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National Academy of Sciences of Armenia

Deutsches Elektronen-Synchrotron

Zeuthen, Germany
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BIOLOGICAL SAMPLES FOR RADIOBIOLOGICAL EXPERIMENTS

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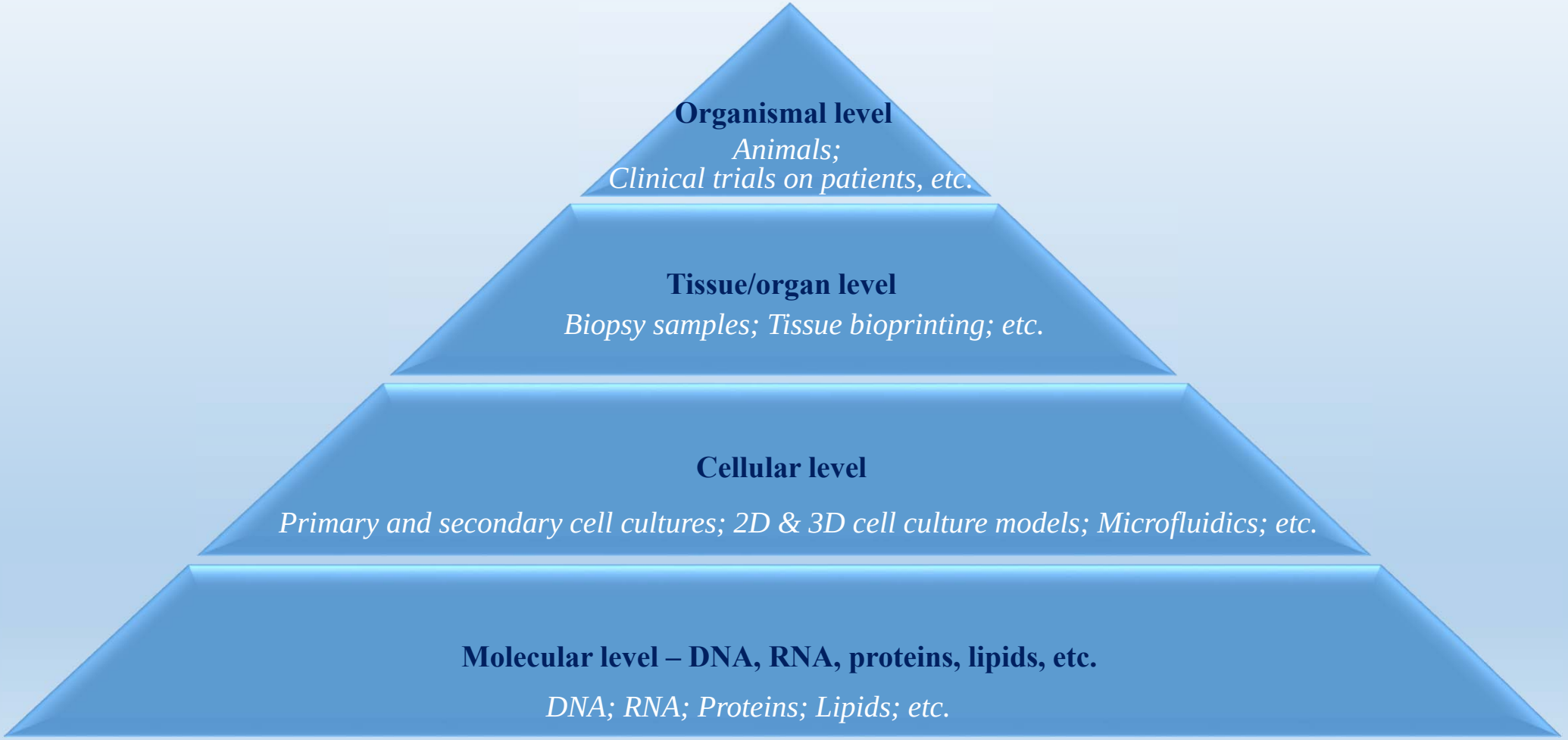
Experiment Types



Experiments on Cellular level

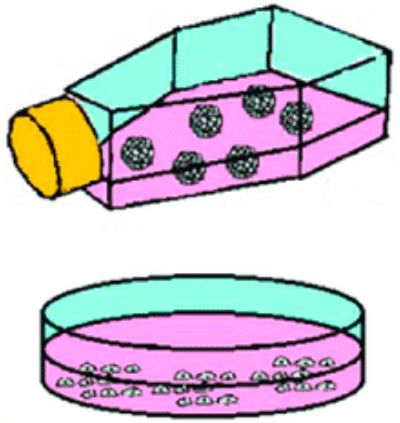
Static 2D and 3D cell cultures:

Pros:

a) Simple realization;
b) Low costs;
c) Simple control;
d) Well standardized;

Cons:

a) Difficult to reproduce cell microenvironment;
b) Difficult to implement in HT systems;
c) Time consuming and laborious.



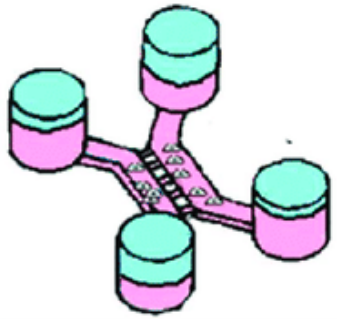
2D microfluidic culture chambers

Pros:

a) Simple realization;
b) Low costs;
c) Simple control;
d) Possible to implement in HT systems;
e) Reduced manual opertion;
f) Sensor integration;
g) Precise spatial/temporal dynamics;
h) Continuous monitoring and feedback.

Cons:

a) Difficult to reproduce cell microenvironment.



