

COMING TOGETHER
TO DESIGN BETTER
HEALTHCARE FOR ALL

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world
CONGRESS

JUNE 25–28, 2024 / SEATTLE, WA
SEATTLE CONVENTION CENTER



Development of 3D innovative tooth organoids for personalised medicine in rare oro-dental diseases

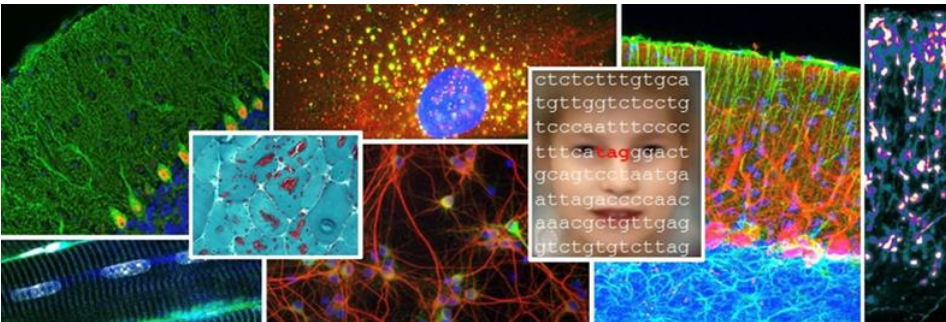
Varvara Gribova, PhD
Strasbourg, FRANCE



➤ Founded in 1994 with the support of CNRS, Inserm, University of Strasbourg and pharmaceutical company Bristol-Myers-Squibb

Departments:

- Development and stem cells
- Functional genomics and cancer
- **Translational medecine and neurogenetics**
- Integrated structural biology





Prof. A. Bloch-Zupan

Prof. Agnès BLOCH-ZUPAN group:

Craniofacial and oral developments, and their associated abnormalities

Oro-Dental Genetic Disorders

Amelogenesis Imperfecta



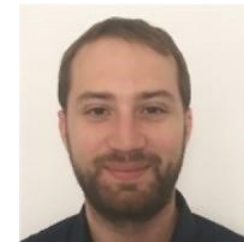
- Incidence: 1:12000
- Defective **Enamel** formation (**Ameloblasts**)
- Hypoplastic (quantitative defect), hypomineralisation, or hypomaturation (qualitative defect)

Dentinogenesis Imperfecta/ Dentin Dysplasia



- Incidence: 1:8000
- Defective **Dentin** formation (**Odontoblasts**)
- Discolored and weakened dentition

Targeted DNA sequencing: GenoDENT NGS panel



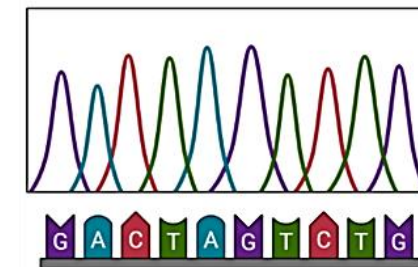
Dr. T. Rey



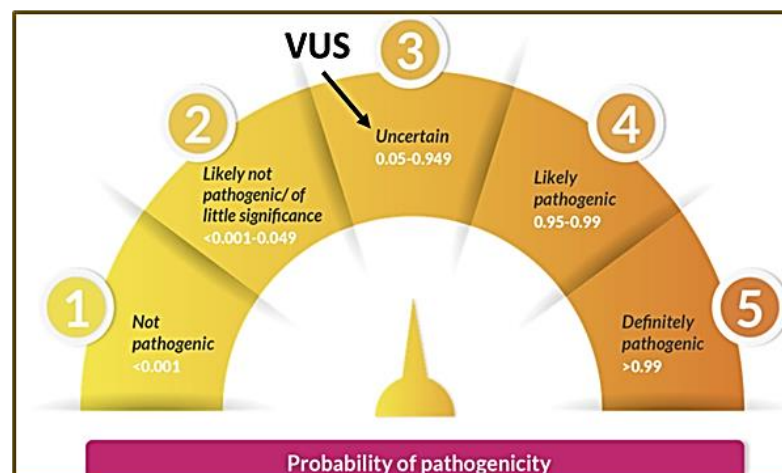
Saliva samples collection



DNA Sequencing



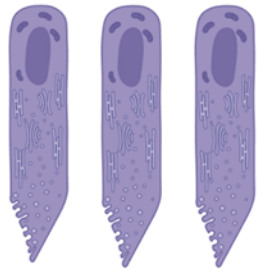
Variants in genes involved in odontogenesis



