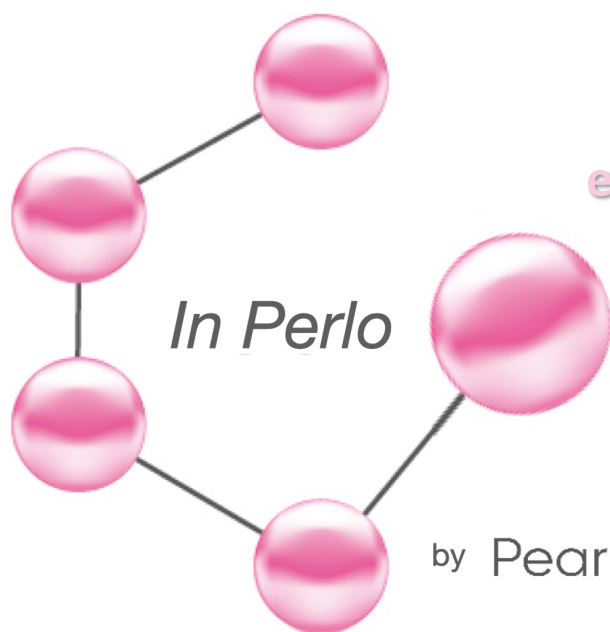
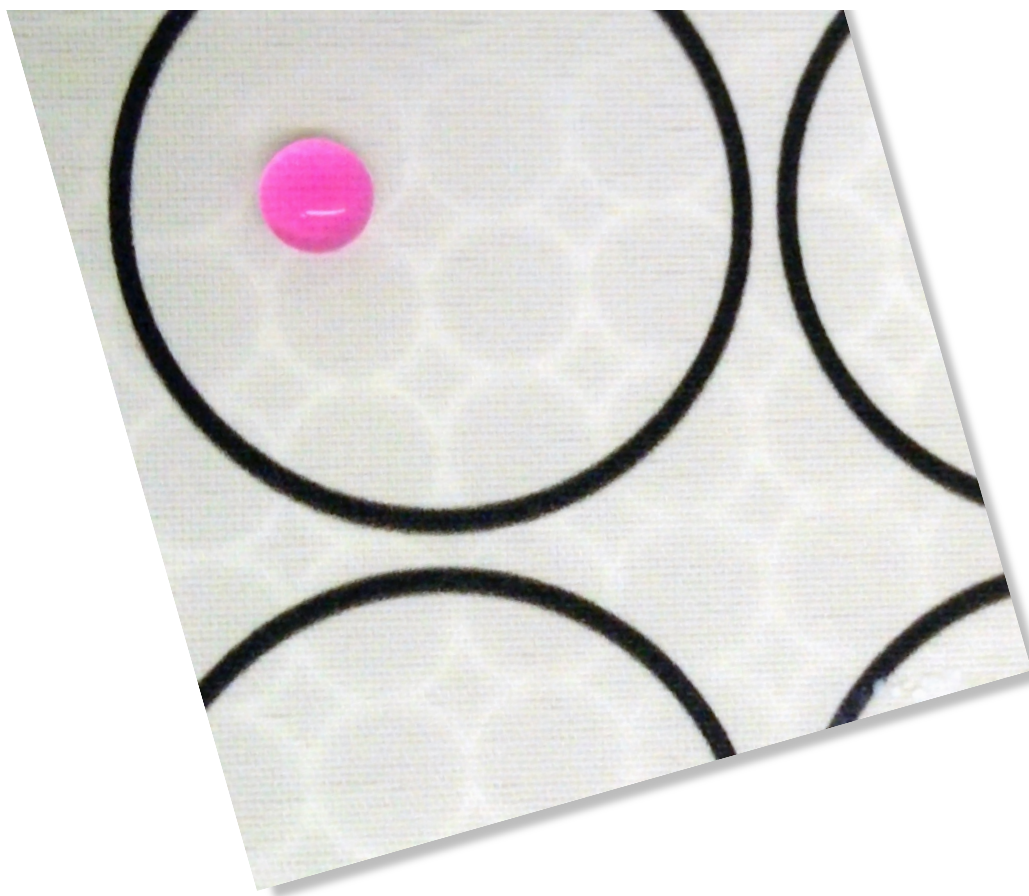


A new innovative disruptive toxicology test close to in vivo models



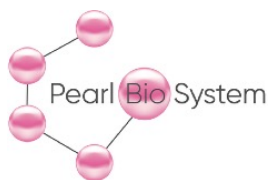
Improve your selection process before starting expensive and sometimes uncertain clinical trials

by Pearl Bio System

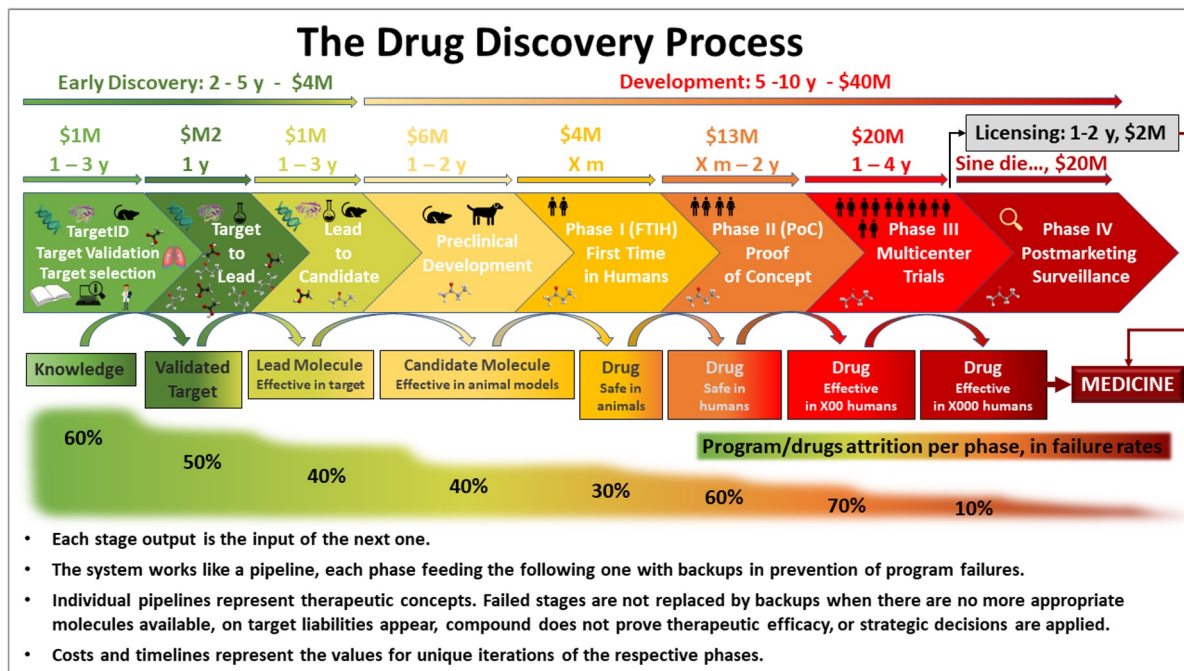


Here we go for the future of your HCS ...

With our Fast and Secured 3D *in perlo*TM Technology Valorize All the Potential of Your Molecules.



