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From science to health

Le programme d'Impulsion MecaCell3D

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Coordinateurs du Programme MecaCell3D

MecaCell3D: *Mechanisms and Mechanics in 3D Multicellular Systems*

- **General objectives:** develop and/or adapt quantitative methods to characterize cell functions in 3D cell assemblies, considering their individual or collective mechanical properties. Use of highly relevant and reproducible models allowing quantitative analyses.

MecaCell3D: Process of selection of the teams

- Organized and proposed by the Cellular Biology, Reproduction, Development and Evolution Program at Inserm (Thierry Galli, Jean Rosenbaum, Christine Lemaitre et Ama Gassama)
- SAB: Orly Reiner (Weizmann Institute); Guillaume Salbreux (Université de Genève), Guillaume Charras (UCL, London) and Meritxell Huch (MPI-CBG Dresden).

- **March 2022:** Call for projects with mini-consorsiums of 2-4 teams
- **July 2022:** Selection by the SAB of **7/49** projects (**18/117** teams)
- **End of september 2022:** Submission of the final project
- **April 2023:** Start of the 3 years contract

MecaCell3D: Overview

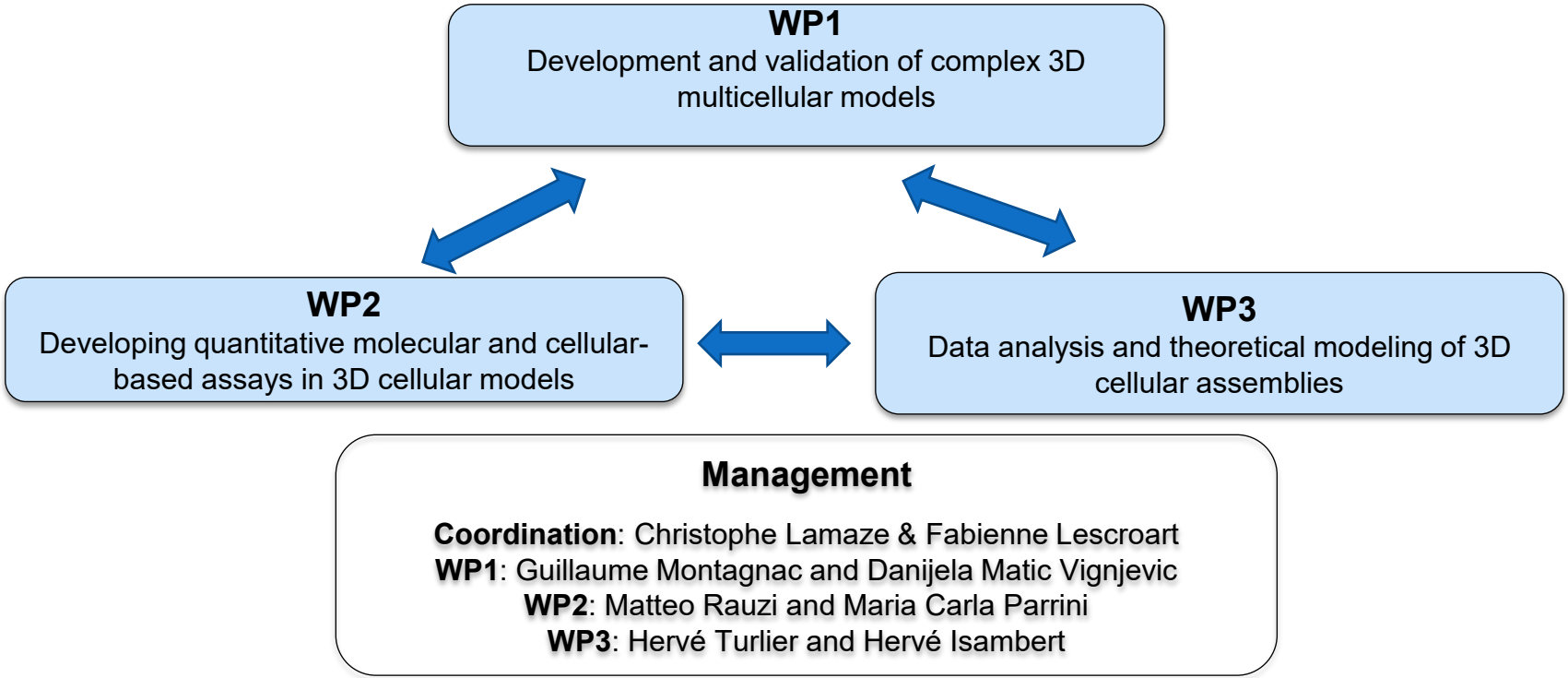
Two unique 3D models:

1) 3D cellular ecosystems of multiple cell populations: reconstitution of tissue environment through encapsulation or microfluidic devices

2) 3D multicellular assemblies: individual 3D structures with multicellular composition, reconstituting tissue heterogeneity.