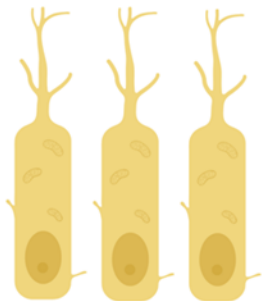
“Variants of Unknown Significance”(VUS)

In vitro models

1. Cells Analysis and Characterization



Ameloblast-like cells

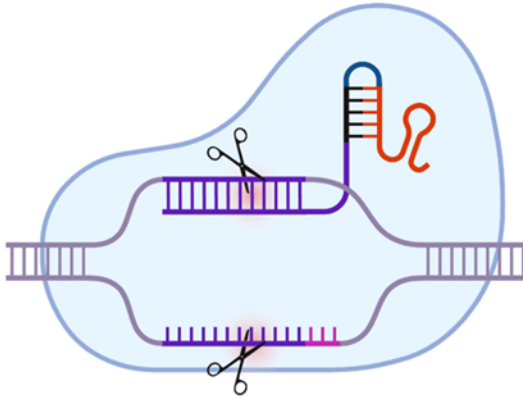


Odontoblast-like cells

2D Cell Analysis

2. Genome editing

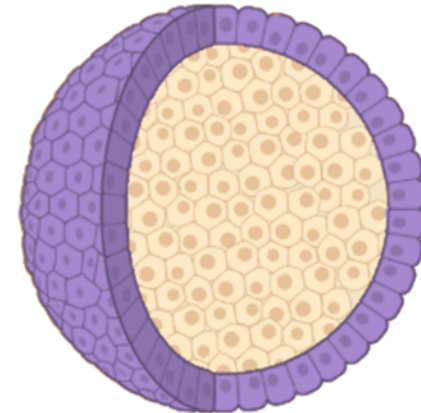
CRISPR-Cas9



Mutant Ameloblastic and
Odontoblastic cell lines

3. Organoids

3D Organoids



3D organotypic model that
mimics **Bell stage** of
odontogenesis

3D Cell Analysis



Dr. Fadi JERBAKA



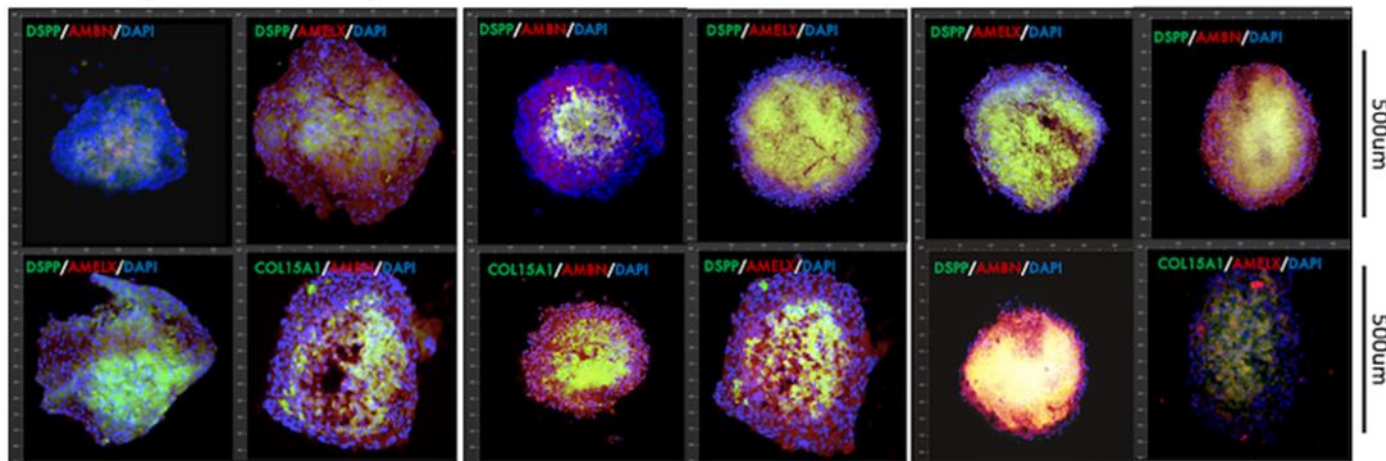
Dr. I. M. BUGUENO

+ Soufian
EL-FALOUSSI

3D Organoids

MOUSE

Mouse (mDPC + Ls8)

