Winter 2023

Pronostic of Colo-Rectal Cancer (CRC) Using Machine Learning Models on Organoids Derived of Patient

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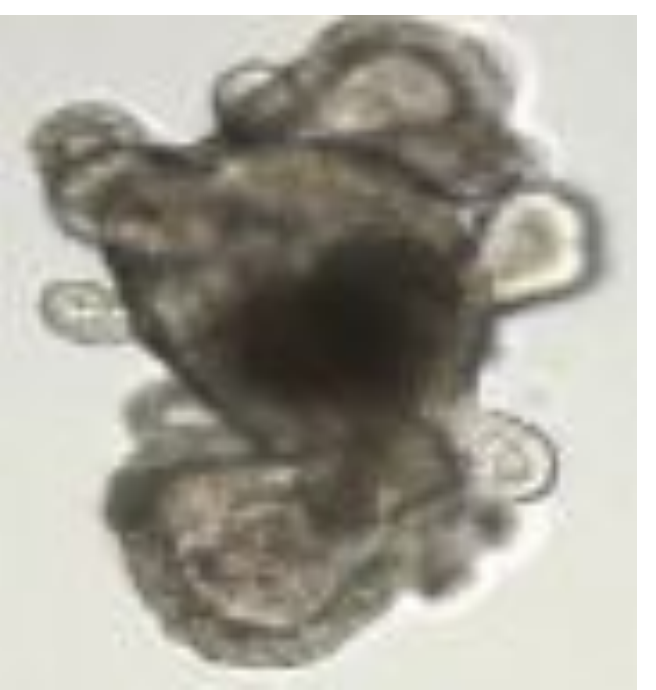
*T. Sato et al., 2009 (Organoid)*

Introduction

Colorectal Cancer (CRC) is one of the most studied carcinomas due to its high incidence in the world. CRC is the second leading cause of death for women and third for men globally. Despite advances in treatment, the mortality rate remains high at 50%.

There are different biological models to study molecular mechanisms through animals, cell lines and, more recently, organoid model. Organoid is a 3D cell culture, generally produced by epithelial cells derived from tumours which can grow under specific conditions of culture.

Organoid offers the potential to further personalised therapies and also eradicating ethical issues. In comparison to other models, this 3D model offers multiple advantages, including greater diversity of cell cancer, biological stability, genetic modification, and extension of the culture.

In recent years, machine learning models have been used to predict the treatment response of CRC using organoids and their tissue of origin. Considering all of this, evaluate the reaction of organoids and tissues further different treatments could help clarify the comprehension and treatment of future CRC patients.
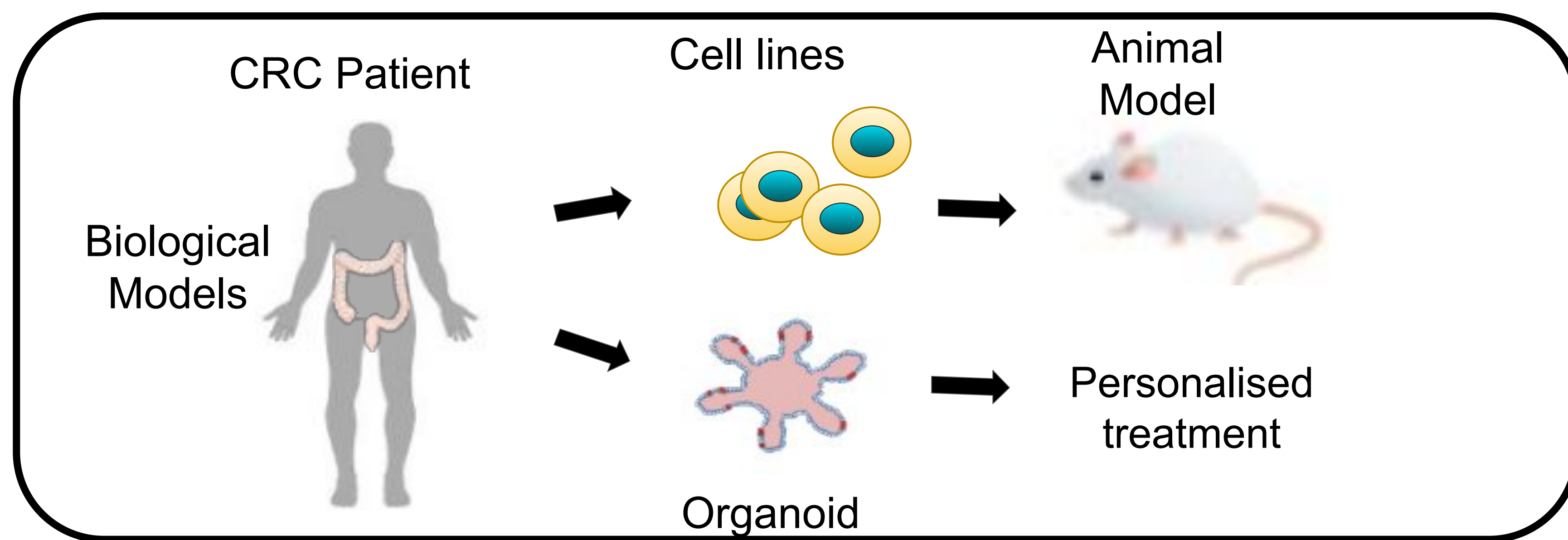
What is the percentage of similarity between the tumour and the organoid? Is it possible to find a pattern between people who do not respond to conventional chemotherapy and those who do?