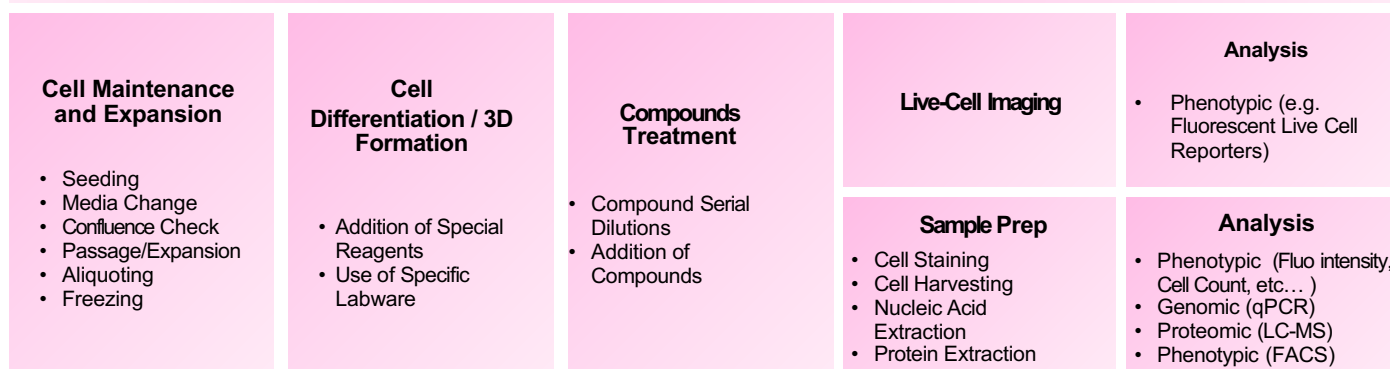
Developing a molecule in various industries or evaluating its toxicological effect requires many costly steps, including a lengthy high-content screening workflow. The exit success rate is very low: between 3 and 12%.



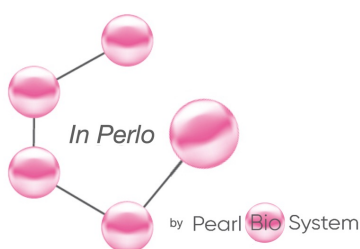
Basic Cell-Based High-Content Screening Workflow

The diagram below shows the most common methods for any high-content cell-based workflow.

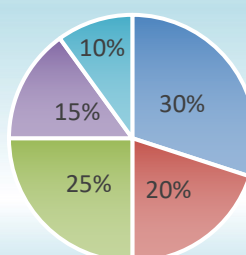
Usually, each of these methods can be partially or fully automated through the integration of third-party devices.



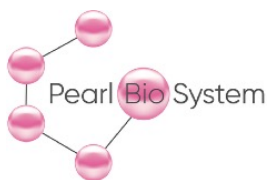
Our *in perlo*TM technology simplifies all these multiple complex steps



Pearl BioSystem brings solutions to various industries



- Pharmaceutical
- CRO - CDMO
- Cosmetics
- Chemical
- Nutraceuticals



Who we are and what we solve with our 3D “*in perlo*™” Technology

- Reliable evaluation of candidate substances is essential for the biopharmaceuticals, skin care and nutraceuticals industries and crucial for appropriate decision-making throughout a development process.
- Pearl Biosystem is a CRO providing 3D screening solutions that help pharmaceutical, cosmetics, and chemical companies to accelerate safety and efficacy testing, and bring better drugs or ingredients to the market in a safer, faster, more efficient, and animal-free way.
- Our patented, 3D liquid pearl technology named *in perlo*™ allows rapid analysis of your identified, promising molecules in a completely safe operational environment. This unique and accurate method for screening provides an animal-free model experimental alternative, free from matrix interference.
- Our unique technology will enable you to explore unlimited applications and empower you to discover your scientific potential.
- The *in perlo*™ solution mimics the “true to life” state. The homogeneity of the 3D liquid pearl is superior to non-homogeneous organoids and more predictable of a molecule.
- The applications are limitless.
- Aligned with FDA to reduce Animal Testing

What is magic in our pearls ?




- Our specific **human cell-line “organoids”** obtained from various cellular phenotypes are in liquid suspension, allowing rapid diffusion of any molecule added to the pearl, whether hydrophilic, lipid-soluble or of a protein nature (e.g., antibodies, nanostructures).
- The added molecules are therefore sure to encounter cells from all sides and will not be hindered or adsorbed by gels or colloids.
- **We are producing several phenotypes of tumoroids and do create organoids by fusing our pearls.**

Click on our video link: Co-culture immunotherapy through the fusion of two or more beads.

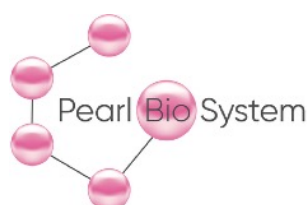
<http://pearlbiosystem.com/oncology.php>

www.pearlbiosystem.com

In perlo™ positioning for compound screening

 In Silico	 In Vitro	In Perlo™	 In Vivo
<ul style="list-style-type: none"> ✓ Low cost ✓ Can be performed with human data = high transferability of results ✓ Ethically favored - 3Rs compliance 	<ul style="list-style-type: none"> ✓ Low cost ✓ Suitable for high throughput/large scale testing ✓ Ethically favored - 3Rs compliance 	<ul style="list-style-type: none"> ✓ Select the best promising molecule before 'in vivo phase' ✓ Accelerate R&D processes = increase drugs success to market access ✓ 3Rs compliance 	<ul style="list-style-type: none"> ✓ Can address the complexity of organ systems ✓ Better evaluate the safety, toxicity and efficacy of a drug candidate in a complex model ✓ Higher translatability to humans

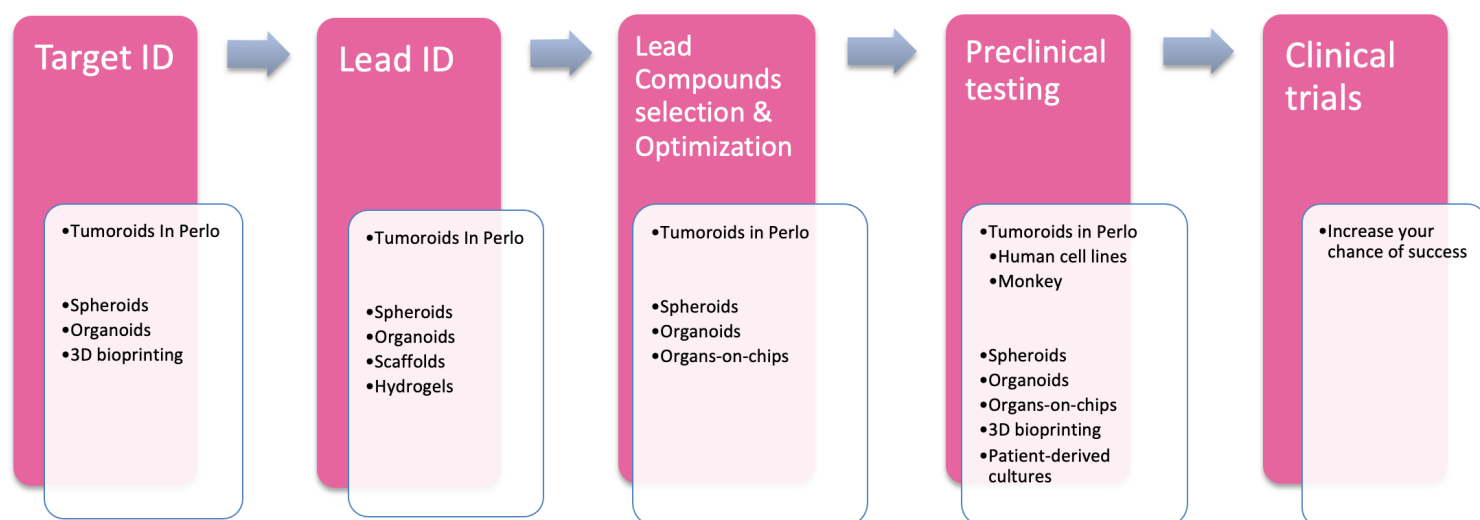
In perlo™ features	In perlo™ benefits	Scientist benefits
Use only liquid media	same as the one used in classic 2D culture	Secure the scientist to easily convert his current phenotype model
Pearl are optically transparent	Compatible with any reverse microscope devices for HCS	Easier integration of the <i>In Perlo™</i> read-out
Possibility to recover treatment molecules	for translational analysis such as proteomics	More insights molecule metabolism
Better diffusion of the molecules to the cells	excellent bioavailability	Closest to the real in-vivo conditions
No need of enzymes to dissociate the scaffold from the tumoroid	Reduces steps in the <i>In perlo™</i> protocol	Automation faster
Only 0.001 g compound vs 15 g	No possibility to characterize the molecule & Samples easy to ship	Secure the confidentiality of the molecules (truly in Pharma - Biotech - CRO - CDMO)
Compatible with hydrophobic and hydrophilic compounds	Multiple applications	Global market approach : DD – Dermo-cosmetic – NutriSciences... Theragnostic
No gel	No need to control the temperature during the 3Dculture process	Automation steps easier – lower cost per assay phase development
Only 3 steps to generate the pearl	Faster assay phase development at lower cost	Increased throughput rate and help to select earlier most promising compounds



Pearl BioSystem Technology: a boost for your R&D funding

Secure your clinical trials with ease with our *In perlo*TM workflow:

The *in perlo*TM 3D: a flexible tumoroid model applicable to all stages allowing it to replace all other models.



