



# UPORT Cancer Biobank

Organoids as a resource for fundamental and applied cancer research

<b>Sub-biobank title (up to 250 characters):</b> Uपोर्ट Cancer Biobank, Organoids as a resource for fundamental and applied cancer research	
Sub-biobank acronym (up to 50 characters): UPORT Cancer	
<b>Details of person with final responsibility and contact person</b>	
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<b>Sponsor</b> , if this is not UMC Utrecht:	N.A.
Grant provider (if applicable):	N.A.
<p><b>Project goal:</b> To create a living biobank (Uपोर्ट Cancer) consisting of organoid cultures derived from healthy and tumor tissues (including body fluids such as blood, urine and ascites) from cancer patients. The Uपोर्ट Cancer Biobank will be used for multiple purposes, including the identification of effective anti-cancer treatments (e.g. through 'drug screens'), the development of personalized medicine strategies (in combination with genetic and clinical data sets), and as a resource for fundamental biomedical cancer research.</p> <p>Healthy tissue (which is often part of the resected tissue) will also be used to derive organoids, for studying the interaction between cancer cells and their microenvironment, and for studying physiological processes to increase our understanding of the organ-specific contexts in which cancer develops.</p> <p><b>Scientific background:</b> Traditional frozen and paraffin-embedded tissue biobanks have proven to be extremely valuable resources for fundamental and applied cancer research. The combination of histopathological, genetic and clinical data has guided the development of many novel diagnostic tools and treatment strategies. However, such tissue biobanks cannot be used to empirically test novel hypotheses relating to tumor development or therapeutic vulnerabilities. Functional cancer research has so far largely relied on the use of immortalized (cancer) cell lines and animal models. However, <i>in vitro</i> immortalization of cell lines is accompanied by extensive genetic changes that allow cancer cells to adapt to the culturing conditions. This creates major and unwanted discrepancies between cancer cell line models and the tissues they are supposed to represent. About 10 years ago, a 3D culturing system was developed which allowed researchers to culture human adult stem cells from (tumor) tissues indefinitely as organoids, or 'mini-organs-in-a-dish' (1,2). Organoid cultures can be established with high efficiency from multiple healthy and diseased human tissues (3-14) whilst maintaining their phenotypic, functional and genetic properties.</p> <p>The unprecedented faithful representation of the (tumor) tissue-of-origin by organoids opens many avenues for <i>fundamental research into the (patho-)physiology of tumor development</i>, for <i>drug discovery</i>, and for developing <i>personalized medicine strategies</i> (e.g.15-24).</p>	

The UMCU, the Hubrecht Institute, and the Prinses Maxima Centrum will apply organoid technology to culture cancer patient-derived healthy and tumor tissue samples for application in these diverse areas of cancer research.

The envisioned UPORT Cancer Biobank, combined with genetic data and long-term patient follow-up, provides a unique resource for many aspects of biomedical cancer research.

**Project members:**

1. UMC Utrecht: Prof. Dr. Onno Kranenburg, Coordinator and project leader of UPORT. Task: coordination of tissue acquisition, culture system development, fundamental research
2. UMC Utrecht: Dr. Jeanine Roodhart, Medical Oncologist. Task: applying organoid technology as a tool in personalized medicine.
3. The Hubrecht Institute: Prof. Dr. Hans Clevers. Task: culture system development, validating organoid technology as a tool in personalized medicine, fundamental research.
4. Princess Maxima Centre: Prof. Dr. Hans Clevers: Task: culture system development, validating organoid technology as a tool in personalized medicine, fundamental research.

The conditions allowing researchers at Hubrecht and PMC to use UMCU patient tissues for derivation of organoid biobanks are described in the accompanying collaboration agreement.

In addition to these project members, the project has been discussed and coordinated with the surgery department, the pathology department and the Central Biobank of the University Medical Centre Utrecht.

The following people are involved:

- *Central Biobank*: is responsible for sample storage, sample coding and sample, distribution (Head: Dr. Imo Hofer).
- *PIs from the Lab Translational Oncology (LTO)*: LTO is headed by Prof. O Kranenburg and includes the following PIs: Prof. Borel Rinkes (surgeon), Dr. Jeroen Hagendoorn (surgeon), Dr. Helma van Grevenstein (surgeon), Dr. Quintus Molenaar (surgeon), Dr. Jeanine Roodhart (medical oncologist), Dr. Richard Meijer, Dr. Paul Coffey, Prof Ronald Zweemer, Dr. Leon Moons and Dr. Hugo Snippert.
- *Pathology*: Dr. Miangela Lacle (pathologist), Prof. Paul van Diest (pathologist and head of the Pathology department).


