

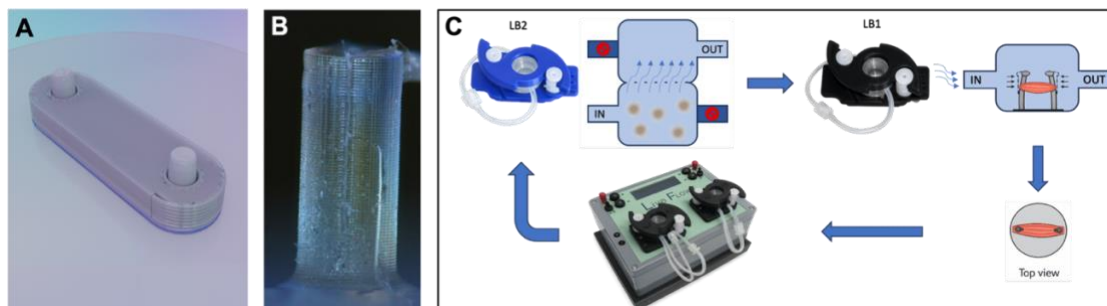


# INFRAFRONTIER Complex *In Vitro* Models:

## 3D bioprinted muscle fibres in tumour-on-chip to study cancer cachexia (MuTu)

### How is the model generated?

1. Isolation, immortalisation, characterisation, and expansion of primary mouse muscle precursor cells (satellite cells - myogenic progenitors) for myobundle establishment
2. Fabrication of engineered tissue culture surfaces with Flexdym-based flexible pillars (Fig. 1A,B)
3. Synthesis and characterisation of GelMA-NaAlg hydrogel and Pluronic F127 as a sacrificial bioink for 3D bioprinting
4. 3D bioprinting of immortalised muscle precursor cells within hydrogels onto engineered tissue culture surfaces for myogenic differentiation into muscle fibres (myobundle) and functional analysis
5. Generation of tumour organoids from colon cancer cells
6. Co-culture between tumour organoids and myobundles in a hydrodynamic system (Fig. 1C).



**Figure 1. Schematic of the MuTu model.**

(A) Rendering of a 3D bioprinted muscle cell construct for myobundle generation fabricated between flexible pillars; (B) A micrograph of a Flexdym-based pillar; (C) Workflow of the MuTu model for the interplay between colon cancer organoids and a myobundle within a hydrodynamic system (IVTech platform). LiveBox2 (LB2) and LiveBox1 (LB1) are featured with flow inlets (IN) and outlets (OUT) for the perfusion of cell culture medium from tumour organoids to myobundles, connected in series via a peristaltic pump (LiveFlow).



### Potential applications:

To analyse functional and molecular alterations of cachectic muscle fibres following colon cancer development with the final aim of testing new potential therapeutic treatments (e.g., anti-tumour and anti-cachexia drugs). In addition, the MuTu model is expected to enable physiologically relevant studies of muscle function in other muscle-impacting pathologies (e.g., diabetes, skeletal muscle dystrophy). Furthermore, MuTu will support drug testing and therapeutic research in a reproducible, ethically responsible system. This platform will offer new opportunities for both basic and translational muscle research.

### Who provides this model?



The Gori and Moretti Labs are fully equipped with the requisite technology and core facilities for derivation and culture of muscle precursor cells and 3D colon cancer cells, including 3D printing and microfabrication facilities (Fig. 2) with one 3D bioprinter and four 3D printers for microfabrication and surface micropatterning. Moretti's group has extensive experience with 3D cancer models and with studying murine muscle in vivo and ex vivo. Gori's group has documented experience in developing new approach methodologies (NAMs) for disease modelling and drug screening, including 3D bioprinted culture models and organ-on-chip technologies.

IBBC hosts INFRAFRONTIER-EMMA infrastructure, providing access to mouse models, data, and scientific platforms and services to study the functional role of the genome in human health and disease; archiving and distribution of scientifically valuable mouse strains through EMMA; access to a whole-organism, systemic analysis of genotype-phenotype interactions using cutting-edge analytical and diagnostic methodology in the INFRAFRONTIER mouse clinics.



Figure 2. Photos of the available 3D bioprinter and 3D printers.

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## References:

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