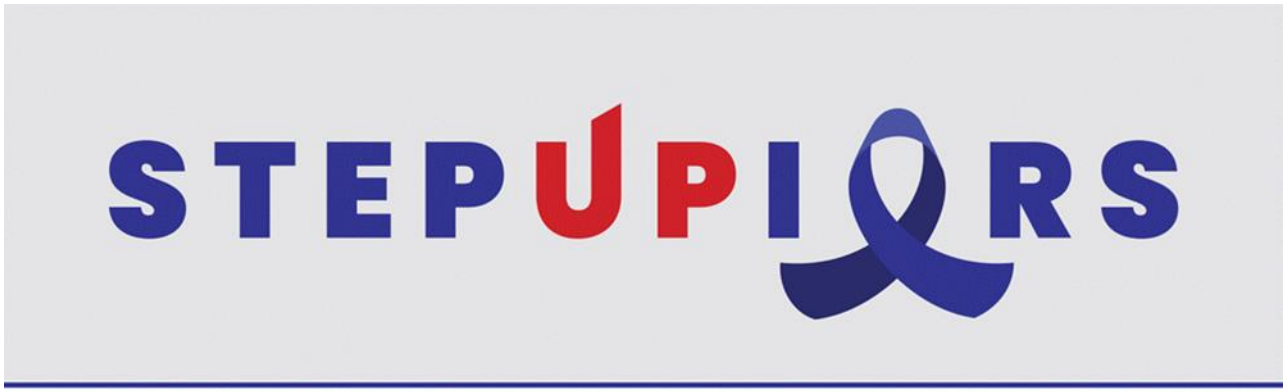

Twinning for a European Consortium of Rectal Cancer Research Institutions through Stepping up Scientific, Technological and Innovation Excellence of IORS

Funded by the European Union Project number: 101079217

Work Package No: 1

Deliverable No: D1.2

Deliverable Name: Increased IORS human capacities for biobank management and oversight

Type: R - Document, report

Dissemination Level: PU-Public

Due Date: September 30, 2023

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The objectives of WP1 - Strengthening the research profile of the Institute for Oncology and Radiology of Serbia (IORS) and establishment of a rectal cancer biobank.

D1.2 encompassed training of IORS personnel for biobank management and oversight with expert advice from partner institutions' biobanking staff and external trainings.

After the kick-off consortium meeting with participants from 4 partner institutions which was held on November 28, 2022, in Belgrade, visits of IORS staff to partner institutions' biobanking facilities were carried out, where the project participants toured their biobanking facilities and discussed operational, logistic, ethical and legal factors related to biobanking with experienced users:

1. Visit to Fundació de Recerca Clínic Barcelona-Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain (Annex Document - 3.1b_23, Report from the training), 10-12.01.2023.
2. Visit to the Netherlands Cancer Institute Antoni van Leeuwenhoekziekenhuis, Amsterdam, the Netherlands, (Annex Document - 3.3b_23 Report from the training), 12-15.02.2023.

IORS staff attended further online and in-person biobanking trainings and webinars, with the goal that future IORS biobanking staff acquire insight into biobanking procedures, preparation of SOPs, accreditation and other regulations:

1. Online educational webinar "BBMRI.QM Academy live Frozen Tissue Collection and biobanking", Graz, Austria, November 15, 2022. Attended by Snežana Bjelogrlić, Ana Đurić, Milena Čavić.
2. Online Workshop on "Implementing Genomic Research Projects" organized by EASI-Genomics and BBMRI, February 1-2, 2023. Attended by Aleksandra Stanojević¸ Miljana Tanić, Ana Đurić.
3. Webinar "The case of data reuse: Ethical, legal, and societal issues in international genomic data access and sharing" organized by EMBL-EBI with lecturers from BBMRI-ERIC and CINECA EU Project (Common Infrastructure for National Cohorts in Europe, Canada, and Africa), Feb 9, 2023. Attended by Kristina Živić, Katarina Mirjačić Martinović, Ana Vuletić, Milena Čavić, Ana Đurić.
4. On-site training "How to Build a Biobank", organized by the International Biobanking and Education Department, Medical University Graz, Austria, on March 13-14, 2023. Attended by Mladen Marinković, Ana Đurić, Katarina Mijačić Martinović, Ana Vuletić, Marija Đorđić Crnogorac, Suzana Stojanović Rundić, Snežana Bjelogrlić, Milena Čavić. (Documents 3.5b_23 Report from the training, and 3.5c_23 Certificates from the training)
5. BBMRI-ERIC Newsroom on biobanking, Mar 21, 2023. Attended by Ana Đurić.
6. Webinar „A guide to identifying suitable patient-derived cancer models in CancerModels" organized by EMBL-EBI, 21 June 2023. Attended by Snežana Bjelogrlić and Ana Đurić.
7. Online meeting with Dr Alexei Levitchi from the Moldavian population biobank. 05.09.2023. Attended by Milena Čavić, Miljana Tanić, Snežana Bjelogrlić, Aleksandra Stanojević and Ana Đurić