Imagine a tool based on tumoroids, growing in close to g_0 gravity, allowing you to select which of your molecules will be the most promising and most effective in the clinic?

Our *in perlo*TM 3D technology based on liquid pearls seeded with **human or animal cell lines** (mouse, rat, monkey, etc.), makes it possible to easily recreate the conditions closest to *in vivo*.

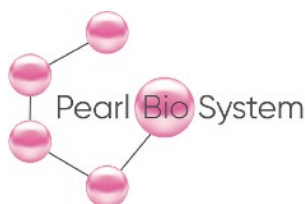
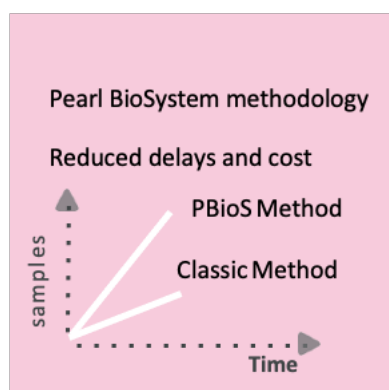
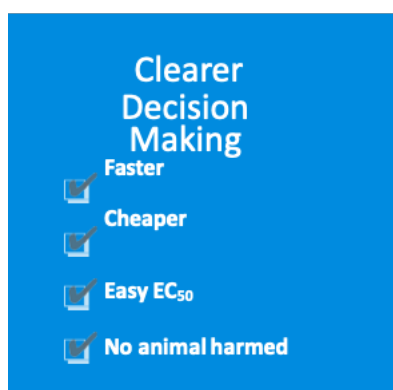
Other 3D culture techniques such as Matrigel (laminin/collagen) offer restricted conditions in terms of diffusion of molecules, working at 4°C, recovery of the supernatant or cells, etc.

Our validated process (CNRS patent) allows manipulation at room temperature and does not require long culture medium validation phases.

This simplicity offers you a considerable range of applications including:

- Monitoring cell-cell interactions through the transparency of the bead;
- The facilitated addition of molecules with excellent diffusion compared to any gel on the market;
- The combination of molecules (e.g. triple therapy) in the context of theragnostic, which will favor the simultaneous development of diagnostic and therapeutic aspects;
- Co-culture by bead fusion (e.g. fusion of pearl filled of activated NK cells with tumoroid seeded pearl for immuno-oncology testing)

Pearl BioSystem Benefits



*In perlo*TM technology: a real boost for your compounds decision-making selection

Biopharma's Pearl BioSystem's Catalog

Early access program: sample testing available in our Oncology program
Breast – Prostate – Pancreatic – Colorectal – Leukemia

Sample Testing on our Prototyping & Validated Assay:

Pearl BioSystem R&D has already developed some assays directly accessible to our customer to evaluate rapidly the added value of the pearl's technology.

Human cancerous cell lines :

- Mammary MCF-7, (ATCC® HTB-22),
- Pancreatic AsPC-1 (ATCC® CRL-1682)
- Pancreatic BxPC-3 (ATCC® CRL-1687)
- Colon SW-620 (ATCC® CCL-227™)
- Testicular NT2/D1 (ATCC® CRL-1973)
- Monocytic leukemia cell line THP-1 (ATCC® TIB-202)

Human control cell line

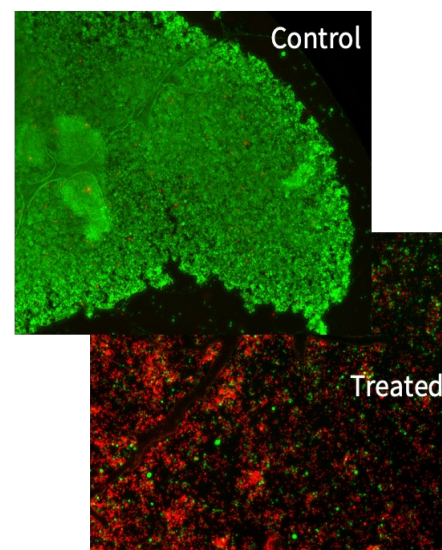
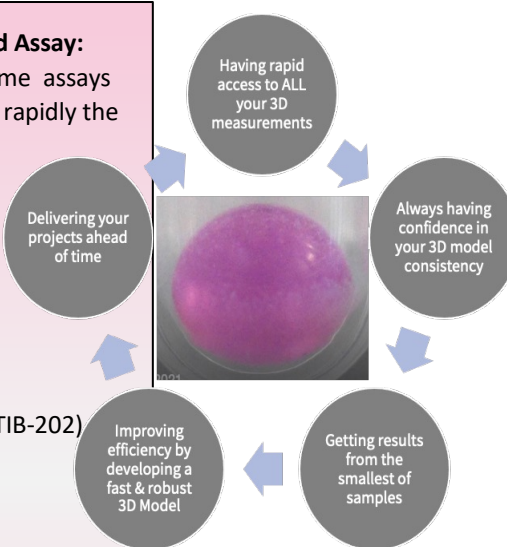
Fibroblasts BJ (ATCC® CRL-2522)

Animal cell lines :

- Mouse
- Rodent
- Monkey
- Dog
- Pigs
- Cow

One assay include :

- Cell growth
- Apoptosis
- Mitochondrial respiratory
- Drug interaction (adding several compounds in parallel)
- Immunotherapy efficacy of any immune activation process just by fusing cancer cell phenotypes with activated immune cells.



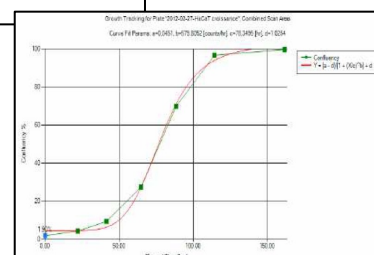
Our biopearl are compatible with :

- Ab
- DNA
- RNA
- Synthetic molecules (biomimetics and peptides)
- your natural extracts in development.

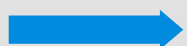
Read-out : Data report in

2D – 3D with EC₅₀ - Images – Curve for :

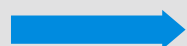
- Your molecule
- Matrix
- Your molecule control or our Celestrol



PILOT STUDY
in 2D

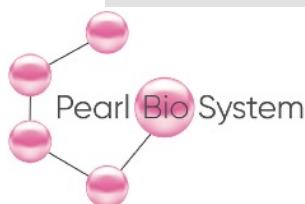


3D testing
Pearl BioSystem
patented tool



Reporting
images + EC₅₀

2-3 WEEKS



Pearl BioSystem technology:
a boost for your oncology preclinical assays

Dermo-cosmetic and Cosmetic's Pearl BioSystem's Catalog

Early access program: sample testing available in our Skin Care program

Sample Testing on our Prototyping & Validated Assay:

Pearl BioSystem R&D has already developed some assays directly accessible to our customer to evaluate rapidly the added value of the pearl's technology.

