

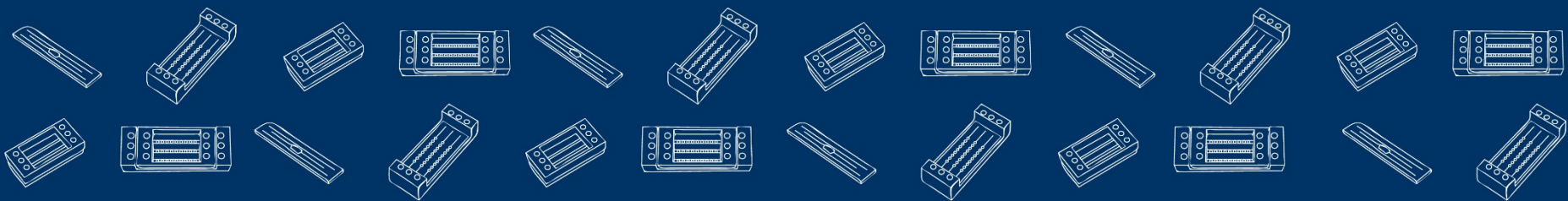
BEOnChip

Biomimetic Environment On Chip

Microfluidic devices for cell culture in biomimetic environments



X Jornada REMA, Madrid 12/12/2019



ORGAN ON A CHIP



DRUG RESEARCH

First studies
Drug discovery



PRECLINICAL

Lab and animal
experiments



CLINICAL TRIALS

THREE PHASES
1000-11000 patients



EVALUATION/ APPROVAL

(Up to 2 years)

PHASE IV STUDIES

(More than 2 years)