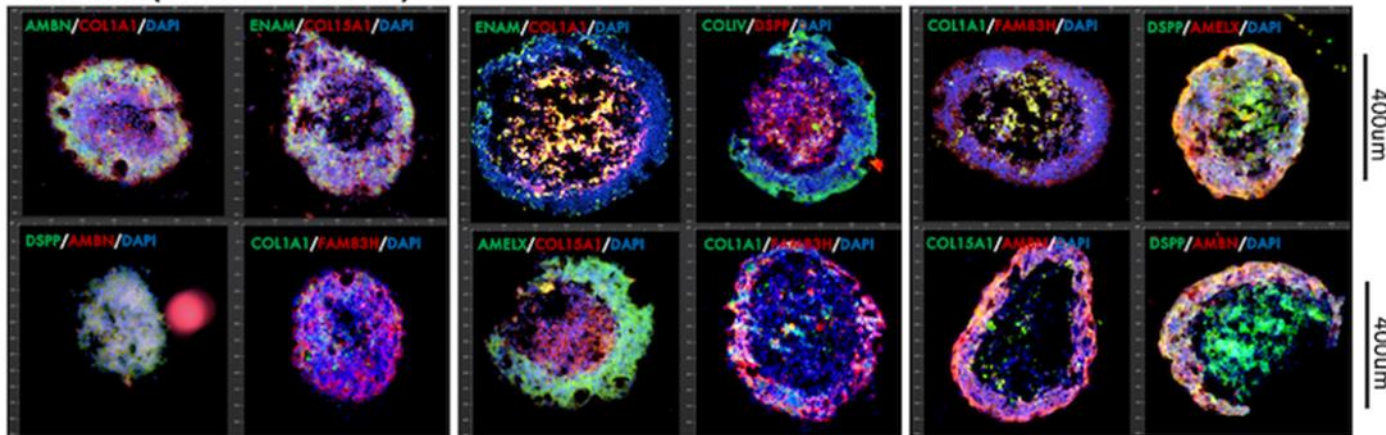


10 – 15d 21 – 30d 30 – 60d



HUMAN

Human (hDPSC + AM1)

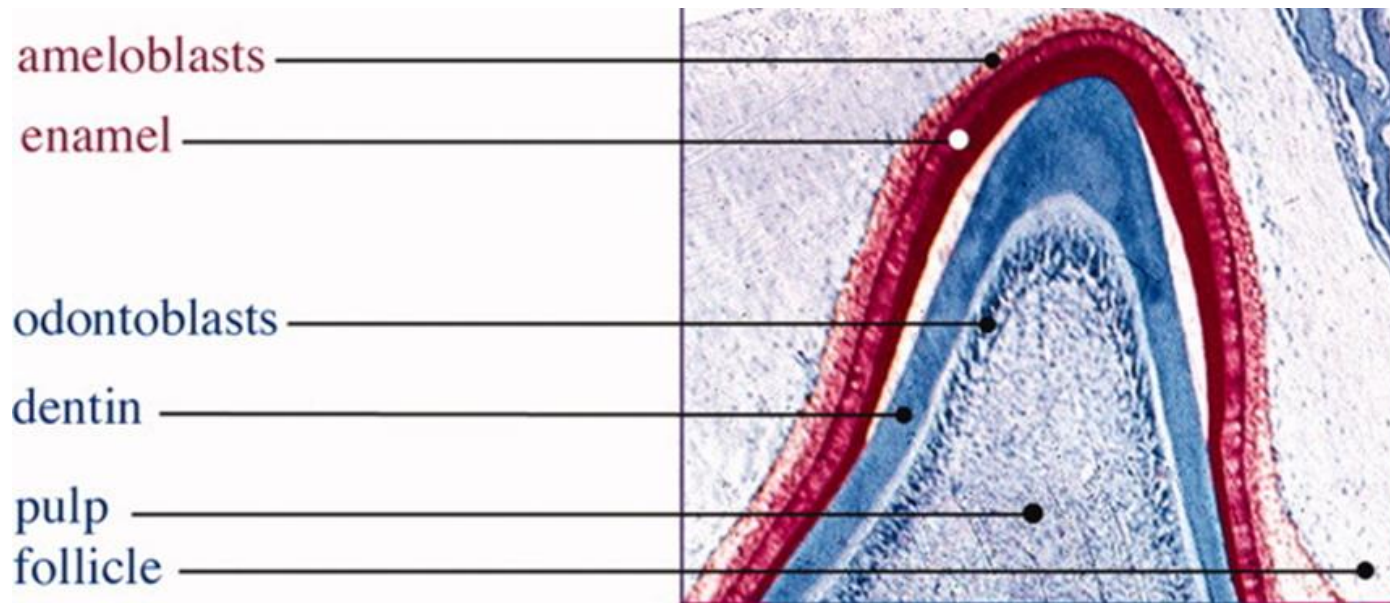


10 – 15d 21 – 30d 30 – 45d

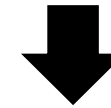


3DBioDENT project:

