CELENYS

Bring a new dimension

Elrig DD – 2nd September 2015

Agathe Devaux
Business Development Director

Good bye flat biology

nature

21 August 2003 Volume 424 Issue no 6951

Goodbye, flat biology?

Seductive highe

When the assistant lished i bacteria on a base anteed his own in microbiology — been unthinkable fundamental labo

But biologists three dimensions have been stunne behave, which is m Cancer biologists malignant and no mental biologists

NATURE | VOL 424 | 21 A

REVIEWS

Drug Discovery Today • Volume 18, Numbers 5/6 • March 2013

ELSEVIER

Reviews • GENE TO SCREEN

Thr link

Susan

School of Ph

Cells, gr effective screenin frequent a drug. (example naturall cancer d each me

The need preclinica

The design follow a similar trend of progression. Typically a potentially dr gable target is identified and, often with the aid of *in silico* mod ling, lead compounds are designed, developed and optimised act on this target. Preclinical testing is then performed w compound libraries to establish which members of the libr exhibit efficacy towards the target in question. Preclinical testi

Published in final edited form as:

Nat Med. 2010 December ; 16(12): 1450–1455. doi:10.1038/nm.2265.

Invasive 3-Dimensional Organotypic Neoplasia from Multiple Normal Human Epithelia

Todd W. Ridky, **Jennifer M. Chow**, **David J. Wong**, and **Paul A. Khavari**+

Programs in E

Abstract

Refined can therapeutics genetic path esophagus, environmen engineered epithelial in malignancy Oncogenic

Advanced Drug Delivery Reviews 63 (2011) vi

Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/addr

ELSEVIER

Preface

3D — A new dimension of in vitro research ☆

Cell culture is prone to artifacts. Cells live — and as any living being, they react to survive. Survival of the most adaptable one: a principle well known in the evolution of organisms holds true also for cell populations under the selection pressure of culture conditions.

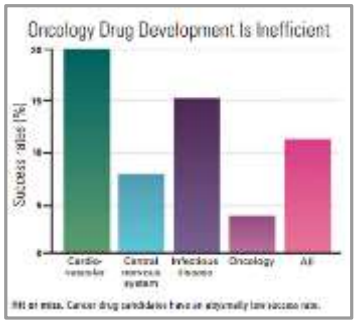
The closer the cellular environment mimics the physiological situation, the less cells need to move away from tissue-type differentiation. And we have first examples that show organo-typic cultures to provide more relevant results. They might help us to make better predictions of the organism's response to treatment, disease agents and chemical ex-

only emerging. We are left with time windows between establishing the 3D culture and critical loss of differentiation. Adding the fourth dimension, time, to make long-term exposures and long-term reactions of our tissue equivalents possible is the next challenge.

There is more to do in order to make a 3D culture organo-typic. Perfusion can make culture more homeostatic, if we are not recirculating the culture media. Each medium change is the most drastic change of environment for a cell that we can imagine. In an instance, all waste is gone, and nutrients are replenished. To adapt, cells need to stay flexible.

Problem solving

- High attrition rate

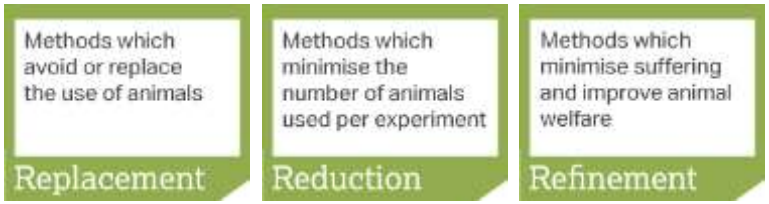


Science 338:29 (2012)

« Almost 90% of the failures accross all therapeutics areas were attributable to **lack of efficacy** (66%) or **safety issues** »

Nature Review Drug Discovery (2011) 10:87

- Reduce use of animals



→ **Need for predictive *in vitro* models**

BIOMIMESYS®

- CELENYS has developed innovative scaffolds for 3D cell culture to better mimic tissue microenvironment