**Study design:** This is an observational project in which we will collect resected healthy and tumor tissue during the course of normal cancer treatment. Blood samples will be drawn during standard care. The blood samples that are obtained will be used to generate genetic (DNA) data and/or will be used for the isolation of immune cells for co-culturing purposes. In addition, depending on the project and cancer type, we will collect urine, ascites fluid, or PAP smears. The tissue samples will be cultured using the 3D organoid culturing method. Cultured normal and tumor tissue organoids will be used for fundamental research, for cancer drug screens, and for patient-specific drug testing and screening.

**Study population:** Adult patients who are treated for a subgroup of cancers (see section 3-2 of the protocol) by surgical resection or a biopsy as a part of diagnosis, standard-of-care, or as part of a clinical trial. Adult patients who are willing to donate blood, urine, Pap-smear and ascites.

**Nature and extent of the burden and risks associated with participation, benefit and group relatedness:** As the participation for this biobank does not require treatment other than medically indicated for the condition, the risk or burden of participating is negligible. The benefits are thought to be long-term and not directly for the patient. No additional biopsies will be taken from lung material. Patients who undergo lung biopsies have a higher risk of complications, in comparison to biopsies from other organs.

## BIOBANK PROTOCOL SIGNATURE PAGE

1. The undersigned, who is the **responsible coordinator** for this **sub-biobank**, declares that:
  - he/she has taken note of UMC Utrecht's biobank regulations ("Kaderreglement Biobanken UMC Utrecht") and will follow this biobank protocol and these UMC Utrecht's biobank regulations;
  - he/she will inform the other parties with responsibility for this biobank protocol about any adjustments to this protocol in connection with questions from the committee and will obtain their approval for these adjustments. Note: If so, this biobank protocol will not need to be re-signed when resubmitted. It is advisable to keep a fully signed version of the final approved protocol in the biobank file.

Name	Signature	Date
Responsible sub-biobank coordinator Prof. Dr. O. Kranenburg Prof Translational Tumor Biology Chair UPORT Head LTO		17-02-2022

### 2. *Signature on behalf of division management*

The management of the imaging and oncology Division hereby declares that:

- they approve of the management of this sub-biobank within the division;
- the entire management team agrees with this approval;
- arrangements have been made about the set-up of this sub-biobank with the management teams of any other institutions/divisions participating in or supporting this sub-biobank.

Place: Utrecht Date: June 2<sup>nd</sup> 2021

Manager:

Name: Prof. Dr. Hendrikse

Signature:



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## LIST OF ACRONYMS AND RELEVANT DEFINITIONS

DPA	Data Protection Authority of the Netherlands
GDPR	General Data Protection Regulation
BC	Broad Consent
CBB	UMC Utrecht Central Biobank
ICF	Informed Consent Form
EB	Executive Board
TCBio	Biobank Research Ethics Committee: independent committee set up by the Executive Board that reviews biobank protocols and the use of the materials for specific research questions.
UPOINT	Utrecht Platform for Organoid Technology

## 1 INTRODUCTION AND RATIONALE

Immortalized cell lines and animals models are routinely used in biomedical cancer research in order to increase our understanding of tumor development and progression, and for drug discovery. Although these traditional models have contributed immensely to our understanding of tumorigenesis, they are not suitable for the development of personalized medicine. During cell line establishment, (tumor) cells undergo major genetic alterations as they adapt to the culture conditions. Following the highly selective culture establishment process, successfully adapted cells no longer form a faithful representation of the original (tumor) tissue. As a result, cell-line-based drug discovery programs have had disappointingly little success in the oncology domain.

Organoid technology is a new method of tissue culturing that was developed in the lab of Hans Clevers at the Hubrecht Institute, and overcomes the limitations that are associated with cell line establishment. The technology is based on insight into the biology of adult stem cells and allows researchers to culture a diverse array of human (tumor) tissues in a dish without the selection process that is associated with traditional cell line establishment. Living organoid biobanks form a faithful representation of the heterogeneity of the disease (e.g. a specific cancer type) and, when coupled to genetic tissue/organoid analyses and to real-world data from patient cohorts, uniquely allow the development of strategies for personalized medicine.

We propose to create an organoid biobank of cultured cancer and paired healthy tissues from multiple defined organs and other patient materials, such as urine, PAP-smear and ascites. In addition, the tissues/organoids will be genetically characterized (DNA/RNA). Paired blood samples will be used to assess germline genetic variation in relation to the variants detected in the tumor, and isolate immune cells for developing cancer-immune cell co-cultures.

The UPORT Cancer Biobank aims to support research on various forms of cancer, as defined in paragraph 3.2. The living biobank, in combination with genetic data and clinical/histopathology data, will contribute to the development of personalized medicine in three ways:

1. *First*, large compound libraries will be tested for their ability to kill tumor organoids in comparison to normal tissue-derived organoids. The identification of drugs that effectively kill (subsets of) cancer organoids will form the basis for developing novel therapeutic treatment strategies.