IORS biobank staff held meetings with governmental and international stakeholders:

- Metting with the Director of the Center for the 4th Industrial Revolution – Dr Jelena Bojovic where we discussed opportunities for IORS to join the National Data Centre and AI infrastructure
- Participation in the working group on biobanking organized by the Minister of Science, Research and Technology – Dr Jelena Begovic and Ms Andrea Wutte, Head of Quality Management Service, Lead auditor, Technical assessor, BBMRI-ERIC – discussing the governmental plan for Serbia to join as on Observer country
- Dr Robert Hewitt, Founder, Biosample Hub, The Old School, The Quay, Carmarthen, Carmarthenshire, United Kingdom - https://biosamplehub.org

IORS staff dedicated considerable time to formulating an adequate informed consent form (ICF) for biobanking sample collection. Since this is the first biobank at IORS, a multidisciplinary team of project staff was formed to investigate different ICF models from relevant international and national biobanks (IARC and other models obtained during visits to other biobanks and online trainings). Using the acquired knowledge, a two-tiered ICF was formulated in accordance with international and local standards and legislative, and adapted linguistically and to local cultural nuances.

IORS project staff performed a thorough market research of available Laboratory Management Information System (LIMS) options, comparing their differing capabilities with regards to ease of implementation in the local information system, sample coding and data protection, entering data into the system and searching for available data. Both commercially available and custom solutions were considered. Partner experience and specific project needs which would best support data collection, analysis and management while providing strong security and protection of patients' privacy, were considered to specify requirements for LIMS public procurement procedure. Finally, we purchased the perpetual license with 3-year upgrade support for the of the Noraybanks, (Noraybio ltd.) software, which was successfully installed on the local IORS server (Annex Document 1.3a_23 Certificate of LIMS installation_06.09.2023).

The intensive and productive trainings, webinars and visits to partner institutionsˇ biobanks increased IORS human capacities for biobank-related procedures and protocols, which lead to the definition of the adequate model for the biobank and organization of the Steering Committee and the Management Committee of the IORS biobank, along with the establishment of appropriate infrastructure/storage facilities and defining standard operating procedures for biobanking (SOPs), a two-tiered ICF and a roadmap for accreditation.

IORS biobank Steering Committee was formed (from IORS – Milena Čavić, Ana Krivokuća, Miljana Tanić, from NKI AVL Remond Fijneman, Mariska Bierkens, from FRCB-IDIBAPS Sergi Castellví-Bel, from BRFAA Ieronymos Zoidakis) with tasks of oversight of IORS biobank management and adherence to OECD best practice, adopting policies/best practices/strategies for biobanking and exchange of information and knowledge on legal and ethics regulation between the partners.

IORS biobank Management Committee was formed (Milena Čavić, Ana Krivokuća, Miljana Tanić, Snežana Bjelogrlić, Mladen Marinković, Jelena Spasić, Suzana Stojanović Rundić, Ana Đurić, Radmila Janković) with tasks of day-to-day implementation of all biobanking activities, regulations, and needs.

The existing IORS Scientific and Ethics Committee will be involved in the approvals of any derived projects and new initiatives pertaining to the advancement of the biobank.