**1 DRUG APPROVED
BY HEALTH AUTHORITIES**



10000
Test compounds

<250
Test compounds

<5 Test compounds

>1 BILLION EURO



Developing a new drug is too slow and expensive



PETRI DISH

Lack of natural environment



ANIMAL EXPERIMENTATION

Expensive and controversial



TIME AND MONEY

Too many false positives



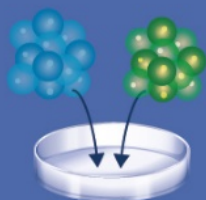
ORGAN ON A CHIP



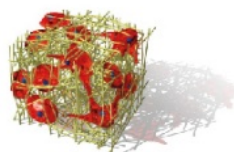
2D CELL CULTURE



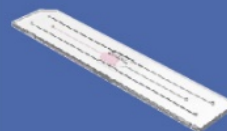
3D CELL CULTURE



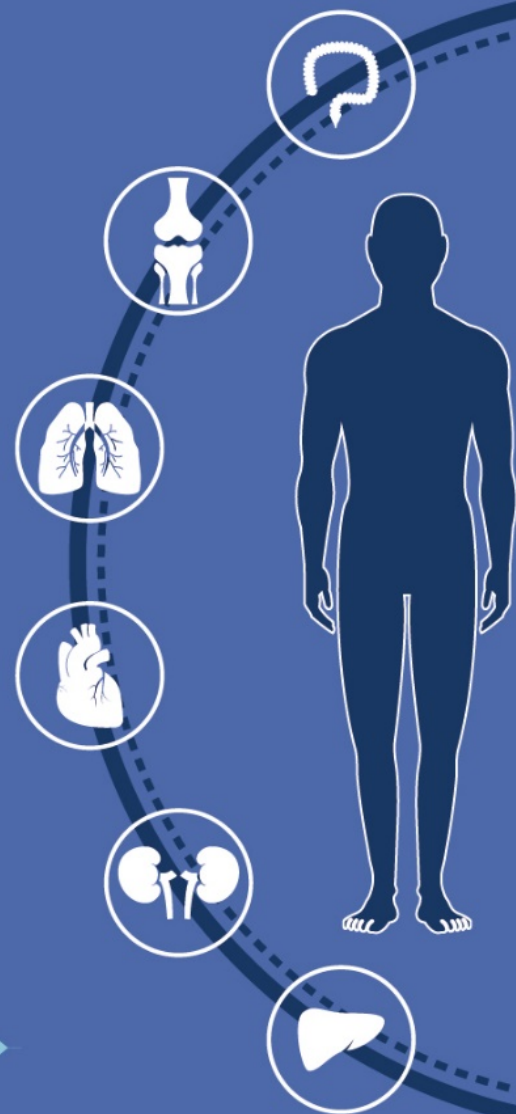
CO-CULTURE



SCAFFOLD-BASED 3D TISSUE

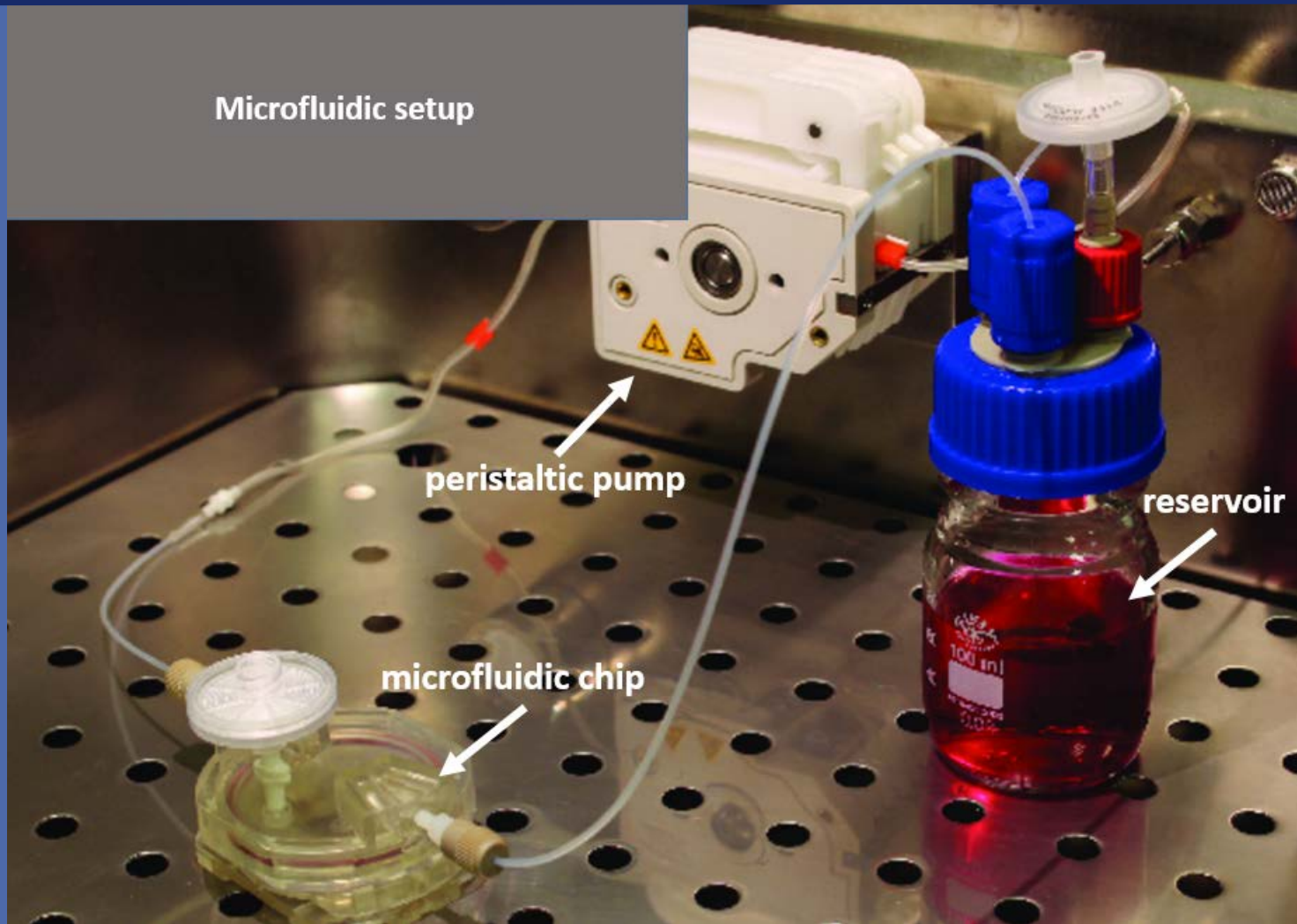


ORGAN ON A CHIP



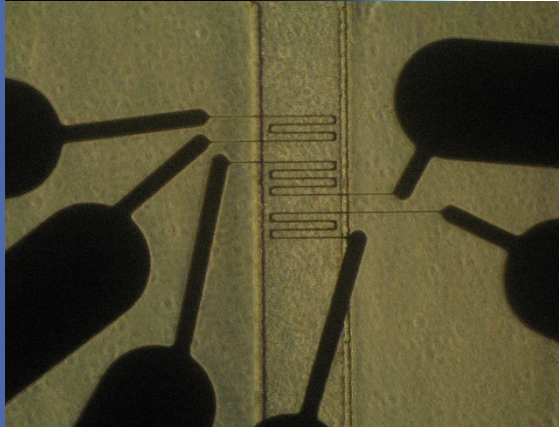
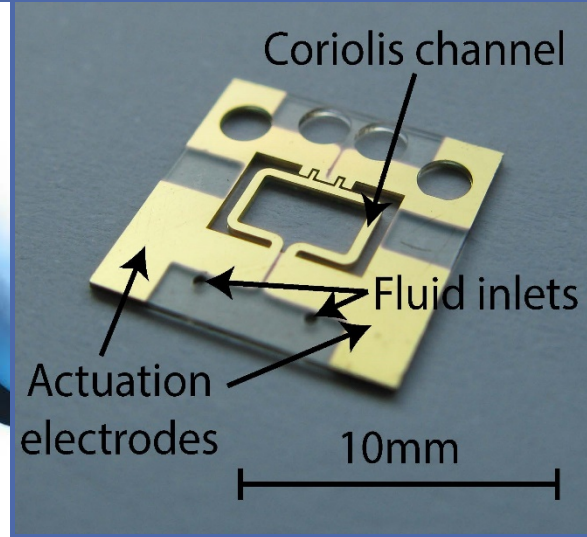
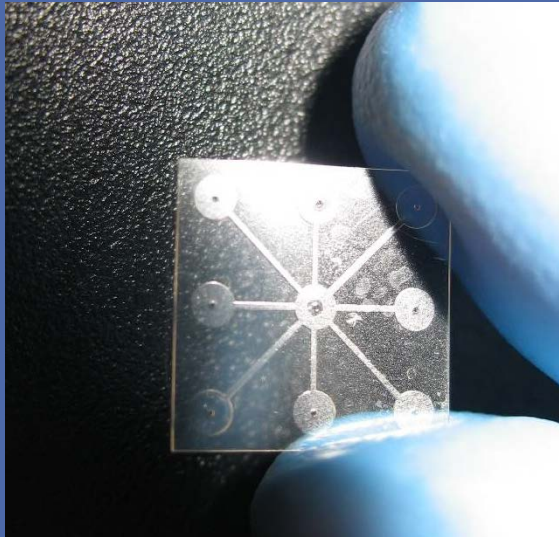
YEARS

Microfluidic setups



Microfluidic

Valve/pump



Coriolis and thermal flow sensors

Microfluidics for cell culture applications

Advantages in tissue engineering and cell culture applications.

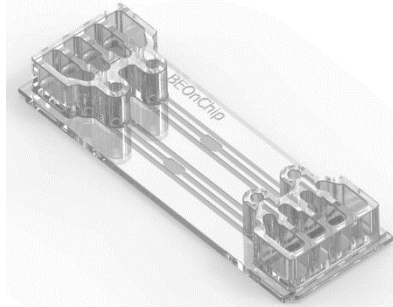
- Reduced size: cost savings, easy storage.
- High parallelization: several experiments in same chip, high-throughput screening.
- Reduction of human error: automatization (less human handling).
- Faster response time (micrometric scale): diffusion, changes in pH, temperature, flow.
- Real time monitoring: optical Access, controlled results.
- Stimuli performance: mechanical, chemical, electrical stimulation.

Microfluidics for cell culture applications

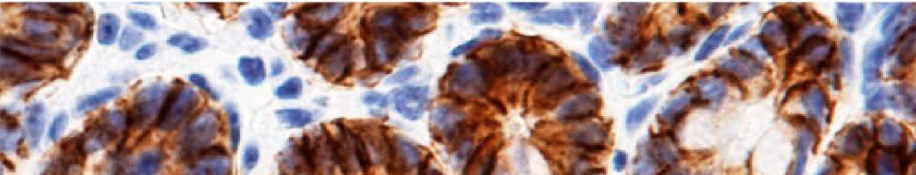
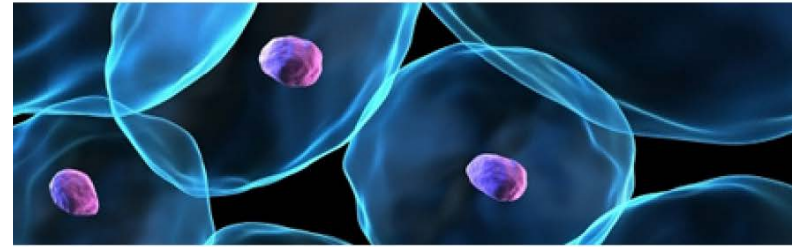
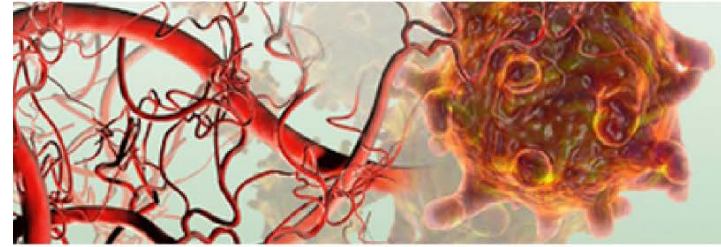
Biomimetic environment

Our goal is to make OoC available to everyone

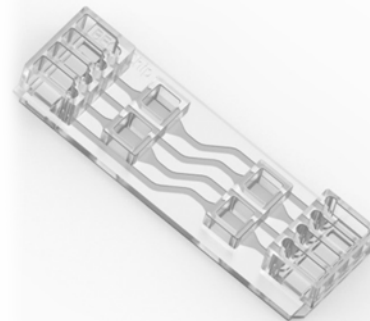
BE-GRADIENT



- APPLICATIONS
- Cell migration
 - Spheroid substitution
 - Necrotic core
 - Immune system
 - Nutrient, O₂ and drug gradient



BE-TRANSFLOW

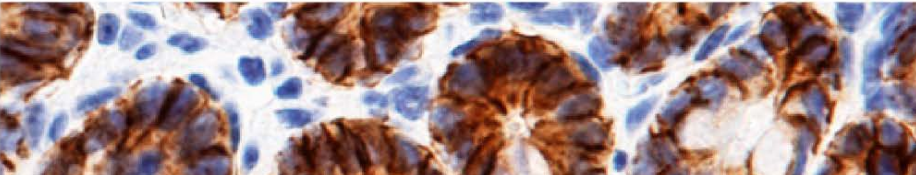
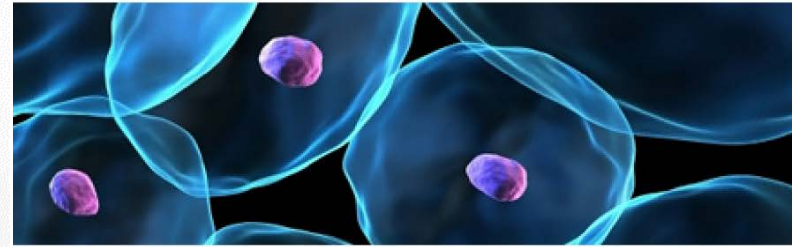
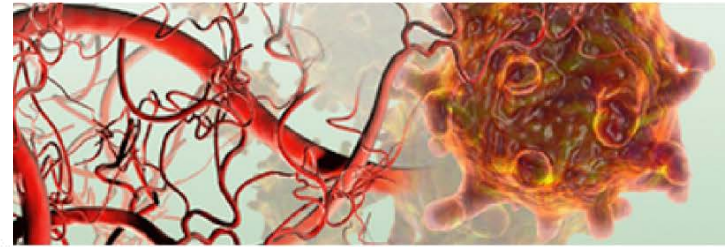
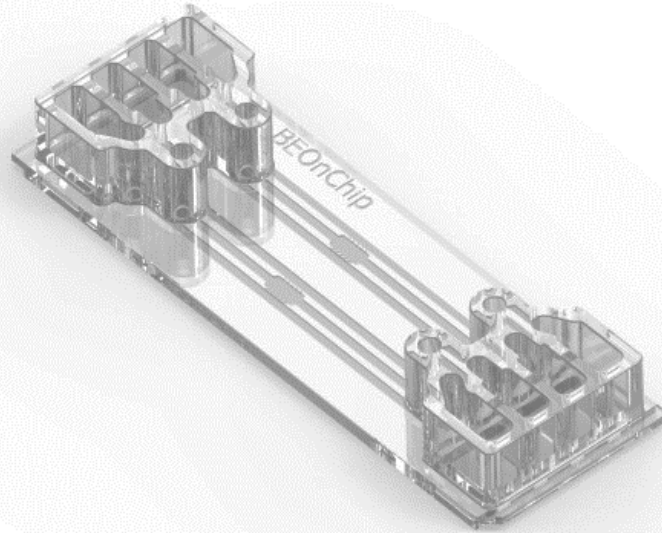