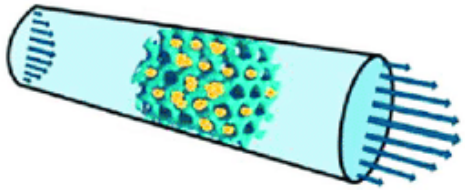
3D microfluidic culture chambers

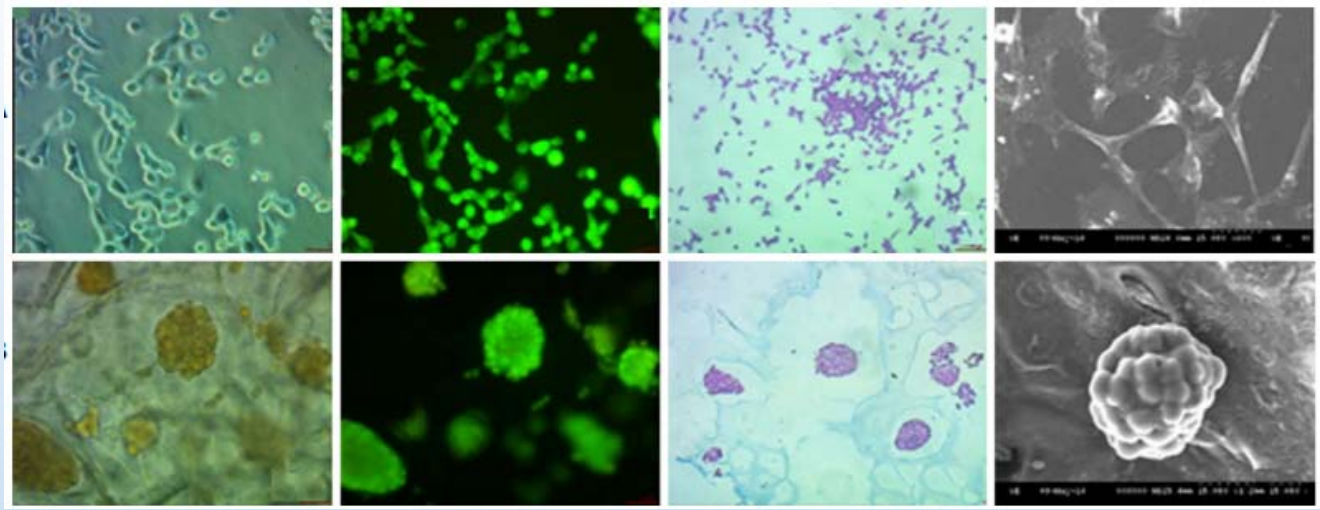
Pros:

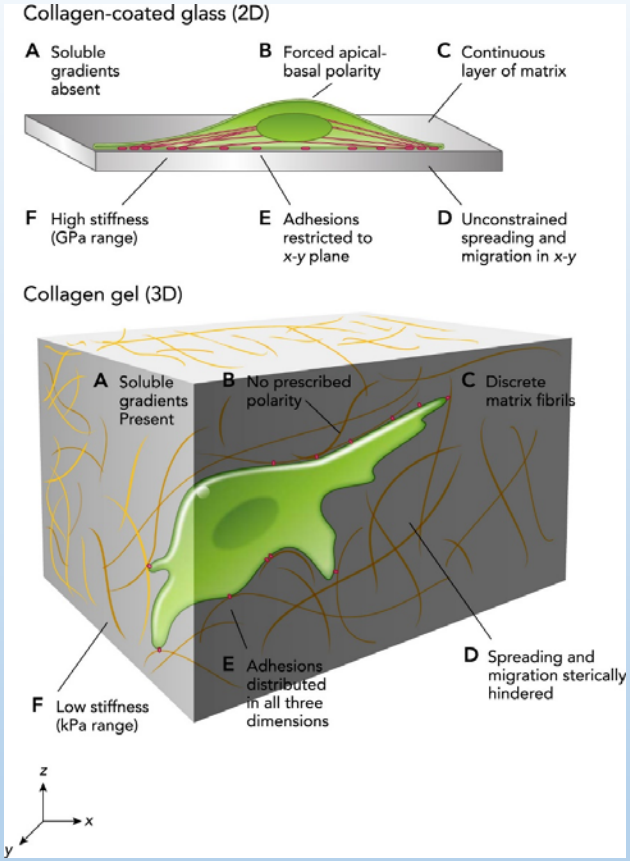
a) 3D microenvironment reproduceable ;
b) Possible to implement in HT systems;
c) Variety of investigations;
d) Scaffold integration;
e) Continuous monitoring and feedback.

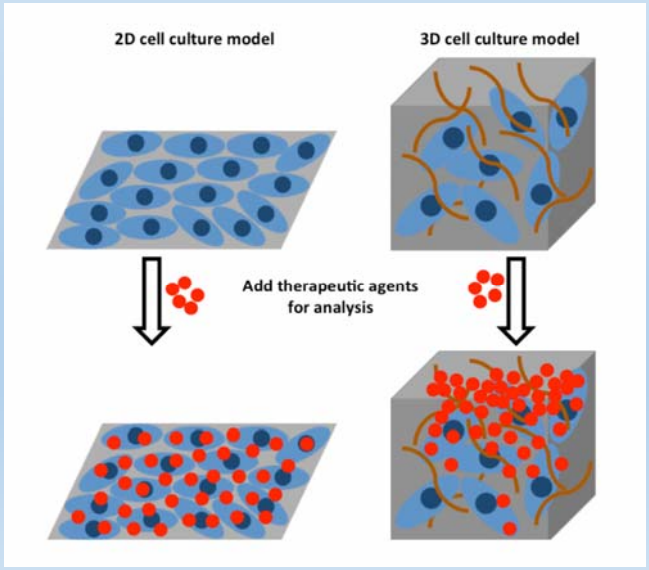
Cons:

a) Limited by diffusion gradients;
b) Difficult imaging;
c) Difficult sensor integration;
d) Costs.






Collagen-coated glass (2D)
A Soluble gradients absent
B Forced apical-basal polarity
C Continuous layer of matrix
F High stiffness (GPa range)
E Adhesions restricted to x-y plane
D Unconstrained spreading and migration in x-y
Collagen gel (3D)
A Soluble gradients Present
B No prescribed polarity
C Discrete matrix fibrils
D Spreading and migration sterically hindered
E Adhesions distributed in all three dimensions
F Low stiffness (kPa range)
z
x
y