MecaCell3D covers different fields of developmental and cell biology focused on **heart diseases** and **cancer**.

MecaCell3D: Organization of the program



MecaCell3D: Management of the program

Our goals:

- to organize and facilitate strong integration and interactions between the MecaCell3D partners
- to ensure an adequate coordination and progress of the scientific program to be developed in WP1 to WP3
- to promote a smooth and efficient implementation of the work plan within the time and budget frame of the project.

MecaCell3D: Management of the program

- Kick-off meeting Septembre 2023 (Marseille)
- Videoconferences (every other 6 months)
- 2 days of work progress presentation in 2024
- Organization of a national or international conference at the end of the program for 2026/2027

MecaCell3D: The different partners

1) Guillaume Montagnac (U1279, Villejuif) / Danijela Vignjevic (UMR 144 CNRS, Inst. Curie)


Model: colon cancer spheroids/organoids embedded in a capsule of CAFs/collagen

► Role of CAFs contractility and of the cellular eco-system (CAF, stem cells, immune cells…)
► Endocytosis, drug and nutrient diffusion, tumor growth,
► Live imaging

2) Maria Carla Parrini (U1339) / Stéphanie Descroix & Hervé Isambert (UMR 168 CNRS) Inst. Curie

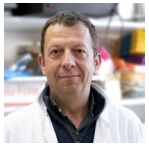


Learning causality networks within the lung tumor ecosystem using a tumor-on-chip approach

► Development of vascularized lung tumor-on-a-chip platform
► Advanced imaging/Transcriptomics
► Machine learning methods to infer causality networks

MecaCell3D: The different partners

3) Christophe Lamaze (U1339, Inst. Curie) / Béatrice Turcq (U1312, Bordeaux) / Pierre Bon (UMR CNRS 7252, Limoges)



Quantification and functions of subcellular structures in 3D spheroids

► Encapsulated breast spheroids/ endothelial vesseloids with fluorescent caveolae (Crispr/Cas9)
► Caveolae visualization by EM metal replica
► Fluorescent and label-free imaging of live samples for AI-assisted analysis

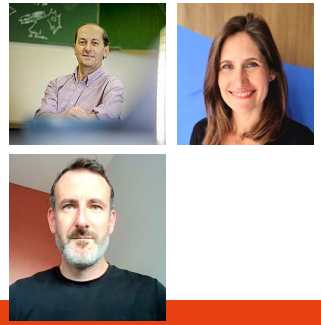
MecaCell3D: The different partners

4) Fabienne Lescroart & Stéphane Zaffran (U1251) / Pierre François Lenne, Sham Tlili & Robert Kelly (UMR 7288 CNRS)/ Marseille

Gastruloid: a 3D model for the early steps of cardiac development

- ► Optimize the gastruloid model for cardiogenesis
- ► Develop advanced imaging approaches / Tissue interactions and dynamics
- ► Simultaneous recording of lineage and transcriptome

5) Michel Pucéat (U1263, Marseille) / Sonia Stefanovic (U1263, Marseille) / Willy Suppato (U1182, Palaiseau)



Mini-heart project

► Engineering cardioids from human ESC with chambers recapitulating contracting/pumping functions & cardiac diseases

► Using advanced techniques (acoustic bioprinting, spatial transcriptomics, 3D cell imaging and biomechanics)

► Cross-validation with embryonic mouse hearts

MecaCell3D: The different partners

6) Matteo Rauzi (U1091, Nice)