2. *Second*, the living organoid biobank will provide a tool for fundamental scientific research into the mechanisms of cancer initiation and metastatic progression in a tissue-type-specific manner. Organoids are amenable to genetic modification, imaging, *in vitro* high-throughput drug screening, etc., which allows them to be used in a wide range of cancer research applications. Examples include the stepwise conversion of healthy tissue organoids into cancer organoids (and/or *vice versa*) by CRISPR/CAS technology. In addition, organoids are now widely used to study the interactions of tumor and normal tissue-derived organoids with immune cells and bacteria.

Normal tissue organoids will be used to model and study physiological processes in distinct organs and tissues, as this may provide insight into the organ-specific contexts that influence cancer development. In addition, normal tissue organoids will also be used to model and study the interaction between cancer cells and healthy cells within the tissue microenvironment.

3. *Third*, the biobank will help validate organoid technology as a diagnostic tool for response prediction. New technology allows organoids to be grown from small amounts of tumor tissue (biopsy) and be rapidly expanded and drug-screened within a period of 2-3 weeks. If such proof-of-concept is delivered, the organoid biobank may start to be used as a standardized drug selection platform for individual patients.

The UPORT Cancer Biobank will be generated in close collaboration between the UMCU, the Hubrecht Institute and the Princes Maxima Centrum, according to the agreements accompanying this biobank protocol.

## 2 OBJECTIVE

### Primary Objective:

To create a living biobank (UPOINT Cancer) consisting of organoid cultures derived from healthy and tumor tissues (including body fluids such as blood, urine and ascites) from cancer patients.

### Secondary Objective(s):

The UPOINT Cancer Biobank will be used for multiple purposes, including the identification of effective anti-cancer treatments (e.g. through 'drug screens'), the development of personalized medicine strategies (in combination with genetic and clinical data sets), and as a resource for fundamental biomedical cancer research.

Healthy tissue (which is usually part of the resected tissue) will also be used to derive organoids, for studying the interaction between cancer cells and their microenvironment, and for studying physiological processes to increase our understanding of the organ-specific contexts in which cancer develops.

## 3 BIOBANK POPULATION

### 3.1 General description of the biobank population

A) Healthy donors and/or patients?

healthy donors  
Number: .....

patients  
Number: 3000-4500

B) From which donor category will materials be collected (more than one answer possible)?

- aged 16 years or over and able to exercise their free will (capacitated)
- aged 16 years or over and unable to exercise their free will (**incapacitated, proceed to question C**)
- aged 12-15 years and able to give informed consent (**proceed to question D**)
- aged 12-15 years and unable to give informed consent (unable to exercise their free will, incapacitated) (**proceed to question C**)
- under 12 years of age (**proceed to question D**)

C) If a donor is unable to exercise his/her free will, which category does he/she belong to?

- people with a mental disability
- people with a psychiatric disorder
- people with a dementing disorder
- people with a reduced level of consciousness
- other, i.e. ....

D) (If applicable:) Why will the materials not be collected from subjects who are of age / capacitated i.e. able to make a reasonable judgement of their own interests with regards to the biobank?

.....



E) Which type or types of disorders/conditions does the biobank concern (up to 3):

- heart disorders
- congenital, familial and genetic disorders
- disorders of the blood and lymphatic systems
- nervous system disorders
- eye disorders
- balance and ear disorders
- respiratory, thoracic and mediastinal disorders
- gastrointestinal tract disorders
- renal and urinary tract disorders
- skin and subcutaneous tissue disorders
- musculoskeletal and connective tissue disorders
- endocrine disorders
- nutritional and metabolic disorders
- infections and parasitic diseases
- injuries, intoxications and complications of procedures
- neoplasms (benign, malignant and unspecified, including cysts and polyps)
- surgical and medical procedures
- vascular disorders
- general disorders and administration site disorders
- pregnancy, perinatal period and puerperium
- social circumstances
- immune system disorders
- hepatobiliary disorders
- reproductive system and breast disorders
- mental disorders
- other, i.e.

### 3.2 Specific description of the biobank population

The patients are selected from those who are undergoing resection and/or biopsy of the below mentioned tumors and the tissues to which these tumors have metastasized. Also patients are selected who are willing to donate urine or ascites fluid, diagnosed with the below mentioned tumors. Some patients undergo a biopsy procedure (no biopsies from lung material) as a part of diagnostics, standard care or clinical trial. If a patient gives consent, an extra biopsy piece will be collected at the time of biopsy procedure.

The patients who will be included are diagnosed with one of the following diseases, at any developmental stage.

1. Colorectal Cancer (including anus cancer)
2. Prostate Cancer
3. Pancreas or bile duct Cancer
4. Mammary Cancer, from male and female patients
5. Liver Cancer

6. Gastric Cancer
7. Oesophagus Cancer
8. Lung Cancer
9. Head and neck Cancer
10. Neuroendocrine Cancer
11. Bladder Cancer
12. Kidney Cancer
13. Ovarian Cancer
14. Cancer of the cervix
15. Thyroid Cancer
16. Cancer of the adrenal glands
17. Appendiceal mucinous tumors (AMTs), including low-grade mucinous appendiceal neoplasms (LAMNs), high-grade mucinous appendiceal neoplasms (HAMNs), and mucinous adenocarcinomas (MACs).