Human skin cell lines :

- Keratinocytes
- Melanocytes
- Sebocytes
- Hair

Human control cell line

- Fibroblasts BJ (ATCC® CRL-2522)

One assay include :

- Cell growth
- Apoptosis
- Mitochondrial respiratory
- Immunotherapy efficacy of any immune activation process just by fusing cancer cell phenotypes with activated immune cells.
- Effect on skin in relation to other organs (isiosyncratic)
- Ingredients interaction (adding several compounds in parallel)

Validated applications :

- Anti Inflammation / Anti Aging
 - Pigmentation
 - Sebogenesis
 - Wound Healing
 - Biofilm co-culture
- with possible recovery for each application of
- Proteome
 - Secretome
 - Fixed cells

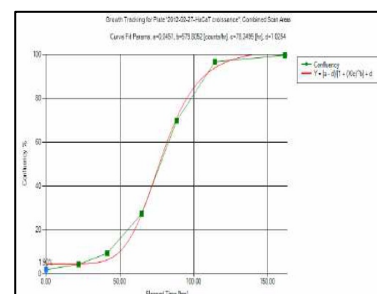
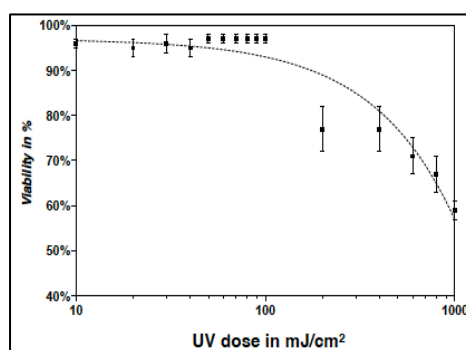
Our biopearl are compatible with :

- Ab
- DNA
- RNA
- Synthetic molecules (biomimetics and peptides)
- your natural extracts in development.

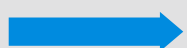
Read-out : Data report in

2D – 3D with EC₅₀ - Images – Curve for :

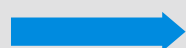
- Your molecule
- Matrix
- Your molecule control or our Celastrol



PILOT STUDY
in 2D

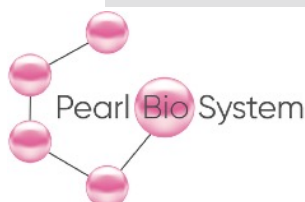


3D testing
Pearl BioSystem
patented tool



Reporting
images + EC₅₀

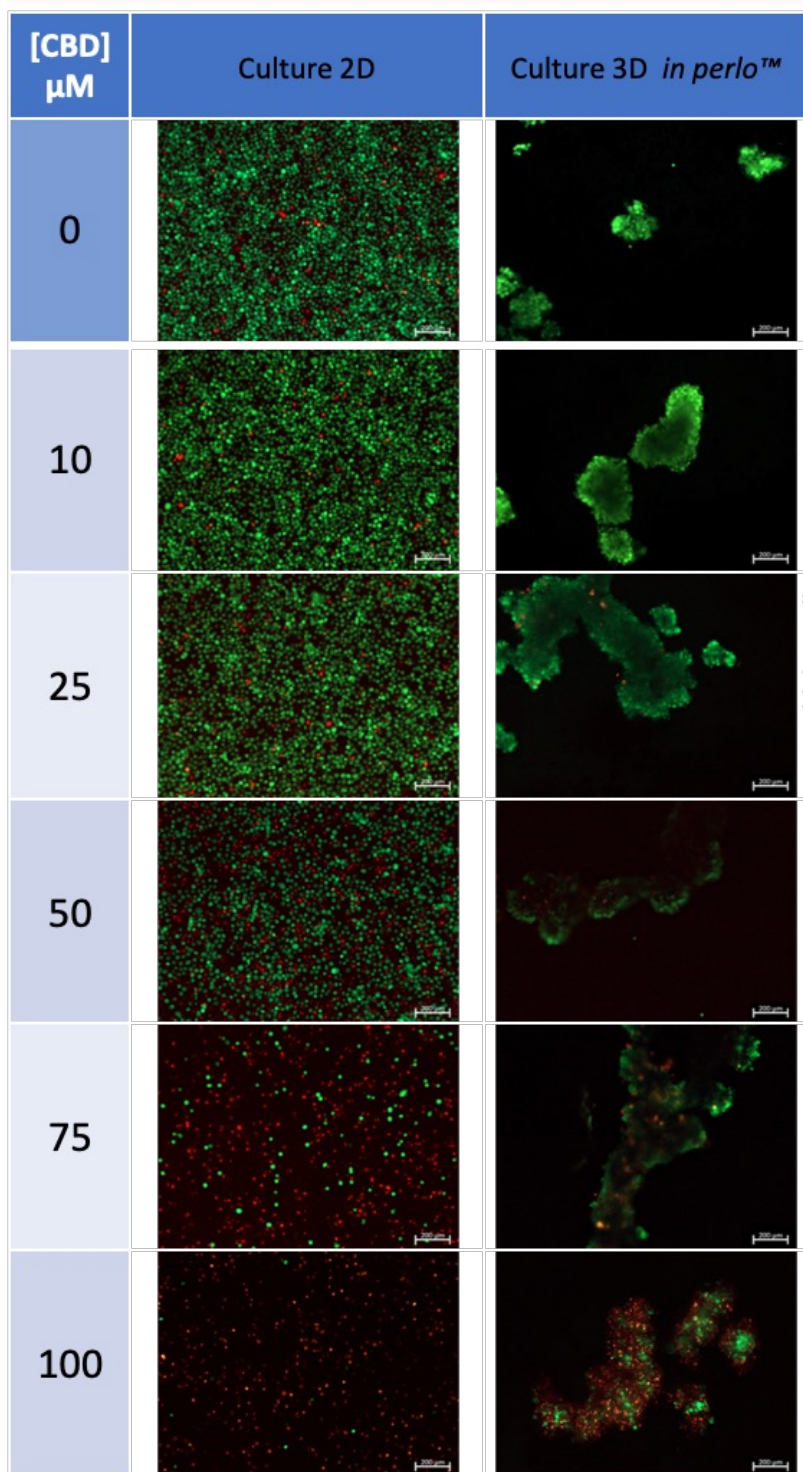
2-3 WEEKS



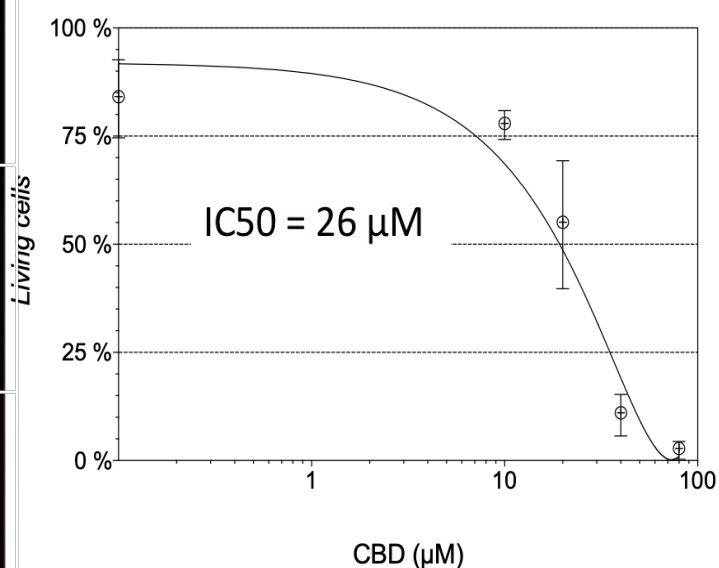
Pearl BioSystem technology:
a boost for your 2D & Skin model preclinical assays

Medicinal cannabis *in perlo*TM testing

In recent years, interest in *Cannabis sativa* L. has been rising as legislation is finally moving in the right direction.



