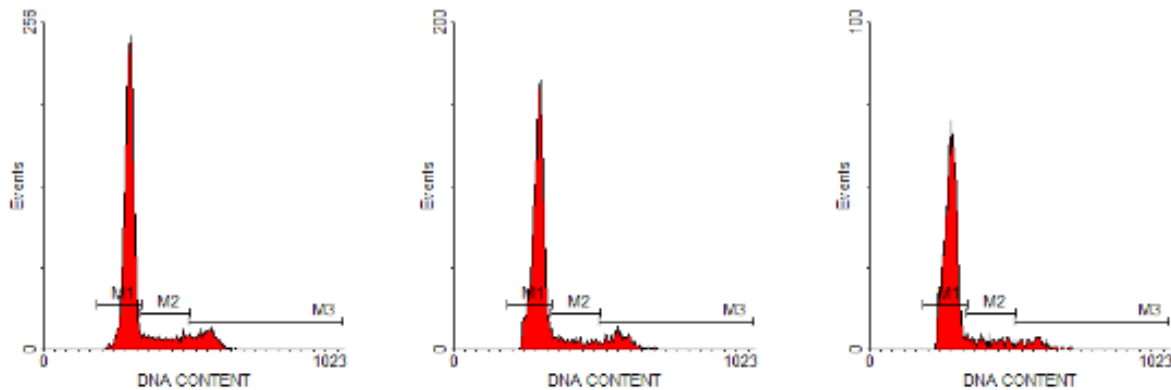
➔ **Biomimesys® is transparent**  
**Time-lapse microscopy**

Mean spheroid diameter ( $\mu\text{m}$ )

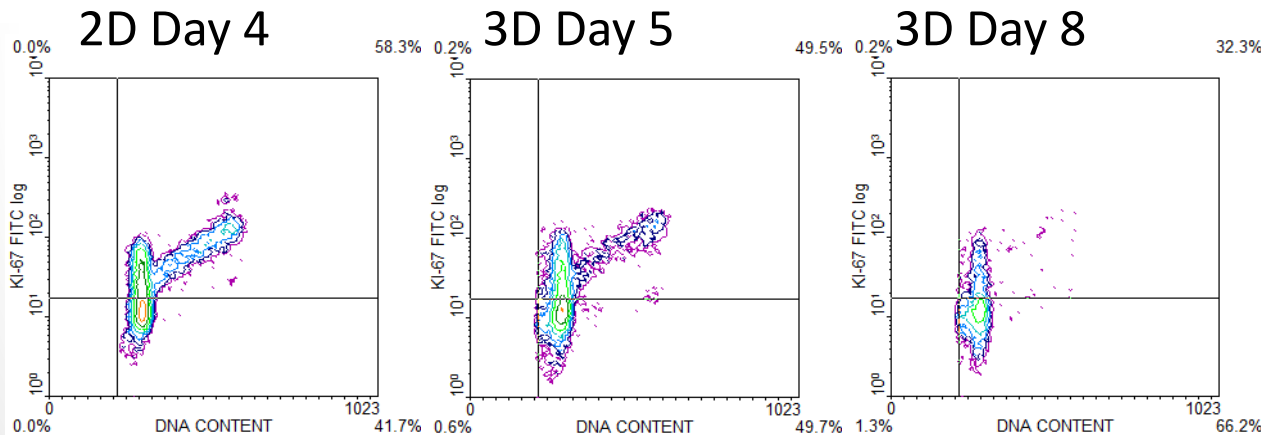


HT29 Spheroid reach maximum size 35 $\mu\text{m}$  after 6 days of culture

# Spheroid formation and proliferation analysis 2/2



Biomimesys® easy  
cell recovery  
Flow cytometry



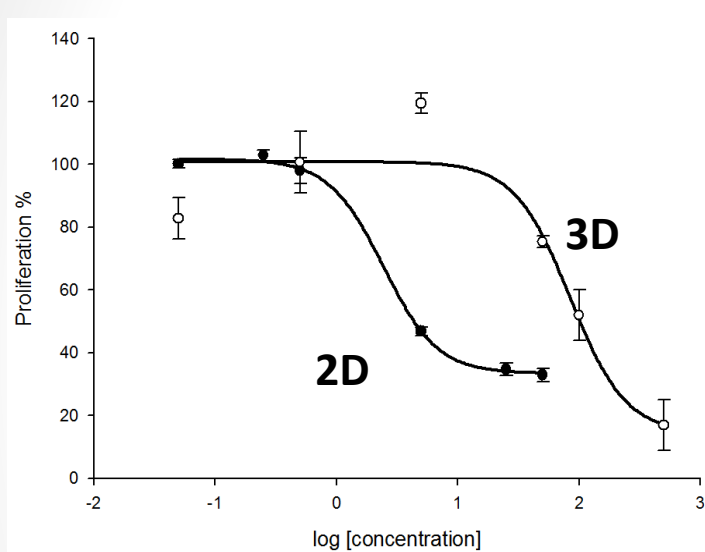
After 5 & 8 days, cells  
in 3D reached max  
spheroid size and  
entered quiescent  
phase compared to  
2D cell culture