A. Is this group of donors also involved (as far as you know) in ongoing research that is subject to the WMO or in an existing biobank of UMC Utrecht?  yes  no

### 3.3 Inclusion criteria

- All cancer patients undergoing (partial) resection or biopsy of any of the organs studied in this proposal and who are older than 16, and mentally competent will be included.
- All cancer patients willing to donate ascites fluid, PAP smears or urine who are diagnosed with the diseases mentioned in this protocol.
- From all of the above patients blood can be withdrawn for the interests of the biobank mentioned in 4.1.

### 3.4 Exclusion criteria

None.

### 3.5 Intended or expected number of donors

We expect to include 3000-4500 patients in 10 years.

## 4 METHODS

### 4.1 Biobank procedures involving the donor

#### Resection:

Resection will take place during standard care. The resection material will be taken to the pathology. The pathologist will check if there is leftover patient material that will not be used for diagnostics. The pathologist will try to sample tumor and normal tissue from the leftover material and place this in tubes with growth medium. The tubes will be labelled with a pseudonymized code (P-number, see 4.3.1) and will then be given to the researcher.

#### Biopsies:

If a patient needs a biopsy for standard care, the patient will be asked if an extra biopsy can be taken for the biobank. The biopsy is placed in a tube with growth medium and taken to the pathology. The tubes will be labelled with a P-number and will then be given to the researcher.

#### Urine:

There are two ways to obtain urine from a patient:

1. During surgery: the surgeon will empty the bladder via a catheter.
2. During outpatient clinic visit: the patient will be asked to donate urine during an outpatient clinic visit that is needed for standard care.

The urine will be collected in a container with PBS and taken to the CDL. The CDL will label the container with a P-number and give it to the researcher.

#### Blood

Extra blood is collected for the biobank. This only happens when the patient undergoes a venepuncture for their regular care process or if the patient has an IV. Blood is never taken for the biobank alone. The blood is collected in an EDTA- tube and taken to the CDL. There, the tubes are labelled with a P-number and then given to the researcher.

#### Ascites fluid:

The patient will be asked to donate a portion of the ascites fluid that will be collected during standard treatment. The ascites fluid is collected in a tube with growth medium and taken to the pathology. There tube is labelled with a P-number and given to the researcher.

#### PAP smear:

Patients with a gynaecological tumor who will undergo a diagnostic procedure will be asked to donate PAP smear during their hospital visit. The PAP smear is placed in a tube with growth medium and taken to the pathology. The tubes will be labelled with a P-number and will then be given to the researcher.

**A)** Will the donors have to undergo additional invasive procedures (which are not part of the standard care) as part of their participation in the biobank?

no. In this case, does it concern:

a) residual materials<sup>1</sup>?  yes  no

b) withdrawal of extra blood during standard venepuncture as part of regular care?

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<sup>1</sup> Materials obtained as part of diagnostics and/or treatment that no longer need to be used for quality assurance and/or further individual diagnostics.

- yes, maximum 6 times 10 ml/procedure in the first year of participation in the biobank
- no
- venepuncture ..... times ..... ml/procedure
- arterial puncture ..... times ..... ml/procedure
- intravenous injection ..... times .....ml/procedure
- intra-arterial injection ..... times .....ml/procedure
- subcutaneous injection ..... times .....ml/procedure
- intramuscular injection ..... times .....ml/procedure
- intra-articular or peri-articular injection ..... times .....ml/procedure
- withdrawal of cerebrospinal fluid .... .. times ..... ml/procedure
- endoscopy, type of endoscopy:  
.....times
- biopsy, type of biopsy:  
..... times
- catheterisation, type of catheterisation:  
..... times
- assessment involving radiation exposure, type of assessment:  
.....times..... mSv/procedure  
.....times.....mSv/procedure  
.....times.....mSv/procedure
- vaginal/rectal examination .....times
- other procedures, i.e. (describe according to severity and frequency):
- 1) An additional biopsy when a biopsy is already being performed in the context of standard care, diagnostics, and/or a clinical trial. No biopsies will be taken from lung material. Patients who undergo lung biopsies have higher risks, in comparison to biopsies from other organs.
  - 2) For cervical cancer, we ask permission to obtain an additional PAP smear during pelvic examinations undertaken in the context of standard care or diagnostics. (note: no additional pelvic examination will be undertaken solely for this biobank)

**B) How much time will donors spend on their participation in the biobank (and any prior examinations)?**

Time to be spent: per visit 15 minutes

Total amount of time for the individual donor: 15 minutes

Donors as defined under [3.2](#) will be approached by the biobank coordinator to ask if they would like to donate their tissue to the biobank. This contact moment, wherein the potential donor is informed about the initiative, on average takes 15 minutes and is not considered to be a significant time burden.