Tridimensional opto-mechanical manipulation and computational cell morphology

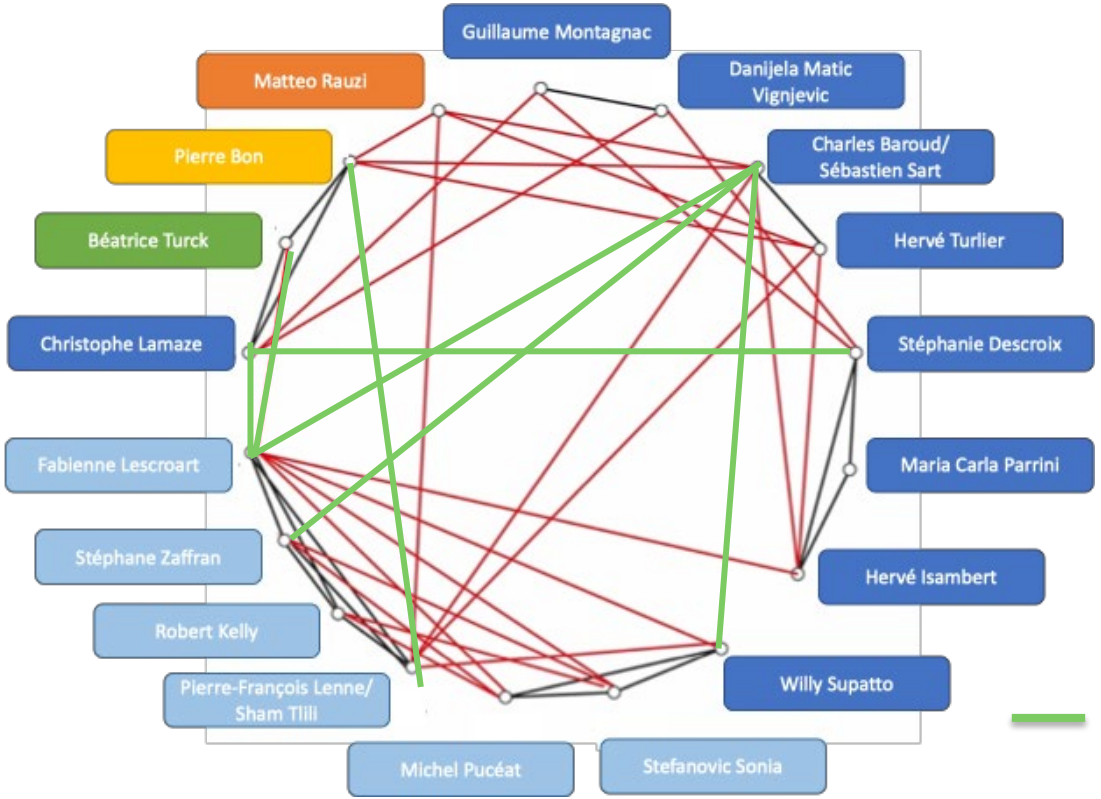
- ► Data processing and cell segmentation to quantitatively measure shape changes
- ► Using 4D segmentation to investigate cell morphology and topological transformations
- ► 4D imaging, mechanical measurements, controlled perturbations, and big data processing

7) Hervé Turlier (U1050, Collège de France) / Charles Baroud (Inst. Pasteur, Ecole Polytechnique), Paris

Mechanical sensing and stimulation of 3D culture models / Mechanical interference & simulations of multicellular systems

- ► Guiding differentiation of pluripotent cells
- ► Measuring mechanical properties on single cells/ detect cell heterogeneities in organoids/tumoroids
- ► Multi-scale mechanical description from nucleus to cell to tissue

18 teams dedicated to **MecaCell3D**



MecaCell3D: Human task forces

équipe concernée	Nom personnel	fonction	durée
Equipe Guillaume MONTAGNAC	Colonne Hugot	Assistant Ingénieur	6 months
Equipe de Michel PUCEAT	Samanta Conte	Ingénieur d'Etude	18 mois?
Equipe de Beatrice TURCQ	Vanessa Bergeron	Ingénieur d'Etude	12 mois
Equipe de Matteo RAUZI	Barthelemy DELORME	IR (half-time)	24 mois?
Equipe de Christophe LAMAZE & Equipe de Stéphanie DESCROIX	**Bastien Guyot**	**M2 Student**	**6 mois**
Equipe de Hervé ISAMBERT	Louis Montagne	PhD student	36 mois
Equipes de Charles BAROUD	Enara Larranaga	post-doc	24 mois
Equipes de Hérvé TURLIER	Nicolas Ecker	post-doc	24 mois
Equipe de Fatima MECHTA-GRIGORIOU (Maria Carla PARRINI)	Ségolène LADAIGUE	post-doc	18 mois
Equipe de Willy SUPATTO	to be recruited	post-doc	15 mois
Equipe de Danijela VIGNJEVIC	to be recruited	post-doc	15 mois
Equipe de Fabienne LESCROART & Equipe de Pierre-François LENNE	**Srivatsava VISWANADHA**	**post-doc**	**24 mois**