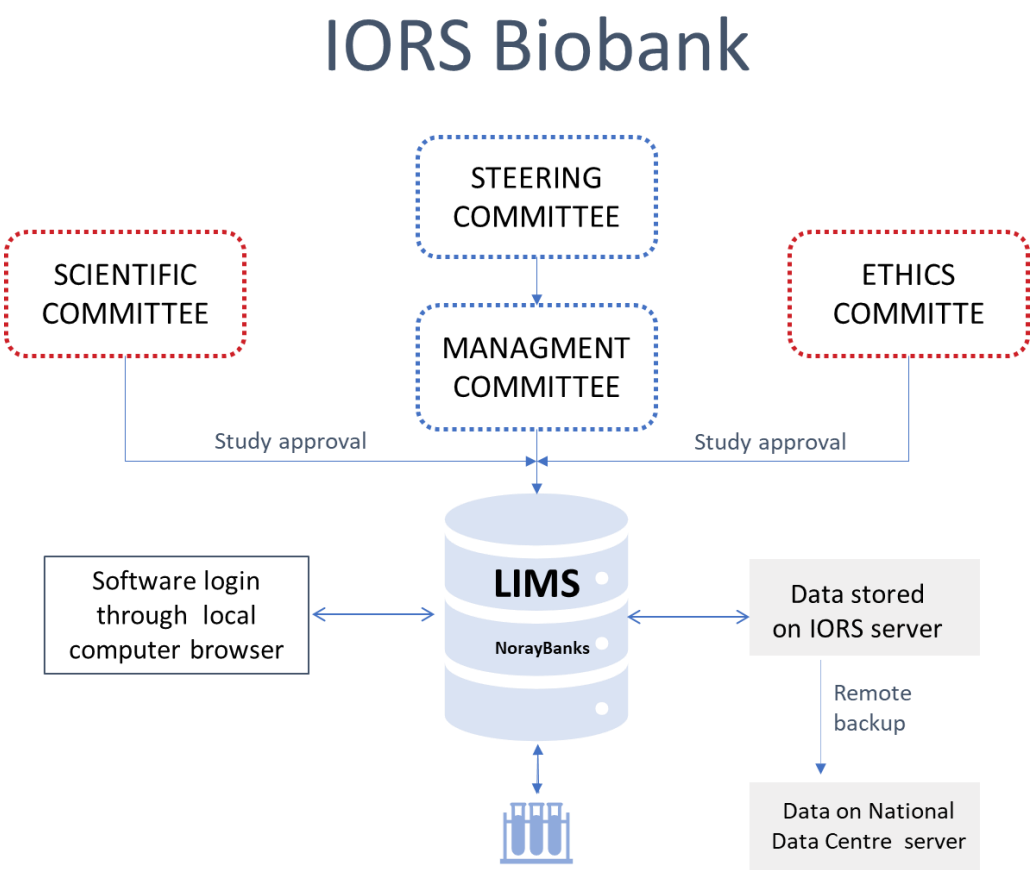


Figure 1. IORS Biobank structure

Based on the trainings and human capacity building performed during this period we were able to identify strengths, weaknesses, opportunities and threats (SWOT analysis) for the future operation of the IORS biobank.