**C) Will the donors be admitted to hospital in connection with their participation in the biobank, or will any hospital admission be extended?**

- yes, their stay in hospital or in the institution will be extended in connection with their participation in the biobank
- yes, they will be admitted to hospital or to the institution for their participation in the biobank
- no

**D)** Describe the extent to which donors will be subjected to procedures or will be required to act in a certain way, such as cooperate with questionnaires, interviews or physical/mental assessments, deny themselves certain things, stick to a particular diet (for invasive procedures, see question A).

No specific lifestyle limitations are required for participation.

**E)** Will the donors be tested for certain disorders/conditions (e.g. HIV, pregnancy)?

yes (explain), i.e. ....

no

**F)** Indicate which risks participation in the biobank carries for the donor.

The risks for patients when participating in this biobank are negligible. We will use leftover material from resections, and the portion urine and extra blood, as well as the ascites fluid will be obtained during standard care. When the patient is undergoing a biopsy procedure, we will ask to obtain an extra biopsy that will be taken during standard care. We will not obtain lung biopsies for the biobank because of the higher risk of pneumothorax. PAP smear will be obtained when the patient has a physical examination. In both cases, the same risks apply as for regular treatment. Mild discomfort may be experienced while taking the Pap smear.

**G)** Will participation in the biobank mean for the donor that the standard treatment or diagnostics can be deviated from or can be postponed?

yes

no

not applicable

**Ga)** If so, what does the deviation or postponement entail, and why is it justifiable?

N.A.

**H)** Why do you consider the risks of collection to be minimal and why do you think the burden is in proportion to the purpose of the future research for which precisely this type of tissue or blood sample must be available?

The risk for the donor associated with the participation in this biobank is negligible (see point 4.1F). The organoids generated from these tissues can be expanded and deployed in many future research projects, upon release approval as specified in paragraph 6.

**I)** Additional information relating to the collection procedure:

The proposed biobank is a collaboration between the following parties:

- 1) UMCU, an academic hospital with experience in the use of organoid technology
- 2) Hubrecht Institute, the group of Prof. Dr. Hans Clevers (HI), the research institute that developed organoid technology and which is a leading expert in the further development of the technology
- 3) Prinses Maxima Centrum (PMC), the group of Prof. Dr. Hans Clevers and other PIs.

The conditions for exchange of patient-derived tissues (UMCU > Hubrecht/PMC), biobanking the generated organoids and the subsequent use of these organoids under a TCBio-approved protocol are defined in a collaboration agreement signed by UMCU, Hubrecht and PMC.

Within the UMCU, one or multiple person(s) is/are identified to fulfill the role of biobank coordinator. At this moment, these persons are Annetta Brousalı and Jorieke Salij. The biobank coordinator has the following tasks:

- Organize the detection of potential donors
- Approaching the potential donor to see if he/she wishes to provide informed consent
- Organize the collection of tissue post operation
- Organize the delivery of tissue samples to responsible UMCU or HI or PMC personnel for further processing (specified under 4.2)
- Maintenance of a database with signed consent forms, the code list, and preferences indicated on the informed consent form.

If the biobank coordinator would be a physician, a potential donor could be under the impression that the level of care that he/she will receive is dependent on his participation. Therefore, the biobank coordinator may not be a physician.

If the biobank coordinator is a researcher aiming to work with organoids generated from the potential donor, there is the risk that the biobank coordinator might put undue pressure on the patient. Ideally, the biobank coordinator should not be a researcher aiming to work with the organoids. However, if no suitable person can be found, this situation may occur. In such events the researcher must be clearly instructed not to put any pressure on the potential donor and that in this capacity he/she is merely there to inform the patient about the option to participate. Ideally, the biobank coordinator should receive training by another biobank coordinator.

## **4.2 Withdrawal of individual donors from the biobank**

Donors can terminate their participation in the biobank at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the biobank e.g. because the donor does not meet the inclusion criteria.

Donors receive a consent retraction form and the contact details of the biobank coordinator that allows them to retract their consent. Upon receipt of the consent retraction form, the biobank's coordinator informs the relevant project partners of the receipt of the form. The patient can choose among the three options that are indicated in the consent retraction form. For more information, see also paragraph 7.2F

### **4.2.1 Specific criteria for withdrawal (if applicable)**

N.A.

### 4.3 Processing and storage of human biological materials

#### 4.3.1 Processing procedures for human biological materials

Patient material is:

- removed from donors, as specified under 4.1, during operation as part of standard treatment.
- collected via an additional biopsy when a biopsy procedure is planned as part of standard care.
- According to the project, also blood, urine and/or other donor material can be obtained.

