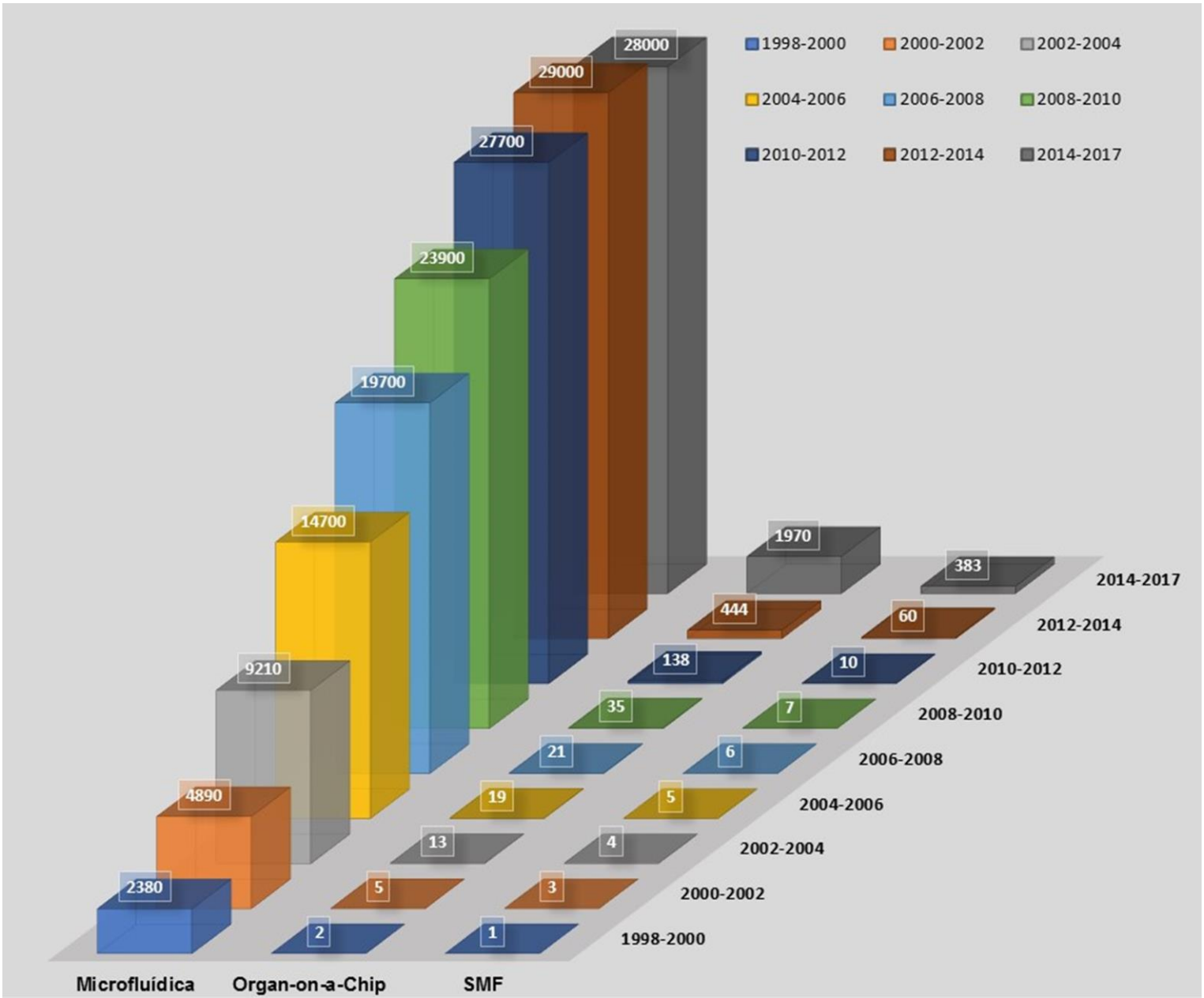
Microphysiological Systems

Principles and applications to health science research.

Talita Miguel Marin

LNBio/ CNPEM

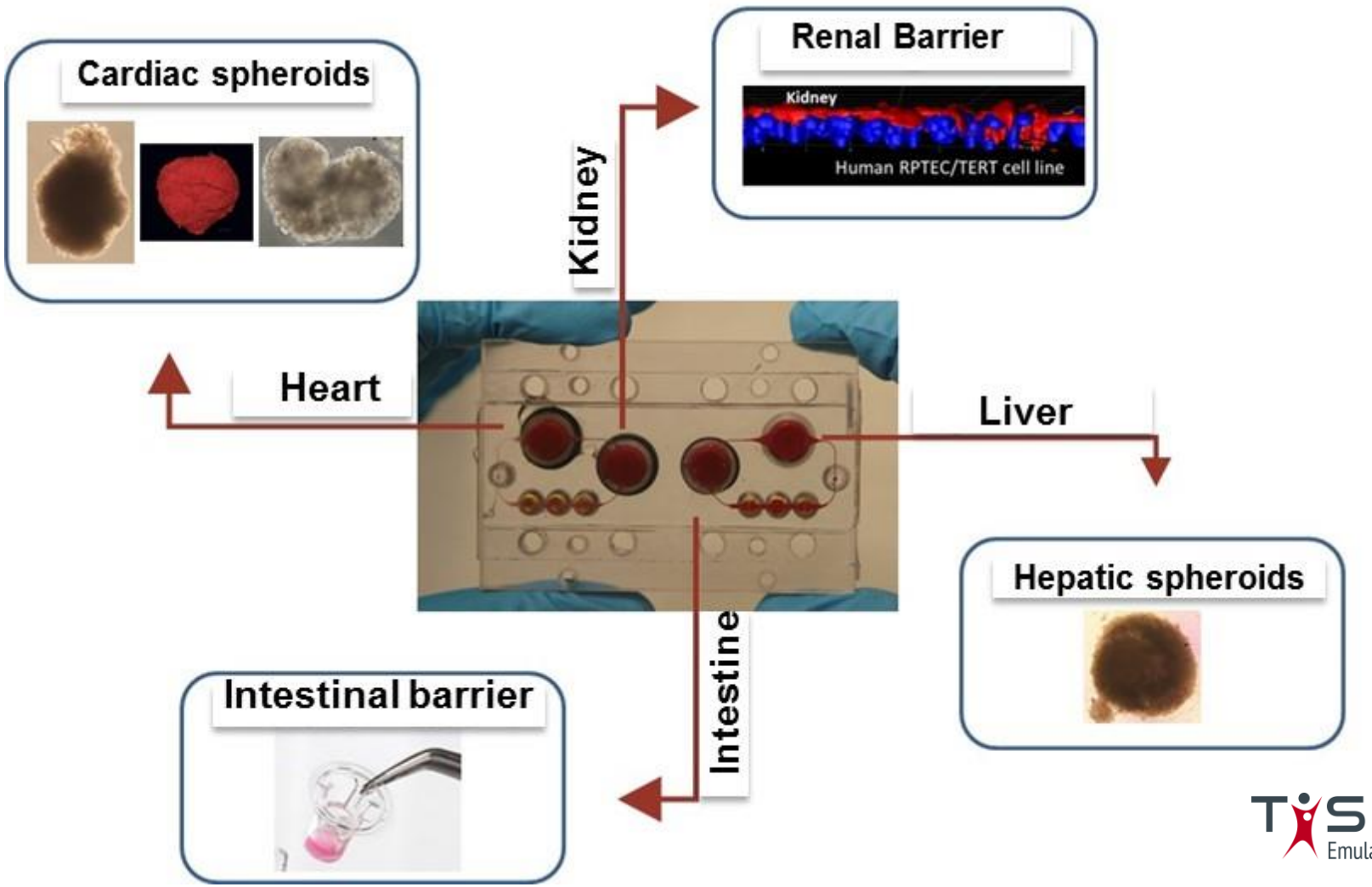
Growing activity and interest in MPS Field.



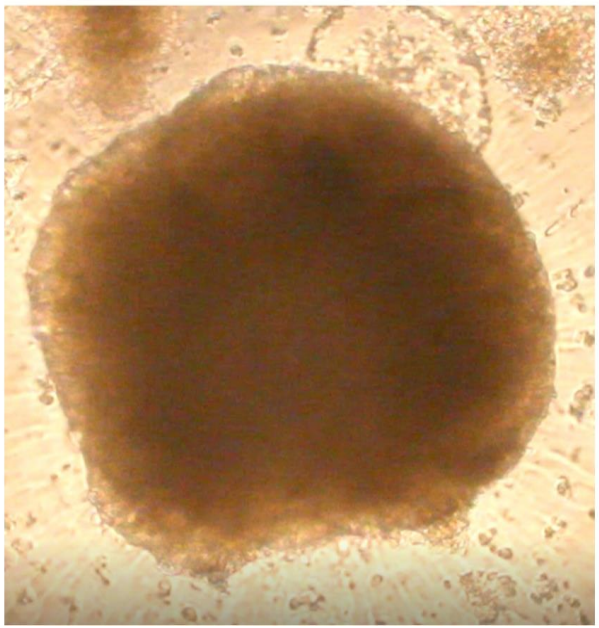
2000 - 2017 increase of academic publications related to the areas of