- Low attachment 96-well plate format
- Quality controlled production

- Bar coded plates
- For research use only

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BIOMIMESYS® 3 key features

1. NATURAL & PHYSIOLOGIC

2. READY-TO-USE

3. COMPATIBLE ANALYTICAL TECHNOLOGIES

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BIOMIMESYS®

3 key features

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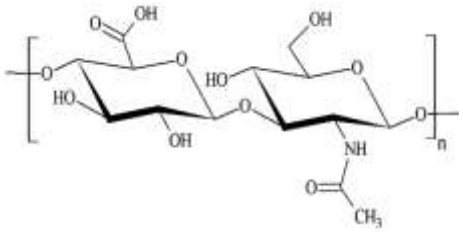

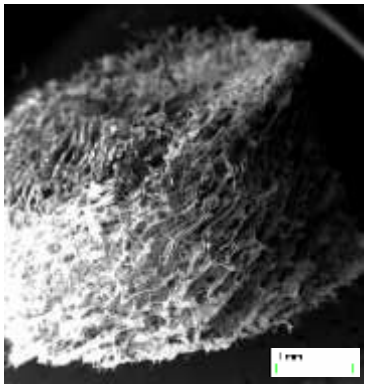

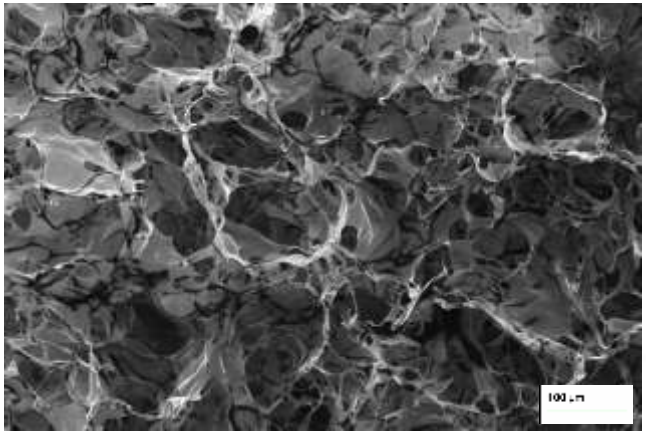

HYALURONIC ACID SCAFFOLD

PHYSICOCHEMICAL FEATURES

- Porosity: 150-200 µm
- Young's modulus: E = 0.5 ± 0.05 KPa
- Swelling ratio:75 ±10 g/g

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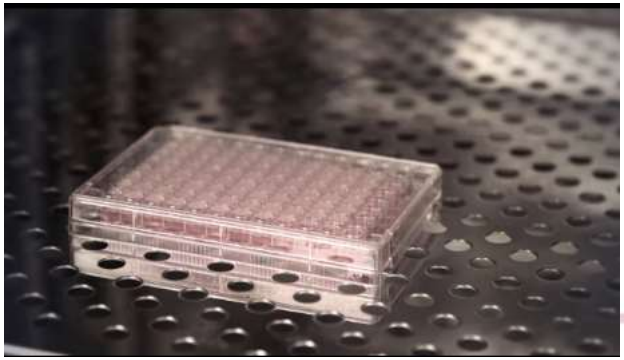
BIOMIMESYS® 3 key features