The resected tissue is transferred to the pathology department of the UMCU. At the pathology department, a piece of tissue that is not needed for diagnostics is placed in medium. The medium is provided by the project partners: HI, PMC or UMCU. The extra biopsy is placed in the medium immediately after collection and then transferred to the pathology department. In both cases, the material is accompanied with a Sample Information Sheet (SIS). The SIS contains information of the sample, a limited amount of information of the donor and a pseudonymized code (P-number) that is generated from the tissue facility.

According to the project, also blood, urine and/or other donor material can be transferred to the researcher. These samples are processed via the CDL and will be accompanied by a CDL form that contains donor information and the P-number. Because of the donor information on the forms, these forms remain with the biobank coordinators. Only the P-number will be handed to the researchers. The biobank coordinators will write the P-number on the tissue SIS form or, in case there is no tissue, a SIS form is made for the samples.

The samples along with the SIS form with every P-number that is generated is transferred to the researchers from either:

- HI
- UMCU
- PMC

The patient material will be generated into organoids on location for research purposes. Eventually a vial from each generated organoid will be stored at the CBB (UMC Utrecht), PMC or HI.

A) Will any cells be amplified to immortal (stem) cells and cell lines?<sup>2</sup>  yes  no

#### 4.3.2 Procedures for encoding and storage of personal and other data and human biological materials

A)

I) Will any personal or other data be encoded?

yes

no, because .....

If the personal or other data will be encoded, please answer the following question:

II) Does it concern:

encoding whereby directly traceable data will be replaced with a random code

---

<sup>2</sup> The donor must consent to this.

pseudonymisation, whereby directly traceable data will be encrypted to a pseudonym using an algorithm (possibly via engagement of a trusted third party).

### III) How will this code be structured?

All biobank samples are provided by the tissue facility (tissue) or the CDL (blood/urine/etc.) with a pseudonymized code, the P-number. This number is made up of a year followed by a consecutive number.

### IV) Who will have access to the key to this code?

The biobank coordinator and data manager of UPORT. In addition, the tissue facility and CDL, who generates these codes, also have access to the key of these codes. (The CBB has access to this key, but only when tissue is stored),

Name: Jorieke Salij, Anneta Brousalı, Jan-Hendrik Venhuizen and new colleagues in the function of biobank coordinator/data manager.

Position: Biobank coordinator and data manager UPORT

Treatment relationship with the patient:  yes  no

Division/department: Imaging & Oncology

### V) Where will the key or keys be stored?

On secure drives of UMCU. (On the T drive, in the G map > CGO > Chirurgie > U-PORT). See also section 'VI) How will the key or keys be secured?'.

### VI) Will there be an extra copy of the key? (for availability reasons)

Yes, all (research) data is stored on UMC Utrecht networked drives from which backups are made automatically twice a day by the division IT (dIT).

### VI) How will the key or keys be secured?

The UPORT team uses the the secured Research Folder Structure on the secure drives of UMCU. That ensures that only authorized personnel has access to the key table. Access is granted by the IT coordinator of the division Imaging and Oncology.

The tissue facility, CBB and CDL have their own internal system that is only accessible for their own staff.

### VII) Who will have access to the source documents and any other data that can be traced back to the person concerned?

The informed consent forms and CDL forms are only accessible for the biobank coordinators and the data manager of UPORT.

Name: Jorieke Salij, Anneta Brousalı, Jan-Hendrik Venhuizen and new colleagues in the function of biobank coordinator/data manager.

Position: Biobank coordinator and data manager UPORT

Treatment relationship with the patient:  yes  no

Division/department: Imaging & Oncology



**VIII) Where will the directly traceable personal or other data be stored?**

Directly traceable personal or other data is stored on the secure drives of UMCU. UPORT uses the the secured Research Folder Structure on the secure drives of UMCU, that ensures that only authorized personnel has access to this date (see above).

The paper originals of these files will be stored in the locked UPORT office.

**IX) Who will have access to the directly traceable personal or other data?**

Name: Jorieke Salij, Annetta Brousalı, Jan-Hendrik Venhuizen and new colleagues in the function of biobank coordinator/data manager.

Position: Biobank coordinators and data manager UPORT

Treatment relationship with the patient:  yes  no

Division/department: Imaging & Oncology

**X) Who will be the data owner?**

UMC Utrecht

**XI) How will the data be secured?**

Personal data: The UPORT team uses the the secured Research Folder Structure on the secure drives of UMCU. That ensures that only authorized personnel has access to the key table. Access is granted by the IT coordinator of the division Imaging and Oncology. The paper originals of these files will be stored in the locked UPORT office.

Non-personal data (pseudonymized data): Is stored in Castor EDC and can only be provided for specific research to the researchers under a 'uitgifteprotocol' (release protocol) which will be approved by the TCBio. After approval of this protocol, a date request can be submitted to the data manager of UPORT. He provides access to the needed data.

The genetic and clinical data that are generated as part of the characterization of this organoid biobank can be coupled to the drug screen data of the same organoids without the need for a separated release protocol.