- **12-fold microfluidics**
- **985-fold Organ-on-a-Chip**
- **380-fold MPS**

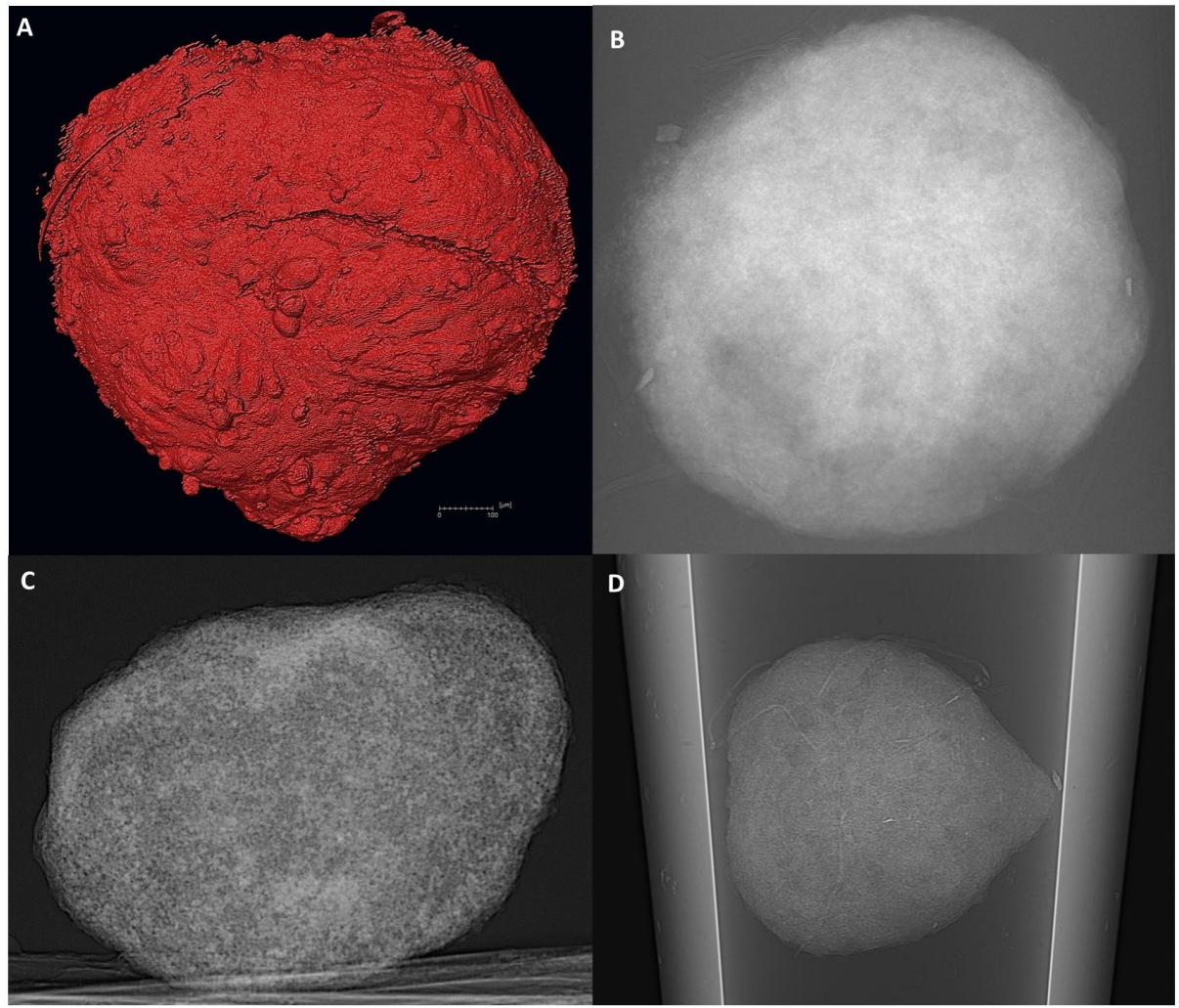
Microphysiological Systems - MPS



Heart –On-a-Chip
Human cardiomyocyte derived from iPSC



Light microscopy image of a cardiac-sphere.4x Magnification



Cardio-spheres - cardiomyocytes derived from human induced pluripotent steam cells - PluriCell. A, B and D-) labeling with Osmium and finalization in ETOH or C-) with critical point. A-) Tri-dimensional Amira reconstruction. B-D-) Images of X-ray. D-) X-ray image showing cardio-sphere inside the sample holder of the Synchrotron Light line..

Heart –On-a-Chip
Human cardiomyocyte derived from iPSC

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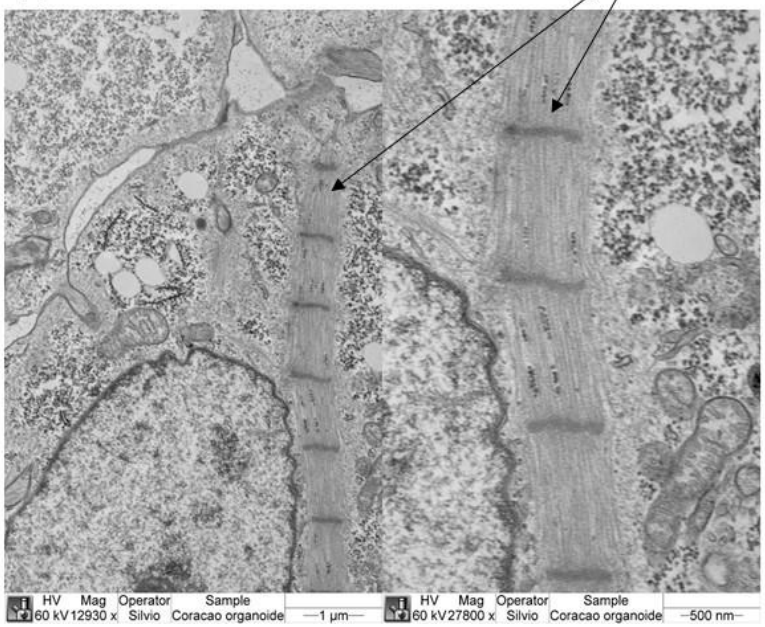
Unidades sarcoméricas

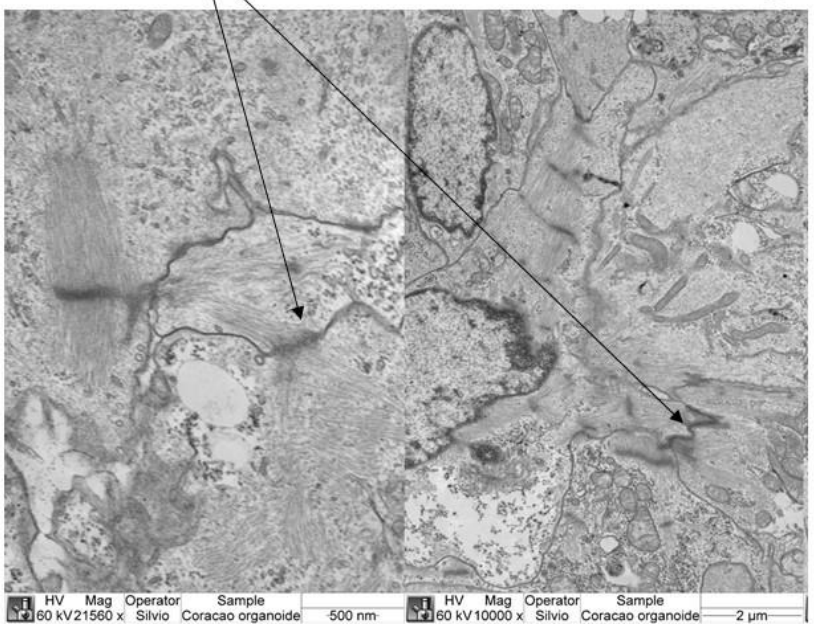
Junções GAP

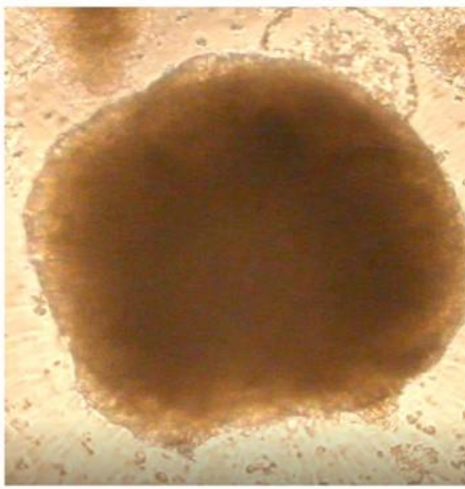
A

B

C







T

S

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Heart –On-a-Chip
Human cardiomyocyte derived from iPSC

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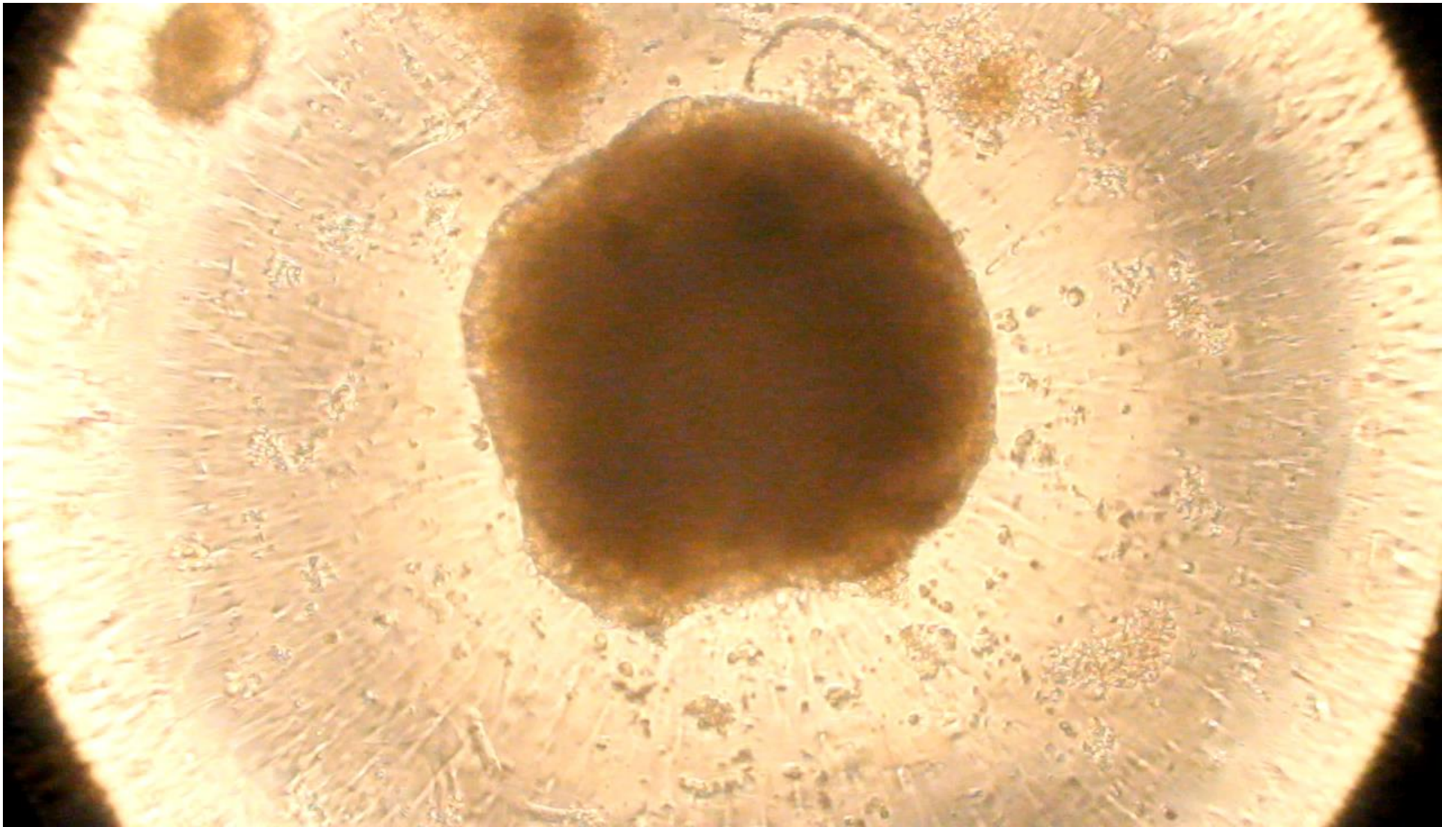

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Heart –On-a-Chip
Synchrotron Radiation Micro-CT