IC₅₀ of CBD on human chemo resistant **pancreatic** cancer cells AsPC-1 (ATCC® CRL-168)

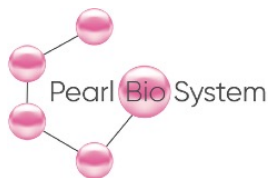


Our *in perlo*TM data, recently published in *Molecules*, supports the notion that CBD is the most effective bioactive molecule for anticancer activity among the components of this plant.

Molecules **2022**, *27*, 1214.

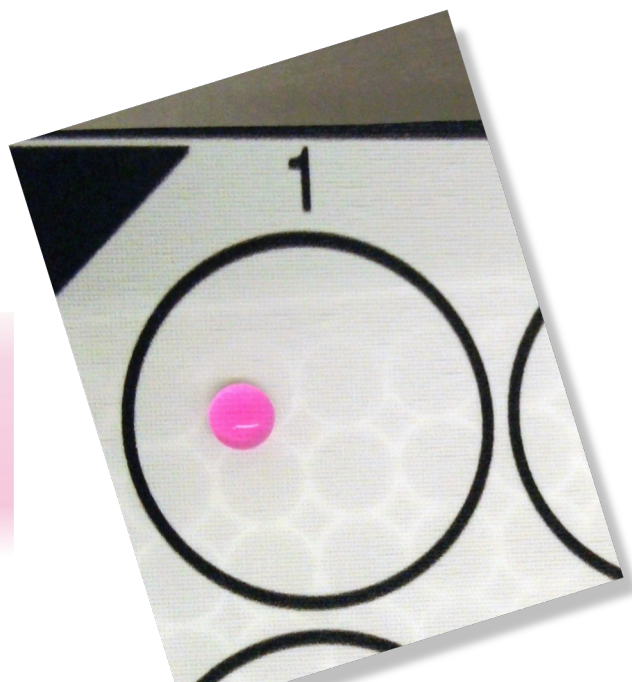
<https://doi.org/10.3390/molecules27041214>

Dose-dependent cell viability after 72H CBD treatment in 2D and 3D culture on chemo resistant **colorectal** cancer cells

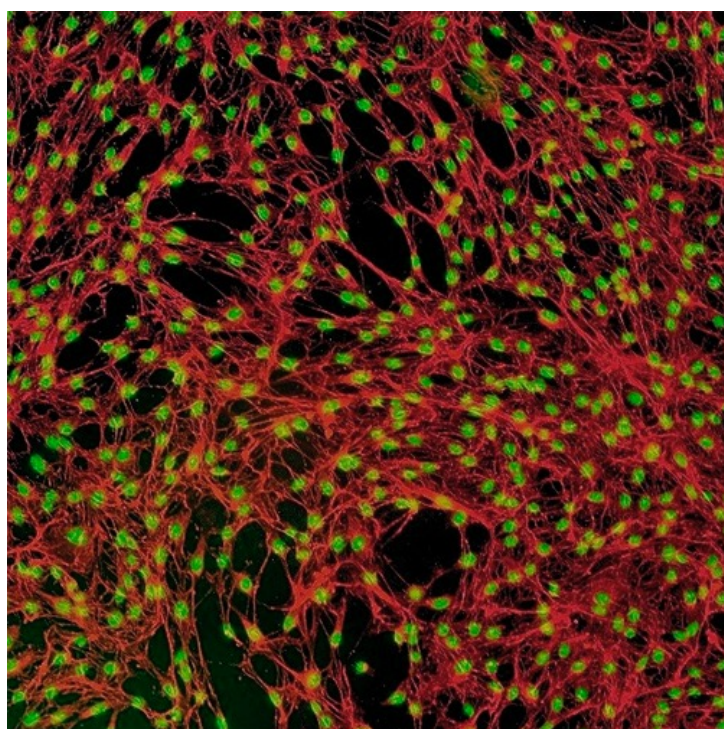


Our ophthalmology application *in perlo*[™]

- To date, there is no 3D cell culture model dedicated to the study of keratitis.



- Keratitis can appear in contact with inflammatory molecules, generally linked to infectious causes: microbial keratitis is the fifth global cause of blindness and visual impairment.



Immortalized Human Keratocytes (IM-HK)

Three human keratocyte cell lines are to be cultivated *in perlo*[™] then activated by injection of several immuno-stimulant molecules.

Custom Assay Development Pearl BioSystem's Catalog

- Mammalian eukaryotic cells (Human, mouse...)
 - Isolated, Stem Cells, Embryonic, induced pluripotent stem cells (iPSCs)
 - Skin cells (keratinocytes, sebocytes, melanocytes...)
 - Eye (keratocytes)
 - Immune cells
 - Cancerous organoid
 - Endothelial cells
- Procaryotes (yeast, bacteria)



- Cell-cell interaction
- Molecule injection
- Combination of molecules
- Co-culture and fusion

Cell Lines

Type of Assay

Prototyping

Optimizing

Sample Testing

Services - Custom assay development program

PHASE 1: Custom Assay Development

Develop the Pearl BioSystem assay to a specific phenotype. It will give a proprietary Design Of Experiment (DOE) cost (DMSO/Pearls concentration/Molecule concentration...) that could be used to do sample testing.

PHASE 2: Sample Testing

Pearl BioSystem will offer to carry out molecule evaluations on the specific DOE assay developed in the first phase.

Molecules samples testing subscription : our offer is fully flexible :

- In house : send us your molecule controls to validate our *In Perlo™* technology

And after Proof of Concept :

- Licensing-out : when validated under your operational criterias

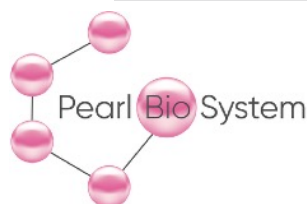
Creation of a proprietary tailor-made assay

PILOT STUDY
in 2D

3D testing
Pearl BioSystem
patented tool

Reporting
images + EC₅₀

3-4 WEEKS

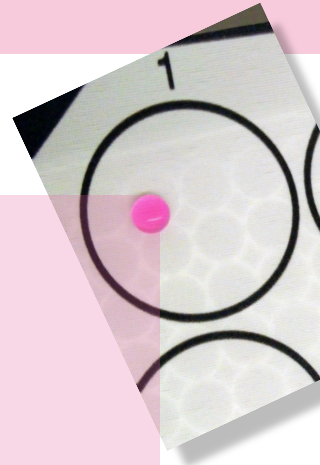


Pearl BioSystem technology:
a boost for your customized preclinical assays

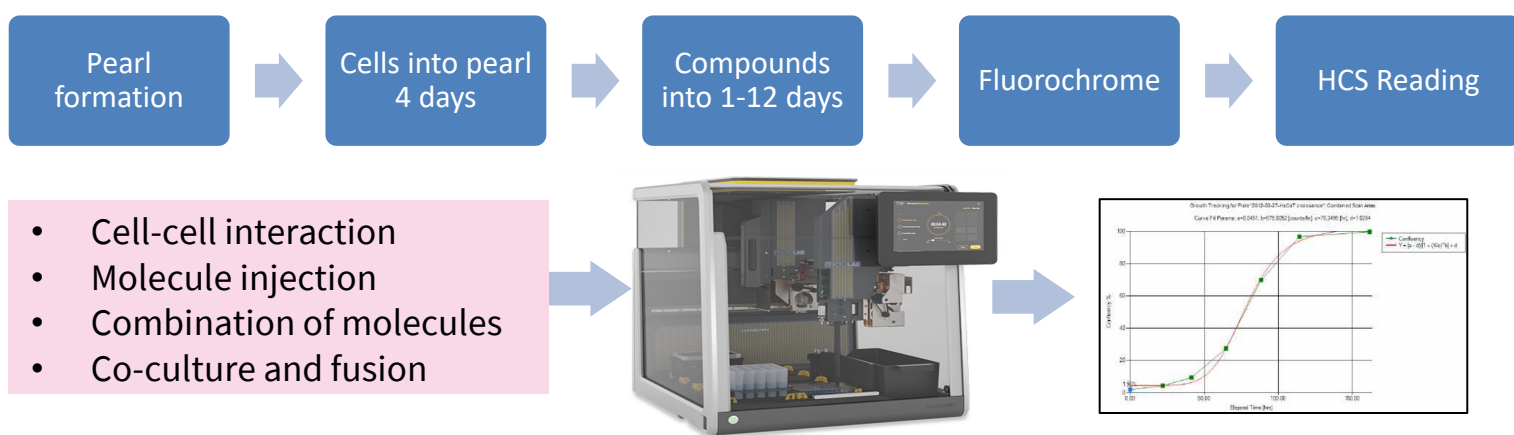
Our Automated Pearl BioSystem's Workflow