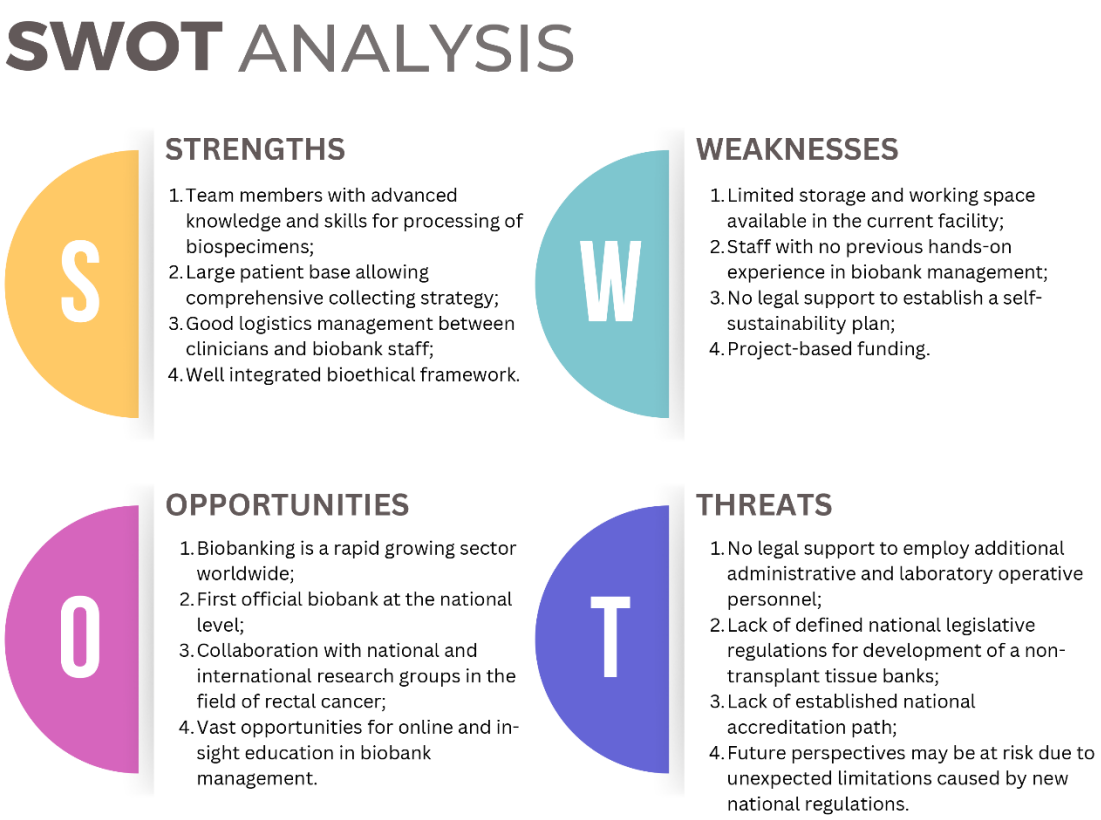


Figure 2. IORS Biobank SWOT analysis

Our mission is that the IORS Biobank will be a place, where all entities from the Institute for Oncology and Radiology of Serbia can store and collect biological material under unified, stable and supervised, continuously monitored conditions.

Our vision is that biological material generously donated by our patients will be stored, used and reused, responsibly, safely, and for the betterment of future patients.

Our biobank management staff is constantly upgrading and updating its policies and practices. We have defined a roadmap towards ISO standard accreditation, and while it is way too early to consider commercialization, we were laying down the principles by which access to data and samples will be permitted.

Achieved outcomes within D1.2 of WP1 until September 22, 2023.

- IORS biobank Steering Committee and Management Committees were formed
- Biospecimens from rectal cancer patients will be processed, organized, and maintained following standard operating procedures (SOPs) related to the IORS biobank which were produced by the IORS biobanking team
- The IORS biobank decided to adopt a management system based on the requirements and principles of ISO 203287:2018.
- The biobank will be research focused with project-funded collections
- A 2-tiered informed consent form for biobanking of Serbian rectal cancer samples was approved by the IORS Ethics Committee on March 27, 2023 (SOP 1.02.01 - Appendix 1 - Informed consent)
- Biobank IT infrastructure set in place –software was acquired Noraybanks by Noraybio ltd. via a public procurement procedure. The data will be stored and maintained on an internal IORS software (daily back-ups and authorized access limited only to researchers involved in this project; samples will be pseudo-anonymized and marked by a unique code prior to analyses), and national centralized AI storage space as per the Data Management Plan (D4.1 - delivered).
- Room No. 152, at the Department of Experimental Oncology on the first floor of IORS was designated as a biobanking space; FFPE collection cabinets and document cabinets for SOPs and ICFs were procured. Freezers at -20°C and -80°C for other sample types are already present in the same facility. Biobanking capacities were expanded by procurement of another high-capacity -80°C freezer compliant with temperature data logging requirement.

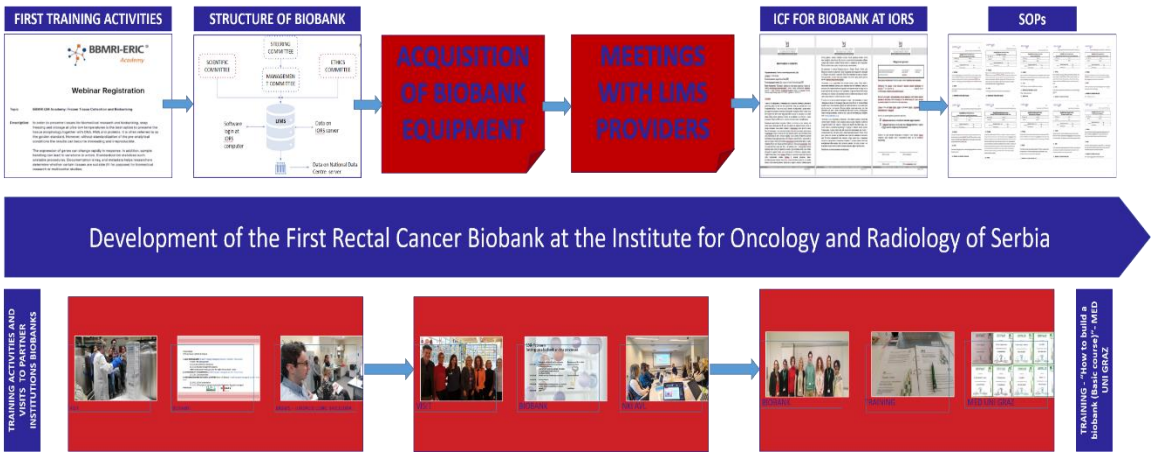


Figure 3. A schematic representation of the IORS Biobank evolution steps

D1.2 DOCUMENTS PROVIDED

- 3.1b_23 Report of IORS visit to IDIBAPS 10-12.01.2023.
- 3.3b_23 Report of IORS visit to NKI AVL 13-15.02.2023.
- 3.5b_23 Report of Biobank training at MedUniGraz 13-14.03.2023. and certificates of training
- SOP 1.02.01 - Appendix 1 - Informed consent
- 1.3a_23 Certificate of LIMS installation_06.09.2023