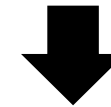
3D models of human tooth development containing patient-specific mutations (VUS)



Bell stage 3D models



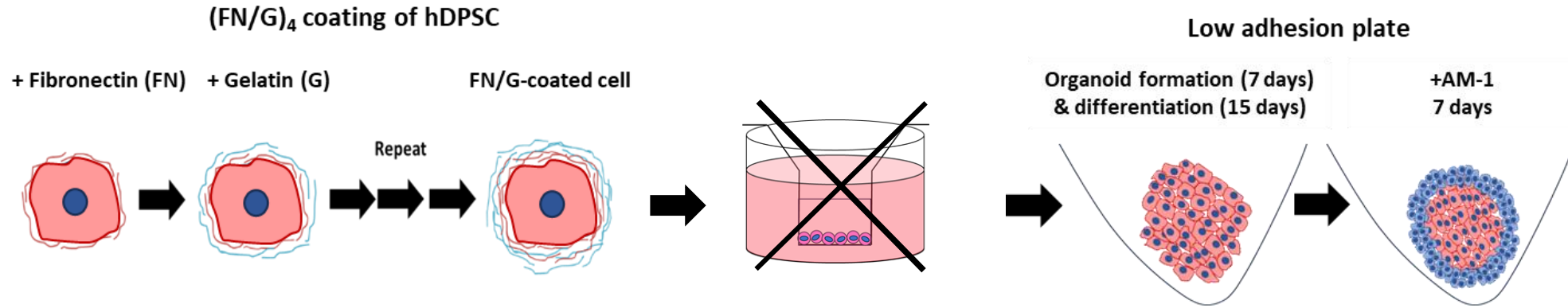
Functional validation *in vitro*



Reduce patient diagnostic wandering

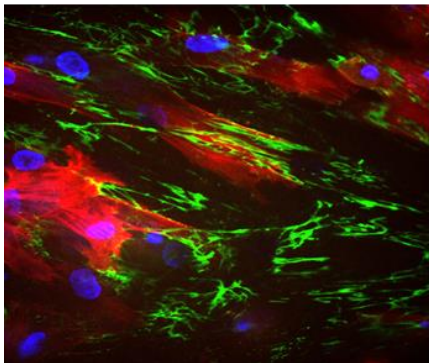
Cell-accumulation method

Fibronectin-Gelatin nanofilms

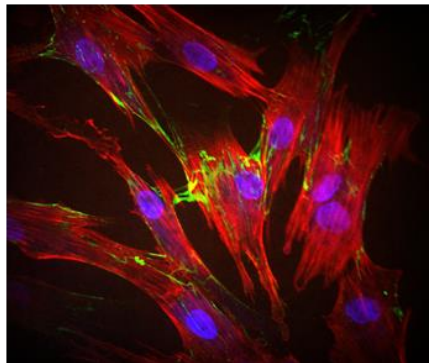


Artificial nanomatrix

FN/G-coated

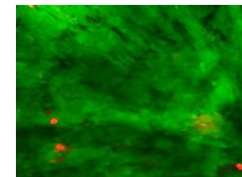


Non-coated

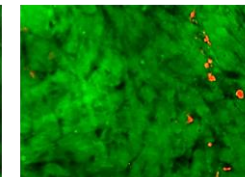


Improved viability

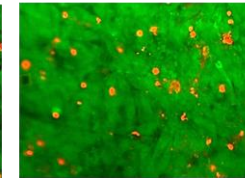
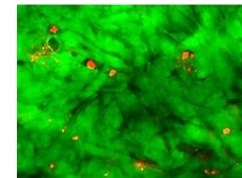
FN/G-coated