MecaCell3D: Toward new funding opportunities

Charles Baroud ⟷ Hervé Turlier — ANR BioMecaNet

Fabienne Lescroart ⟷ Robert Kelly — ANR Heartist

Hervé Isambert — ANR Patterning

Michel Pucéat ⟷ Willy Supatto — ANR Compacard

Charles Baroud — ERC Advanced (MELCART)

Stéphanie Descroix — PEPR MEDOOC

EU project Arturo — Maria Carla Parrini

EU project OASIS — Guillaume Montagnac

MecaCell3D: Publications

2 accepted publications
3 submitted manuscripts (2 as preprints)
1 book chapter


New Results

Follow this preprint

Marangoni-like tissue flows enhance symmetry breaking of embryonic organoids

Simon Gsell, Sham Tlili, Matthias Merkel, Pierre-François Lenne

doi: https://doi.org/10.1101/2023.09.22.559003

accepted in *Nature Physics*


New Results

Follow this preprint

Cardiopharyngeal Mesoderm specification into cardiac and skeletal muscle lineages in gastruloids

Laurent Argiro, Céline Chevalier, Caroline Choquet, Nitya Nandkishore, Adeline Ghata, Anais Baudot, Stéphane Zaffran, Fabienne Lescroart

doi: https://doi.org/10.1101/2023.05.15.540476

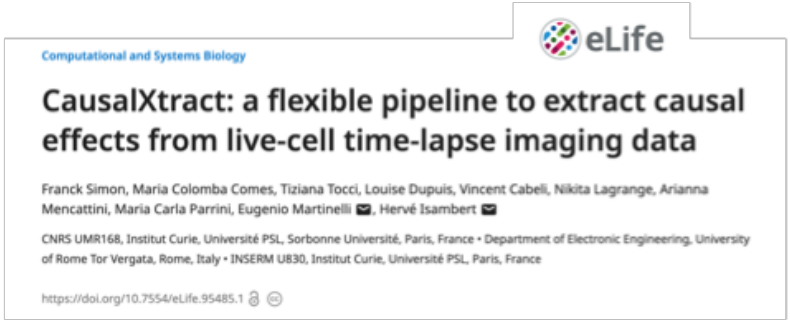
accepted in *Nature Communications*


New Results

Follow this preprint

A quantitative pipeline for whole-mount deep imaging and multiscale analysis of gastruloids

Alice Gros, Jules Vanaret, Valentin Dunsing-Eichenauer, Agathe Rostan, Philippe Roudot, Pierre-François Lenne, Léo Guignard, Sham Tlili


eLife

Computational and Systems Biology

CausalXtract: a flexible pipeline to extract causal effects from live-cell time-lapse imaging data

Franck Simon, Maria Colomba Comes, Tiziana Tocci, Louise Dupuis, Vincent Cabeli, Nikita Lagrange, Arianna Mencattini, Maria Carla Parrini, Eugenio Martinelli, Hervé Isambert

CNRS UMR168, Institut Curie, Université PSL, Sorbonne Université, Paris, France • Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy • INSERM U830, Institut Curie, Université PSL, Paris, France

https://doi.org/10.7554/eLife.95485.1

+ Lansche & Ladaigue et al, submitted

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- Sophie Picci, DR PACA
- Laurence Guitton, DR PACA
- Vincent Biscaras, DR Paris

- **Christophe Lamaze, coordinator**
- Guillaume Montagnac (WP1 leader)
- Danjela Vignjevic (WP1 leader)
- Matteo Rauzi (WP2 leader)
- Maria-Carla Parinni (WP2 leader)
- Hervé Isambert (WP3 leader)
- Hervé Turlier (WP3 leader)

- Charles Baroud
- Pierre Bon
- Stéphanie Descroix
- Robert Kelly
- Pierre-François Lenne
- Michel Puceat
- Sébastien Sart
- Sonia Stéfanovic
- Willy Supatto
- Sham Tlili
- Beatrice Turcq
- Stéphane Zaffran