1. NATURAL & PHYSIOLOGIC

2. READY-TO-USE

3. COMPATIBLE ANALYTICAL TECHNOLOGIES



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BIOMIMESYS® 3 key features

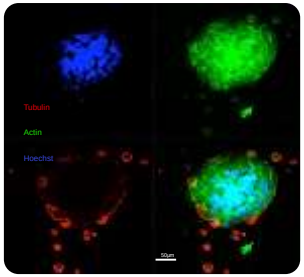
1. NATURAL & PHYSIOLOGIC

2. READY-TO-USE

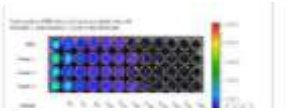
3. COMPATIBLE ANALYTICAL TECHNOLOGIES

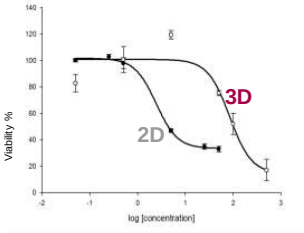
TRANSPARENT

- Microscopy
- Immunofluorescence



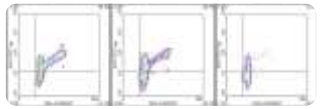
- Plate Reader (OD, fluorescence)





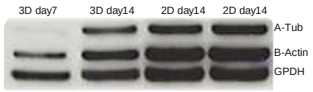
BIODEGRADABLE

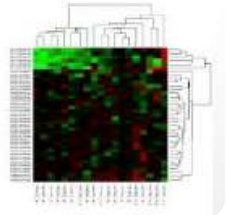
- Flow cytometry



POROUS

- PCRs
- Western-Blot
- ELISA





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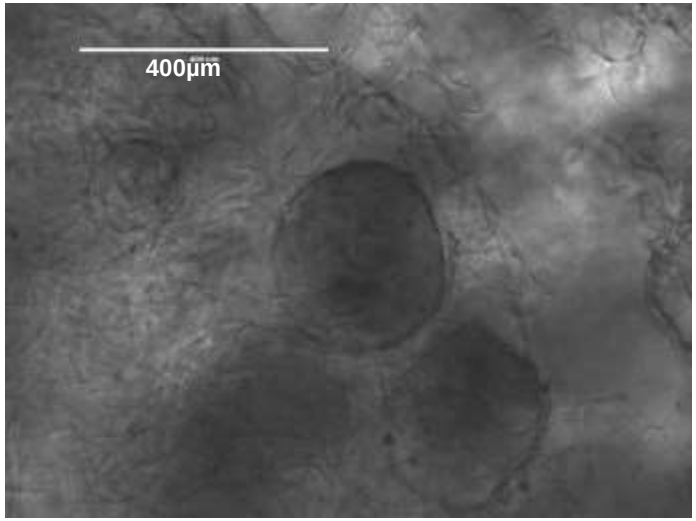
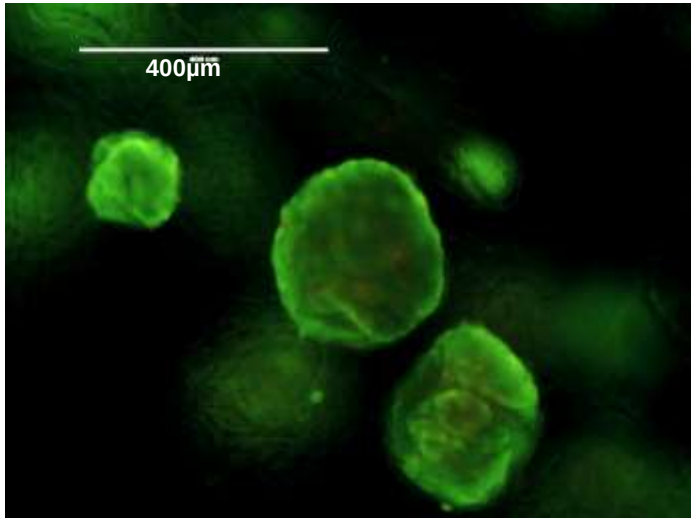
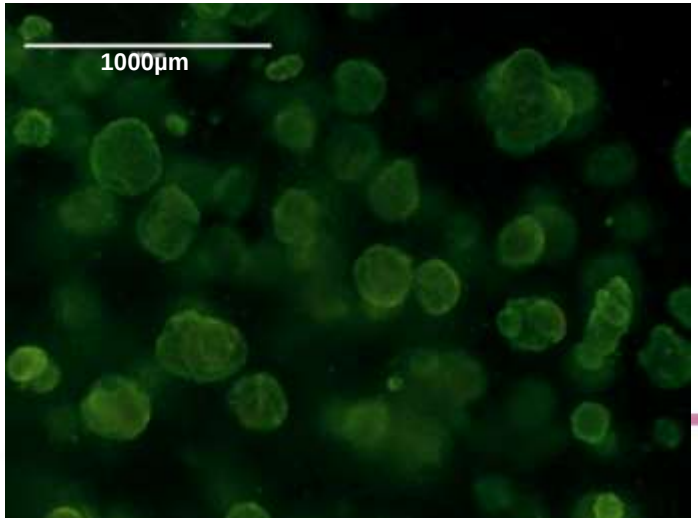
Cell viability