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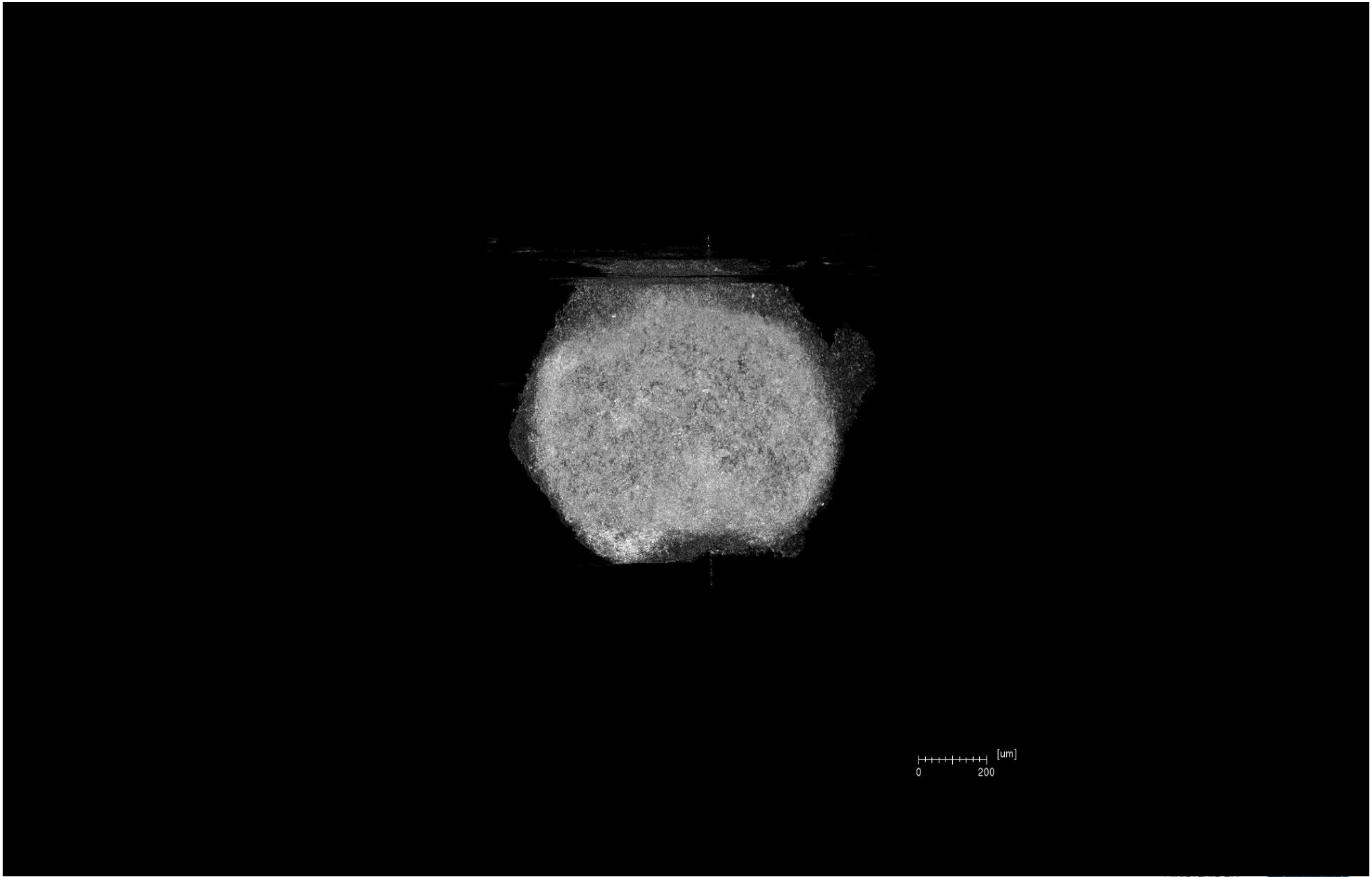
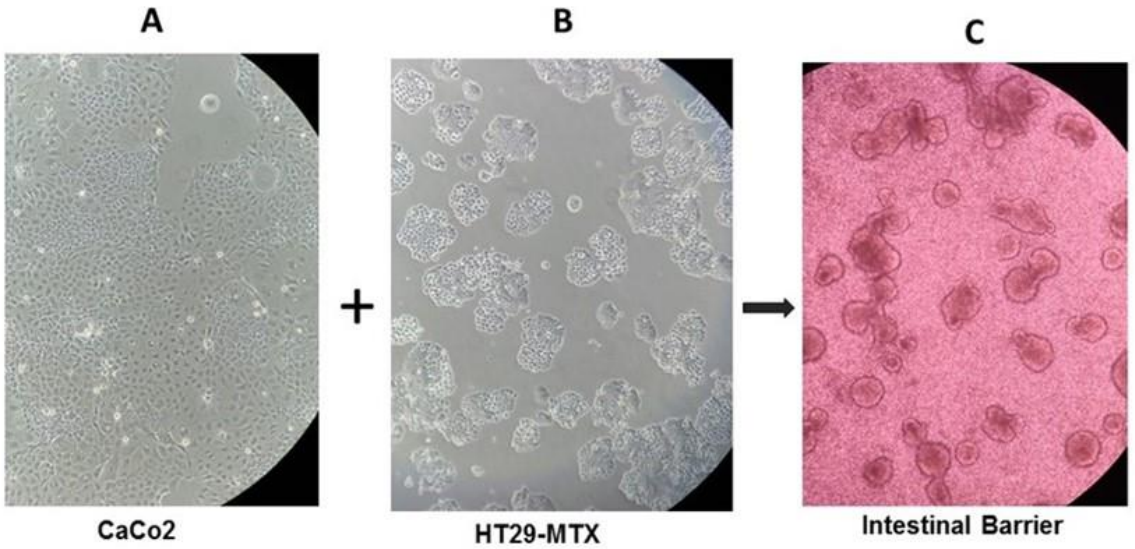
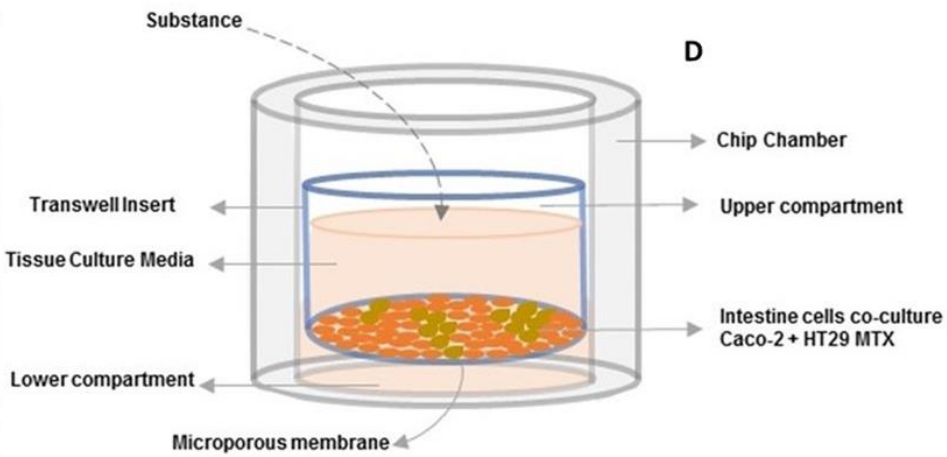
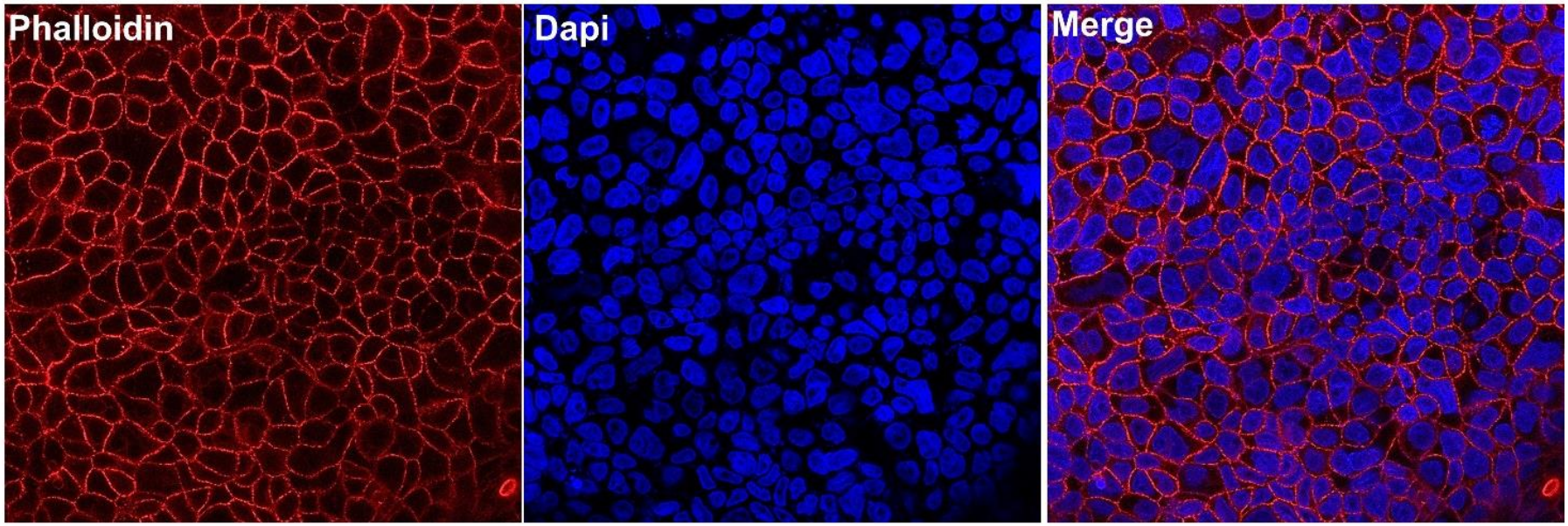