2D cell culture model
3D cell culture model
Add therapeutic agents for analysis

Experiments on Cellular level

Primary cell lines **Secondary cell lines** **Matched normal and cancer cells**

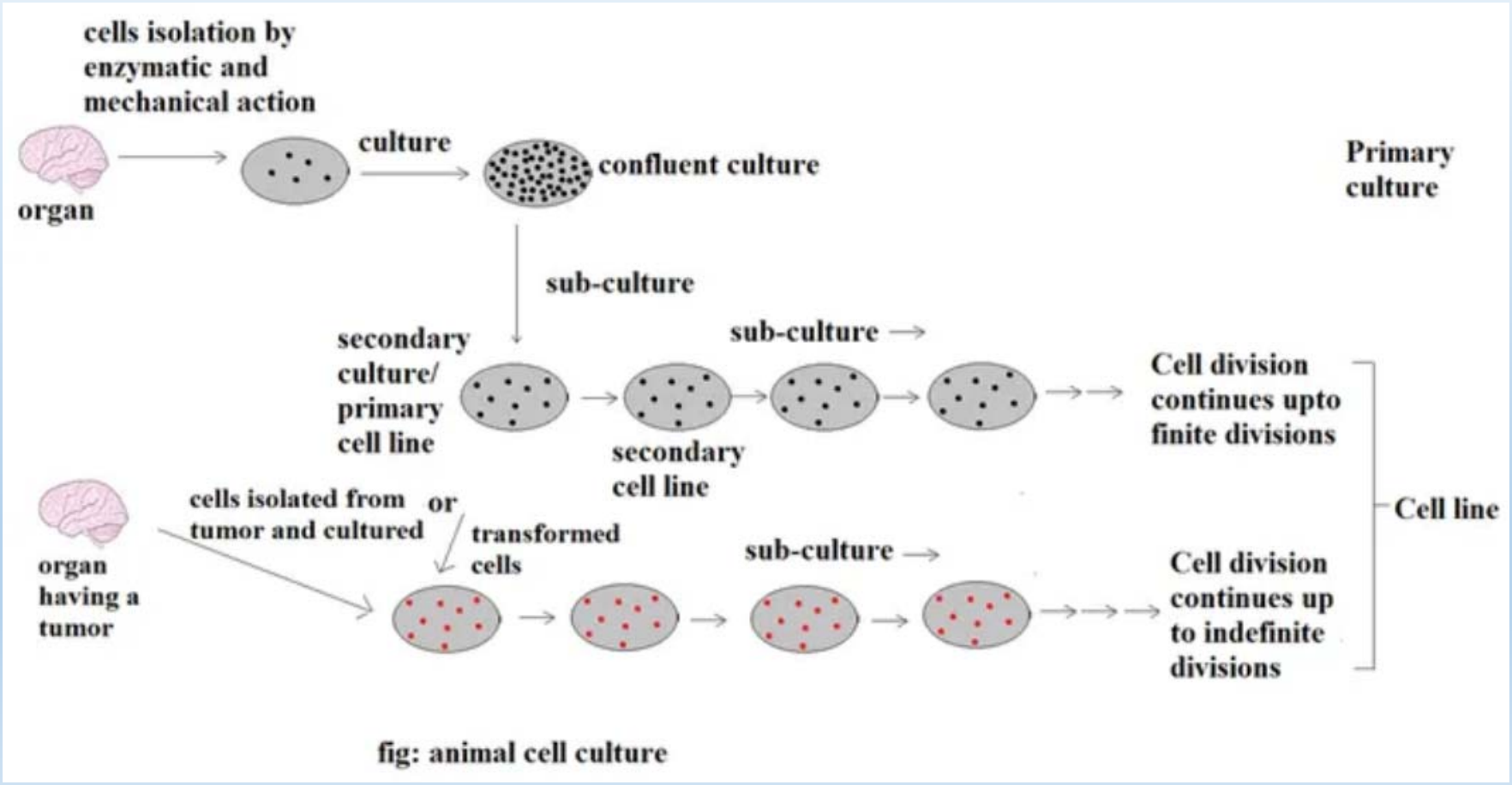
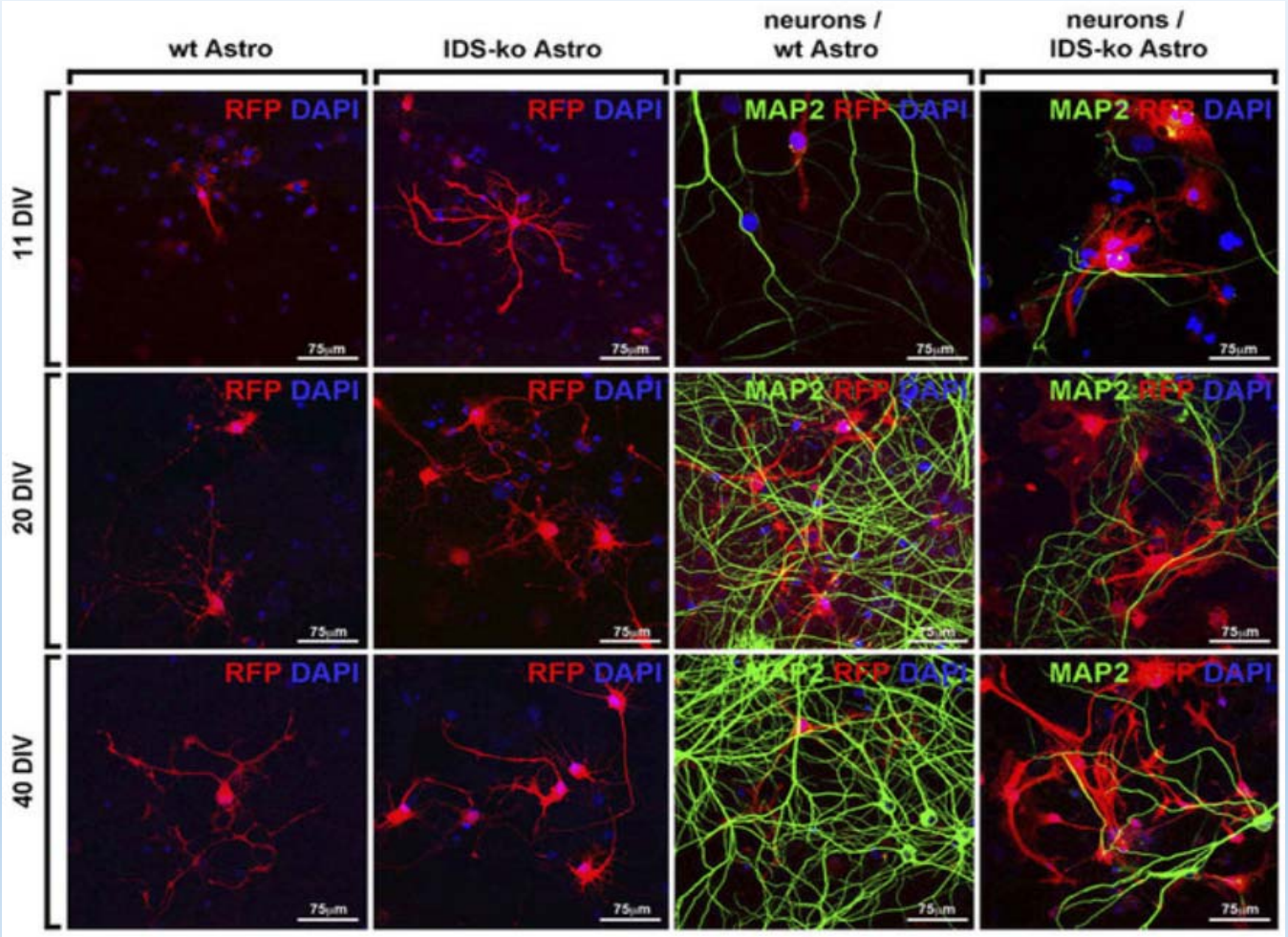