Brightfield microscopy



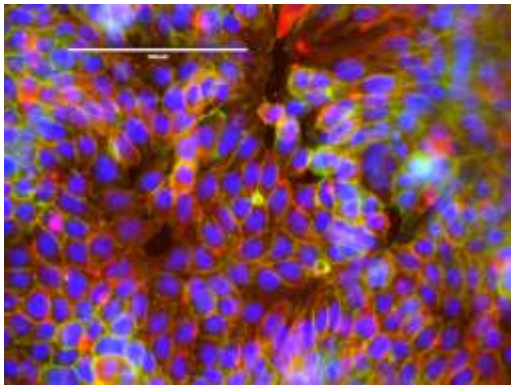


Confocal microscopy

HT29 day28 live/dead kit

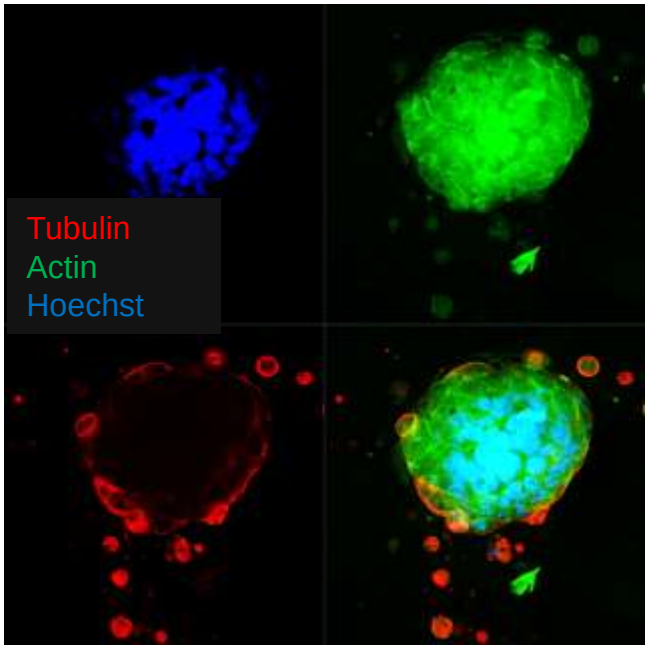
Cytoskeleton organisation

2D

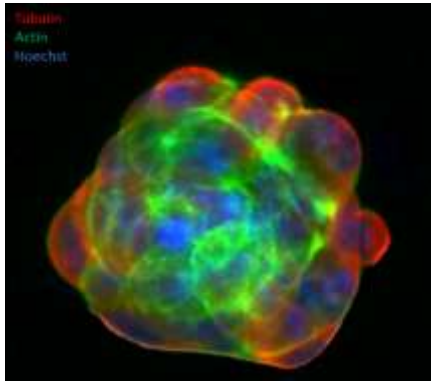


HT-29 day9

3D



HT-29 spheroid, day12

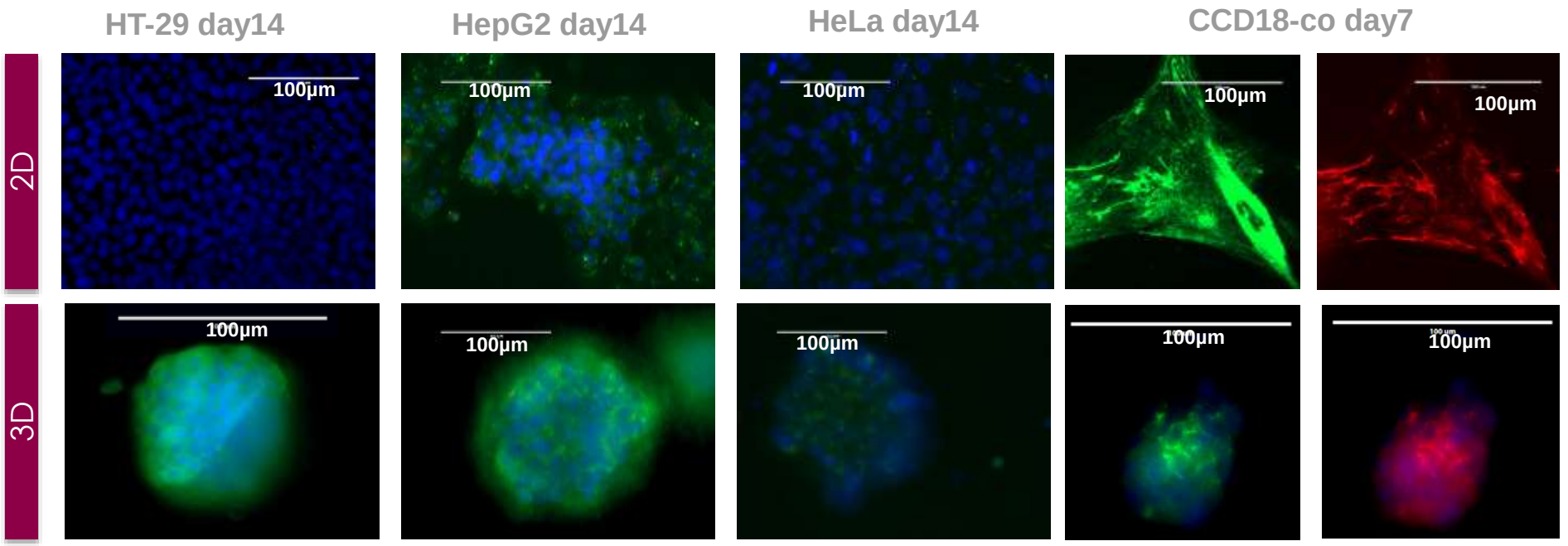