**XII) For how long will the data be retained? <Note: If the intention is to use data from HiX, these must be extracted from Hix in encoded form before the retention period of the HiX data has expired.>**

indefinitely

..... years.

**B) Storage in the CBB is compulsory at UMC Utrecht. If the materials will not be stored in the CBB but externally, please answer the questions below:**

**I) How will the human biological materials be stored?**

with a code that is indirectly traceable to the subject (code list)

in a form that cannot be traced back to the subject (pseudonymised)

anonymously; please note that this option is not useful for a biobank.

**II) How will this code be structured?**

All biobank samples are provided by the tissue facility (tissue) or the CDL (blood/urine/etc.) with a P-number. This number is made up of a year followed by a consecutive number. The biobank coordinator ensures that the P-number is placed on the SIS form that accompanies the sample to HI, UMCU or PMC. This P-number always stays with the tissue and/or the final cultured organoids. If necessary, the patient can be traced back by the UPORT team or the CBB (only if tissue with this P-number is stored before) via the P-number and the link table. A link table will be kept by the Biobank coordinators so that the P-numbers can be related to UMCU patient numbers. The tissue facility, CDL and CBB have their own link system. They only have the code of the samples they have received and processed.

**III) Who will have access to the key to the code?**

As described above, the biobank coordinator and data manager of UPORT have access to the key to the code. Indirectly the CBB has access when samples are stored in there biobank. Also, the tissue facility (only tissue) and the CDL (Blood/urine/etc.) have access to the key but are not involved in this part of the process.

Name: Jorieke Salij, Annetta Brousalij, Jan-Hendrik Venhuizen and new colleagues in the function of biobank coordinator/data manager.

Position: Biobank coordinator and data manager

Treatment relationship with the patient:  yes  no

Division/department: Imaging & Oncology

**IV) Where will the key or keys be stored?**

On secure drives of UMCU. (On the T drive, in the G map > CGO > Chirurgie > U-PORT).

**V) Will there be an extra copy of the key? (for availability reasons)**

All (research) data is stored on UMC Utrecht networked drives from which backups are made automatically twice a day by the division IT (dIT). Also the internal LMS system from CBB, tissue facility and CDL (in case of collecting blood and/or urine) is an indirect copy.

**VI) How will the key or keys be secured?**

The UPORT team uses the the secured Research Folder Structure on the secure drives of UMCU. That ensures that only authorized personnel has access to the key table. Access is granted by the IT coordinator of the division Imaging and Oncology.

They tissue facility, CBB and CDL have their own system that's only accessible to their own staff.

**VII) Who will have access to the materials?**

UMCU, HI and PMC: see Collaboration agreement UPORT-UMCU-Hubrecht-PMC

Researchers who would like in the future to use organoids for their own research purposes, will have to present an approved release protocol in order to gain access to the organoids of the UPORT Cancer Biobank, via the procedure specified in section 6.

VIII) For how long will the materials be retained?

indefinitely.

..... years.

## 5 INCIDENT REPORTING

### 5.1 Reporting of data breaches

For incidents involving personal data, a statutory reporting duty applies (even if the personal data have been pseudonymised/encoded). For this reason, anyone who observes a data breach must report this to the Data Protection Officer immediately, using the reporting form via the ICT Portal on Connect.

A data breach is a technical or organisational security breach whereby personal data are accidentally or unlawfully destroyed, lost or modified, or are disclosed or rendered accessible without authorisation. In case of any doubts as to whether it concerns a data breach, the incident should still be reported. Incidents can be reported via the ICT Portal on Connect: [Selfserviceportal \(umcutrecht.nl\)](https://selfserviceportal.umcutrecht.nl)

As the project partner HI does not have access to the UMCU connect working environment, they shall report data breaches to their own data protection officer and to the biobank coordinator at UMCU, who will then forward this information via the procedure described above to the data protection officer of the UMCU.

## 6 USE OF BIOBANK MATERIALS FOR SPECIFIC RESEARCH QUESTIONS

The organoid lines that are generated for this project are used only for the research as described in the proposal. The aim of setting up this well characterized Biobank of living cell is so future experiments will benefit from the collected data.

Before the human biological materials and the associated clinical and other data from this biobank can be used for specific research questions, approval must first be obtained from the TCBio. For this purpose, investigators must submit a release protocol to the TCBio, making use of the most recent version of the release protocol template, which can be downloaded from the TCBio's website. They must follow the submission instructions on the TCBio's website for this. Among other things, the committee will review the scientific value of the research proposal and assess whether the use of the materials will be in keeping with the donor's control rights. For example, the use of the materials must be covered by the scope of the broad consent given. For the release of materials, the responsible sub-biobank coordinator must also give his/her approval, by co-signing the release protocol.

At the end of a specific research project, body material that is left over will always be returned to the UPORT Cancer Biobank or will be destroyed.