➔ 3D cell culture better mimics *in vivo* model

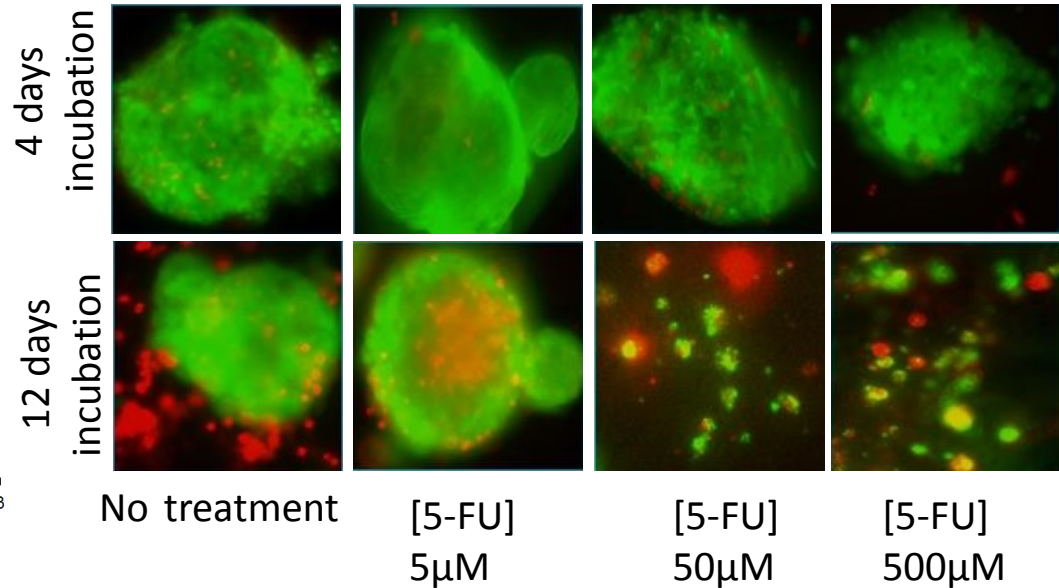


# Drug discovery

## IC50 on DLD-1 using 5-FU



## DLD-1 viability using 5-FU



More drug is needed in 3D cell culture to kill cancer cell

$$\text{IC}_{50_{2D}} = 4,32 \mu\text{M} \quad \text{IC}_{50_{3D}} = 101,7 \mu\text{M}$$

**x 23,5**

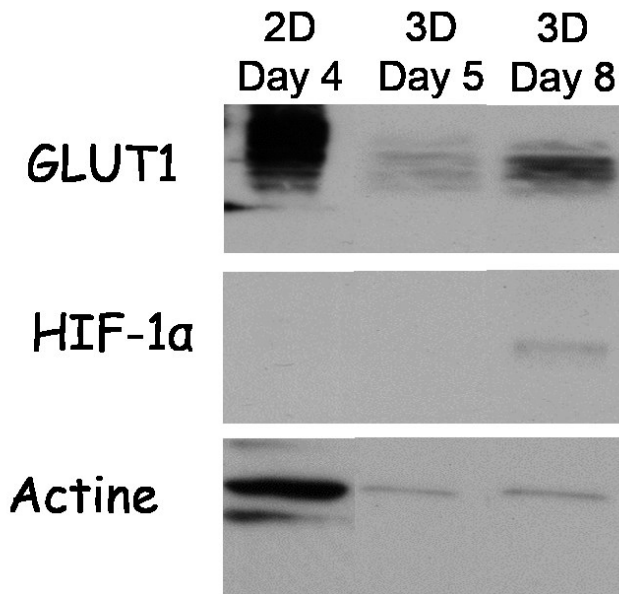
Chemotherapeutic treatment influences 3D spheroid growth and structure

In Red : necrotic cells, In green : live cells

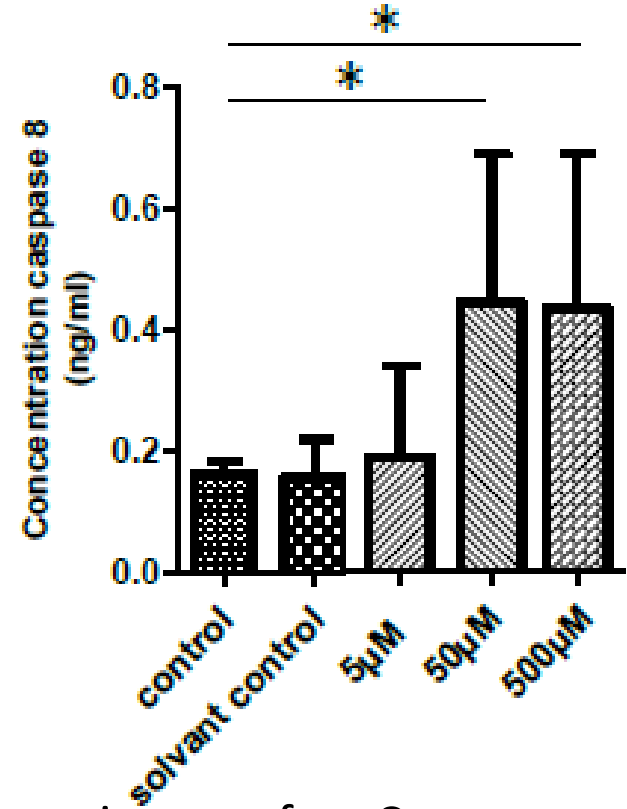
➔ 3D cell culture is a predictive model for drug discovery application