Intestine-on-a-Chip

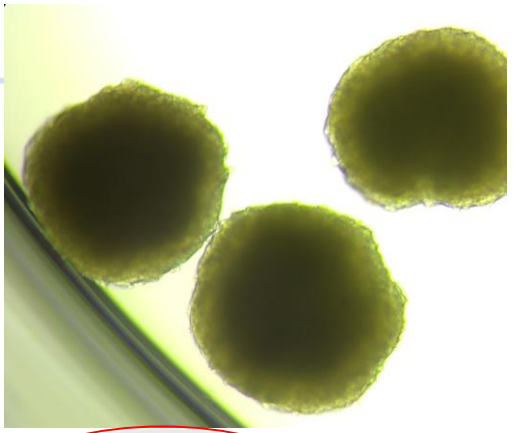




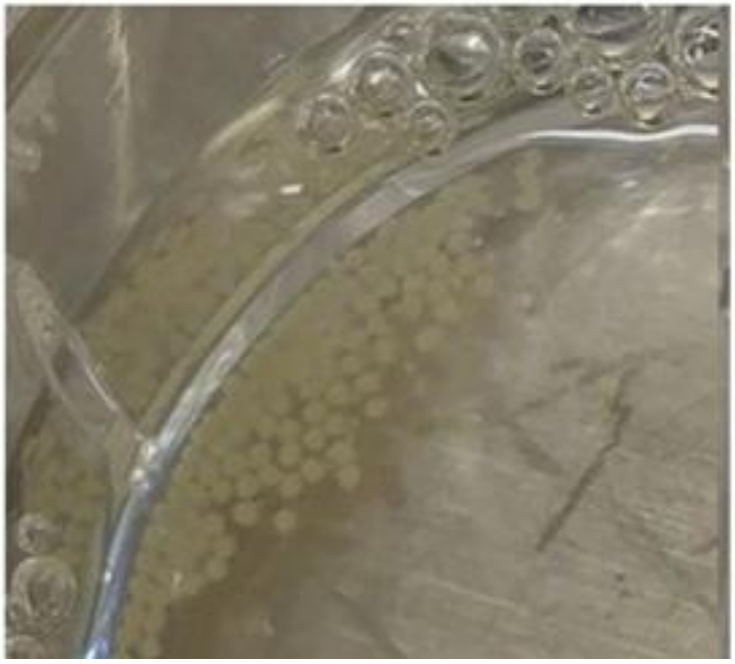


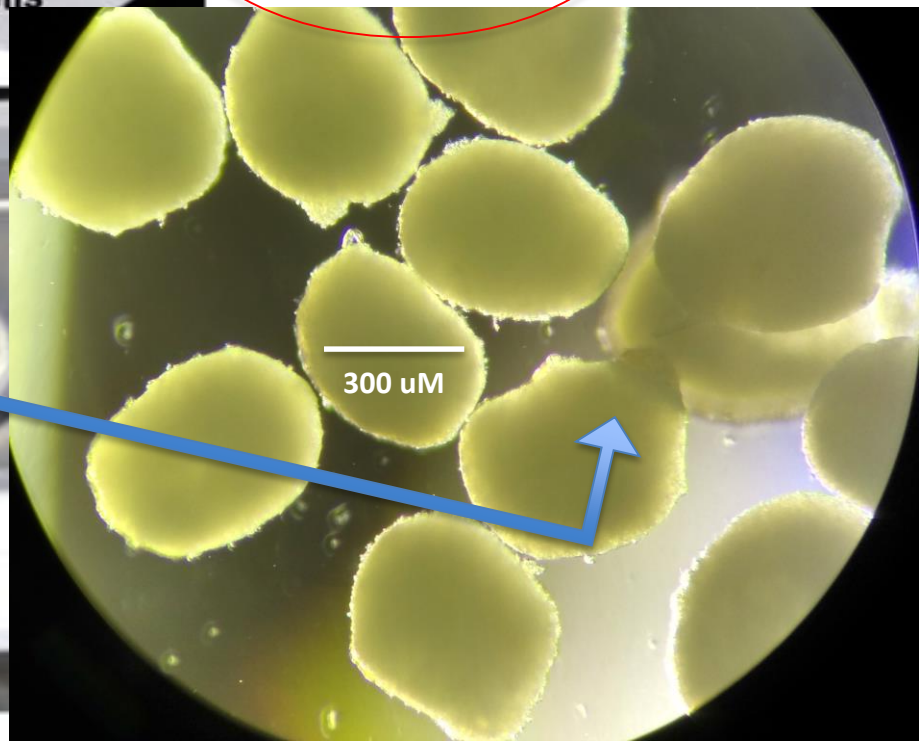
Liver Equivalent

+



UGT
SULT
Cyp2E1, 3A4, 1A2, 2B6 e 2C9





Liver Equivalents
Synchrotron Radiation Micro-CT

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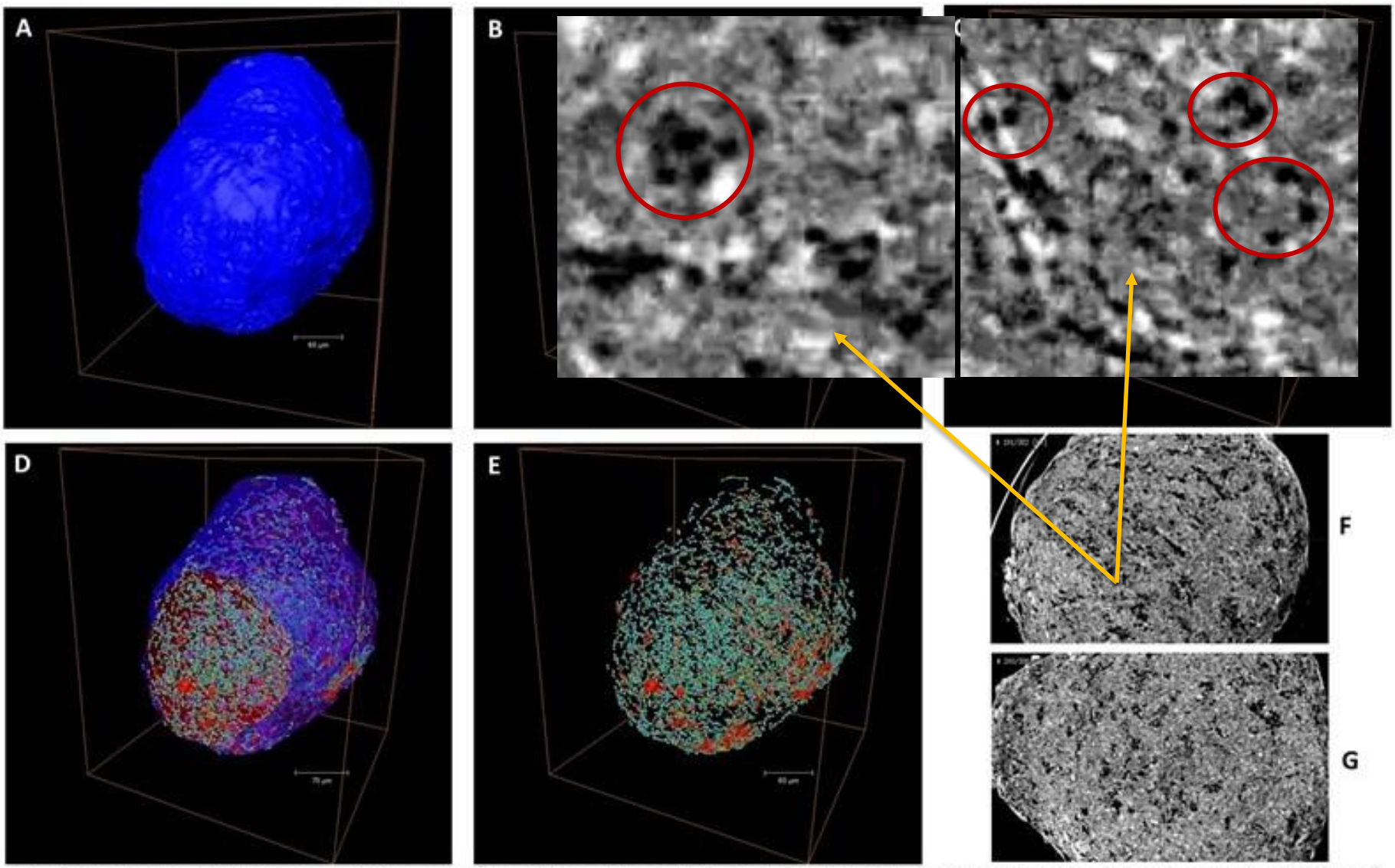

Fig. Surface image of liver organoid stained with PTA. A-) Surface image without and B-) with cut of organoid showing 3 porous or ducts. C-) image of segmented and isolated pores. D-) image of the cut surface with the pores skeleton internally. E-) image of pores with "skeleton" that highlights the scale, the sizes and connections. F and G-) "virtual histology" with thickness of 5 micrometers using "minimum intensity projection" (MIP).

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Liver Equivalents
Synchrotron Radiation Micro-CT

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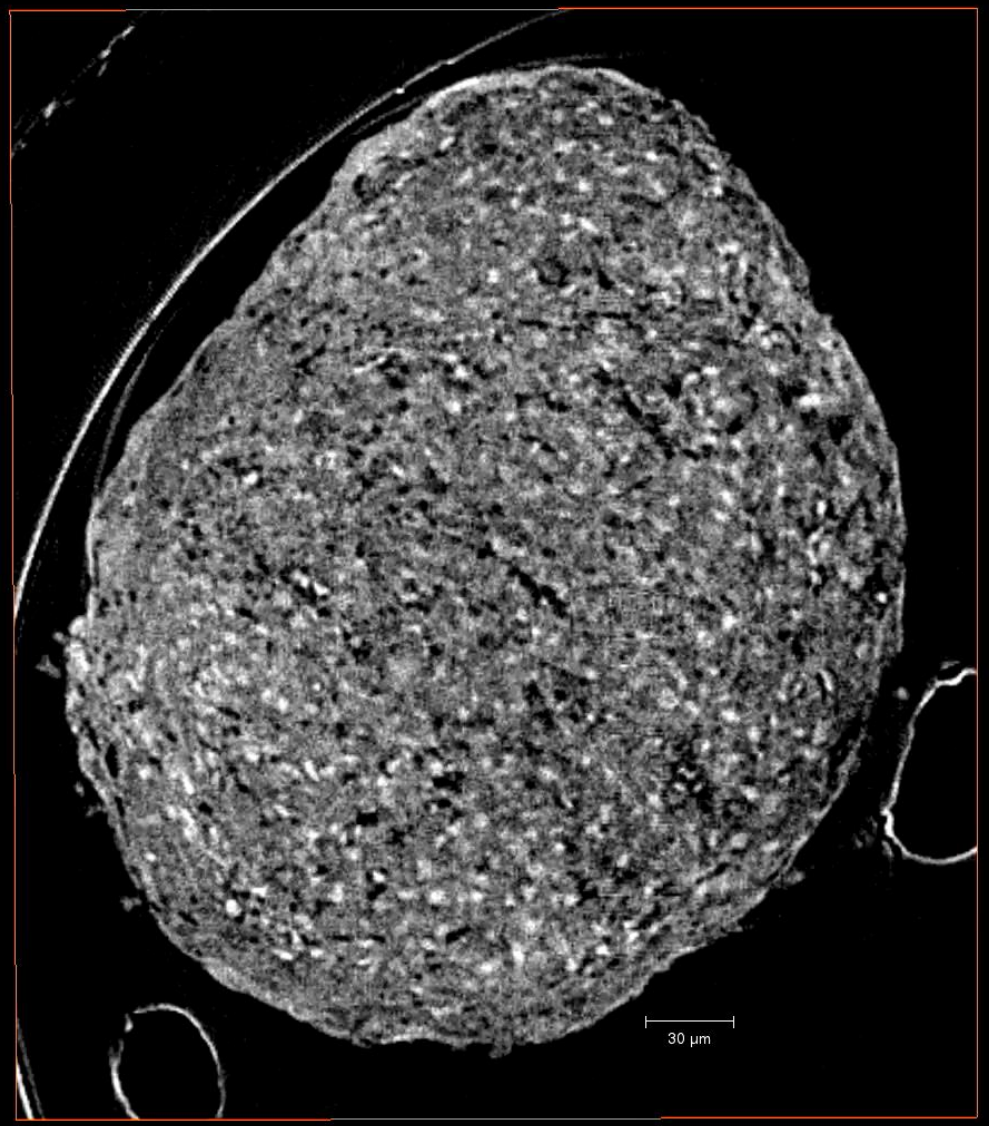