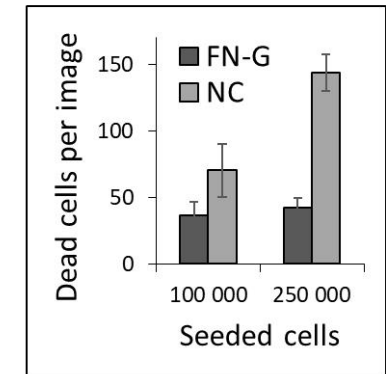
Non-coated



1*10⁵

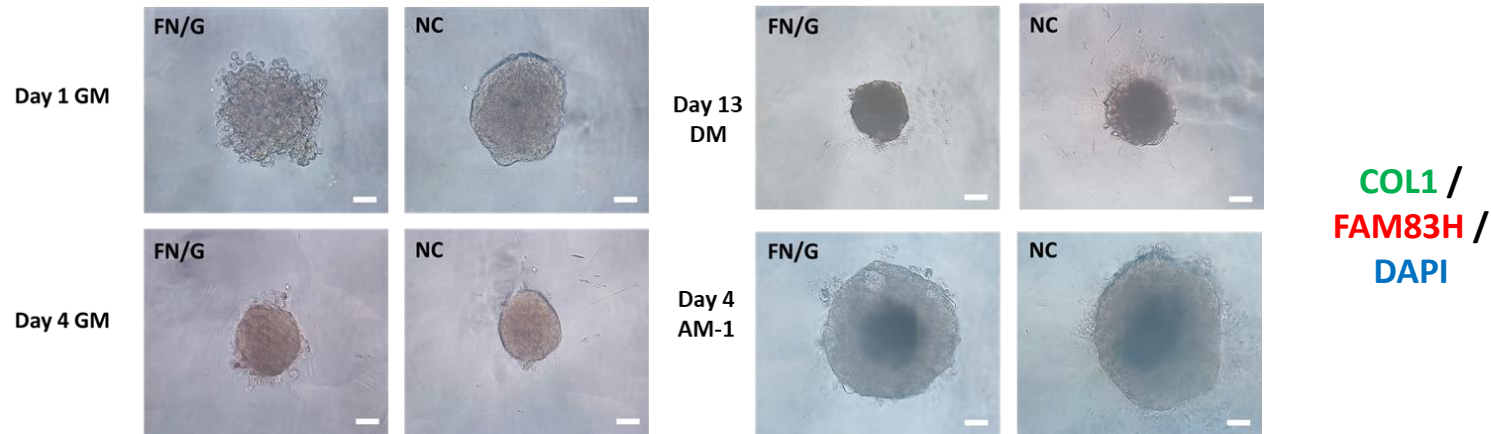


2.5*10⁵

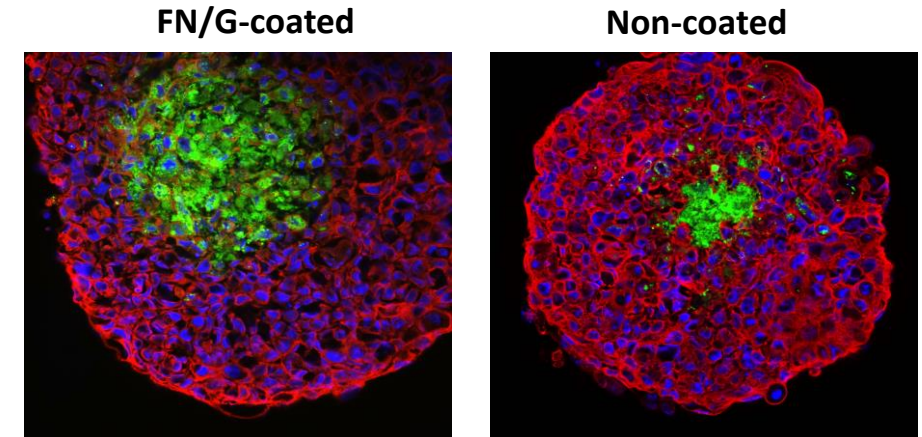


Bilayered organoids

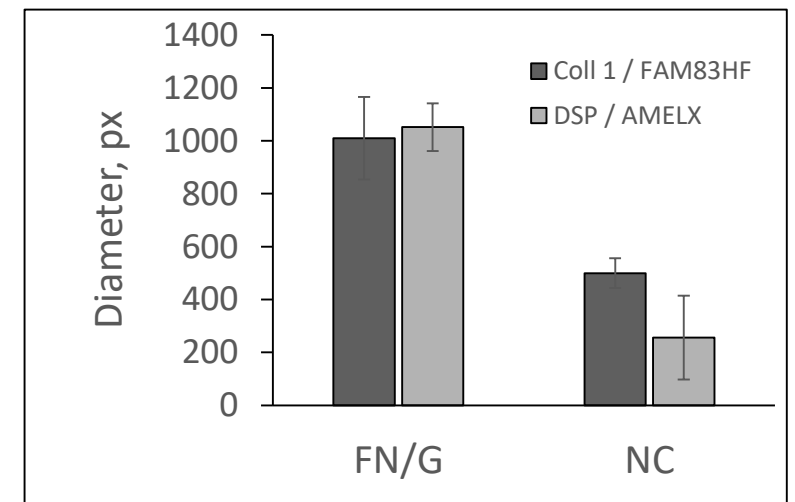
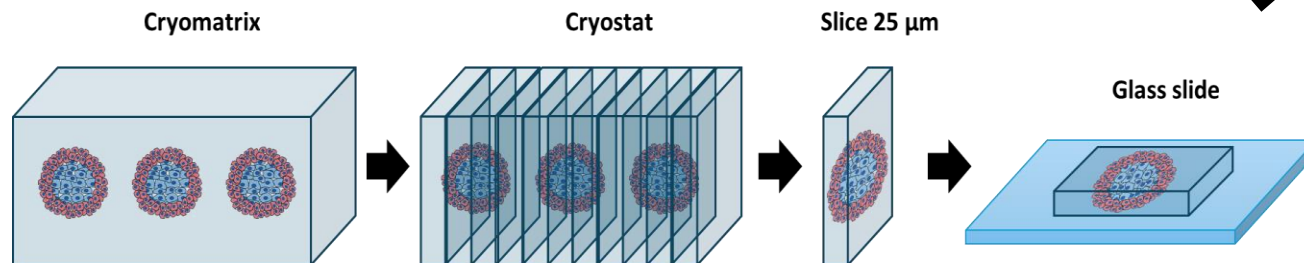
Organoid formation