fig: animal cell culture

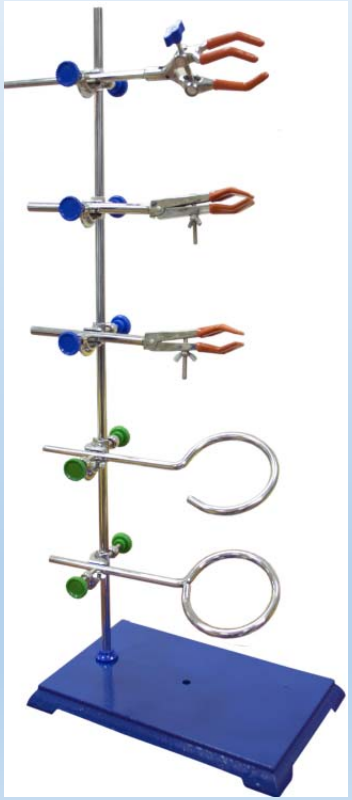
Experiments on Cellular level



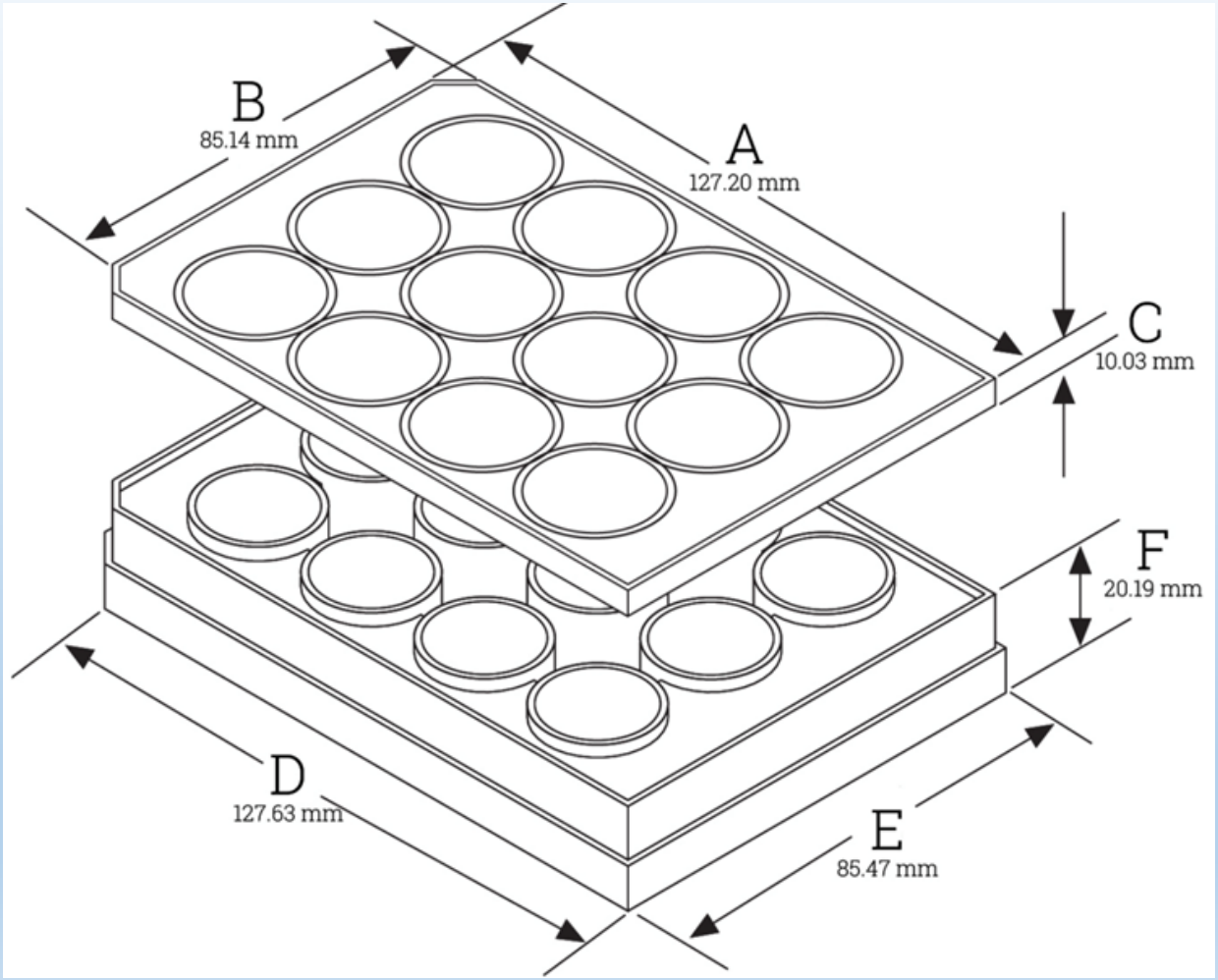
Samples at Experimental Station

New solutions

Sample holder



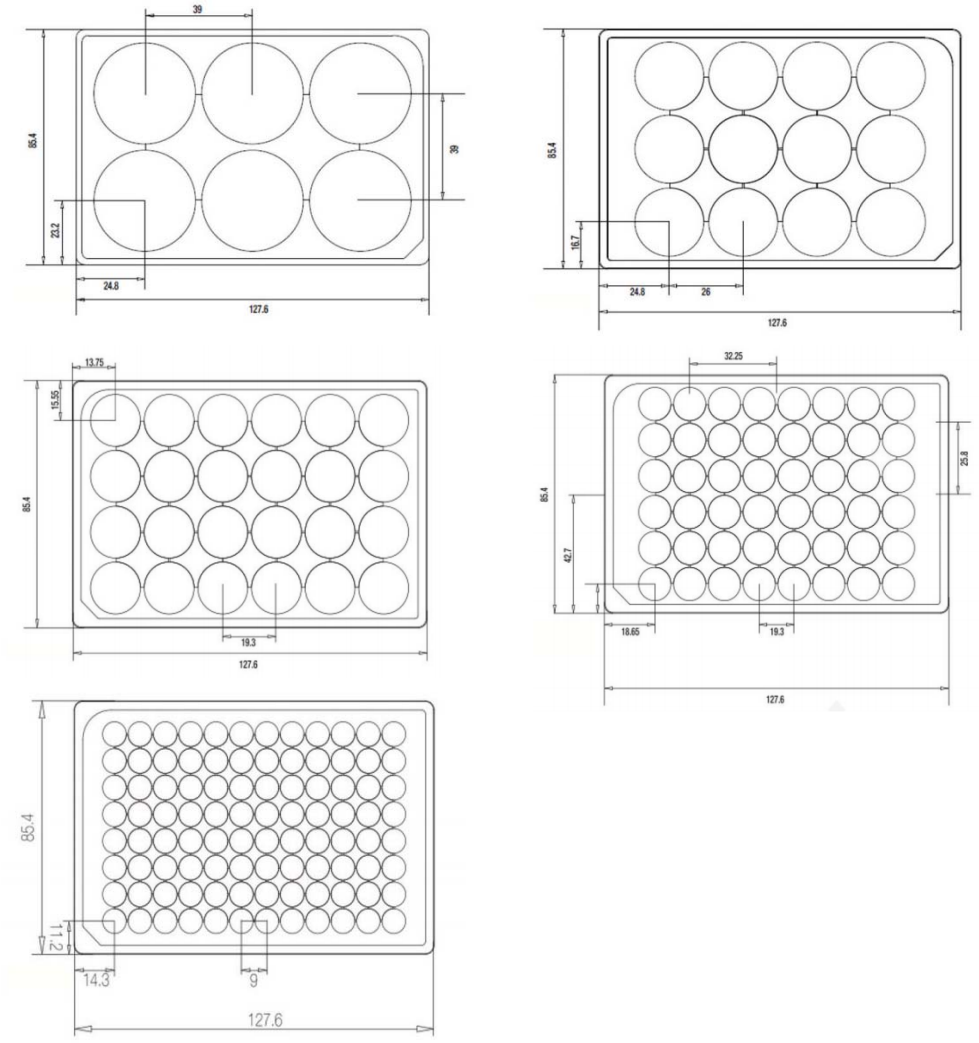
Tripod, Laboratorie Stativ



A: Lid Length
B: Lid Width
C: Lid Height
D: Plate Length
E: Plate Width
F: Plate Height

Well Dimensions:
Top Internal Diameter: 22.75 mm
Bottom Internal Diameter: 22.09 mm
Depth: 17.65 mm