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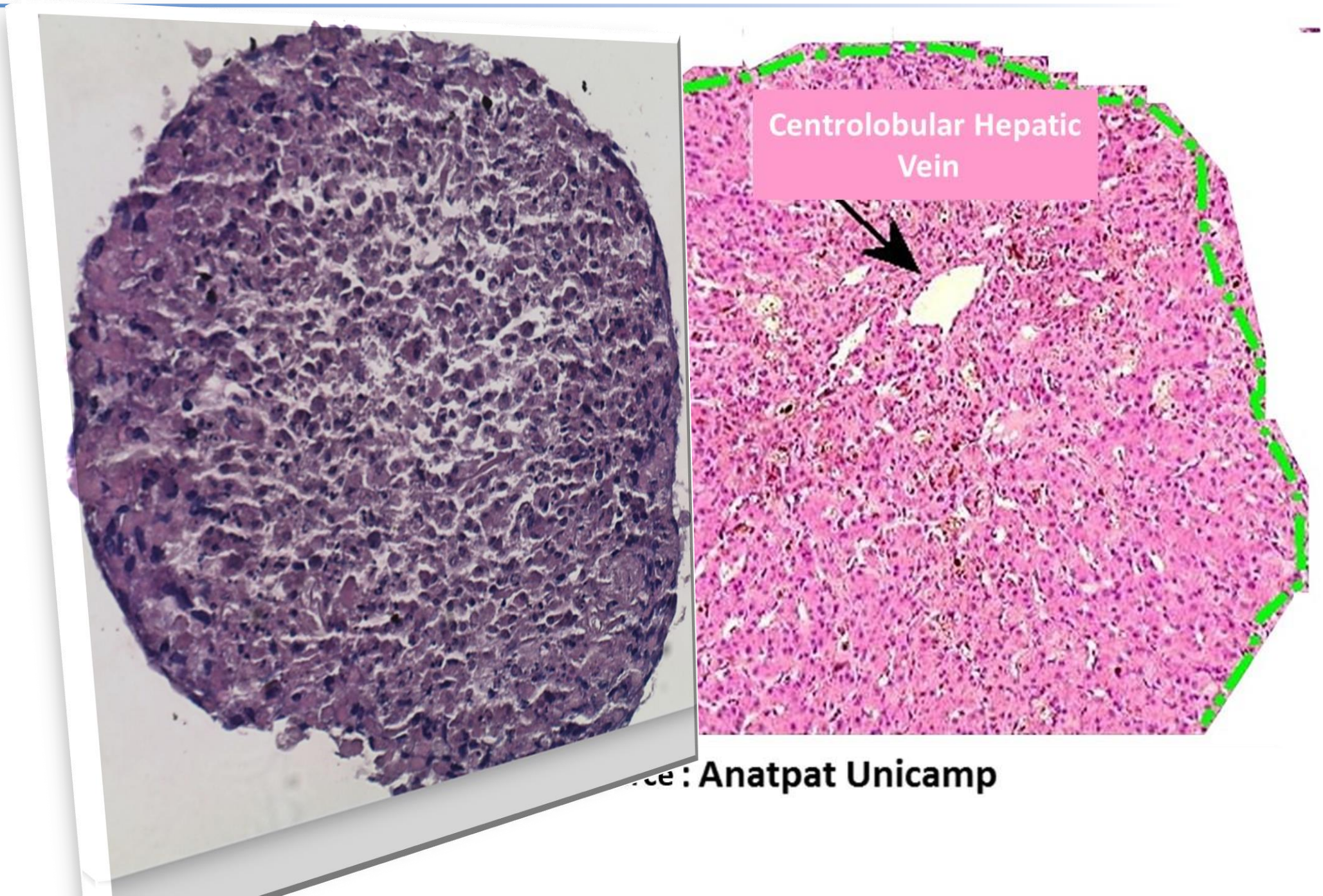
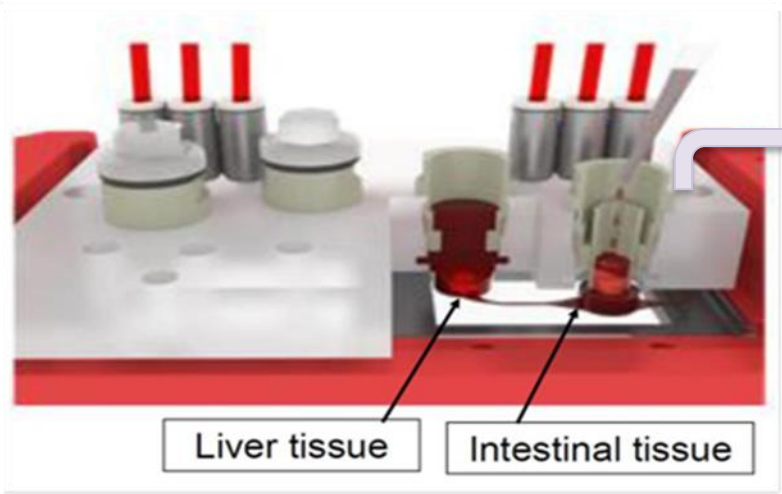
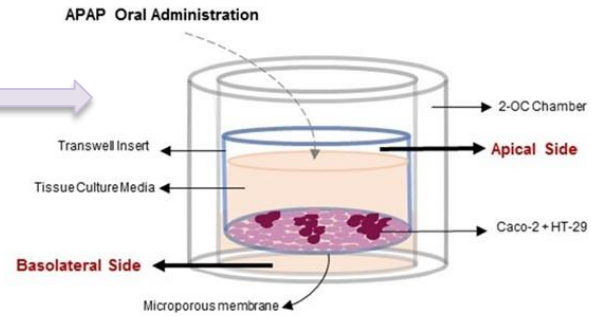
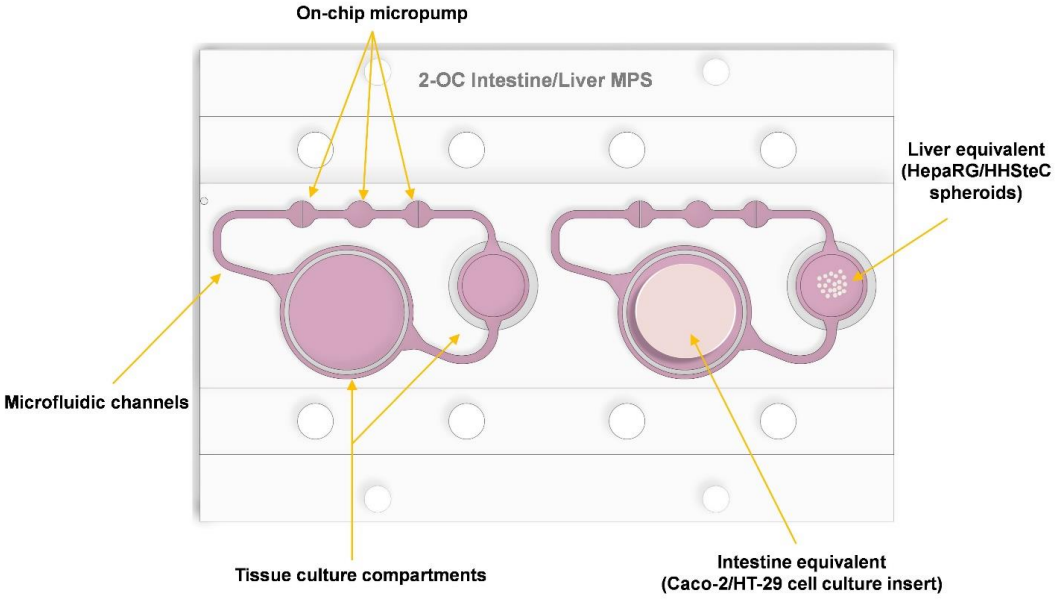
Liver Equivalents
H&E Histology

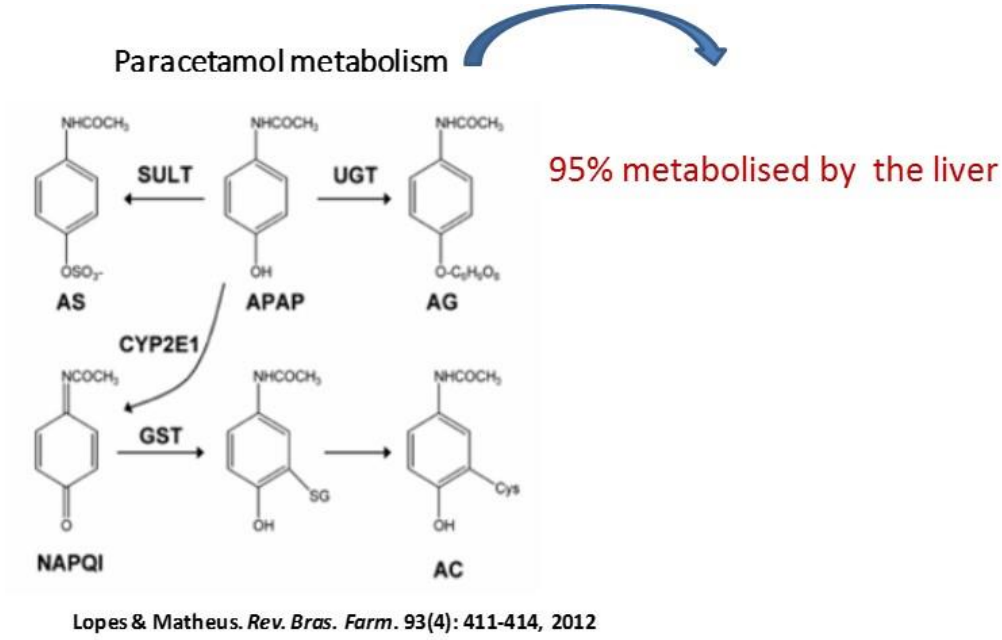


Acetaminophen Absorption and Metabolism in TissUse® Microphysiolgical System









Lopes & Matheus. *Rev. Bras. Farm.* 93(4): 411-414, 2012

(APAP-gluc, 52-57% of urinary metabolites) and sulfate (APAP sulfate, 30-44%)

Marin TM. et al 2018 under review

Acetaminophen Absorption and Metabolism in an Intestine/Liver Microphysiolgical System