Odontoblast differentiation



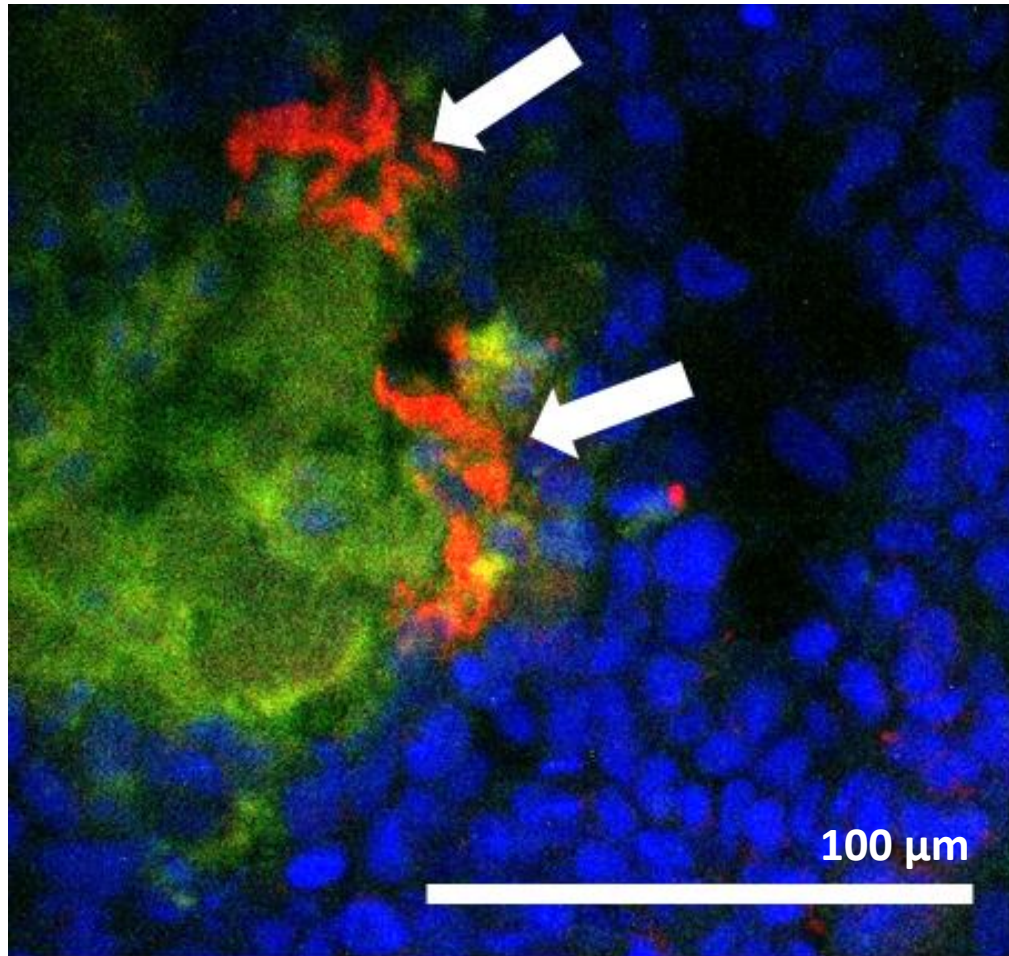
Sample preparation



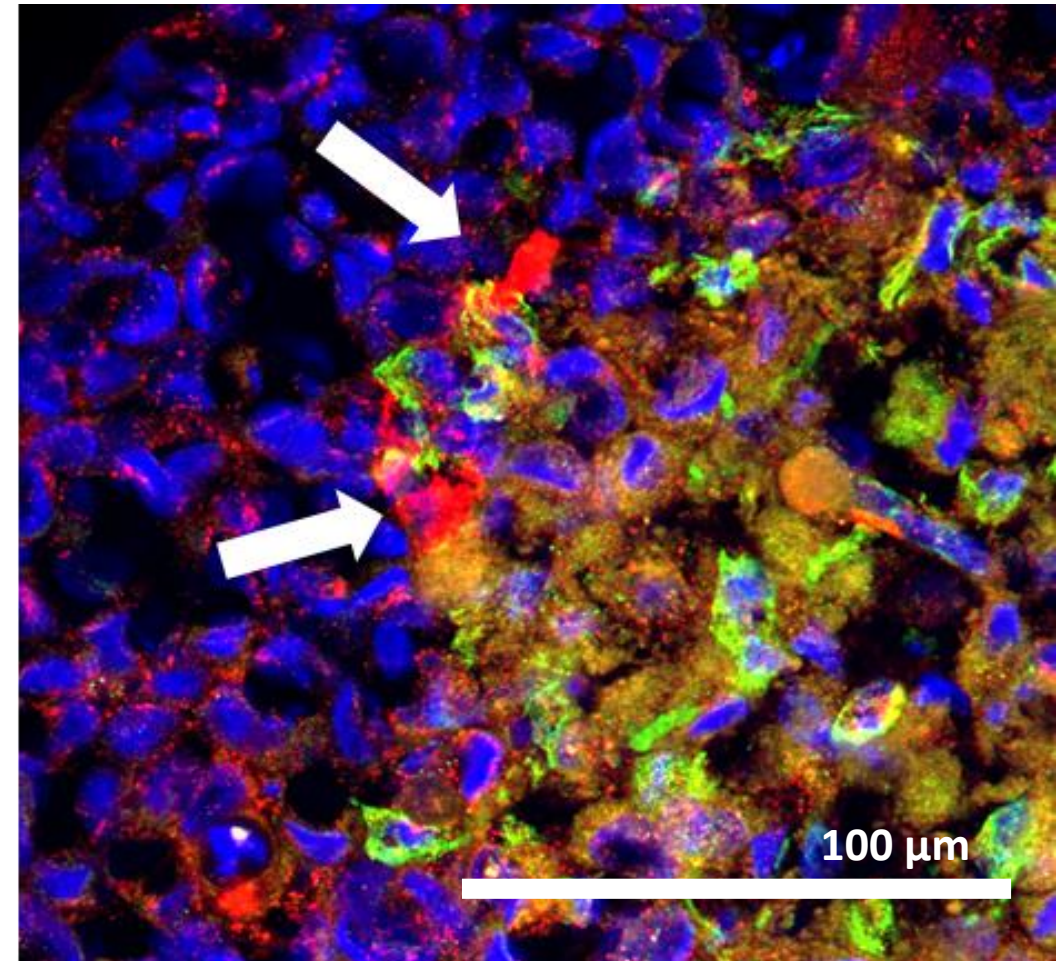
Ameloblast differentiation

Experiment 1

DSP /
AMELX /
DAPI

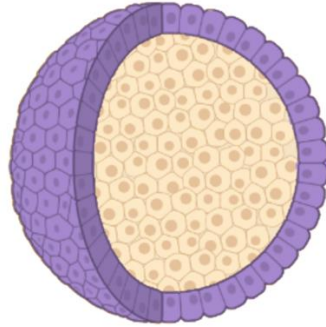


Experiment 2



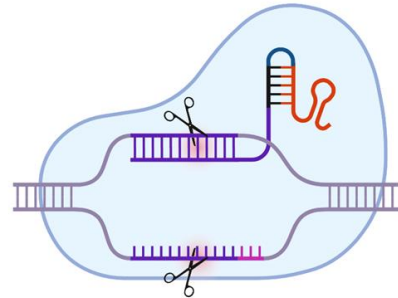
- **3D models (Varvara GRIBOVA):**

- Organoid optimisation
- Gene & protein expression



