INFRAFRONTIER Complex *In Vitro* Models:

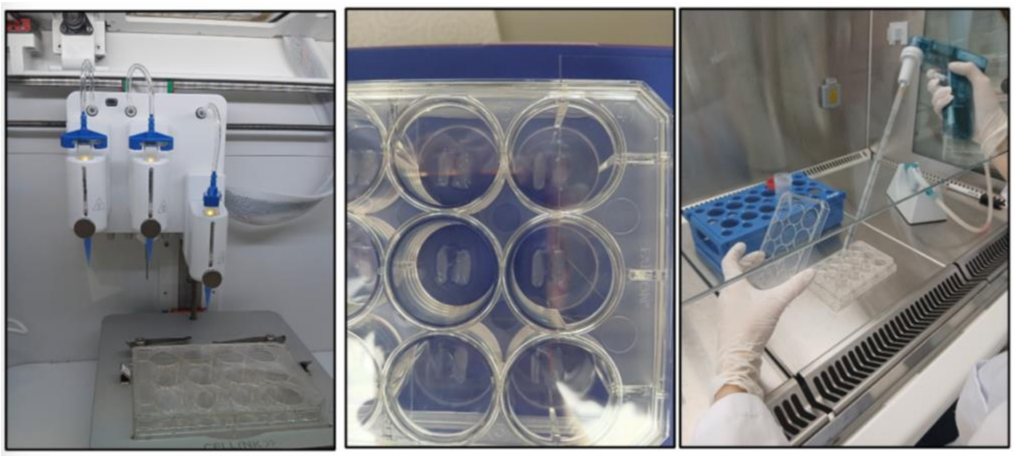
3D bioprinted tissue for colorectal cancer (CRC)

Brief description:

Cells derived from a spontaneous, inducible murine colorectal cancer (CRC) model will be utilized to establish a physiologically relevant *in vitro* 3D bioprinted system. This advanced model is designed to recapitulate key features of the native tumor microenvironment by spatially organizing multiple cell types such as tumor cells, fibroblasts, and potentially immune components within a defined architecture that closely mimics *in vivo* tissue organization.

3D bioprinting enables the precise deposition of cells in combination with biocompatible bioinks composed of materials such as collagen, alginate, or gelatin, which provide structural support and promote cell viability. In addition, Matrigel will be incorporated as an extracellular matrix (ECM) surrogate to supply essential biochemical cues that regulate cell behavior, including proliferation, differentiation, and cell–cell interactions. This approach facilitates the formation of complex, multicellular 3D constructs that better reflect the heterogeneity and functionality of CRC tissue compared to conventional 2D cultures.

The resulting 3D bioprinted CRC models are intended to serve as robust platforms for the preclinical evaluation of novel anticancer therapeutics, allowing for more predictive assessment of drug efficacy and resistance mechanisms. Furthermore, these constructs provide a powerful tool for fundamental research, enabling detailed investigation of molecular signaling pathways, tumor–stroma interactions, and disease progression in a controlled and reproducible environment.



How is the model generated?

Using an extrusion-based 3D bioprinting platform, colon substitute tissues are fabricated employing a highly biocompatible bioink composed of gelatin, alginate, and Matrigel. This composite bioink provides a supportive extracellular matrix–like environment, enabling precise spatial deposition of cells while maintaining structural integrity during and after the printing process. Compared to conventional two-dimensional (2D) cell culture systems, this approach offers a significant advantage by allowing cells to be organized in a physiologically relevant three-dimensional (3D) architecture. Furthermore, cells within these 3D constructs exhibit enhanced viability over extended culture periods and retain their tissue-specific cellular phenotypes and functions to a much greater extent than in 2D systems.

The resulting 3D bioprinted constructs are composed of colonic epithelial cells, stromal cells, and x cells. These distinct cell populations are simultaneously deposited using a multi-head extrusion system, enabling controlled spatial arrangement and the recreation of complex tissue-like microenvironments. This precise organization facilitates cell–cell and cell–matrix interactions that are critical for mimicking native colon tissue physiology.

All cells used in this system are derived from genetically engineered mouse lines obtained from the European Mouse Mutant Archive (EMMA), specifically the Apc^{Min}/5H and Cdx2-Cre^{ERT2} strains, which are maintained and bred in our institutional animal facility. A key feature of this model is the inducibility of the Apc^{Min}/5H mutation via tamoxifen administration. *In vivo*, these animals develop colorectal tumors only upon tamoxifen-induced activation of Cre recombinase.

In our approach, induction of the Apc^{Min}/5H mutation is performed directly within the 3D bioprinted constructs through the application of tamoxifen *in vitro*. This strategy enables the controlled initiation of tumorigenesis within an engineered tissue context, thereby decoupling tumor induction from the *in vivo* environment. As a result, the model allows for the generation of 3D constructs representing defined and reproducible stages of tumor development.

This system is particularly well suited for investigating early events in colorectal tumorigenesis, as well as for evaluating potential therapeutic compounds targeting initial stages of cancer progression. Such analyses are not feasible in traditional 2D cell culture models, where the lack of structural complexity and altered cellular behavior limit their physiological relevance. Consequently, the described 3D bioprinting approach represents a substantial advancement over existing *in vitro* models, offering a more predictive and biologically relevant platform for cancer research and drug testing.

Potential applications:

The 3D bioprints are intended for use in the evaluation of novel therapeutic compounds in oncology. Tumor growth and the proliferation of tumor cells can be effectively analyzed using the 3D bioprints. In addition, these constructs may serve as valuable platforms in basic research to enable a more detailed investigation of molecular and cellular processes underlying tumor biology. The 3D bioprints can be applied in both basic and industrial research.

Who provides this model?

vetmeduni
University of Veterinary Medicine, Vienna

The laboratory that develops and produces the 3D bioprints is part of the Laboratory Animal Medicine unit at the University of Veterinary Medicine. This unit focuses on the generation of genetically engineered mouse models in the field of gastrointestinal diseases, including pancreatic ductal adenocarcinoma (PDAC) and colorectal cancer (CRC). These *in vivo* models are used to investigate the molecular biology of these diseases in basic research and to support the development of novel therapeutic approaches. These in vitro models are intended to be standardized to a degree that allows the 3D bioprints generated *in vitro* to be made available to other researchers and industry partners.

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References:

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