The *in perlo*[™] advantages

- Automated dispensing without temperature control
- No auto-fluorescent signals as there is no matrix present
- No protein matrix interference for the same reason
- No needs of any enzymatic cell recovery
- Scale your assays up with confidence (until x 100 compounds per week)
- Repeatability up-from 6 until 96 well-format (CV <3%)



Automation validated steps



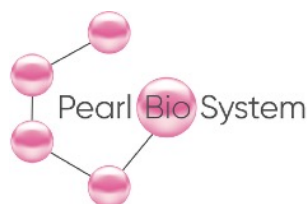
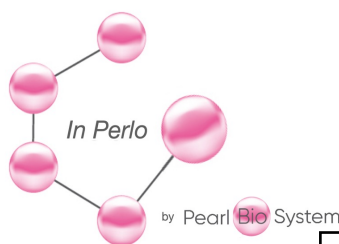
HOW PEARLBIOSYSTEM
CHANGES THE ODDS

A disruptive liquid pearls
based technology

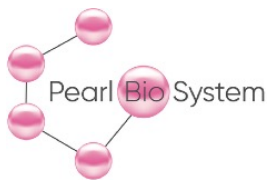
Real High Content
Screening possibilities

Low cost 3D cell culture
technology

Consistent culture conditions
Low plasticware waste



Pearl BioSystem technology:
a high throughput for your customized preclinical assays
and secured your expenditures in your R&D pipeline



How to reach us ?

Would you like to learn more and develop a proof of concept on your compounds currently in development before using our ***in perlo™*** technology on a larger scale?

We offer global presence and support.

Do not hesitate to contact one of our representatives based in your region:

For Europe, UK, Switzerland, South Africa, South America :

Mrs Claire Bottero @ cbottero@pearlbiosystem.com

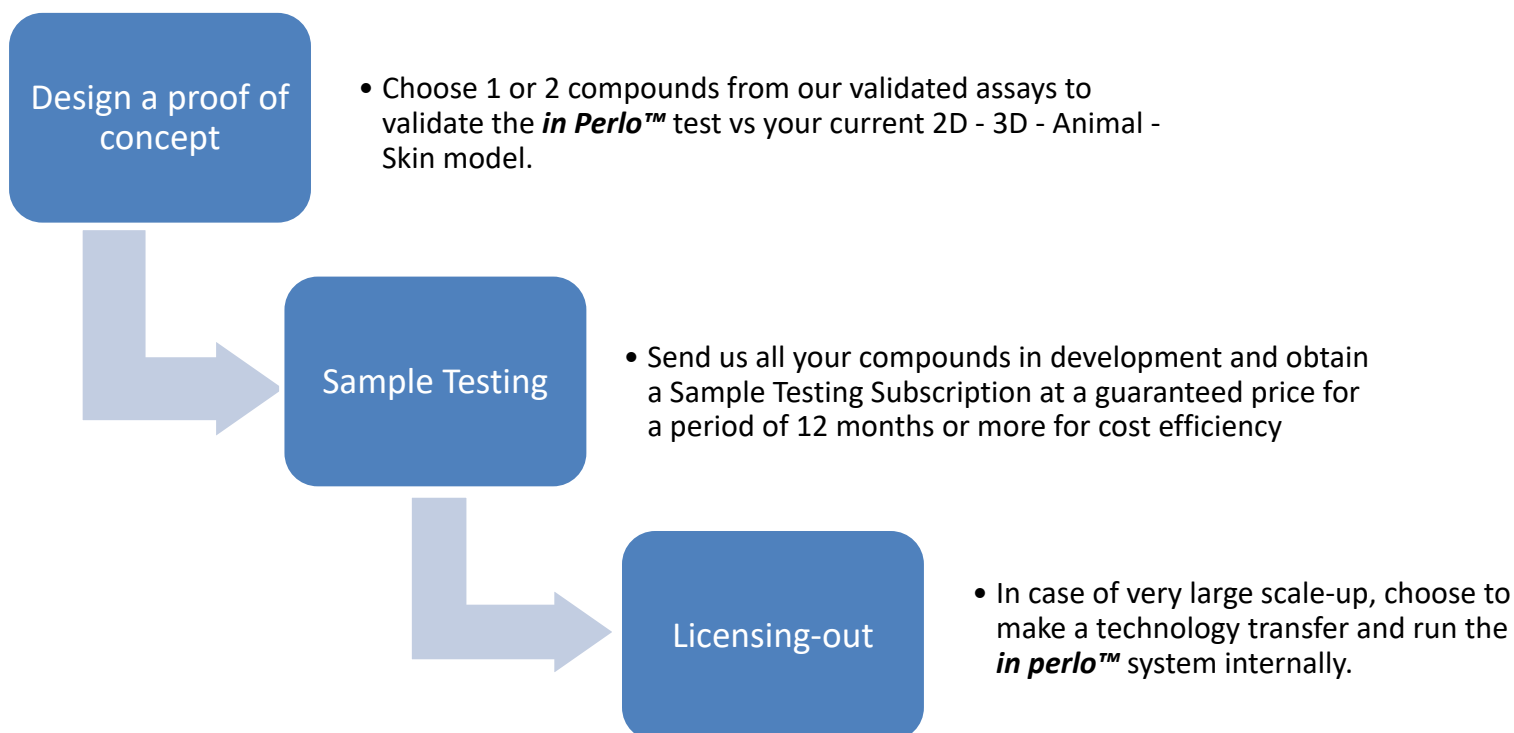
For North America & Canada :

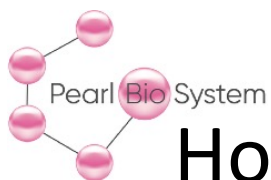
Mrs Martha Miles @ mmiles@pearlbiosystem.com

For APAC :

Martha and Claire @ myproject@pearlbiosystem.com

To discuss the easiest way to integrate our 3D ***in perlo™*** methodology into your preclinical compound screening process.

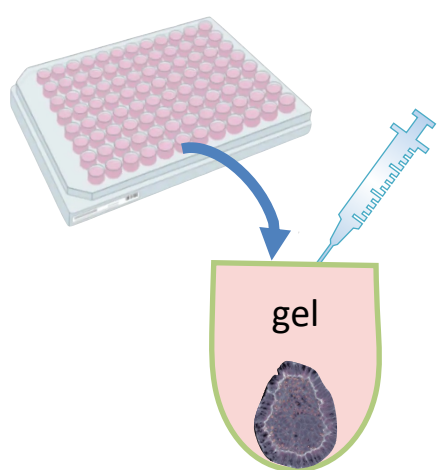




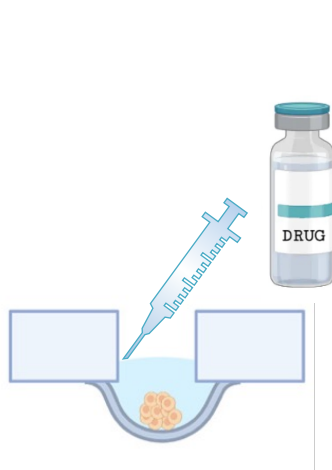
Various 3D culture ?

How the *in Perlo*TM is so revolutionary ?