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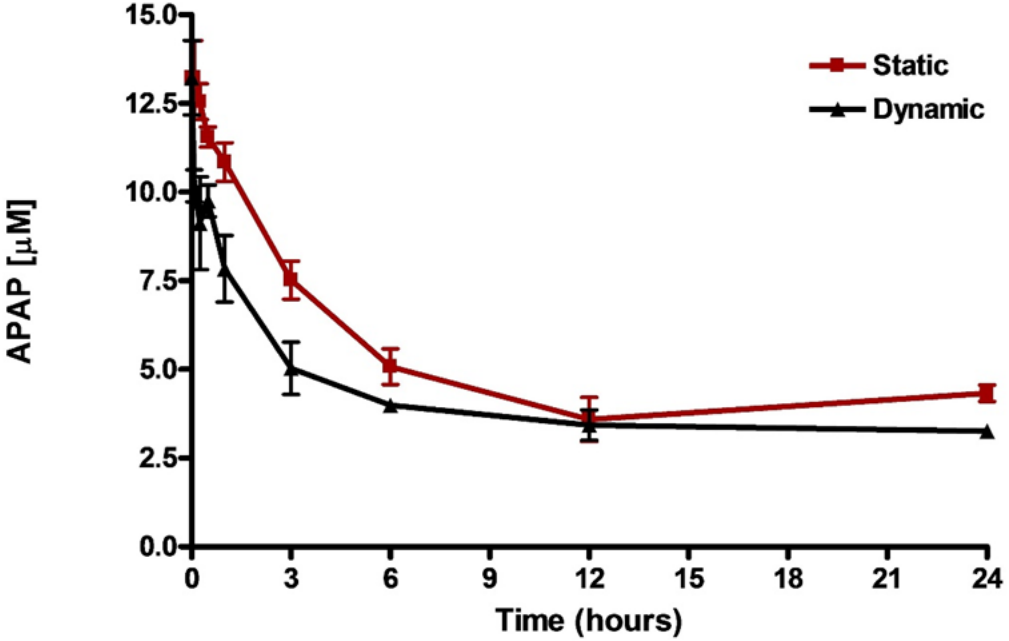
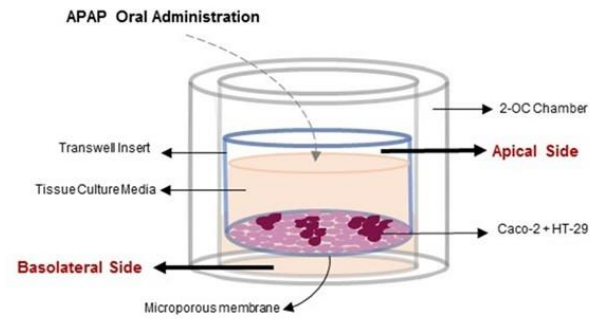
CNPEM Brazilian Center for Research in Energy and Materials

A





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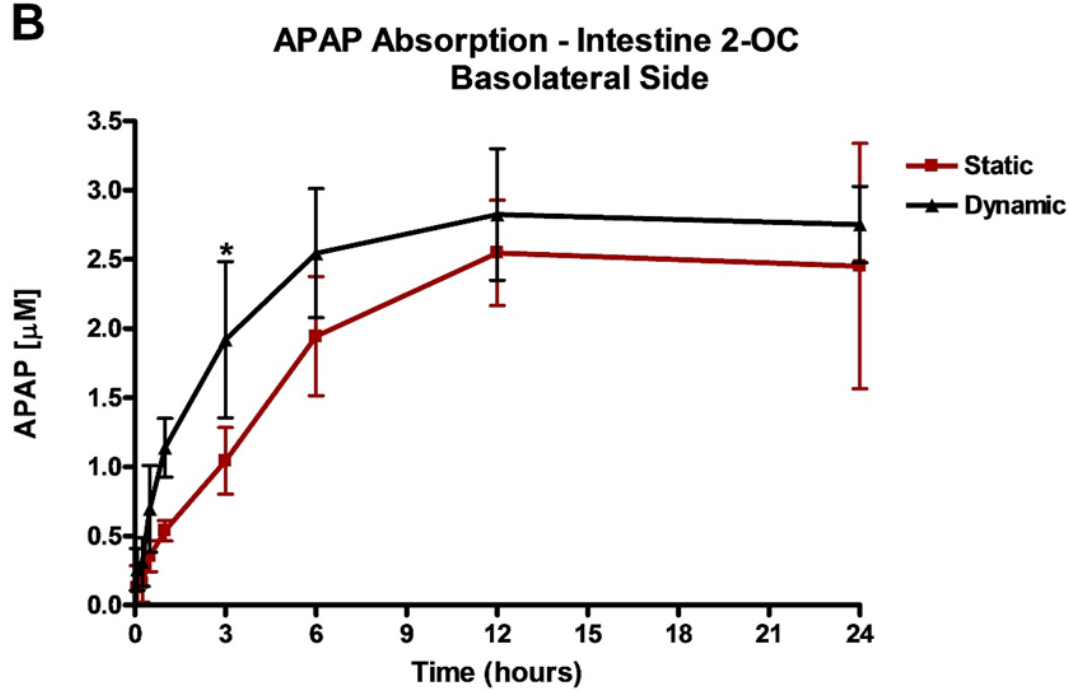

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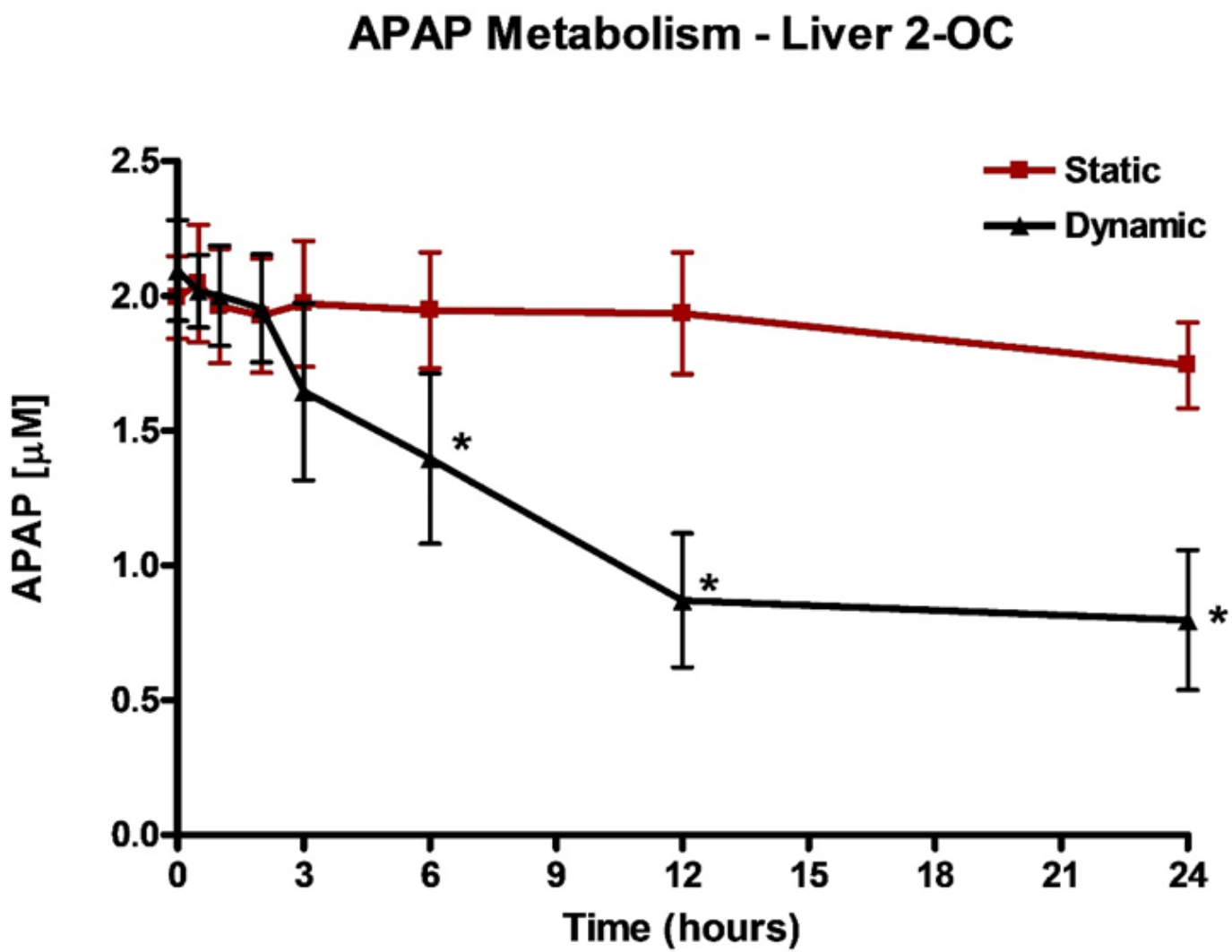
Acetaminophen Absorption and Metabolism in an Intestine/Liver Microphysiolgical System



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Acetaminophen Absorption and Metabolism in an Intestine/Liver Microphysiolgical System