## 7 ETHICAL CONSIDERATIONS

### 7.1 Applicable regulations

This biobank will be set up and managed in accordance with UMC Utrecht's biobank regulations, as adopted by the Executive Board of UMC Utrecht in June 2013.

### 7.2 Recruitment and consent

The responsible sub-biobank coordinator must ensure that broad consent is obtained and that the consent form is signed. The person obtaining consent must ensure that the donor and/or his/her representative possesses the information referred to in Article 4, under h, of UMC Utrecht's biobank regulations, and has received specific verbal and written information on the release, retention, use and destruction of human biological materials, including information on the burden and risks associated with the collection of human biological materials. The donor and/or his/her representative may revoke broad consent at any time after granting it. This revoking of consent only applies to future research involving the collected human biological materials and the associated data.

The responsible sub-biobank coordinator must also ensure that a record exists for each donor, in which any consent and revocation forms are retained.

**A)** How will the donors be recruited, and who (investigator, treating physician, other person) will inform the donor or his/her legal representative and ask for their consent?

Patients will receive the information during an outpatient clinic visit or by post or email. The biobank coordinator will then contact the patient to give information about the biobank and answer any questions that may have risen after reading the Patient Information File (PIF). This will allow the possible donors to make an informed and careful consideration of the participation.

The biobank coordinator will ensure that the patient understands the intentions of the project and the procedure. In addition, the patient is informed that he or she can retract the permission at all times, without having to provide a reason for doing so. If the patient decides to give consent, he/she will sign two consent forms which will then also be signed by the biobank coordinator (or the patient will send the signed informed consent through the mail or by post. In that case, the biobank coordinator will send a copy back to the patient). The patient will keep one copy of the consent form and the biobank coordinator will keep the other.

**B)** Are any donors dependent in any way on the investigator or the party recruiting the participants?

yes

no

**B.b)** Why will human biological materials be collected from these particular donors, and how will the donors' interests be protected?

Advances in clinical science require tissue samples of patients with malignant disease, or precursor lesions thereof. The risk associated with biobank participation is negligible as material will only be collected during planned procedures in the context of standard care. Furthermore, patient data will only be provided in a pseudonymized manner to ensure researchers will not be able to ascertain the identity of the patients.

The decision not to participate or to retract initial consent does not have any negative influence on current or future treatment. It will not have any negative consequences for the care and attention the patient receives at the UMCU.

C) How much time to reflect will the donors or their legal representatives have when deciding on participation?

At least 2 days

D) Can the donors be approached again during their participation in the biobank (for instance for further testing or follow-up)?

- yes  
 no

E) Will the donors be asked to consent to this during the consent process for this biobank?

- yes  
 no

F) Can donors revoke their consent for participation, and how will this be recorded?

Donors will receive along with the patient information sheet and informed consent form a consent retraction form. The consent retraction form can be sent to the biobank coordinator of the UMCU. If permission is withdrawn, this means that no new material is collected for the UPORT Cancer Biobank. In addition, a choice is made from the following options:

1. The material already collected for the UPORT Cancer Biobank will remain available for scientific research as specified in the consent form. In addition, new medical data can be collected to link to material that has already been collected.
2. The material already collected for the UPORT Cancer Biobank will remain available for scientific research as specified in the consent form. No new medical data or material is collected.
3. All material collected from the patient for the UPORT Cancer Biobank will be destroyed, except for material that has already been approved for use in a specific scientific study. If measurements have already been taken with that material, those data will also still be used.

### 7.3 Findings

If the donor and/or his/her representative grants broad consent, the donor will be told that he/she will be informed of any findings that may result from the actual use of the human biological materials and that may be important to the donor. If the donor and/or his/her legal representative does not wish to be informed, the human biological materials cannot be included in the sub-biobank.

Findings based on the biobank materials that offer information on serious conditions that may be clinically relevant to the donor and/or his/her relatives will be reported to the TCBio. The committee will assess all relevant information and will decide, together with the medical head of the department who is responsible for the sub-biobank, whether or not the donor will be informed. Feedback to the donor will be given via the treating physician.

#### 7.4 Resistance by incapacitated adults (if applicable)

N.A.

#### 7.5 Compensation (if applicable)

N.A.

### 8 ADMINISTRATIVE ASPECTS AND PUBLICATION

#### 8.1 Amendments

Amendments are changes to the management of the biobank after the TCBio has issued a positive opinion before the start of the biobank. All amendments must be submitted to the TCBio for review.

Non-substantial amendments will not be submitted to the TCBio for review, but will be recorded and included in the biobank file by the responsible sub-biobank coordinator.

#### 8.2 Disclosure and publication of results

Investigators will make results of research for which materials from this biobank have been used available in the public domain. Investigators are responsible for the completeness and accuracy of the publications. Investigators must adhere to the accepted guidelines for ethically sound result reporting.

Publications on research for which materials from this biobank have been used will be sent to the TCBio within 1 year after the end of the study in which the material has been used.

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