PANC-1 spheroid, day12

- Tubulin expression is localised in 3D at spheroid periphery

Microscopy - IF

ECM secretion

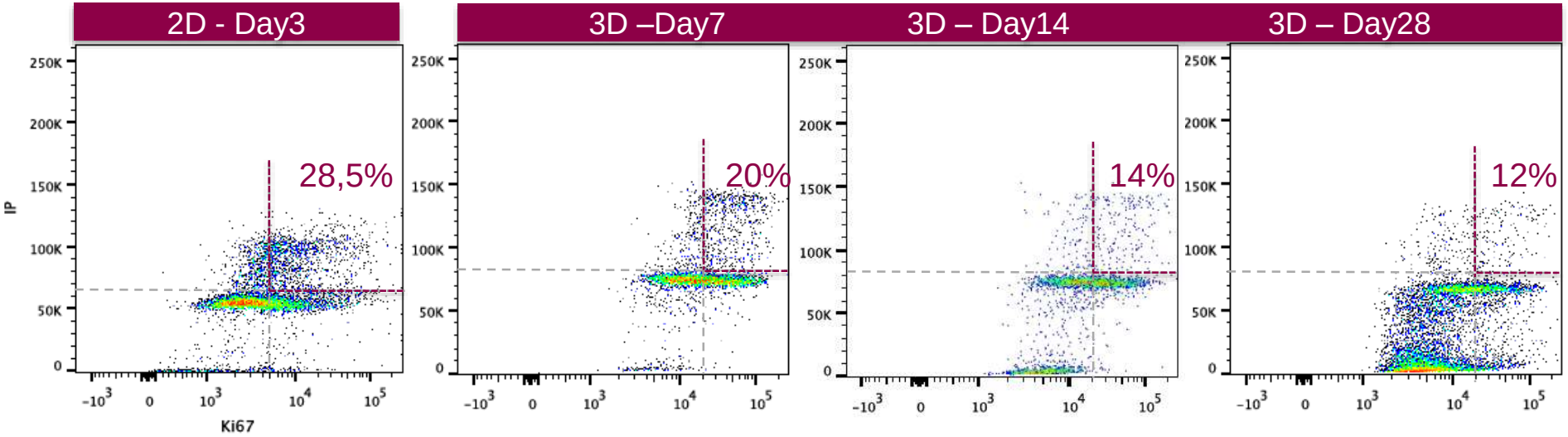


- Collagen and fibronectin expression vary in 3D compare to 2D

Collagen
Fibronectin
Hoechst

Cell retrieval

Cell cycle analysis



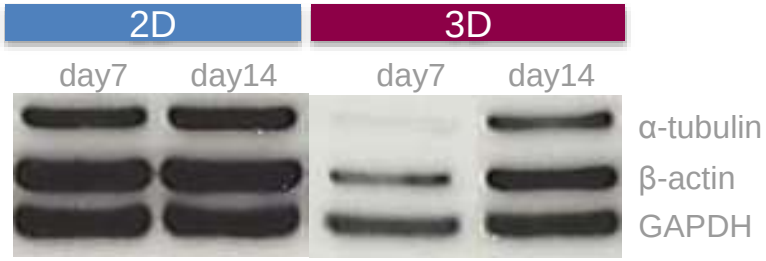