- **Genome editing (Eve SUSS):**

- Transfection protocol setup
- CRISPR/Cas9 modification → selection

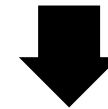


Dr. V. Gribova



Eve Suss

3D models with VUS



Diagnosis

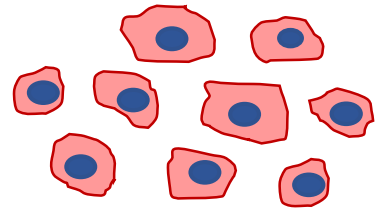


3D culture in hydrogels and bioprinting

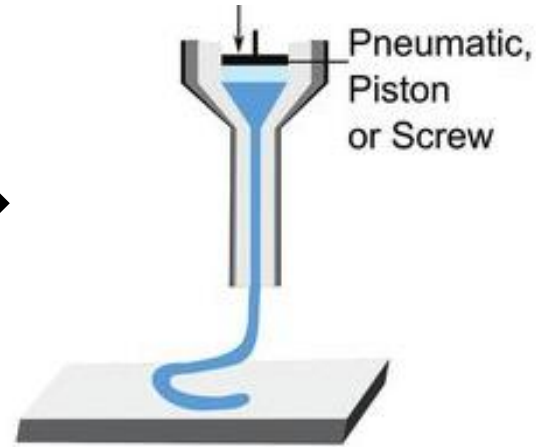


Bioink

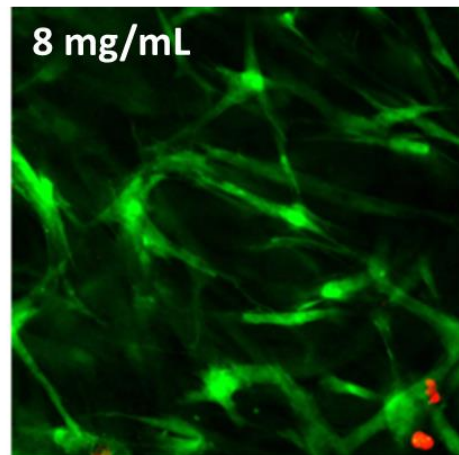
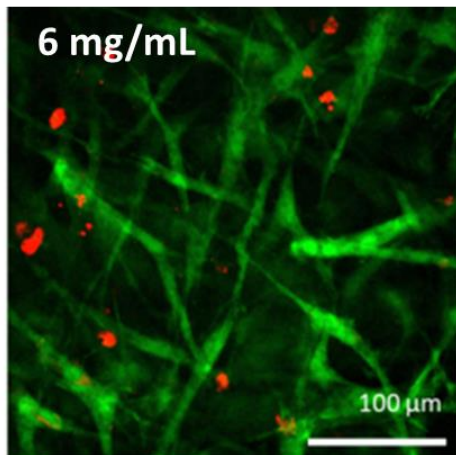