Research Objective
Generate a new Machine Learning Model (ML) capable of predicting the development and response of CRC patients further different chemotherapy treatment.

Specific Objectives
1. Prepare and clean data prior applying an unsupervised machine learning model.
2. Classify different organoids derived from CRC tissue and **previous tissue stored** based on diagnosis, morphological characteristics and molecular consensus of CRC.
3. Evaluate drug tolerance of organoid, comparing the tissue derived or/and tissue with the same or similar classification.
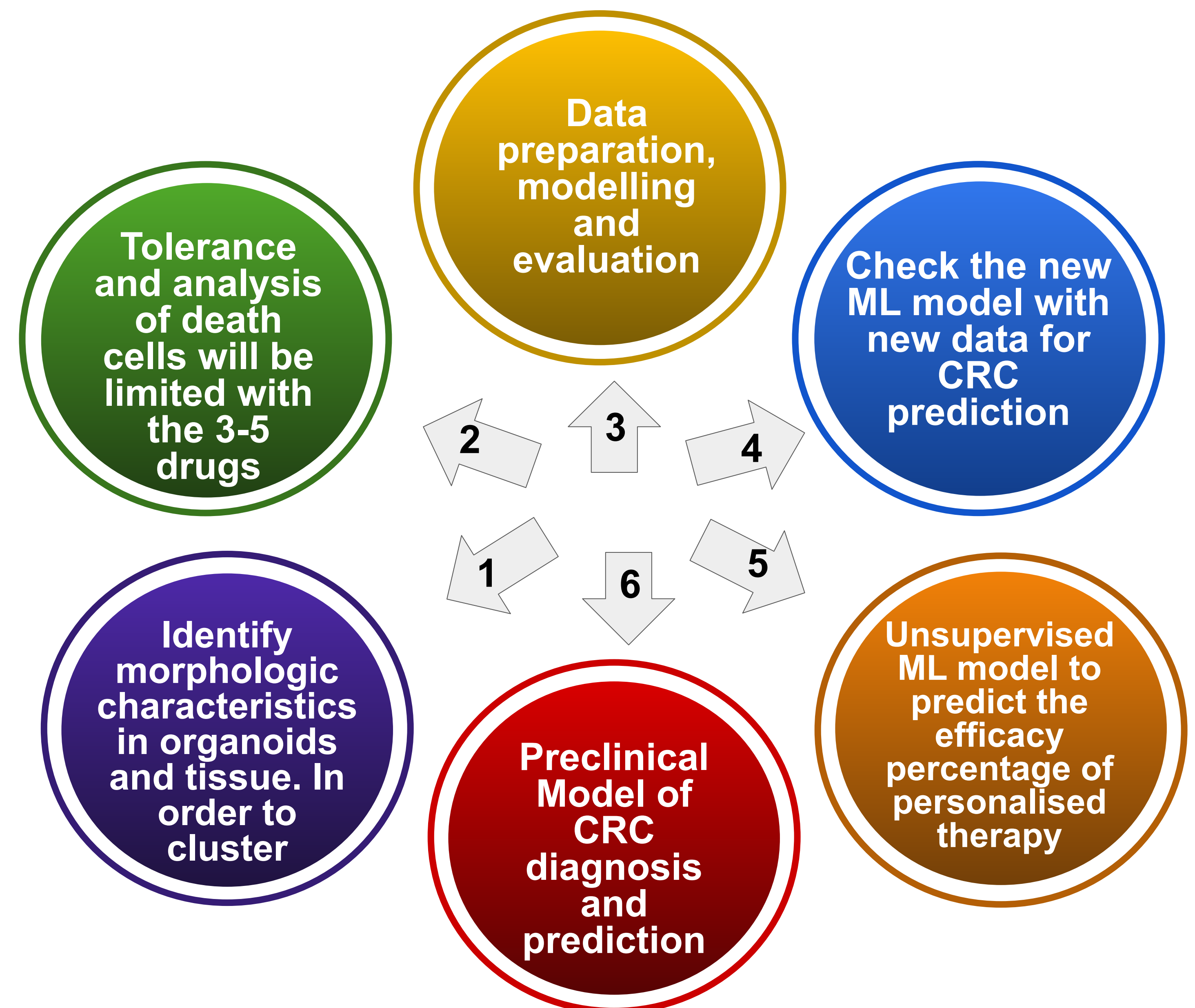
Methodology
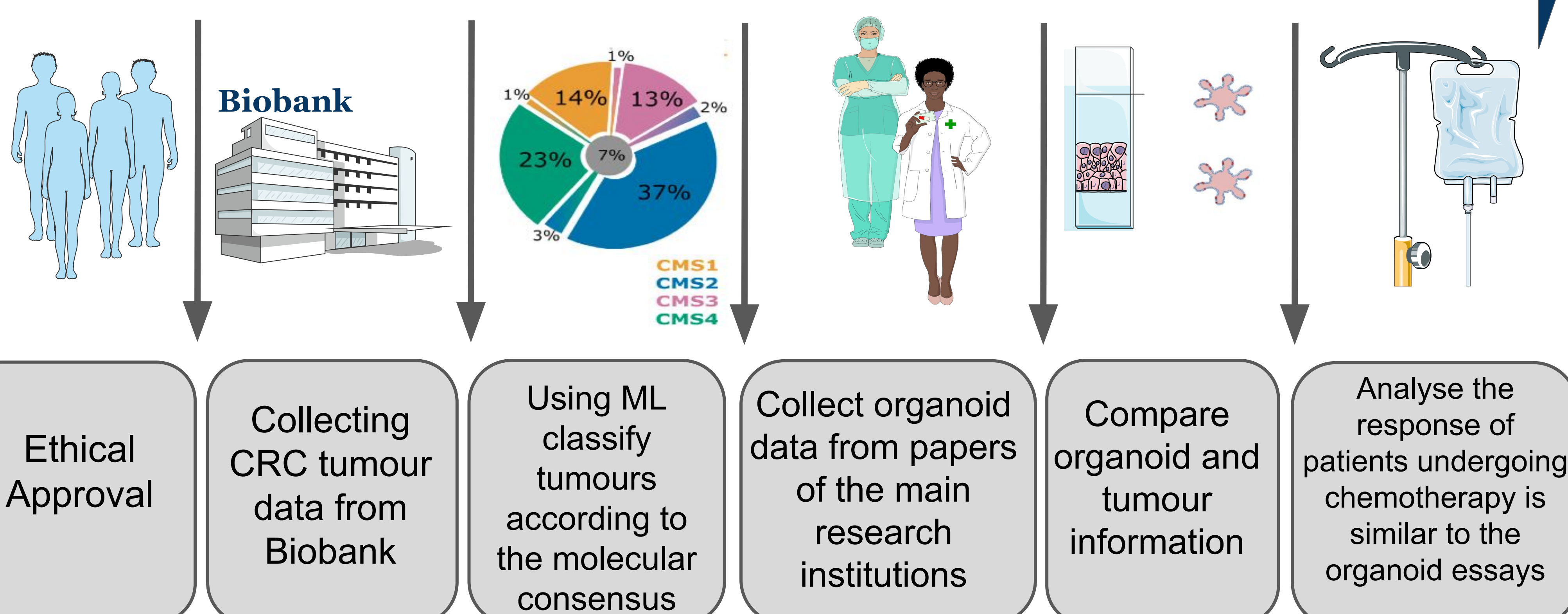
The ethic committee must approve the study. It will also monitor practices during the project develops. A critical step is to obtain informed consents from participants. The privacy, confidentiality and protection of the data will be the responsibility of the biobank and research team to provide the necessary data for the study. Organoids and tissues will be organised according to the same diagnosis and molecular similarity. Followed by drug screening essays and the response is evaluated.