Flow cytometry IP and KI-67/FITC

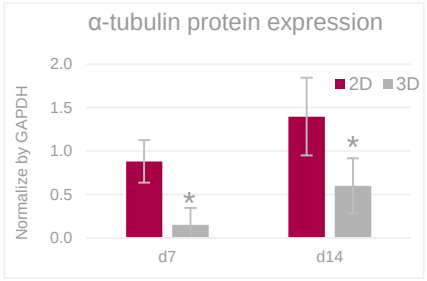
- Proliferation rate in 3D is lower compared to 2D

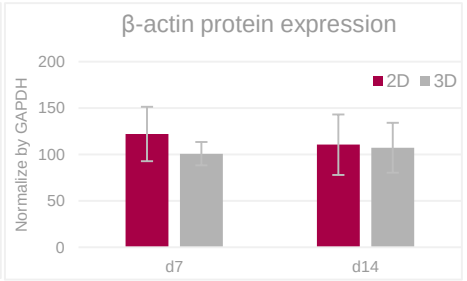
DNA/RNA/protein extraction

Cytoskeleton organisation

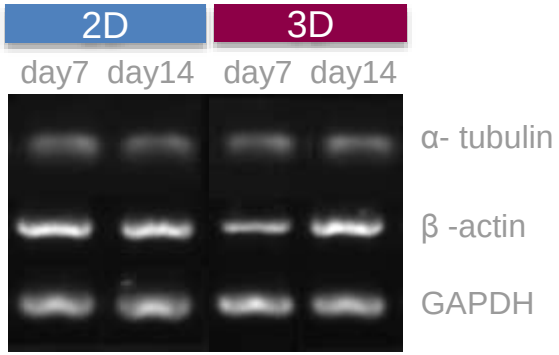
Protein analysis
(Triton-based buffer)