- APPLICATIONS
- Cancer-metastasis
 - SKIN on chip
 - GUT on chip
 - Toxicity testing



Our goal is to make OoC available to everyone

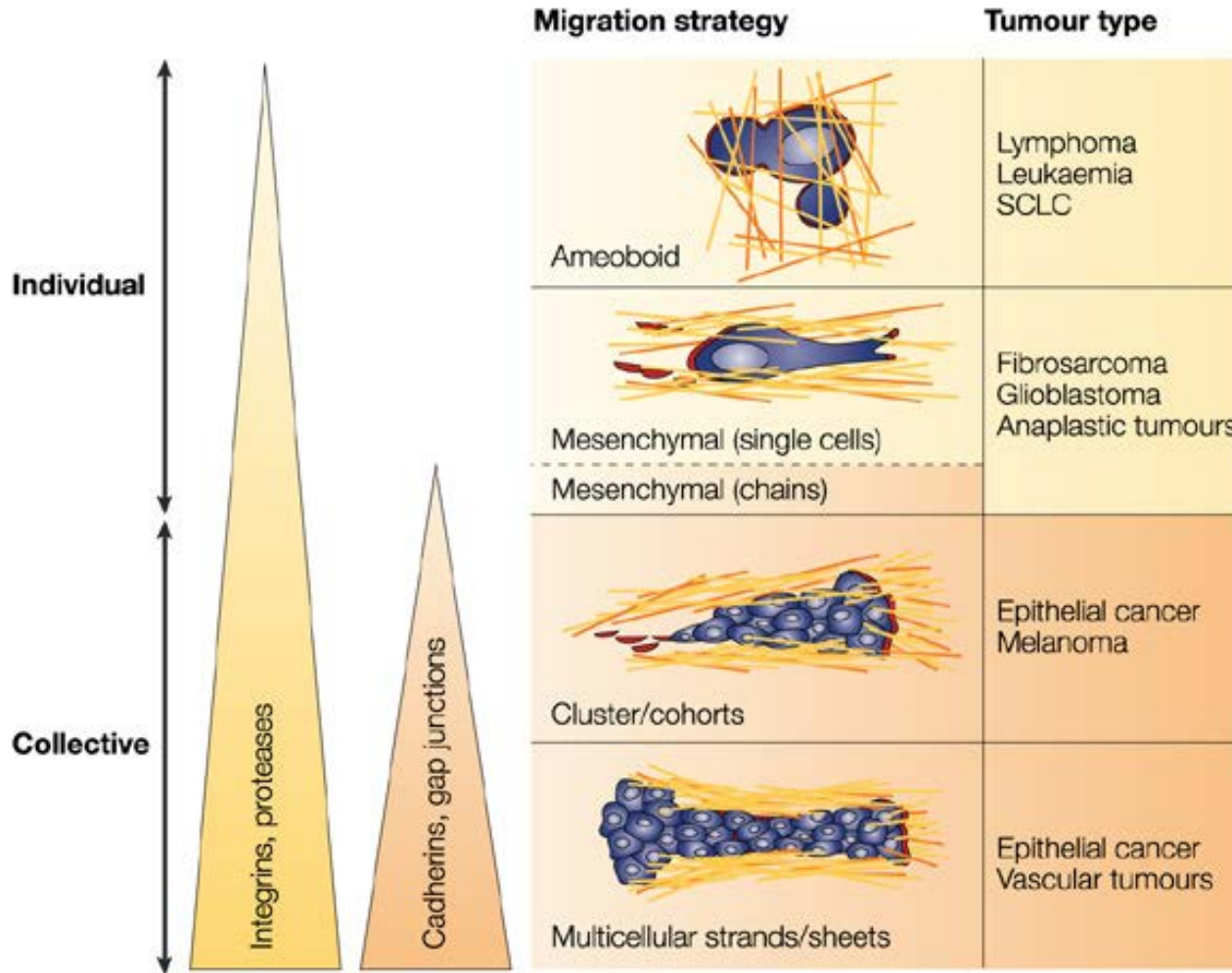
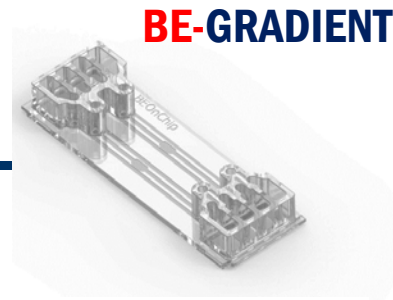
BE-GRADIENT



In vitro model of tumours migration
in 3D

In vitro model of Glioblastoma based
on microfluidics

In vitro model of tumours migration in 3D



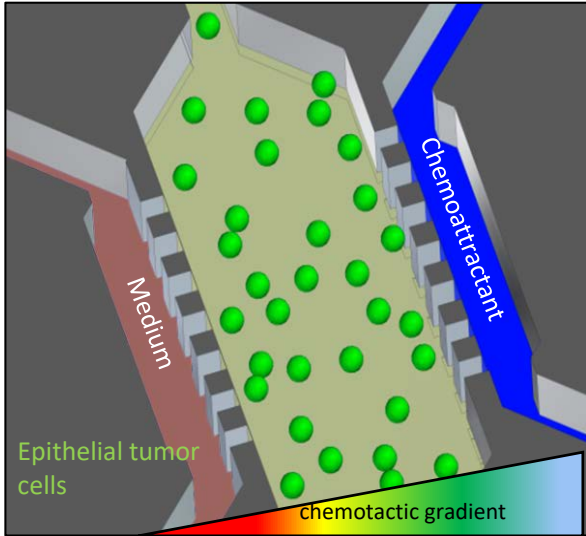
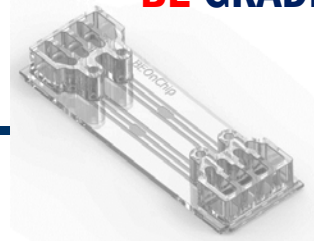
Universidad Zaragoza



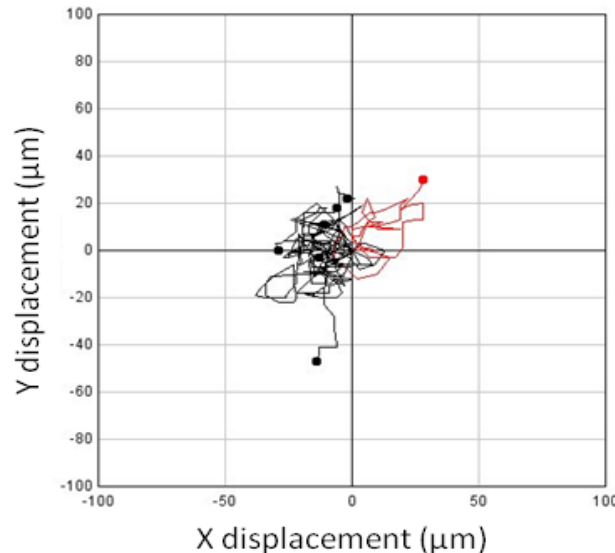
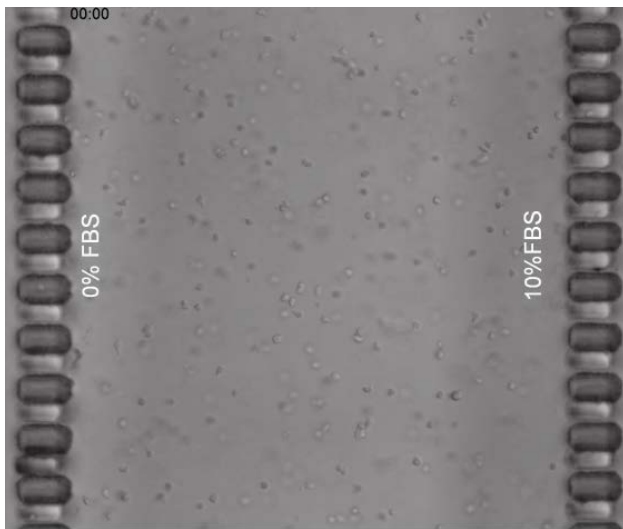
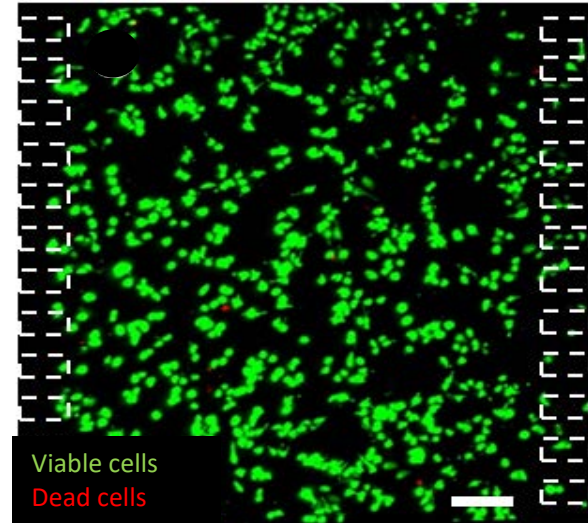
Instituto de Investigación Sanitaria Aragón

Peter Friedl & Katarina Wolf; *Nature Reviews Cancer* volume 3, pages 362–374 (2003)

In vitro model of tumours migration in 3D



OSC-19 and U-87 cells at 2 millions cells/ml in collagen hydrogel at 1,5 mg/ml.