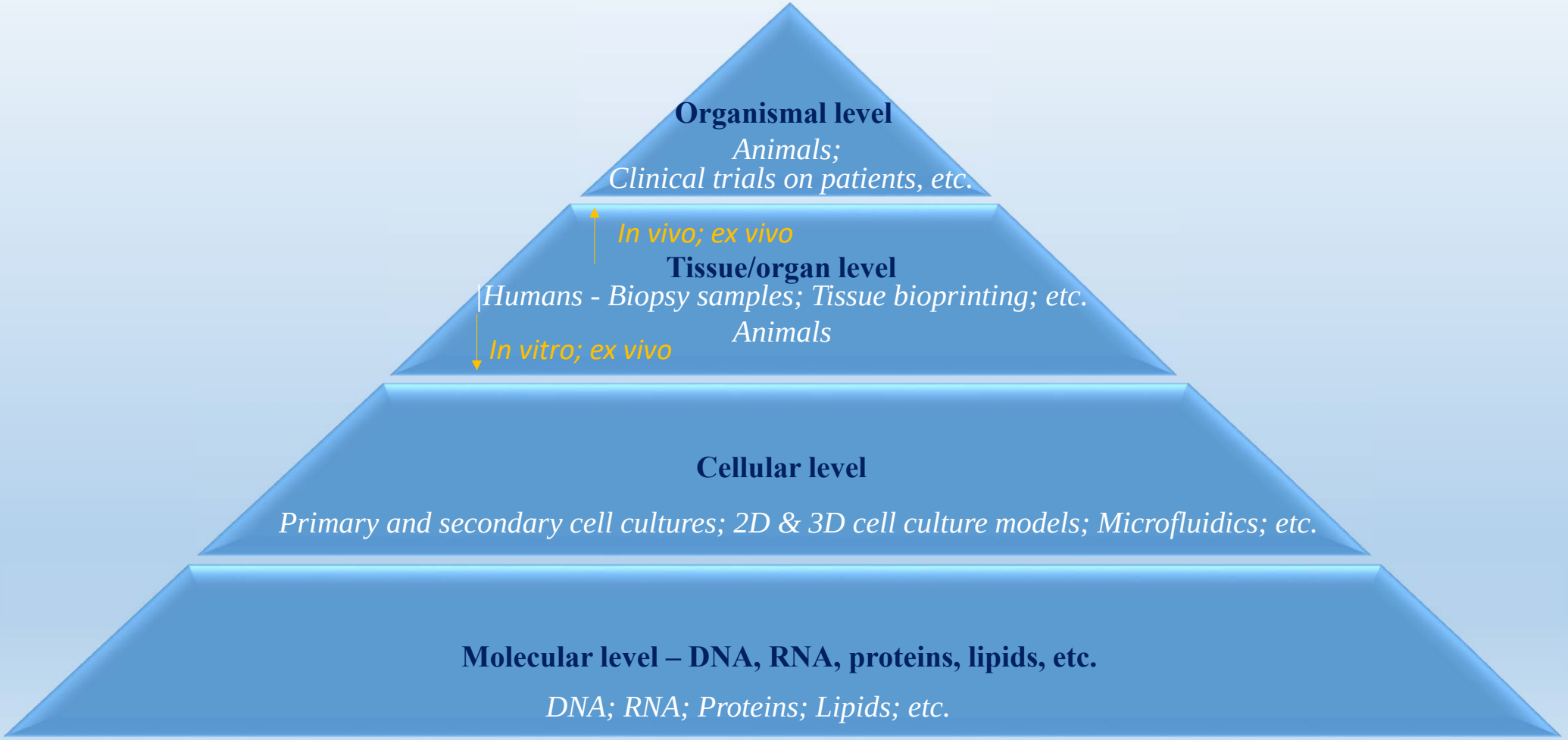
Cell culture plates



Sterilin Petri Dishes, 30 to 140mm

Description	Base OD x OH (mm)
Petri dish, 30mm	35.0 x 11.0
Petri dish, 50mm	52.0 x 14.5
Petri dish, 50mm, deep form	50.0 x 20.3
Petri dish, 55mm	55.5 x 12.0
Petri dish, 55mm	55.5 x 12.0
Petri dish, 60mm	60.0 x 15.1
Petri dish, 140mm	138.9 x 21.1

Experiment Types



Animal Models

The development and importance of animal models in radiation research has a historical context.