Report is publicly available at:
https://www.stepupiors.eu/deliverables-and-milestones/#wp1

Report from a visit of IORS staff to IDIBAPS within WP3 of the project STEPUPIORS – 101079217

for project participants Aleksandra Stanojević, Snežana Bjelogrlić, Mladen Marinković, Ana Đurić, Marko Radulović and Milena Čavić in the period 10-12.01.2023.

1. STEPUPIORS project participants Aleksandra Stanojević, MSc, Dr Snežana Bjelogrlić and Mladen Marinković, MD, went on a training-visit to the partner institution August Pi i Sunyer Biomedical Research Institute (IDIBAPS) in Barcelona, Spain, in order to gain knowledge in the field of biobanking, in the period from 10-12.01.2023. During the training, biobanking procedures were theoretically and experimentally presented. The training was be hosted by Dr Aina Rodríguez, the event coordinator was Dr Teresa Botta, and the speakers Dr Teresa Botta, Èlia Alcañiz, MSc, Dr Ada Soler and Dr Gemma Aragonès. All staff from HCB-IDIBAPS Biobank contributed to the visit.

The training visit had the following agenda:

Day 1 (Tuesday 10/01)

BIOBANK INFRASTRUCTURE AND ORGANIZATION

- technical aspects of storing tissue samples and liquid biopsy samples (whole blood, isolated sera or plasma, leukocytes, cerebrospinal fluid)
- advantages and disadvantages of tissue cryopreservation in relation to tissue preservation in paraffin blocks
- methods for processing and aliquoting liquid biopsy samples
- preparation of tissue microarrays
- the importance of immortalization of isolated B lymphocytes as an infinitely viable source for DNA isolation.

ETHICS AND LAW IN BIOBANKING

- establishing a biobank and the importance of creating a long-term and short-term plan
- periodic evaluation of set goals
- organization of employees within the biobank sector
- the importance of cooperation with institutions that have the same/similar activity
- types of models when establishing a biobank
- how to formulate informed consent for patients
- how to protect the identity of patients from a third party that uses the collected samples for scientific purposes
- the difference between anonymity and pseudo-anonymity
- roles of local and central ethics committees
- European regulations dealing with the management and organization of the biobank
- similarities and differences of existing legal regulations in Spain and Serbia.

Day 2 (Wednesday 11/01)

QUALITY MANAGEMENT

- the quality of the biobanking is evaluated bilaterally, by internal (QMS, Quality Management System) and external auditors
- The QMS defines the goals and activities of the biobank and by monitoring the appropriate pre-defined indicators ensures that they are achieved
- QMS defines quality indicators and activities in accordance with European standards ISO 9001 and ISO 20387:2018
- ISO 9001 includes a set of indicators that are not specific to the organization's activity
- ISO 20387:2018 defines indicators specific to the work of a biobank.

ADMINISTRATIVE TASKS IN BIOBANKING

- how to promote and develop biomedical research by ensuring the availability of biological samples and related data to the scientific community
- how to become a reference platform for the use of human biological samples
- how to strengthen the position of the biobank at the national level and increase its contribution at the international level
- how to ensure compliance with legal and ethical provisions
- how to correctly define the activity plan as part of the existing infrastructural and operational possibilities
- how to properly conduct a SWOT (Strengths, Weakness, Opportunities, Threats) analysis
- the importance of the timely formulation of the CAPA (Corrective action, Preventing action) strategy

SAMPLE MANAGEMENT AND BIOBANK VISITS

- bank of neurological tissues, which was organized with the aim of collecting samples from patients suffering from neurodegenerative diseases
- bank of tumor and healthy tissues
- bank for liquid biopsies
- freezing and cryopreservation service

Day 3 (Thursday 12/01)

DATA MANAGEMENT

The LIMS (Laboratory Management Information System) of the NorayBanks company was presented as part of the practical lecture. During the session, coding of samples, entering data into the database and searching for available data were processed.