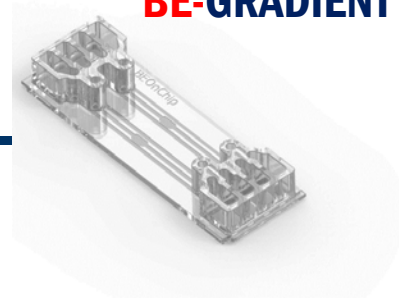


Cell viability was evaluated, showing viable cells in green and dead ones in red. Scale bar is 200 µm.

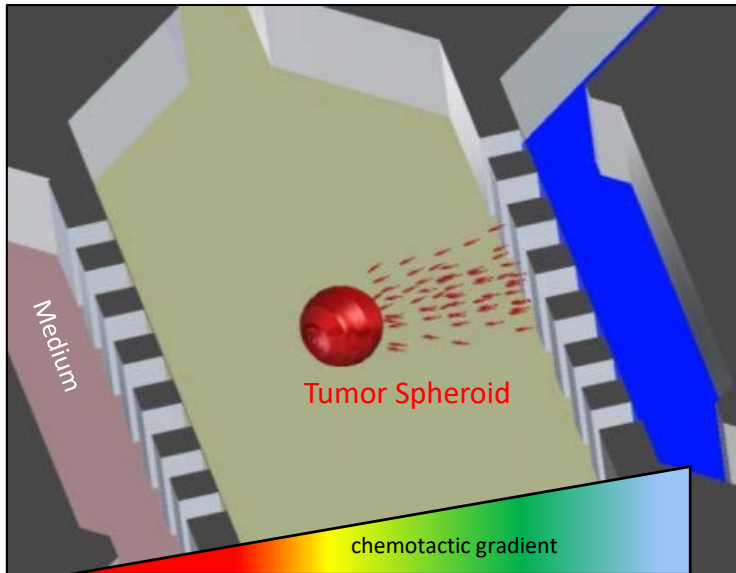
FBS-free medium was perfused through the left lateral microchannel, whereas 10% FBS-containing medium was used on the right lateral microchannel. Scale bar is 200 µm.

In vitro model of tumours migration in 3D

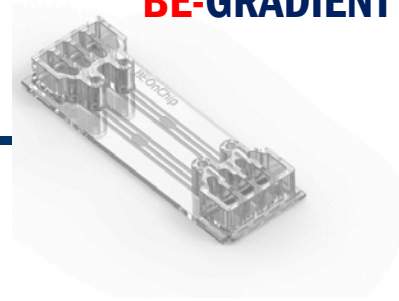
BE-GRADIENT



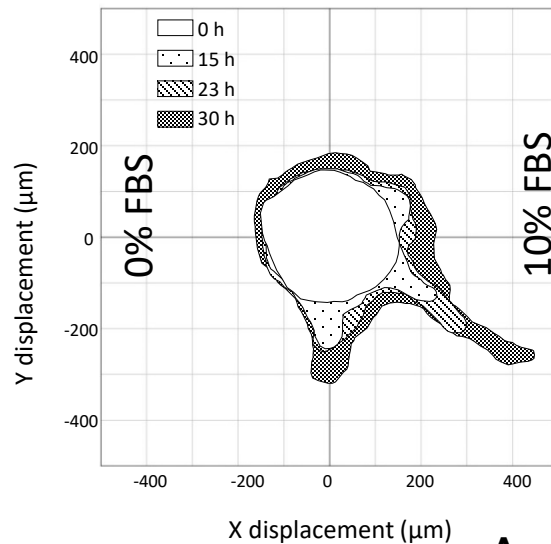
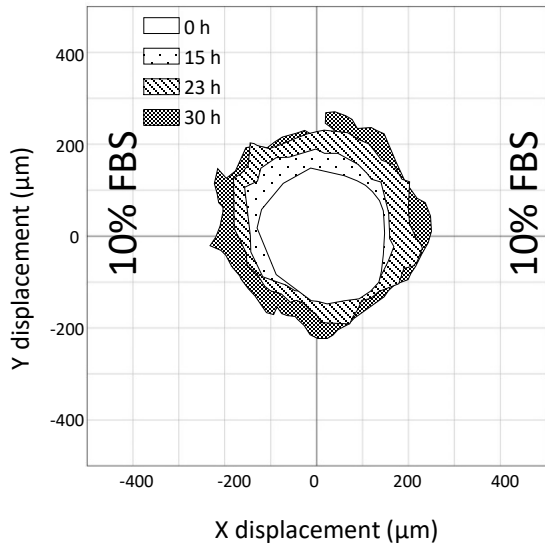
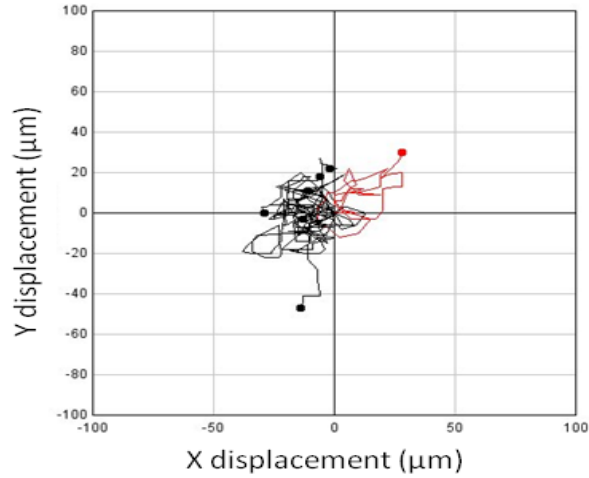
Head and Neck (epithelial tumour)



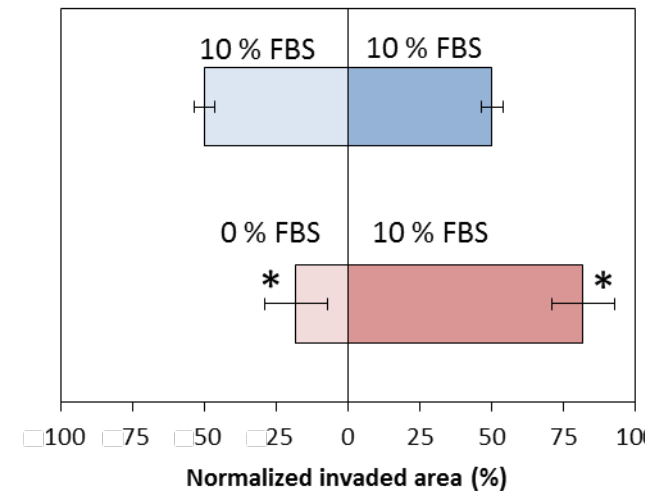
In vitro model of tumours migration in 3D



Head and Neck (epithelial tumour)