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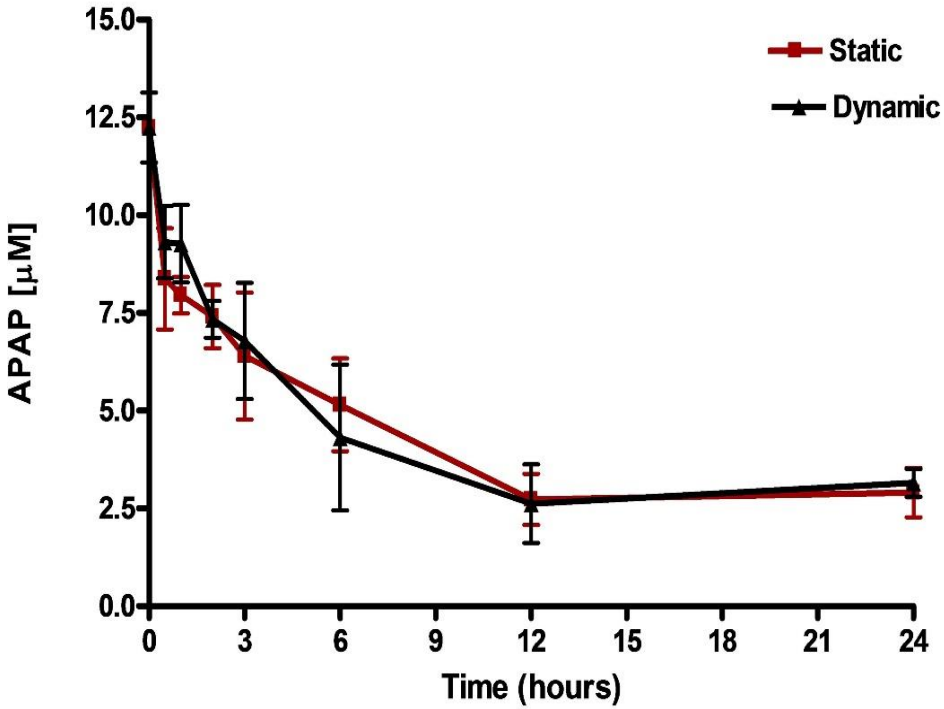
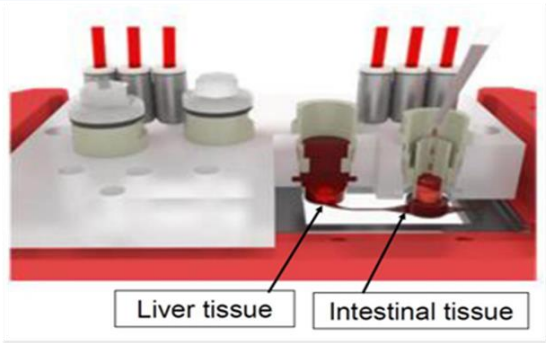
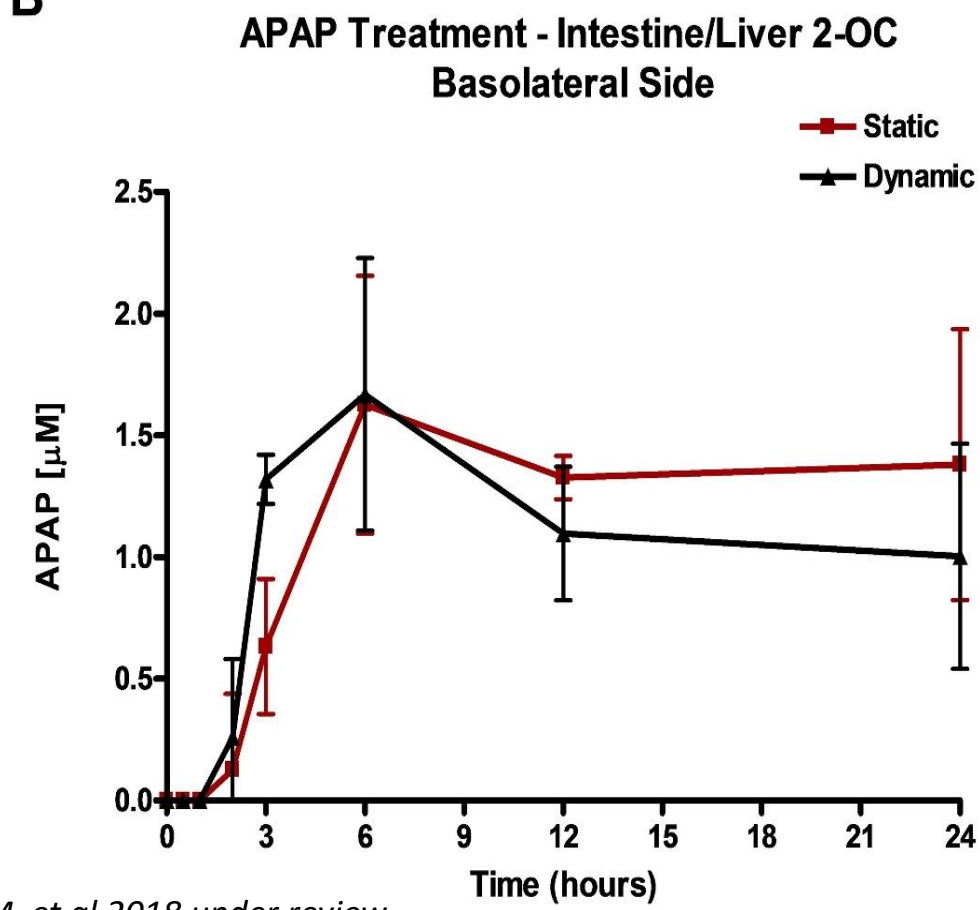
A





B



Marin TM. et al 2018 under review

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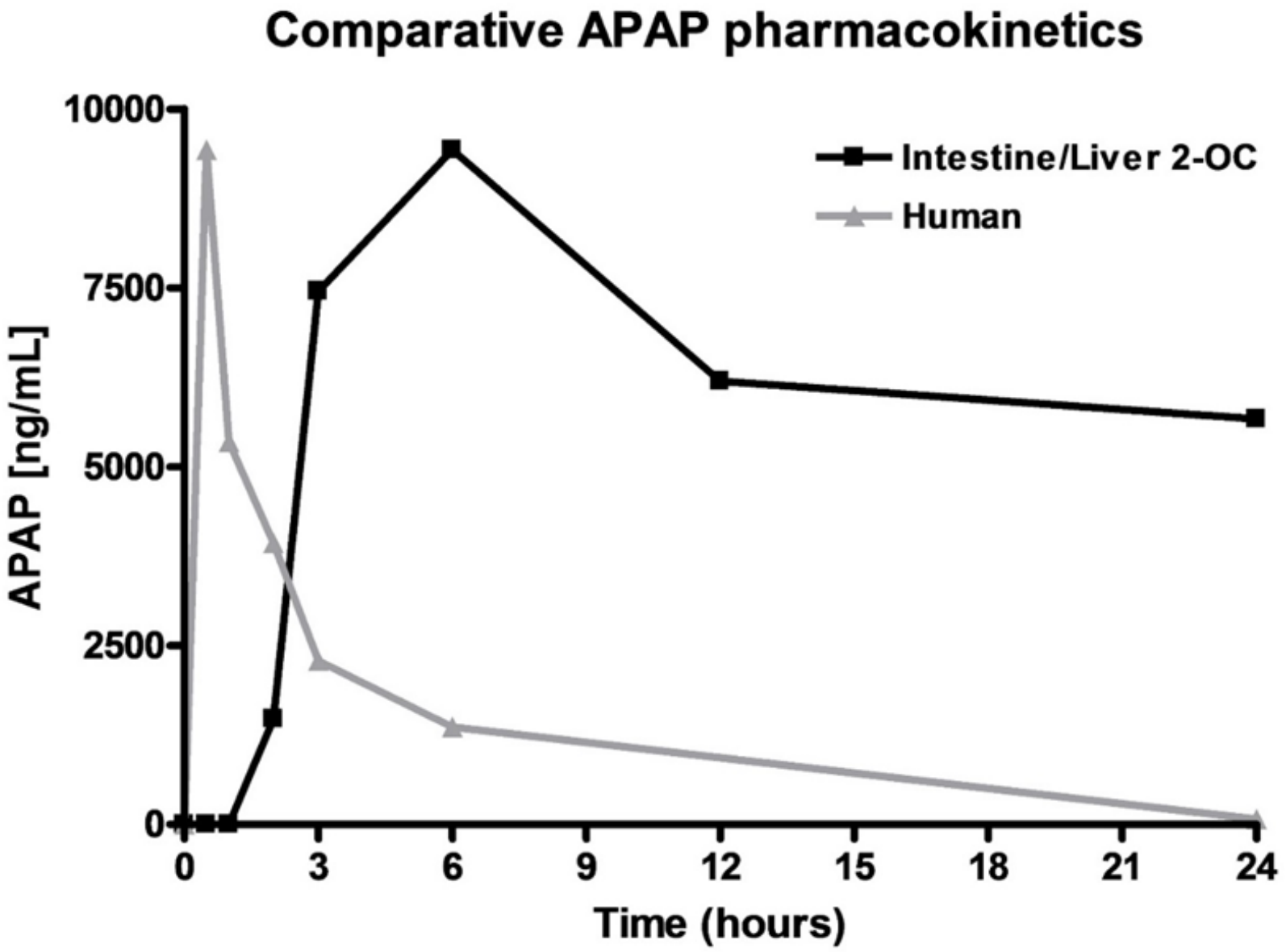
Comparative APAP pharmacokinetics
10000
7500
5000
2500
0
APAP [ng/mL]
Intestine/Liver 2-OC
Human
0
3
6
9
12
15
18
21
24
Time (hours)

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Intestinal Barrier

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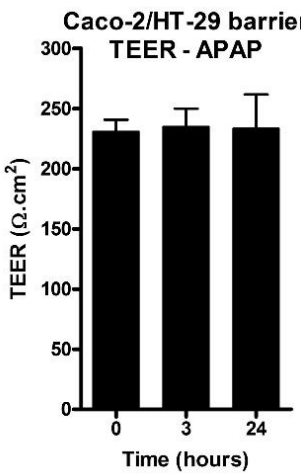

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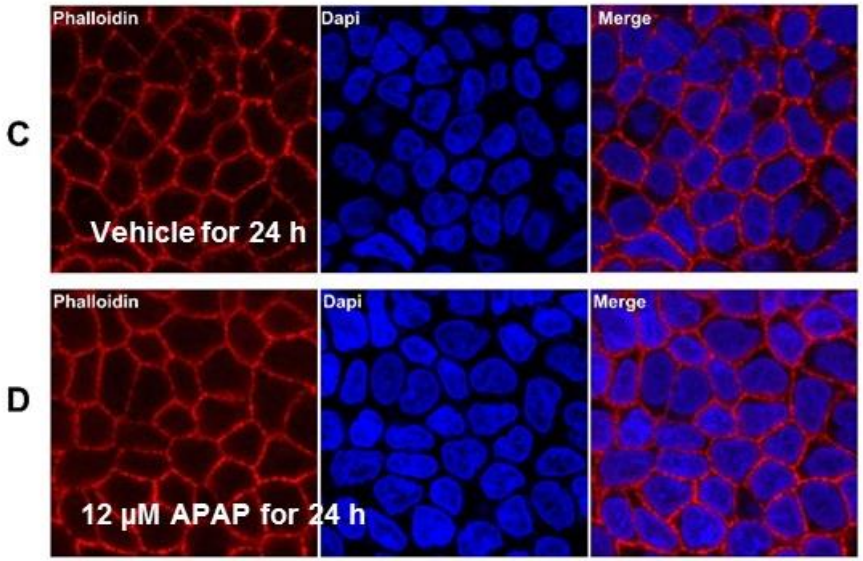