SUSTAINABILITY IN BIOBANKING

Sustainability of the biobank - how to organize a complex system within the framework of limited infrastructural possibilities, while meeting quality standards and fulfilling previously defined goals. Since this topic was the most complex, the focus of the lecture was on defining the basic aspects of sustainability:

- operational - refers to effective optimization in the context of sample types (e.g. storing frozen tissues vs. tissues in paraffin molds), the number of aliquots per sample of each liquid biopsy isolate, etc., with the aim of avoiding sample accumulation and reducing the existing capacity of the biobank
- financial - requires the creation of a clearly formulated strategic plan that identifies goals in the direction of focusing on certain types of pathology and types of biological samples that are of greatest interest to the scientific community at a given moment
- social - accreditation, dissemination, and participation in scientific projects.

DISSEMINATION AND OUTREACH ACTIVITIES

Dissemination was the only topic that did not relate to the organization of work within the biobank, but is a strategy that plays an important role in its sustainability. The lecture was about various forms of spreading awareness in the scientific and general population about the importance of collecting and storing human samples for the purpose of researching the mechanisms of disease occurrence and their treatment. As a concrete example, after the lecture, all participants of the STEPUPIORS project were involved in a well-designed game based on the escape room model, during which participants can perceive various aspects of the work of the biobank in an interesting and fun way, such as the importance of informed patient consent, protecting the patient's identity, taking a sample, sample processing according to SOP (Standard Operating Procedure) and the like.

2. STEPUPIORS project participants Dr Ana Đurić, Dr Marko Radulović and Dr Milena Čavić went on a training visit to the partner institution August Pi i Sunyer Biomedical Research Institute (IDIBAPS) in Barcelona, Spain in order to gain knowledge in the field of project management, in the period from 10-11.01.2023. and biobanking 11-12.01.2023. The training was hosted and organized by IDIBAPS European and International Projects Research Management Office, led by Juan Abolafia, and the presenters included Dr Isil Tekeli, Dr Haritz Plazaola, Dr Ruth Conesa, Dr Arnau Llobet and Dr Nuria Ferrer.

The training included:

10.01.2023.

- Presentation of the Pre-award grant management office at IDIBAPS
- Presentation of promotion activities of the Pre-award grant management office
- Discussing calls prospection and dissemination
- Presentation of funding opportunities for the project line of research
- Presentation of ResearchConnect software
- Discussing the identification of networks, actions and initiatives for collaboration
- Presentation of proposal preparation activities
- Eligibility check of the calls and handling of questions
- Discussing how to define project objectives according to the call requirements
- Advising on the work plan and implementation
- Discussing Budget preparation
- Discussing General administrative support - Mock exercise in Funding and Tenders Portal

11.01.2023.

- Presentation of the Post-award grant management office at IDIBAPS
- Discussing financial reporting (personnel cost, equipment depreciation, internal invoicing, and other direct cost)
- Discussing differences in personnel costs calculation in Spain and Serbia
- Discussing reporting on travel costs, publications
- Discussing financial reporting on publication costs
- Discussing funding and tenders

- Presentation of IDIBAPS practice in continuous reporting
- Presentation of financial statements
- Presentation of IDIBAPS Timesheets tool
- Discussing good practice in communication with the Project Advisor and European Commission

12.01.2023.

Project participants joined the biobanking personnel and followed the previously outlined agenda.

STEPUPIORS

Twinning for a European Consortium of Rectal Cancer Research Institutions through Stepping up Scientific, Technological and Innovation Excellence of IORS

Funded by the European Union Project number: 101079217

Report from a visit of IORS staff to NKI AVL within WP3 of the project STEPUPIORS – 101079217

for project participants Milena Čavić, Radmila Janković, Miljana Tanić, Suzana Stojanović Rundić, Marija Đorđić Crnogorac, Ana Đurić and Marko Radulović in the period 13-15.02.2023.

1. STEPUPIORS project participants Dr Milena Čavić, Dr Suzana Stojanović- Rundić, Dr Ana Đurić and Dr Marko Radulović went to an expert visit to the partner institution the Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital (NKI AVL) in Amsterdam, Netherlands, to get familiar with the overall organization of the NKI AVL as a research and healthcare center. Dr Milena Čavić, Dr Ana Đurić and Dr Marko Radulović participated in the presentation of project management activities of the NKI AVL in order to gain knowledge and practical skills in the field of project management. The visit took place in the period February 13-14, 2023. and was hosted and organized by Dr Remond Fijneman from NKI AVL. The presenters who participated in this part of the training were: Dr Marjolijn Mertz, Dr Roderick Beijersbergen, Dr Elise van Bree, Dr Beatriz Carvalho, Dr Carmen Rubio Alarcon, Dr Soufyan Lakbir, Dr Baukelien van Triest, Dr Paula Hoekstra, Dr Sacide Ekiz, Dr Omied Horati, Dr Gerrit Meijer, Dr Henri van Luenen and Dr Meike de Wit.