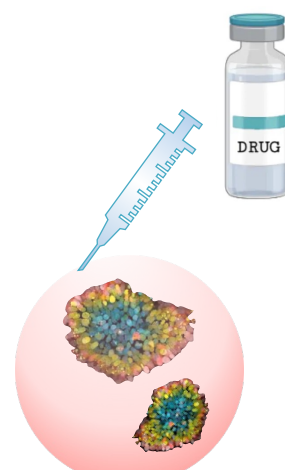
3D culture screening techniques



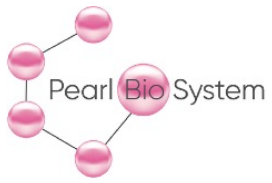
Low adhesion wells



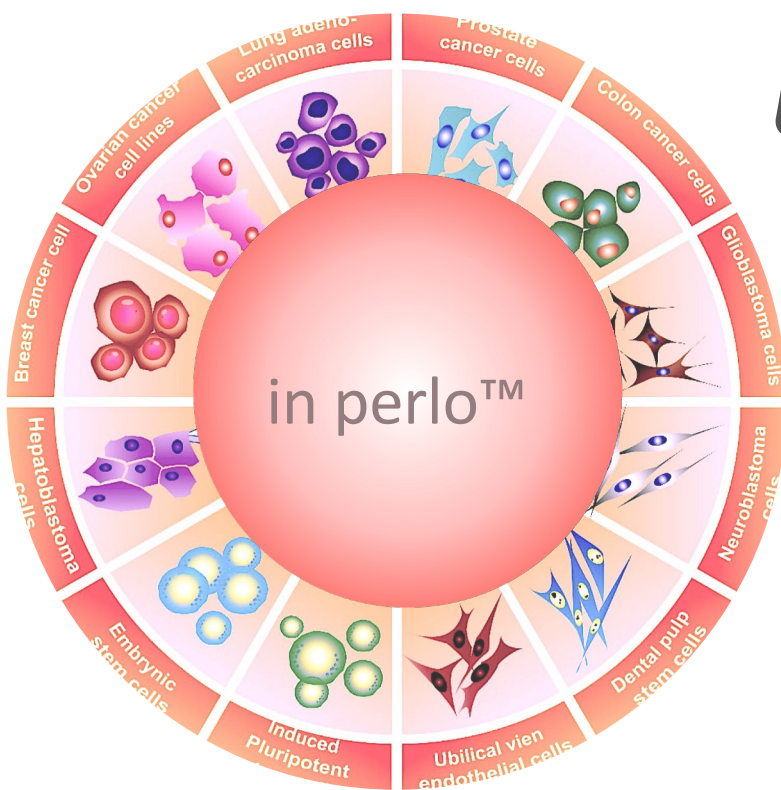
hanging drop



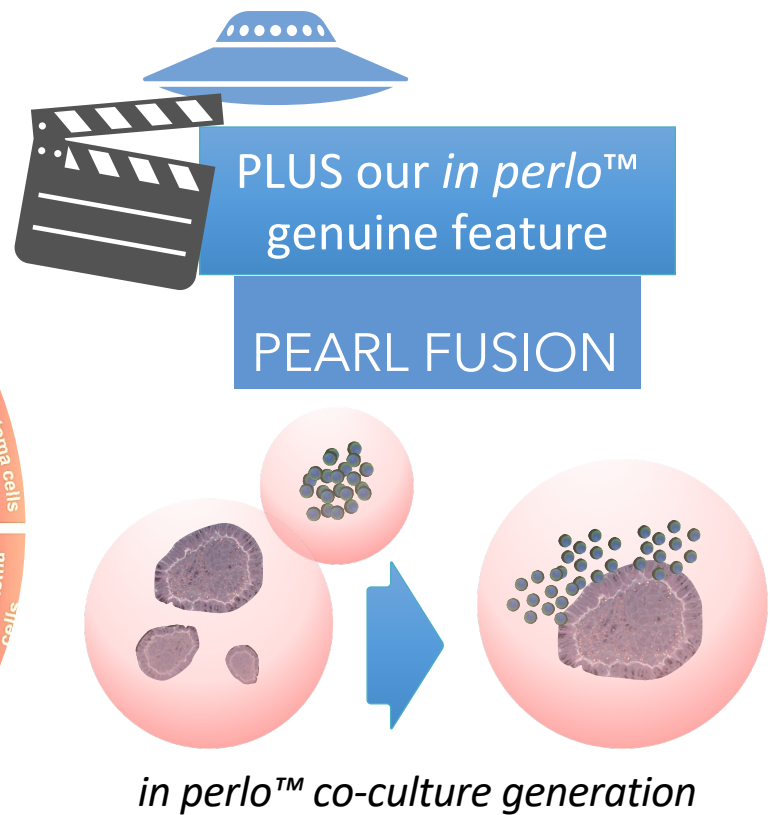
*in perlo*TM



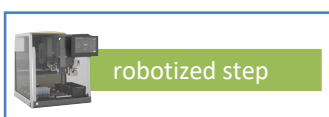
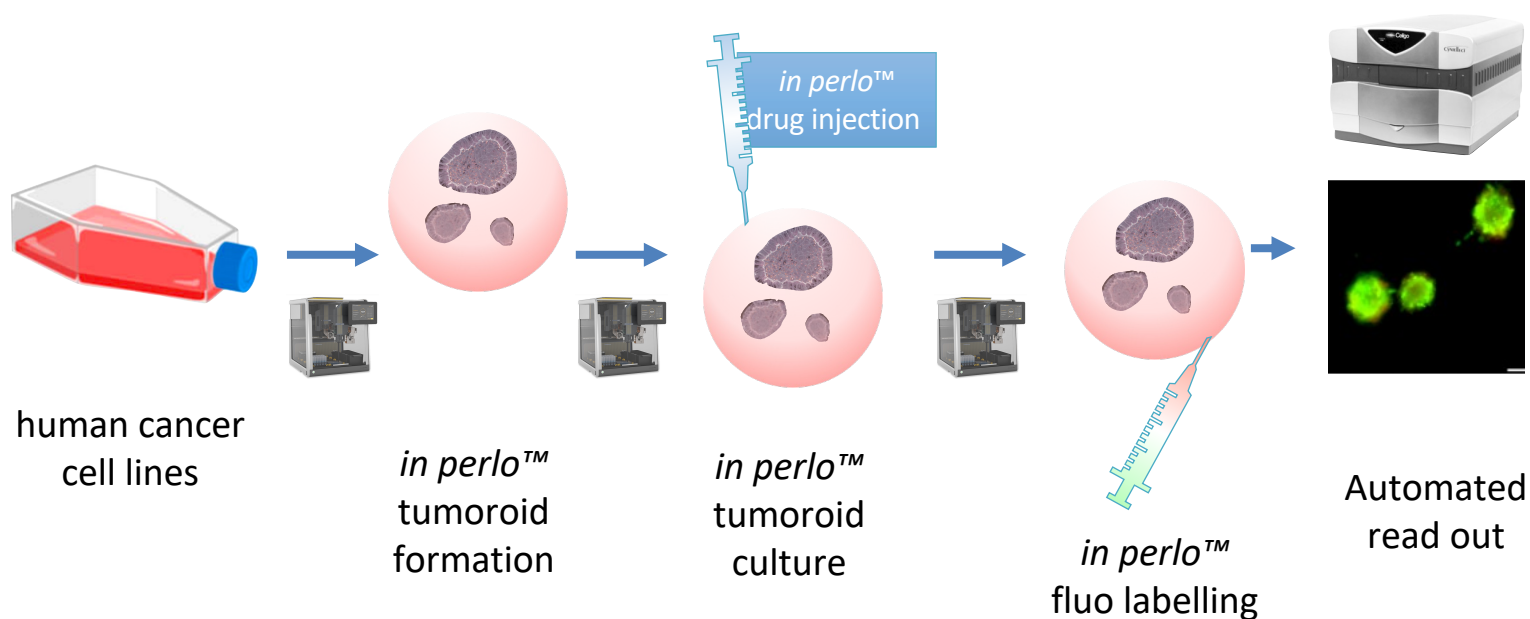
Any phenotype application