- In the 1950s, public concerns about the peaceful and military deployment of atomic power led to large-scale, mission-oriented research into the genetic consequences of radiation exposure.
- Most of this effort was performed in Germany, U.S. and Britain and was directed toward low-dose radiation experiments in mice with the aim of evaluating the genetic risk of radiation exposure.
- While not fully successful in achieving their goal, these studies had a profound effect on biomedical science, laying down the foundation for research into human genetics, transplantation, cancer, immunity and other fields.

Animal Models

Besides the direct radiation effect it is also very important to take into account confounding effects, such as:

- Dose rate
- Peak dose rate
- Bunch repetition rate
- Concomitant exposure to burns or trauma
- Infections resulting from immune suppression
- Availability of timely supportive care.

Radiation exposure types and designs

Whole body irradiation

Partial body irradiation

Organ/Tissue irradiation

Tumor volume irradiation

Investigations on systemic level (immune system, antioxidant system, inflammation, apoptosis, etc.)

Genetic studies (DSB, etc.)

Genomic studies (SNPs, CNVs, deletions, etc.)

Epigenetic studies (DNA methylation, etc.)

Studies on cellular level

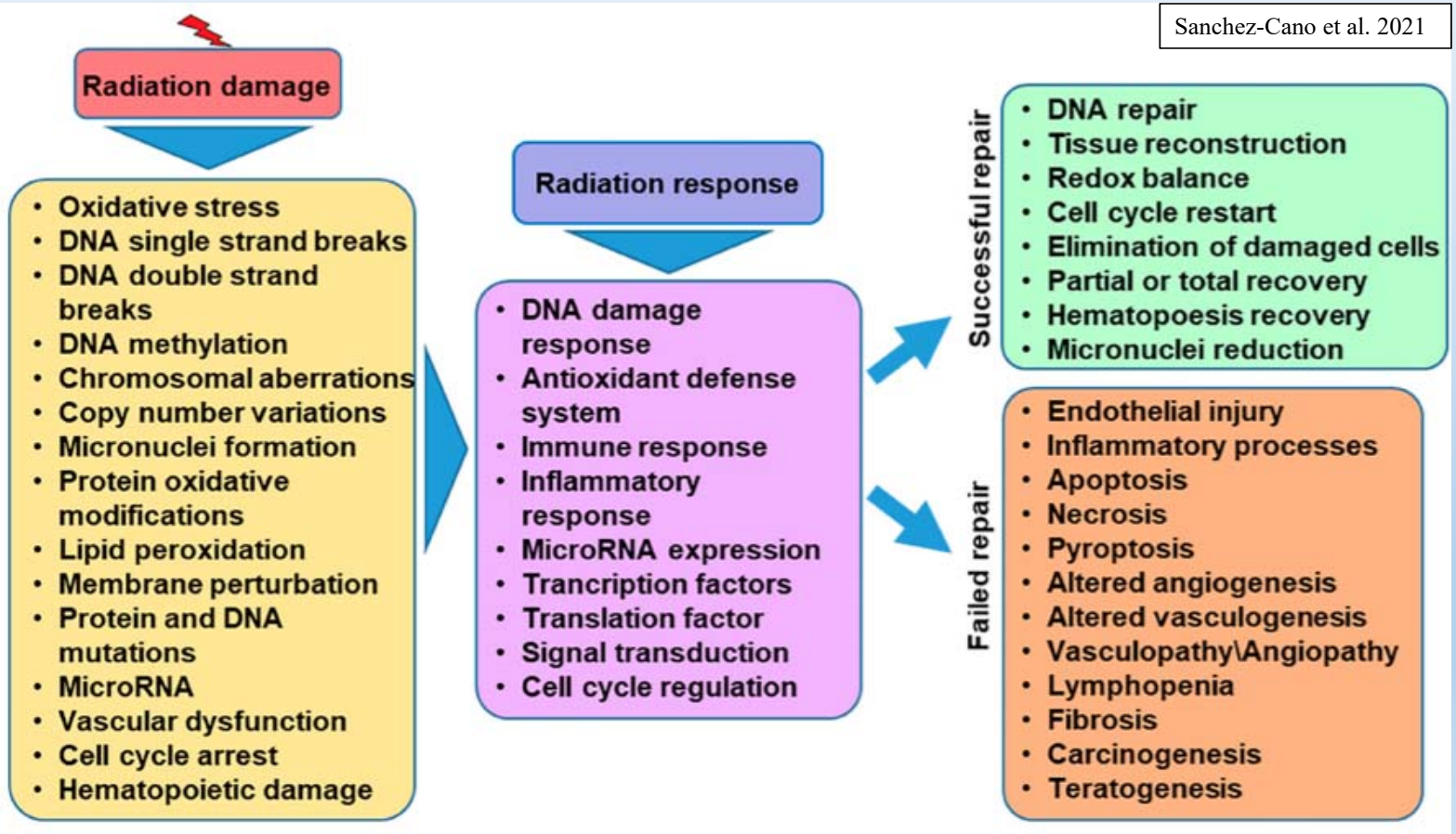
Studies on molecular level

***In vitro* studies**

***In vivo* studies**

***Ex vivo* studies**

Mechanisms involved in radiation damage and subsequent radiation response



Organs at most risk

- ✓ **Immune system**
- ✓ **Hematopoietic system (bone marrow)**
- ✓ **Gastrointestinal tract**
- ✓ **Kidney**
- ✓ **Skin**
- ✓ **Lung**

Little is known as to how the systemic effects of radiation exposure influence local organ function or how damage to one system affects others.

If early failure of one organ is prevented, another tissue could later fail.