The visit included:

13.02.2023.

- Presentation of the NKI AVL by Dr Remond Fijneman
- Presentation of activities handled by the research part of the NKI AVL
- Presentation of the BioImaging Department at the NKI AVL by Dr Marjolijn Mertz
- Presentation of the Genomics Core Facility by Dr Roderick Beijersbergen
- Discussing differences and similarities in the organization of work at the Genomic Facilities at the IORS and the NKI AVL
- Presentation of the Organoids (TGO research) Department by Dr Beatriz Carvalho, Dr Carmen Rubio Alarcon
- Presentation of the Radiotherapy Department by Dr Baukelien van Triest
- Discussing differences and similarities in the organization of work at Radiotherapy at IORS and Radiotherapy at NKI AVL, Dr Baukelien van Triest, Dr Suzana Stojanović-Rundić

14.02.2023.

- Presentation of the Project Administrative staff and good practices for managing projects at the NKI AVL by Dr Paula Hoekstra, Dr Omied Horati, Dr Sacide Ekiz
- Presentation of PaNaMa RMS system - software for Project Management - used by project management staff at the NKI AVL
- Discussing the connection of the Project Management system with the HR and the Accounting system at the NKI AVL
- Discussion on the NKI AVL practice for usage of overheads
- Discussion on the practice of engaging researchers in different projects, both national and international, at the NKI AVL
- Discussing templates for financial reporting
- Discussing good practice for on-time preparation of Timesheets
- Presentation of the Antoni van Leeuwenhoek Hospital (AVL) and Netherlands Cancer Institute (NKI) by Dr Henri van Luenen, Head of Operations
- Presentation of the AVL expertise center for several rare tumors, rehabilitation and

training centers and treatment departments
- Presentation of the AVL in numbers: patients, clinical trials, operations, treatments etc.
- Presentation of the AVL activities
- Presentation of the NKI in numbers: scientists, scientific support staff, postdoctoral fellows etc.
- Presentation of the NKI research facilities
- Presentation of training and development programs for PhD students, postdocs, PIs, and technicians at the NKI
- Presentation of Pre-award grant management activities at the NKI
- Discussing the NKI's practice of internal peer review of grant applications
- Discussing the NKI's practice of hiring external support for organizing and writing collaborative proposals
- Presentation of Post-award grant management activities at the NKI (financial, legal, IPR and data management support)
- Discussing the software for access to all financial and other project-related data
- Discussing funding opportunities for cancer research in the Netherlands
- Discussing the overall approach to management of particular projects - Dr Meike de Wit, Dr Remond Fijneman

2. STEPUPIORS project participants Dr Milena Čavić, Dr Suzana Stojanović-Rundić, Dr Radmila Janković, Dr Miljana Tanić, Dr Marija Đorđić Crnogorac, Dr Ana Đurić and Dr Marko Radulović went to an expert visit to the partner institution Netherlands Cancer Institute Antoni van Leeuwenhoek Hospital (NKI AVL) in Amsterdam, Netherlands to get knowledge in establishing and organizing a biobank. The visit took place in the period February 14-15, 2023, and was hosted and organized by Dr Remond Fijneman from NKI AVL. The presenters who participated in this part of the training were: Dr Susanne Rebers, Dr Annegien Broeks, Dr Wouter Kievit, Dr Daan van den Broek, Dr Hylke Galama, Dr Margriet Lemmens and Dr Lana Meiqari.

14.02.2023.

- Presentation of the Code of conduct by Dr Susanne Rebers
  - Legal framework – most relevant regulations on the preservation of tumor tissue and research
  - Discussing the informed consent
- Presentation of regulations and organization for clinical investigators by Dr Annegien Broeks
- Presentation of regulations for human samples and data by Dr Hylke Galama
  - Discussing the GDPR consent (must be specific), OPT-IN and OPT-OUT in practice
  - Discussing other topics in Code of Conduct Data Management Plans, DPIA, GDPR rights, publishing, archiving

- Presentation of the IRB (application form for the biobank)

- Presentation of the registration and sample request procedures by Dr Wouter Kievit
  - Discussion about tissue procedures and organization, biosample processing
  - Presentation of SOPs: collection, storage, annotation; sample requests (track and trace)
  - Presentation of software (ART – Application request tool, BAT – Biobank application tool) – used by all facilities: Clinical chemistry, TGO, Pathology etc.
  - Discussing translational research in the NKI-AVL
  - Presentation of Datadesk
  - Presentation of Core Facility Molecular Pathology and Biobanking – CFMPB Margriet Lemmens

- Visit the CFMPB and labs for tissue procedures with Dr Wouter Kievit
  -Visit the biobank facilities

15.02.2023.