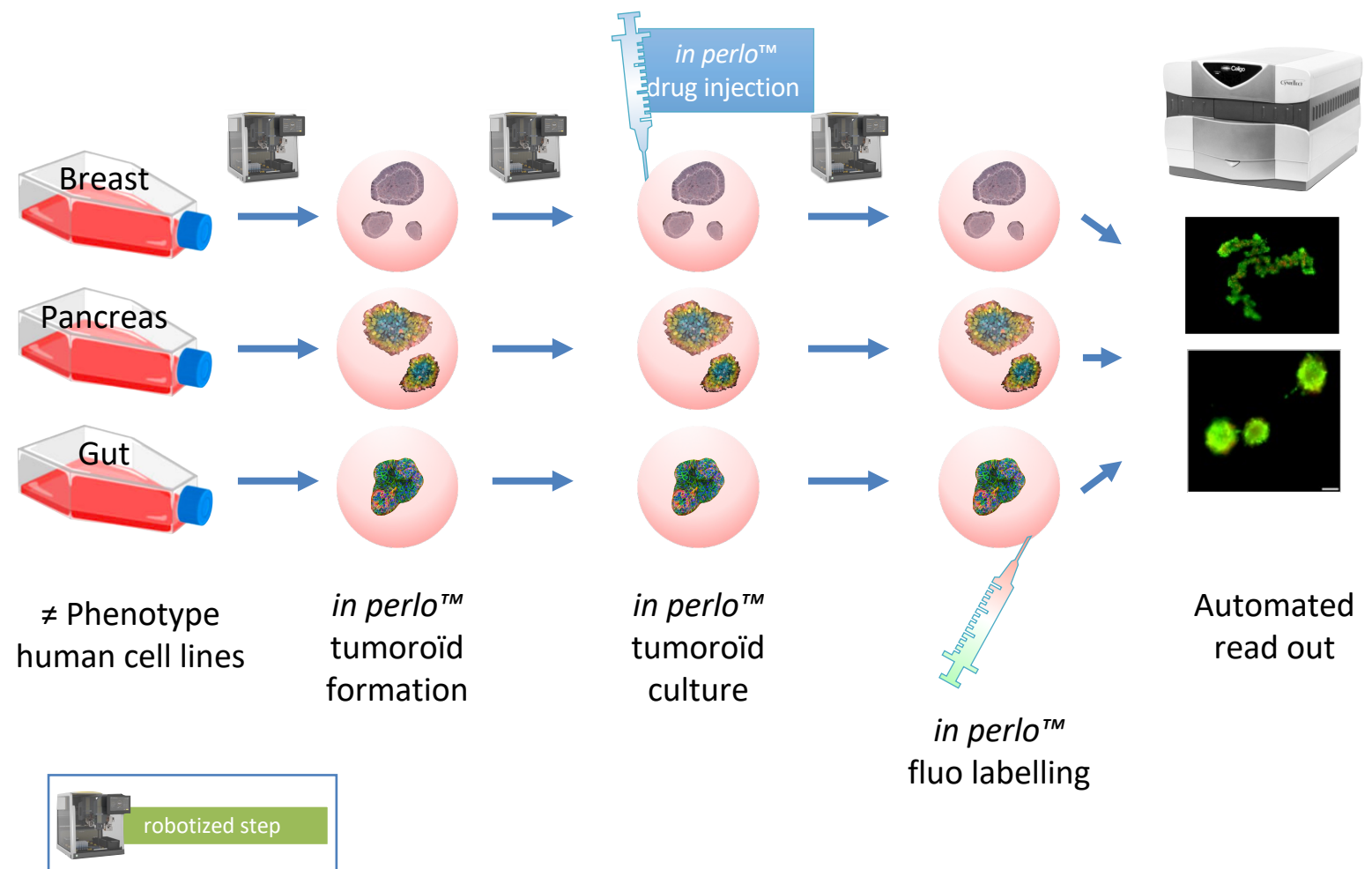
≠ phenotypes cell lines



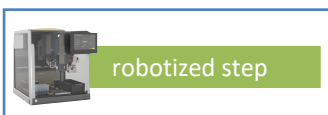
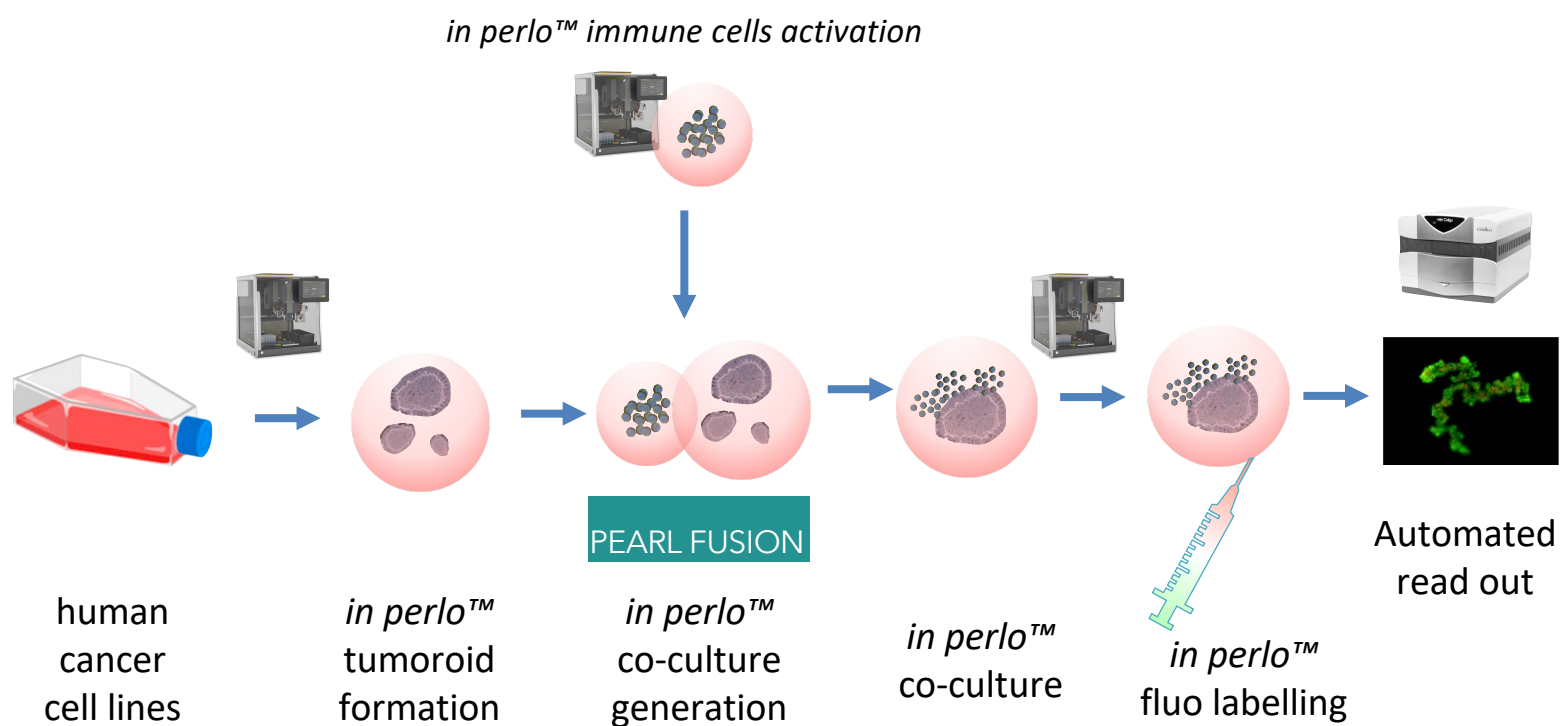
Automated workflow for screening



Automated workflow for screening



Workflow for immune stimulation



Workflow for immune stimulation