Parameters for optimizing experimental designs so as to allow valid comparison between studies

- ✓ Gender – Male and female animals
- ✓ Dose
- ✓ Dose rate
- ✓ Homogeneity of dose
- ✓ Total time of exposure
- ✓ degree of shielding
- ✓ microbial status
- ✓ supportive care
- ✓ Selection of animal strains and species

Animal models

Mouse

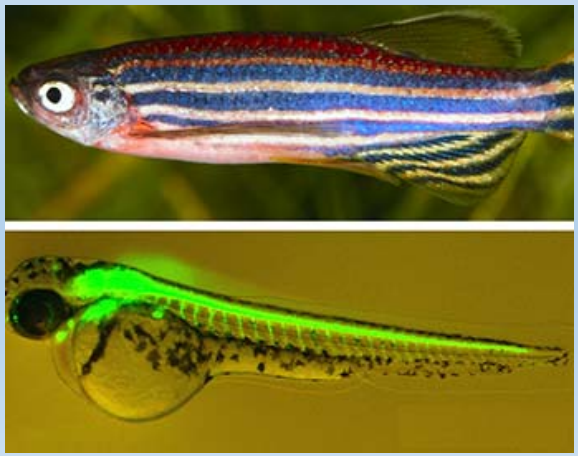
C57BL/6 and C3H/HeN

Rat

Wistar rats

Pig/Minipig

Zebrafish



Crab

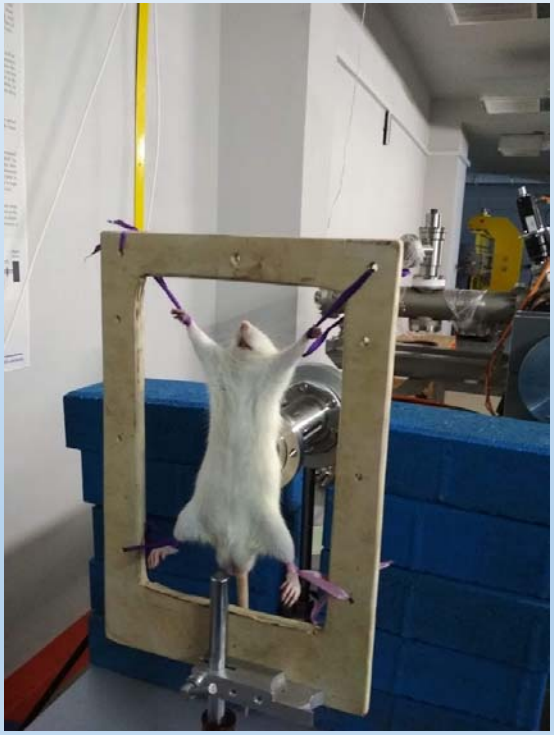
Flies (Drosophila melanogaster)