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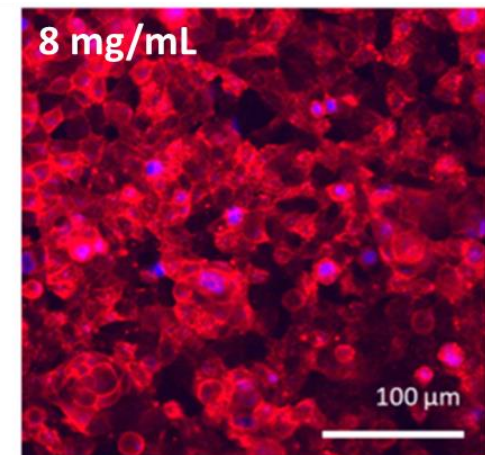
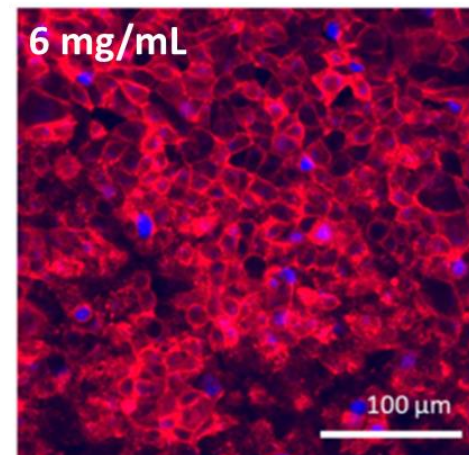
Cells



hDPSC viability



AM-1 adhesion



The team

Prof. Agnès Bloch-Zupan
Dr. Isaac Maximiliano Bugueno
Dr. Youri Arntz
Eve Suss
Marie-Christine Fischer
Dr. Yann Hérault



Alumni

Dr. Tristan Rey
Dr. Fadi JERBAKA
Soufian EL-FALOUSSI

Travel fellowship