# Pathway analysis



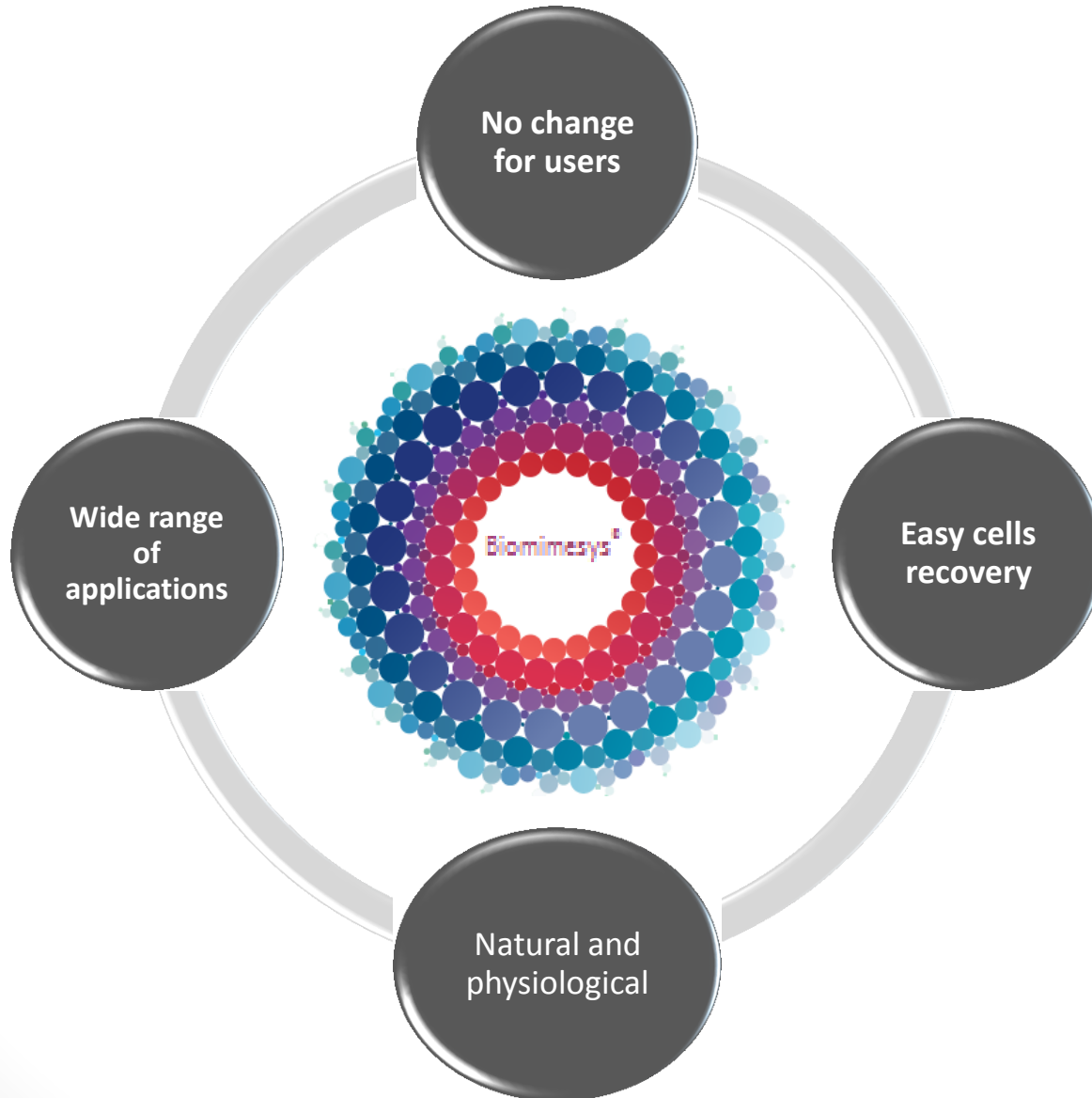
Increased level of HIF-1 $\alpha$  and Glut-1 correlated with spheroid formation and hypoxia increase with HT29 cells culture.



Concentration of Caspase 8 significantly increased at 50 $\mu$ M of 5-FU compared to the control (\*=P<0.05) which correlate with the spheroid dissociation observed during HT29 culture

➔ 3D cell culture is closer to in vivo metabolism

# Benefits for the use of Biomimesys



✓ welcome experts to test our scaffolds

If you are interested please contact us :

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[agathe.devaux@celenys.com](mailto:agathe.devaux@celenys.com)

# Thanks for your attention

## Questions ?!

<http://www.celenys.com>



Catégorie émergence2012  
Catégorie Créa / Dev 2013