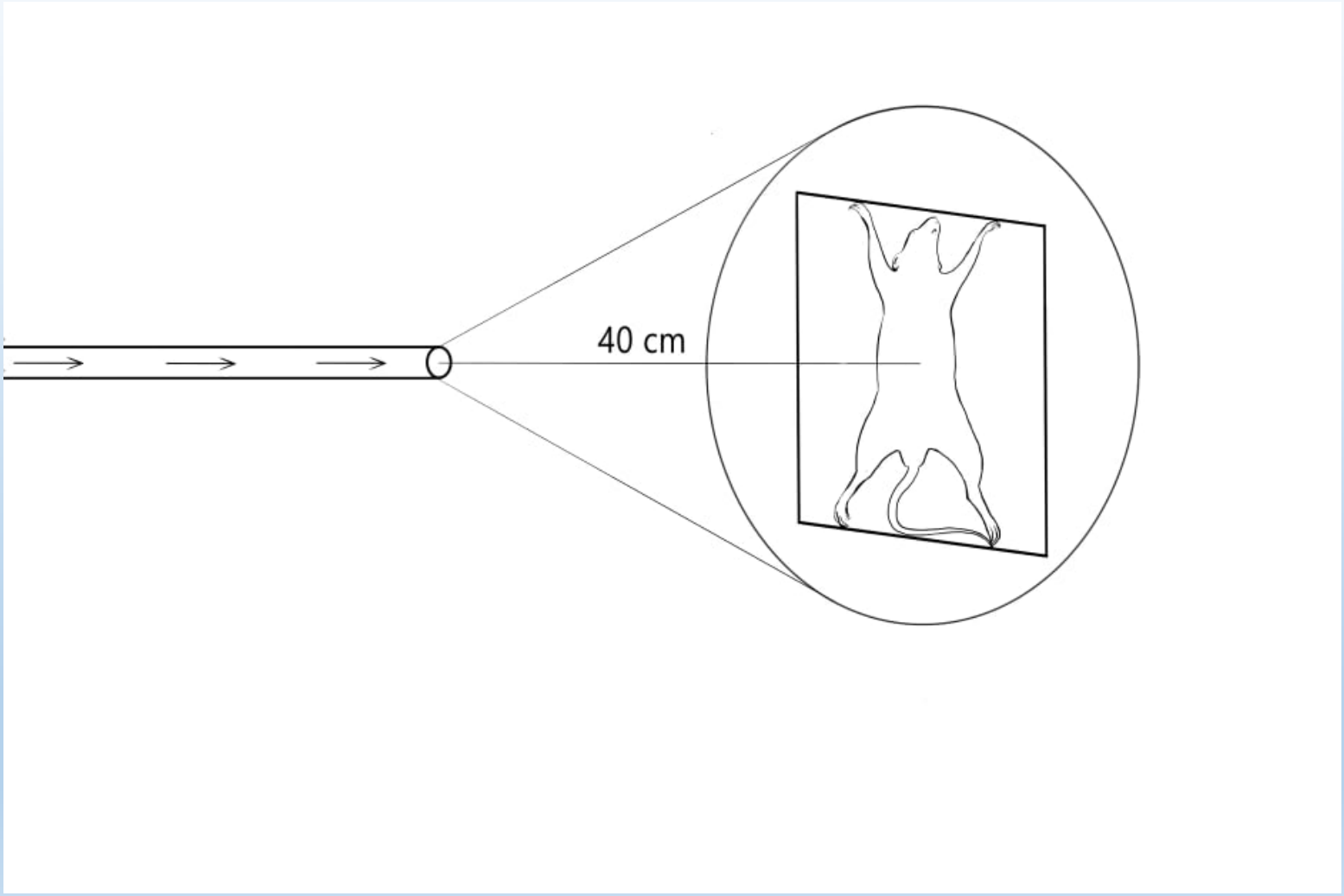
Worms

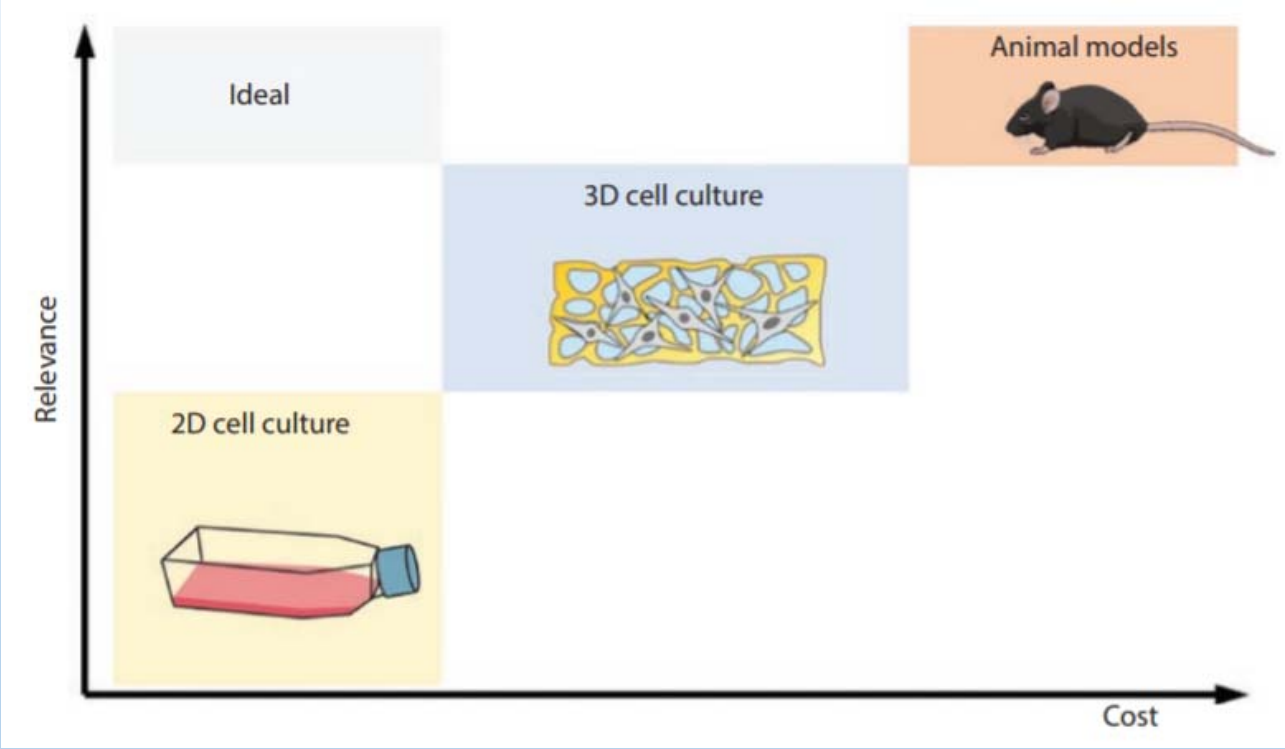
Non human primates (Rhesus macaques)

Samples at Experimental Station

Sample holder




40 cm

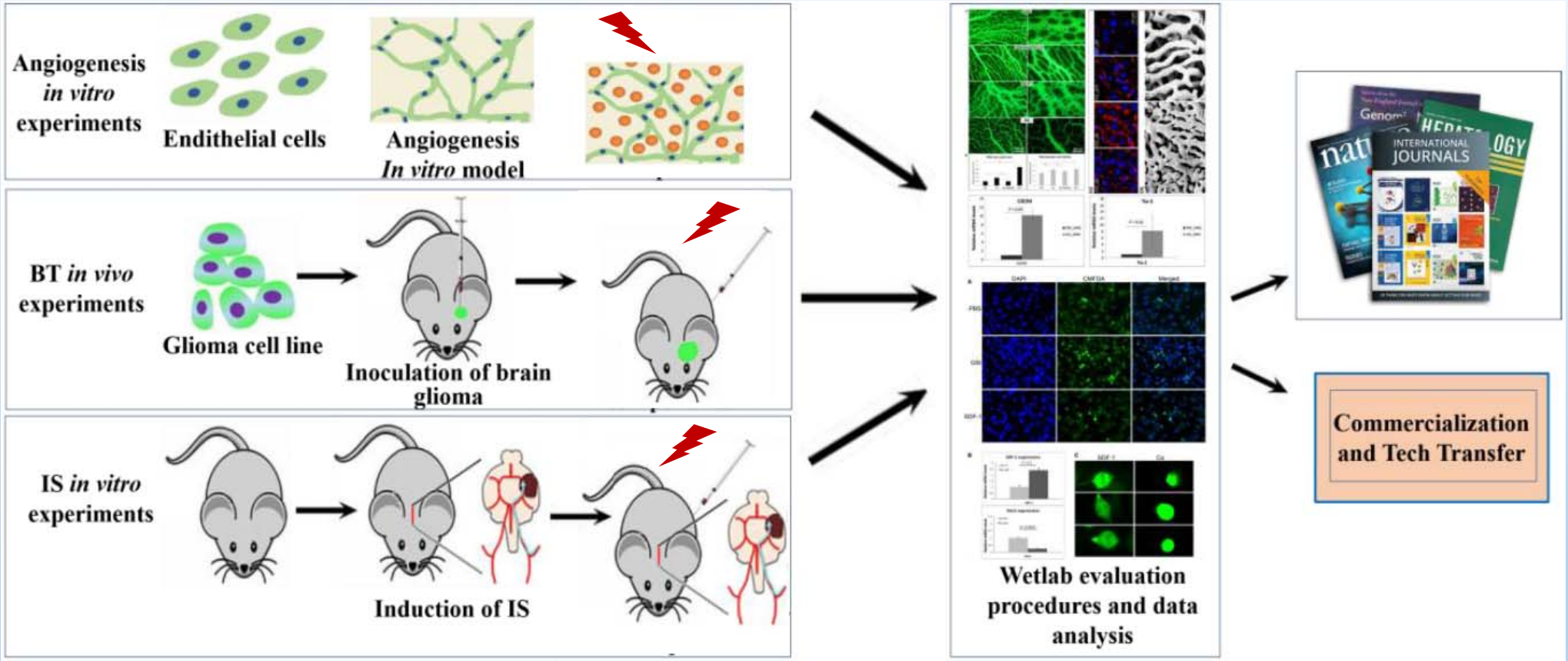

Ideal
Animal models
3D cell culture
2D cell culture
Relevance
Cost

First Experiments

- Toxicological studies
- Dose-response correlations
- Threshold limit values

Study Design Principle in Toxicological Studies

Example of Study Design



Pre-irradiation preparations
From several days to several weeks

Irradiation
From several hours to several days

Post-irradiation analyses and procedures
From several weeks to several months, years

THANK YOU