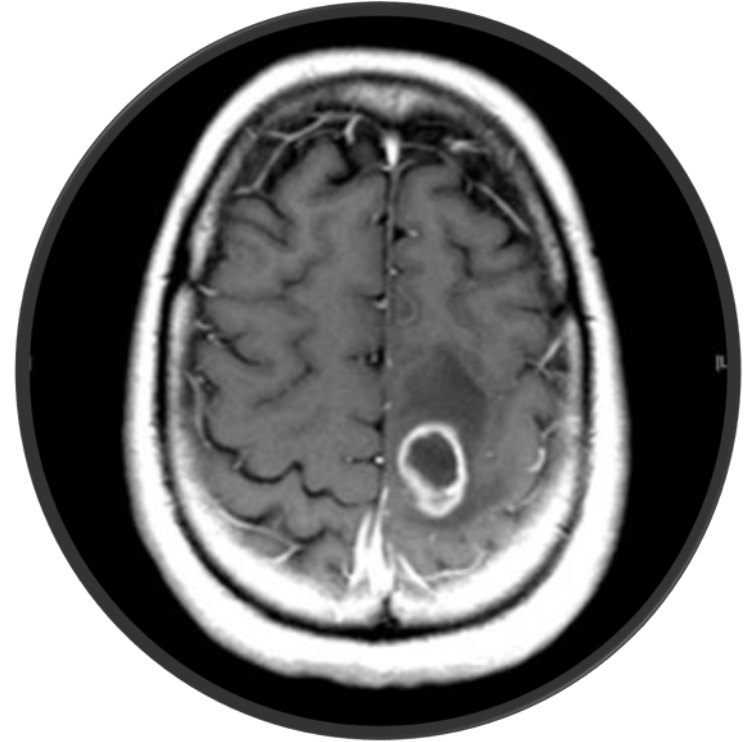
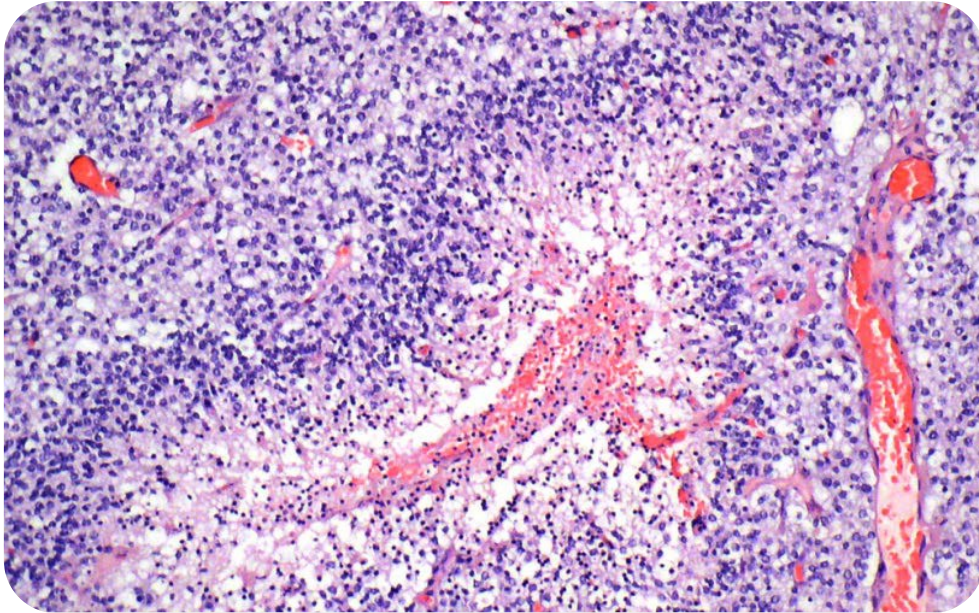
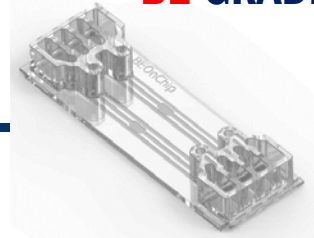


Invasion ratio

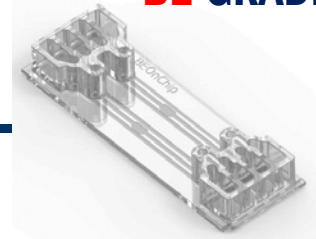


In vitro model of Glioblastoma

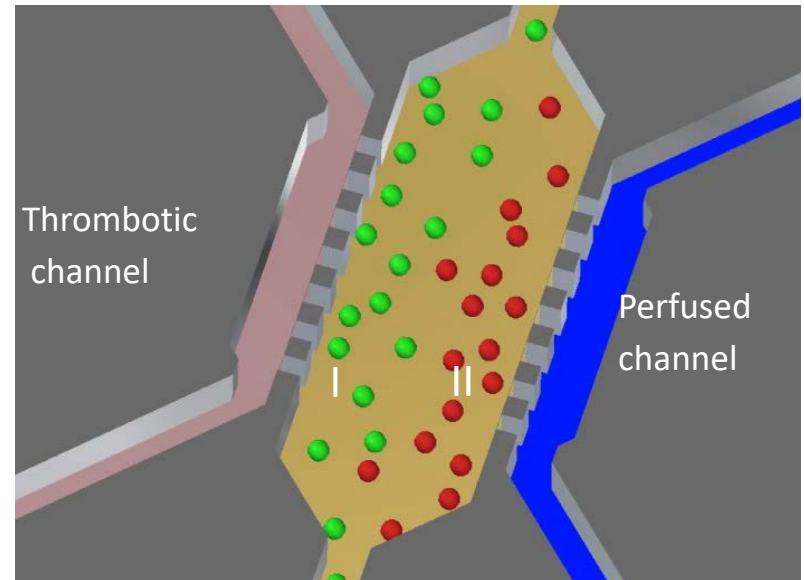
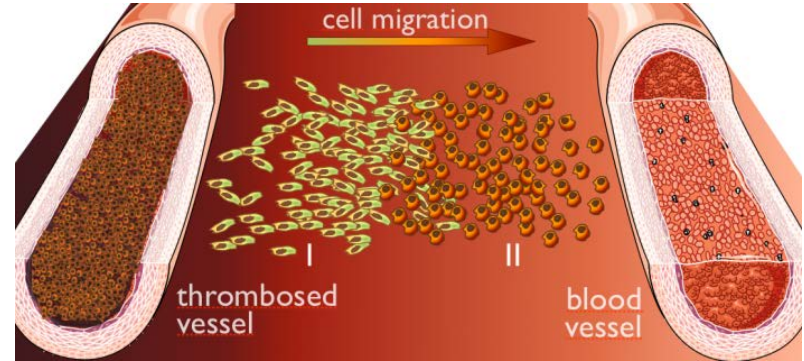
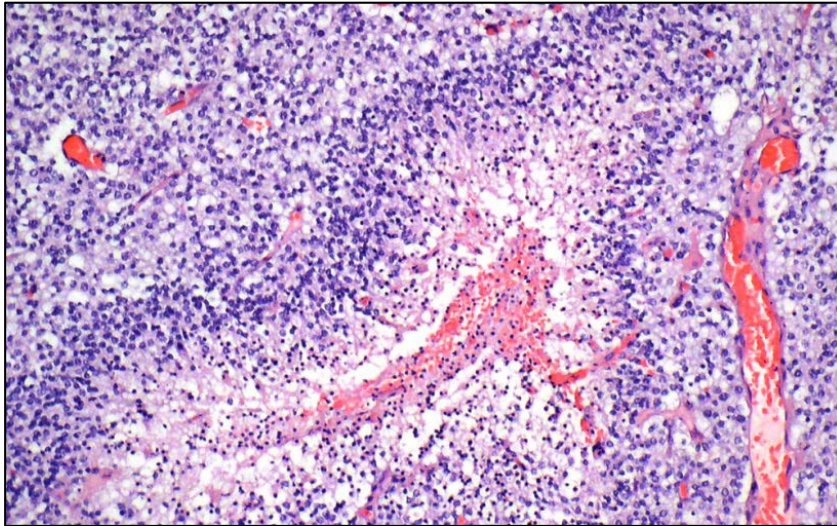
BE-GRADIENT



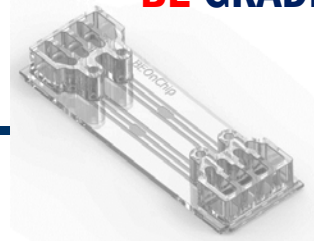
In vitro model of Glioblastoma



Vascular-tumour interactions



In vitro model of Glioblastoma



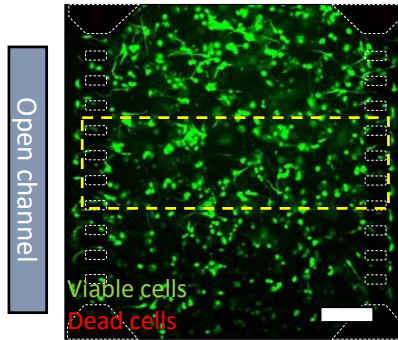
3 days

6 days

9 days

Unrestricted

Thrombotic



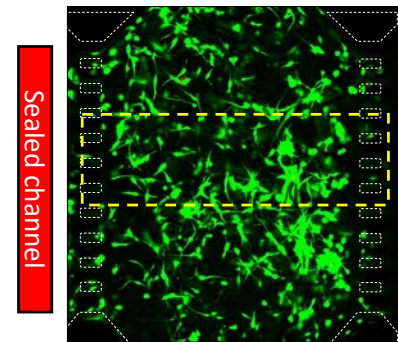
Open channel

Open channel

Open channel

Open channel

Open channel



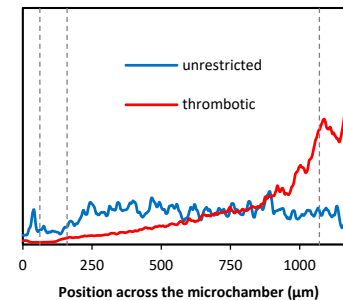
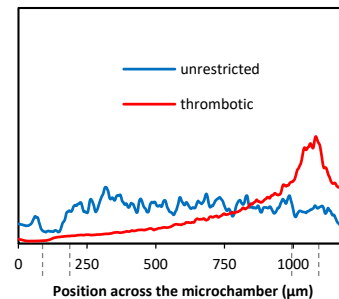
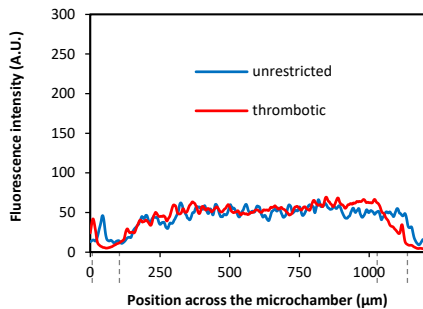
Medium flow