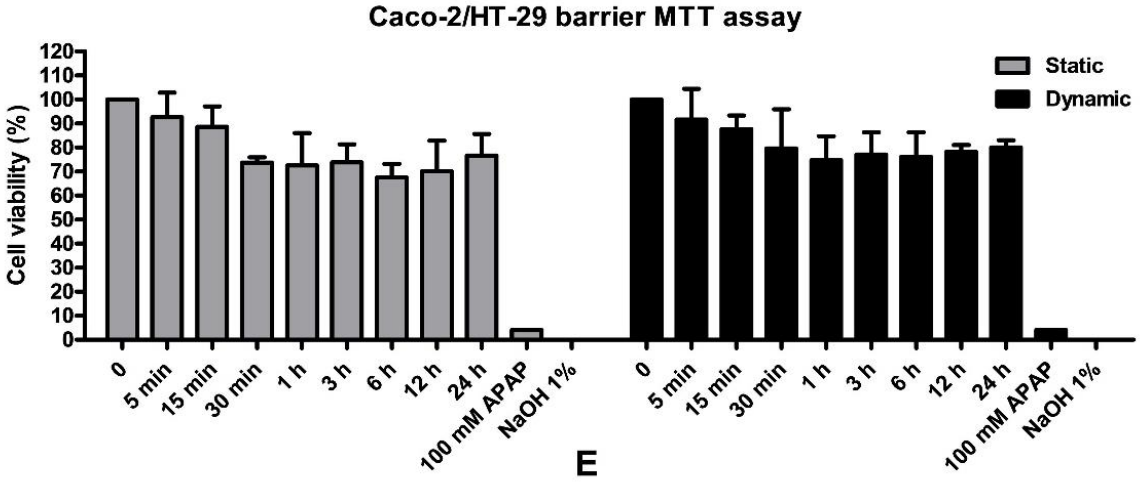

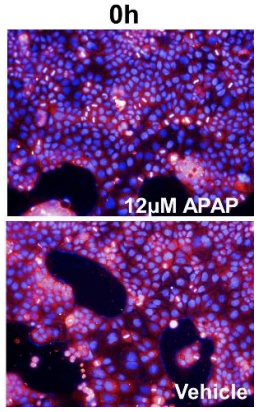

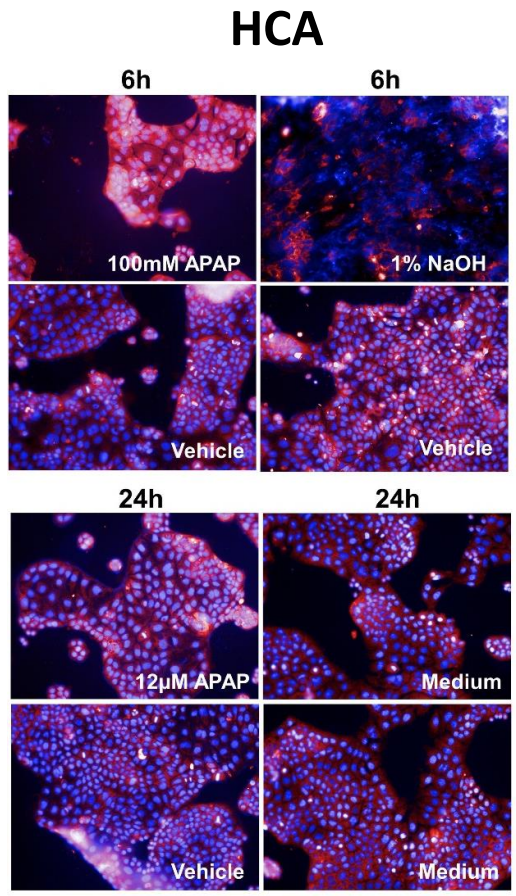

Liver Equivalents
Toxicity assessment

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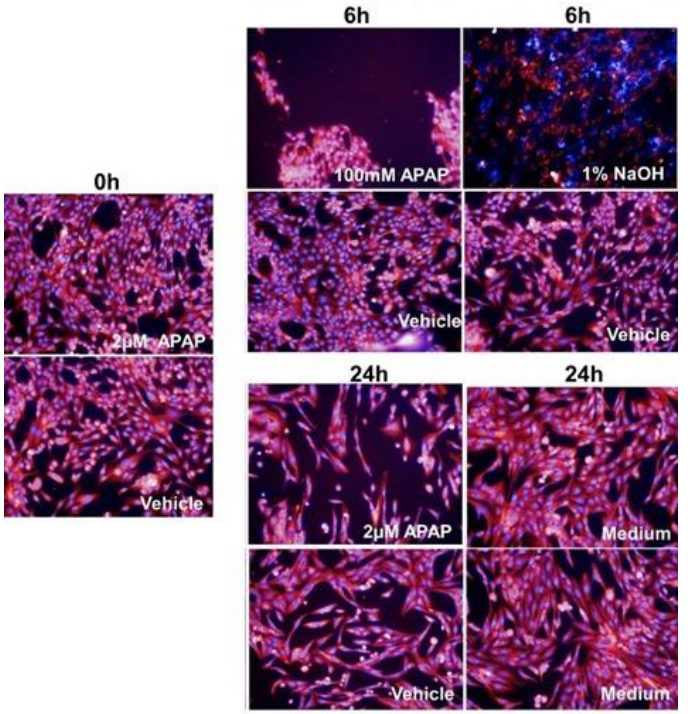
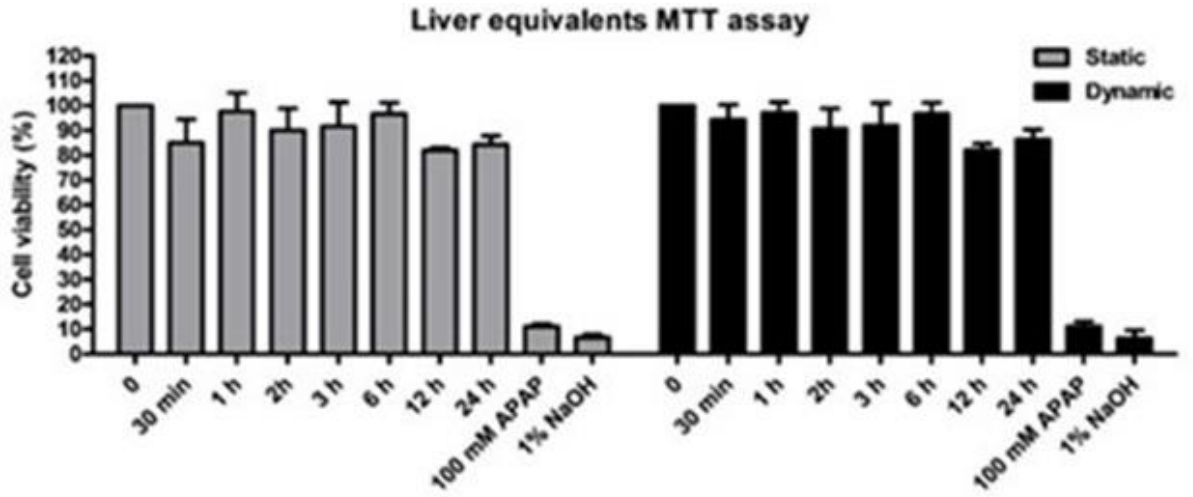
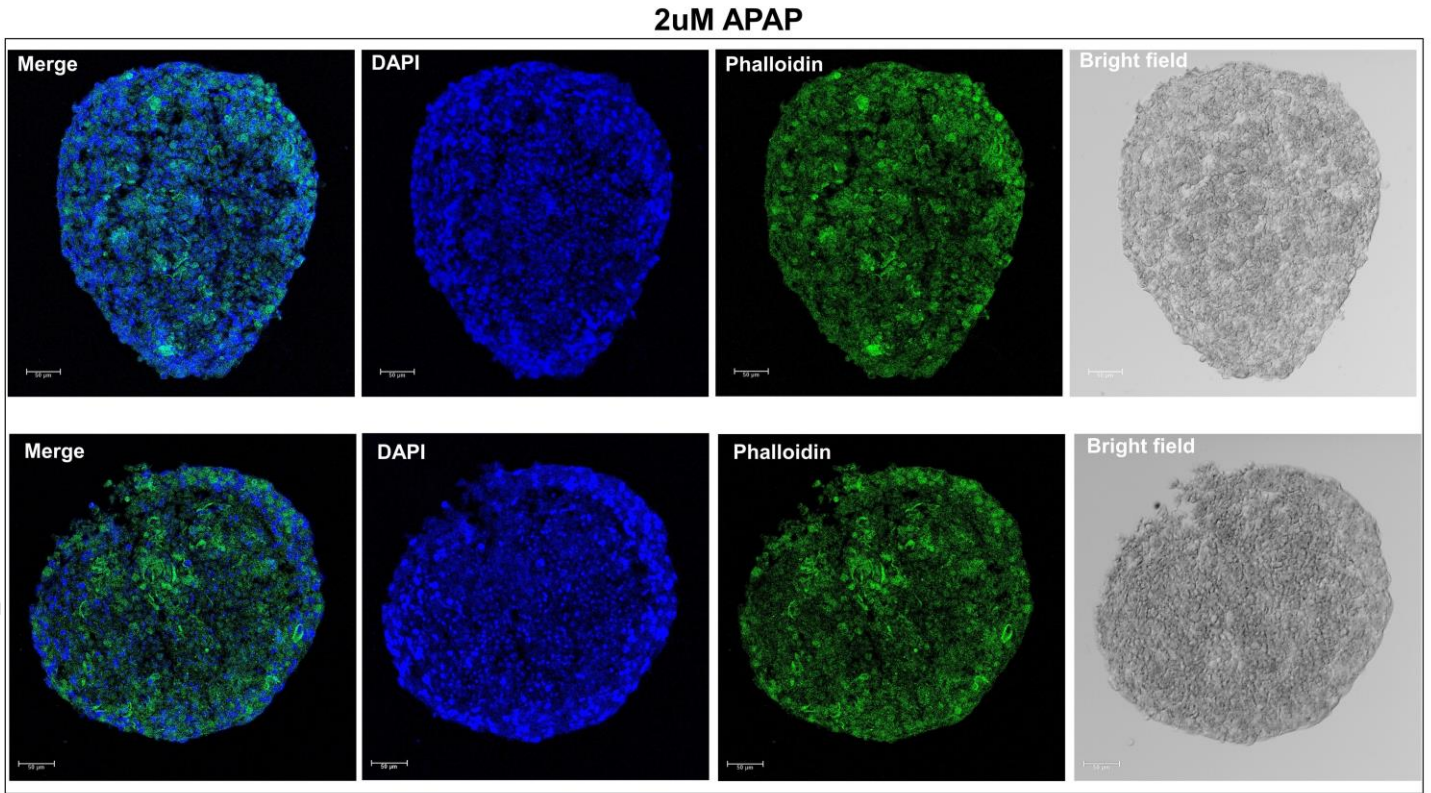
HCA







Summary

- The APAP intestinal absorption and hepatic metabolism could be emulated in the MPS
- Media circulation or microfluidics flow application seems to improve significantly the liver spheroids functionality
- The MPS *in vitro* assessments can be associated to *in silico* biological modeling to better predict the pharmacokinetics and toxicological profile of new drugs under development, thus decreasing costs and time for clinical trials and hopefully providing better accuracy than animal models soon

Acknowledgment

LNBio

Dr. Eduardo Pagani
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Dr. Murilo Carvalho
Dra. Kaliandra Gonçalves
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Dr. Kleber G Franchini

Dr. Diogo Biagi
Dr. Marcos Valadares

Unicamp

Dr. Silvio Roberto Consonni

Talita Miguel Marin,
PhD - Coordinator of the Human Tissue Culture Laboratory

LNBio- CNPEM

+55-19-35175131

email: talita.marin@lnbio.cnpem.br

Eduardo Pagani
Pharmaceutical Development Manager

LNBio- CNPEM.

+55-19.3512-1099
- Fax: 19.3512-1006
Cel. 11 99102-0285
eduardo.pagani@lnbio.cnpem.br

http://www.lnbio.cnpem.br/site/home.aspx

Kleber Gomes Franchini
Director - LNBio- CNPEM.

Tel. 55 19 3512-1244


Thank you !