| Ethical Approval | Collecting CRC tumour data from Biobank | Using ML classify tumours according to the molecular consensus | Collect organoid data from papers of the main research institutions | Compare organoid and tumour information | Analyse the response of patients undergoing chemotherapy is similar to the organoid essays |

Analysis

1. Identify morphologic characteristics in organoids and tissue. In order to cluster
2. Tolerance and analysis of death cells will be limited with the 3-5 drugs
3. Data preparation, modelling and evaluation
4. Check the new ML model with new data for CRC prediction
5. Unsupervised ML model to predict the efficacy percentage of personalised therapy
6. Preclinical Model of CRC diagnosis and prediction

Comments

In contrast to previously reported ML models, this new proposal takes into consideration tissue with diagnostic and molecular similarities and not just the tissue utilised for creating organoids. This will be increase the accuracy of the model to continue on the clinic validation stage.

In numerous cases, it is impossible to grow organoids from patient tissue and biobank of organoids has not yet been established. Thus, an organoid biobank is essential for the advancement of this field. Adjuvant therapy can be considered for future research, even though chemotherapy is the only treatment considered in the present research for the prediction of the progression of CRC and reactions.
ML will help us determine whether greater recurrence and a poor response to the existing medication could be related to patient subgroups that were improperly diagnosed.

Recommendations

If the organoid's negative response to medications is identical to tissues with similar diagnoses and morphological characteristics, considered a combination of new drugs or novel therapies.
Consider also including the stroma or microenvironment in the culture for a more representative model, not only epithelial cells.

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Acknowledgements