Medium flow

Medium flow

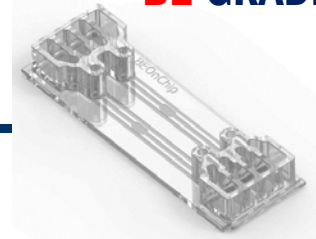
Medium flow

Medium flow



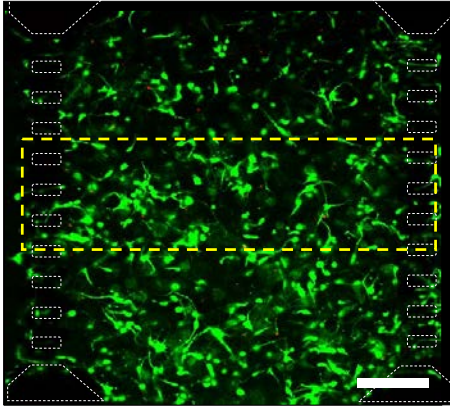
U-251 at 4 millions cells/ml in collagen hydrogel at 1,5 mg/ml. Medium flow was enable only through right microchannel. Cell viability was assessed using fluorescein diacetate 5 μ g/ml (green) and propidium iodide 4 μ g/ml (red). Scale bar is 200 μ m.

In vitro model of Glioblastoma



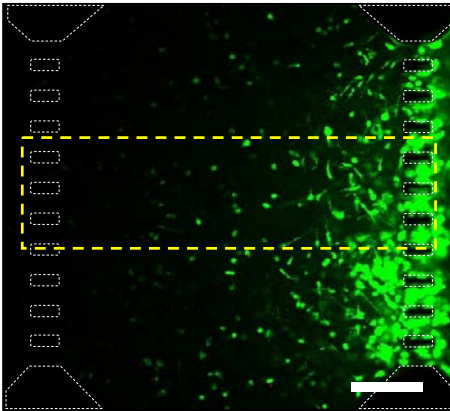
9 days

Open channel

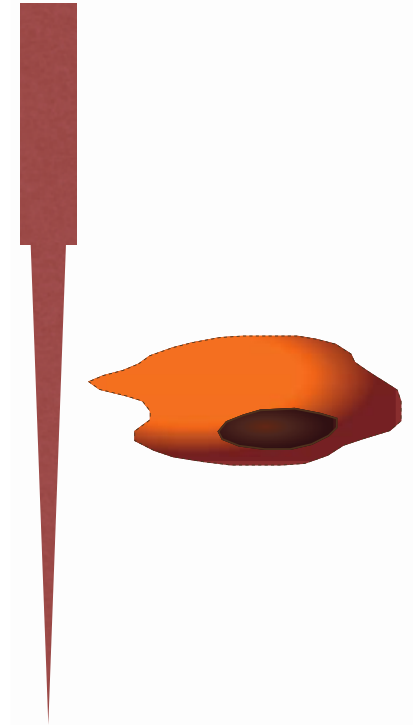
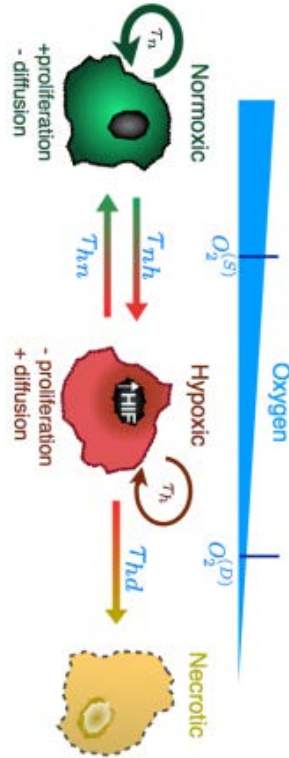


Open channel

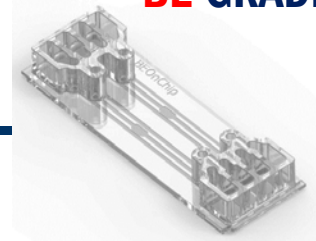
Sealed channel



Medium flow



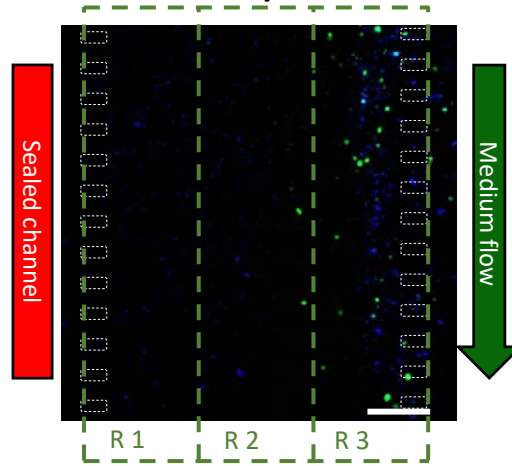
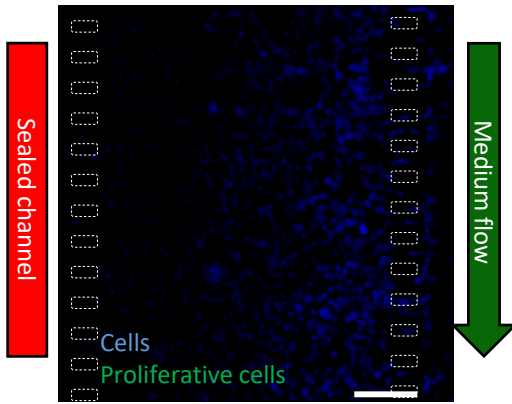
In vitro model of Glioblastoma



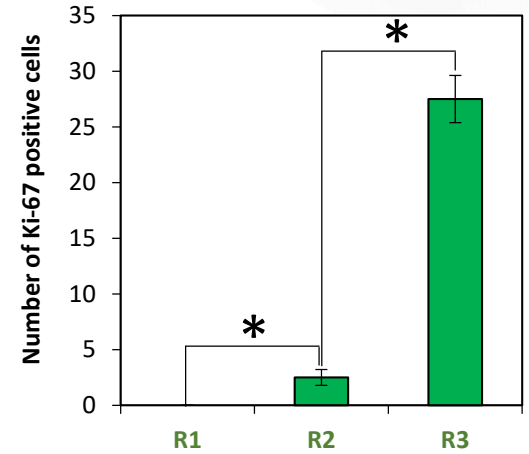
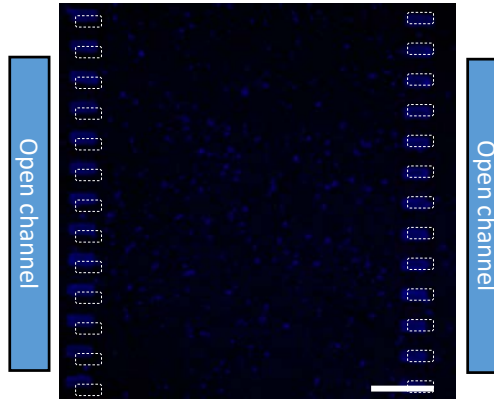
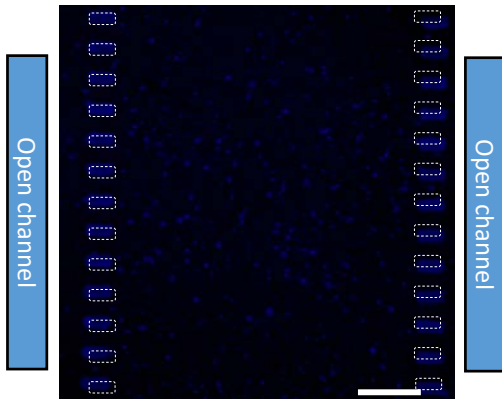
5 days

9 days

Thrombotic



Unrestricted

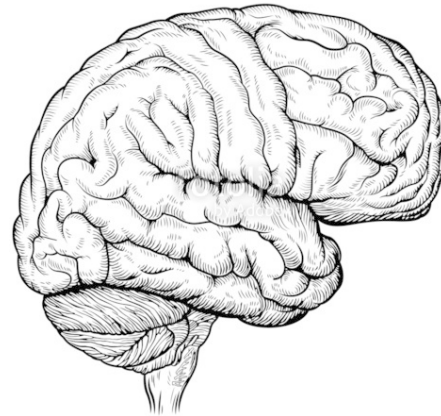
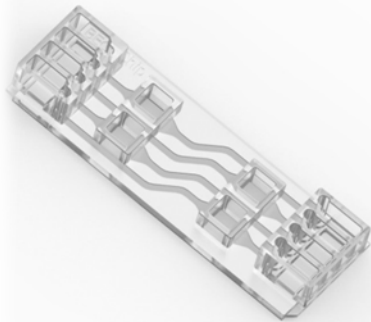


Ki-67 immunofluorescence showing GBM cell proliferation. U-251 MG at 4 millions cells/ml in collagen hydrogel at 1,5 mg/ml. Scale bar is 200 μ m.