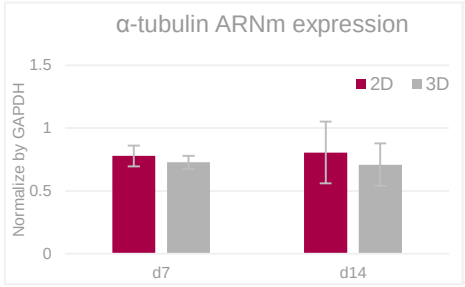


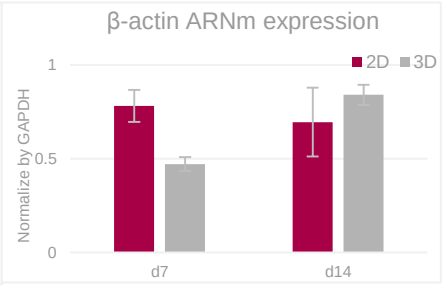




RNA analysis
(TRIzol buffer)



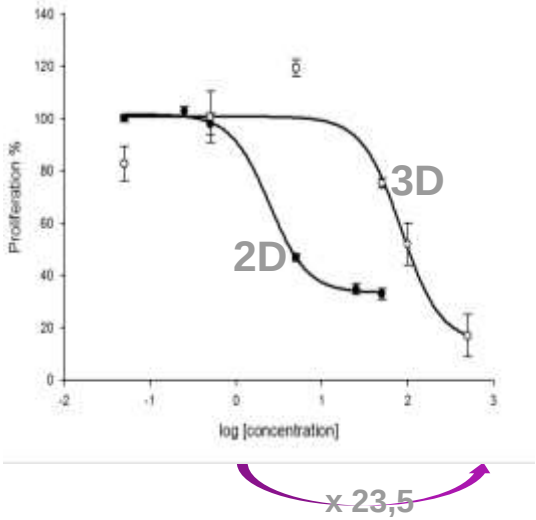




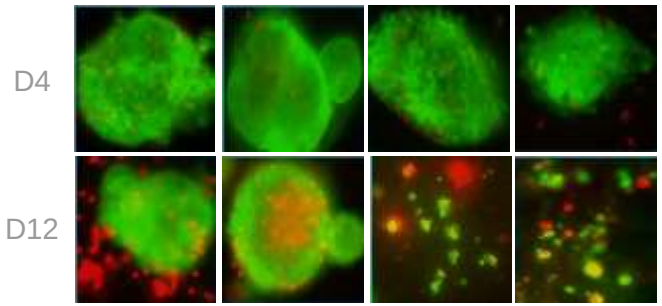
* : p<0,05 Two-ways Anova with Bonferroni post-test

The use of 3D cell culture in drug discovery

IC50 on DLD1 using 5-FU

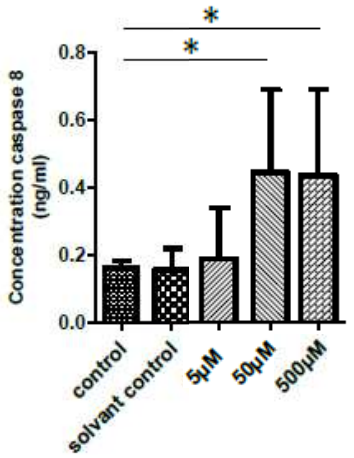


DLD-1 viability using 5-FU



In Red : necrotic cells, In green : live cells

Pathway activation



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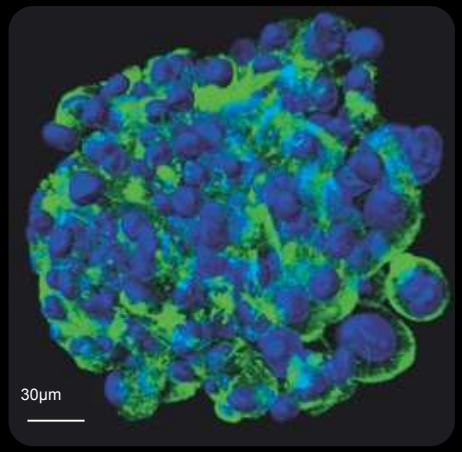

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