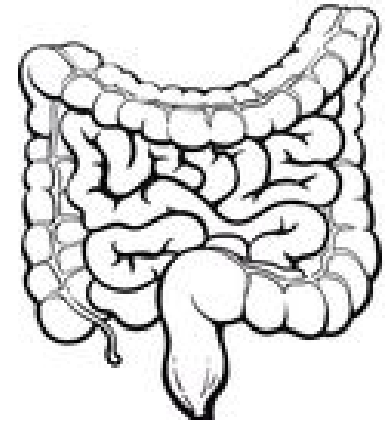
What do we do

We are validating different organ models in our devices

BE-TRANSFLOW



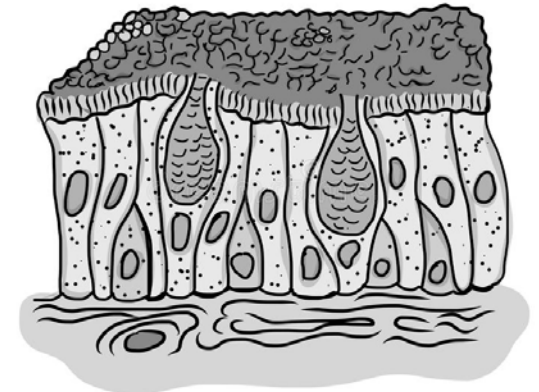
Blood-Brain-Barrier



Gut model



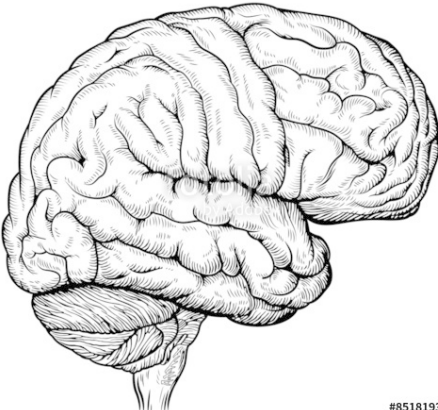
eurostars™ Bone model



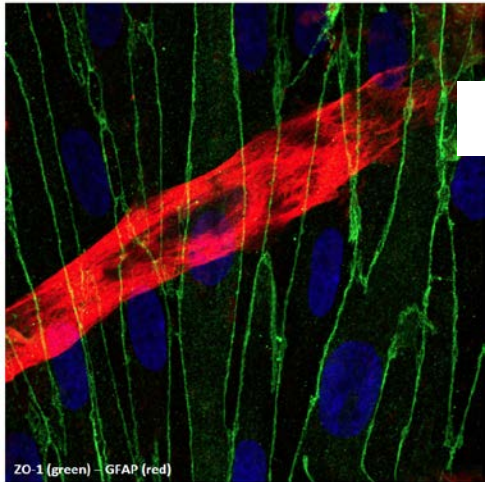
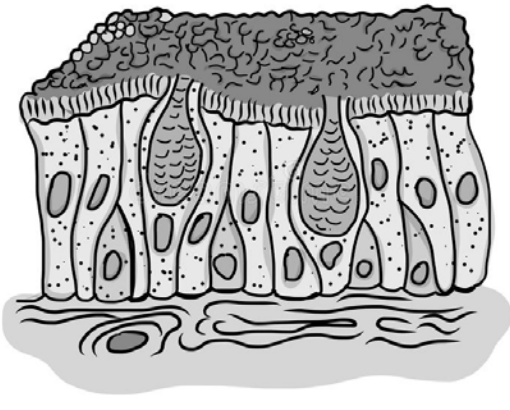
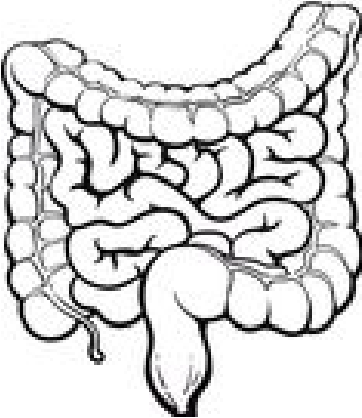
Skin model

What do we do

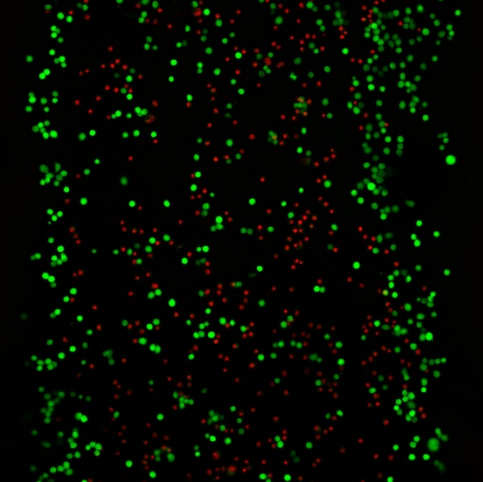
We are validating different organ models in our devices



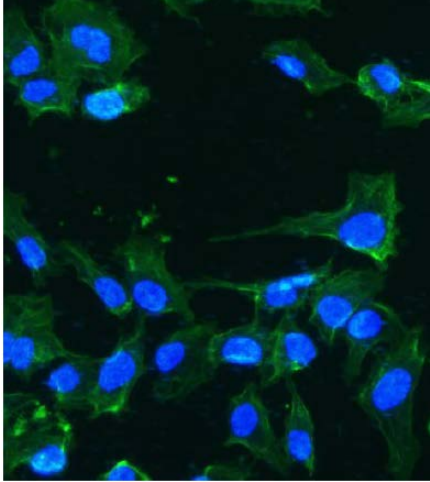
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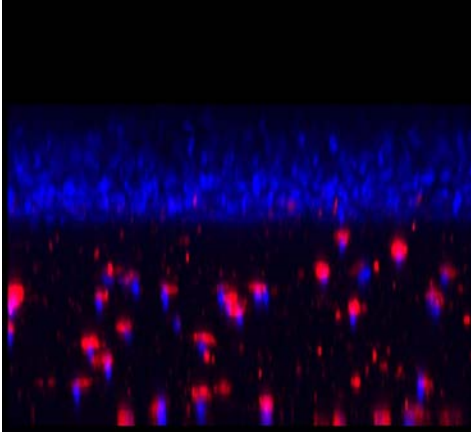
BMEC + astrocytes



Ht29, colon carcinoma



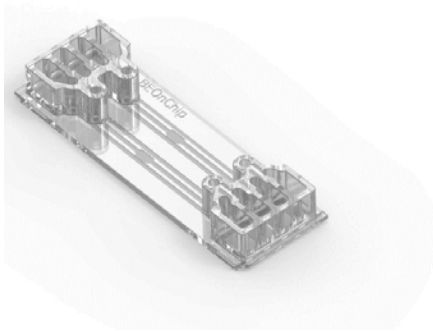
U2OS



Epithelial + HaCaT

Business model

**OWN
DISTRIBUTION**
(Device
+
protocol)



- Europe
- China, Japan
- Central America
- South America

**MICROFLUIDIC
CONSULTANCY**



IDEA



DESIGN



PROTOTYPE



VALIDATION



INDUSTRIALIZATION

PARTNERS

Flow control companies



Research Institutions



Instituto de Investigación
Sanitaria Aragón



Inserm


























La science pour la santé
From science to health

European projects

- H2020-FETOPEN-2018-2020 Advanced and versatile PRInting platform for the next generation of active Microfluidic dEVICES- PRIME
- BEONCHIP is leading a EUROSTARS project (BONAFIDE E!10530, EU). Project leaders. 1,647,240.15 €, 36 months
- SME Instrument phase I (H2020-SMEInst_762315_B-On-Chip, EU) 50.000€
- CISTEM (MSCA H2020 RISE, Project number: 778354). 364.500€, 48 months
- At the national level, BEONCHIP is participating in a RETOS project (PRENOMON, Spanish Government). 691.482,27€, 48 months

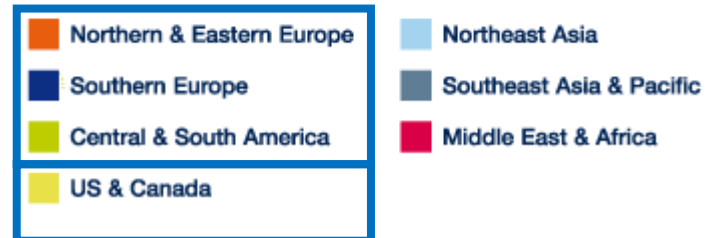
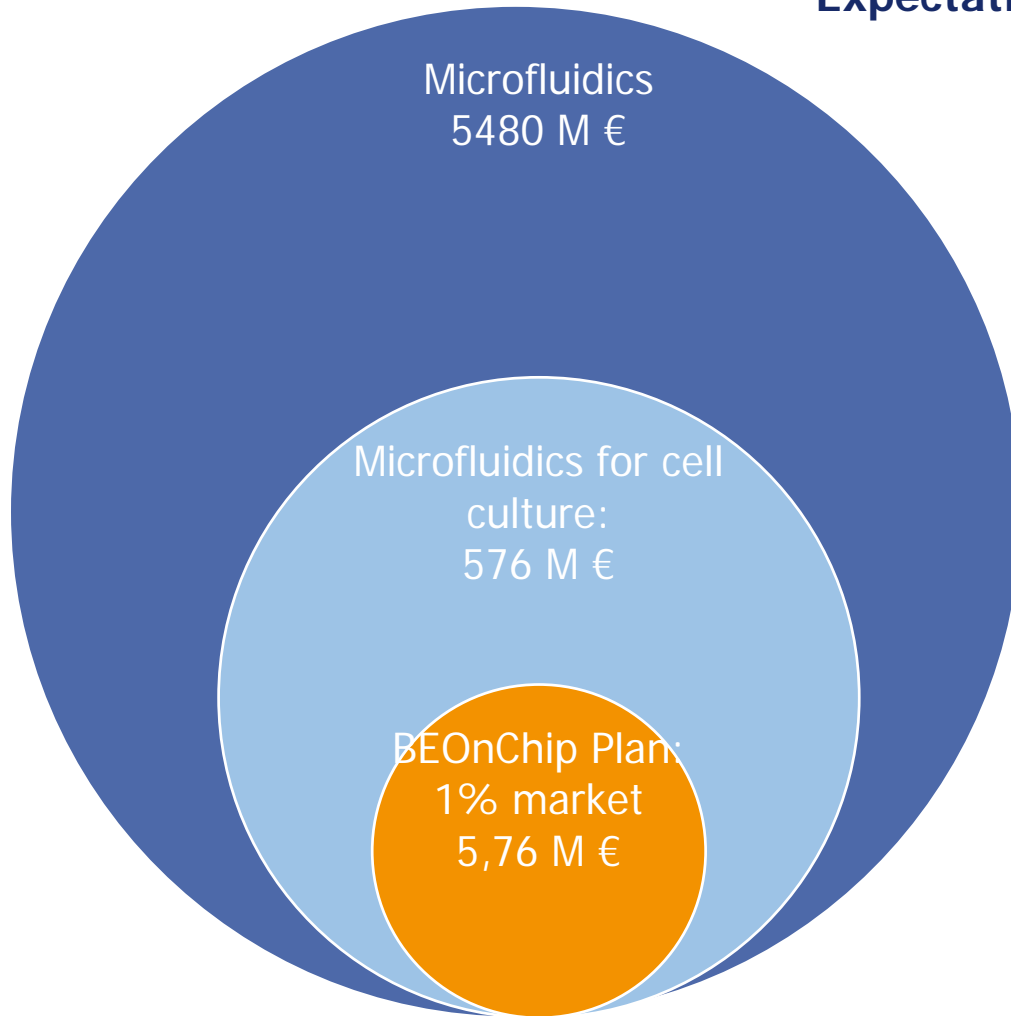


Competition

					
Easy to use					
biomimetic environment					
range of products					
services					

OoC is an emerging market with a huge potential

Expectations 2021 ↑ 20%

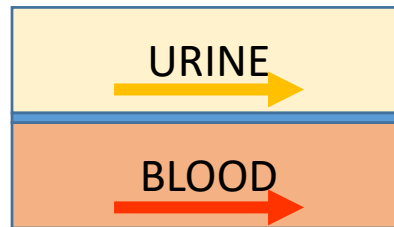


What's next? 2019

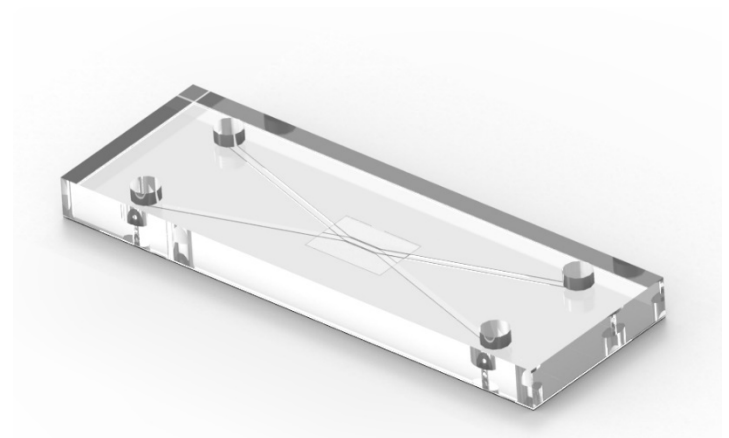
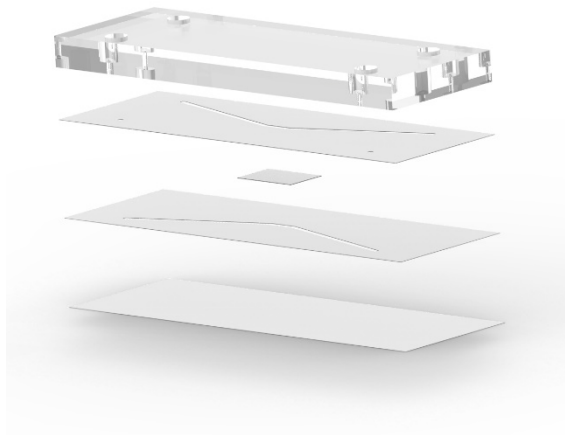
New devices and models



Kidney-on-a-chip

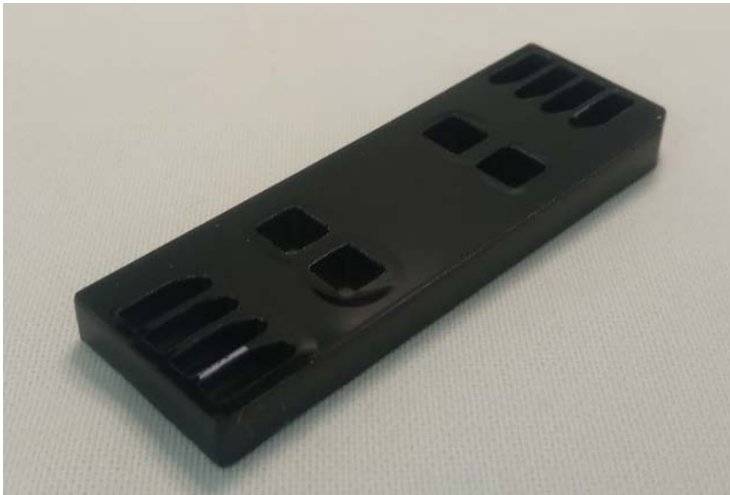


Channel
Porous membrane
Channel



What's next? 2019

BE-TRANSFLOW FAMILY



Black material:
improving microscopy
analysis



**Custom porous
membrane:**
pore size, material

What's next? 2020

BE-ROCKER

Novel design of a rocker device for the laboratory.

Its **compact design** and material selection **allow** its introduction in **cell culture incubators** in conditions of **saturated humidity**.

The device is equipped with a **high precision silent rotor**.

The dimensions of the device are:
295x255x185 mm.

Connection to computer via **USB**.



Working team

MIT
Technology
Review

INNOVATORS
UNDER 35
SPAIN



Dr. Rosa Monge
CEO



Dr. Luis E. Serrano
Head of sales



Sara Aldea
Head of product



Lara Pancorbo
R&D technician



Sandra González
Biologist technician

Working team

Collaborators



Bea Cativiela

Javi Henriques-Gil

Raquel Naranjo

Ruth Sánchez

Advisory board



Dr. Manuel Doblaré

Dr. Ignacio Ochoa

Dr. Luis J. Fernández



BEOnChip

Biomimetic Environment On Chip



X Jornada REMA, Madrid 12/12/2019