- Presentation on Setting up a biobank and its processes (focus on liquid biopsy) by Dr Daan van den Broek
  - Visit the Department of Clinical Chemistry
  - Presentation of liquid biopsies procedures: sampling and processing of samples by various methods (types of tubes and labeling, lab equipment)
  - Discussing SOPs: collection, storage, annotation
  - Discussing Monthly biobank report and Molecular Tumor Board (weekly meetings)
  - Discussing Hix system – system for requesting blood collection
  - Presentation of types of requests (internal, external), a system of coding and marking samples
  - Discussing procedures for external sample – from external studies or another clinical center
  - Presentation of national consortium: COIN
  - Discussing health technology assessment
  - Discussing collaboration between countries in health technology assessment through different EU initiatives

- Presentation of the Biobank use for secondary purposes, i.e., research by Dr Lana Meiqari
  - Requesting samples; who decides on the secondary use of samples;
  - Use of samples and dataflows in research: example - CAIRO5 Multicentre, randomized, phase 3 clinical study
  - Presentation of Data Management in Translational Research
  - Using of BioPortal platform
  - Organizing and saving the study results
  - Data interview: Where to find data in prospective studies
  - Presentation of projects: PLCRC-MEDOCC/CrEATE/PROVENC3-
  - Presentation of Data capturing platforms
  - Presentation of cBioPortal– tools for cancer genomics
  - Presentation of MtFIT (multi-target FIT) prospective study – gathering stool

- Presentation of PROVENC3 Observational study
- Discussing Data Quality/Verification and Integration
- Discussing Data Automatization and Integration
- Discussing FAIRification Process Components-Creation, Capture, Quality Check

STEPUPIORS

Twinning for a European Consortium of Rectal Cancer Research Institutions through Stepping up Scientific, Technological and Innovation Excellence of IORS

Funded by the European Union Project number: 101079217

Report from a Course "How to Build a Biobank" at Medical University of Graz within WP1 and WP3 of the project STEPUPIORS – 101079217

for project participants Snežana Bjelogrlić, Suzana Stojanović Rundić, Ana Vuletić, Katarina Mirjačić Martinović, Marija Đorđić Crnogorac, Ana Đurić, Mladen Marinković and Milena Čavić in the period 13-14.03.2023.

STEPUPIORS project participants Dr Snežana Bjelogrlić, Prof Dr Suzana Stojanović Rundić, Dr Ana Vuletić, Dr Katarina Mirjačić Martinović, Dr Marija Đorđić Crnogorac, Dr Ana Đurić, Mladen Marinković, MD, and Dr Milena Čavić attended a two day course "How to Build a Biobank" at Medical University of Graz in the period 13-14.03.2023. During the interactive lectures and two workshops, the course participants gained knowledge on the basic principles of Biobanking as a new discipline that aims to be an integral part of biomedical research in the future. The course was led by Prof Dr Karine Sargsyan, Managing Director for International Biobanking and Education, Vice Scientific Leader and Lecturer of the Master's University programs Biobanking and Human Centered Artificial Intelligence in Medicine at the Medical University of Graz and President of ESBB. Prof. Dr. Karine Sargsyan was one of the founders of this Biobank and its Director until recently.

The other lecturers at the Course were: Dr Anna Michalska-Falkowska, Deputy head of Quality Management in Biobank at The Medical University of Bialystok, Andrea Wutte, MSc, Head of BBMRI-ERIC QM Service and Denis Marino, MSc Operational co-director at the Geneva pediatric onco-hematology biobank.

The course included the following topics:

13.03.2023.

1. **Welcome & Introduction, Prof Dr Karine Sargsyan**

2. **Definition, Function and Challenges of Biobanks - Prof Dr Karine Sargsyan**

Definition of biobank (OECD preferred),

- types of biobanks – disease-focused, population-based, clinical biobanks, traditional biobanks, virtual, fully virtual/distributed
- Key components of Biobank at MedUniGraz – output of around 1 million used samples per year - good usage
- Biobank system – should be tightly regulated, not incorporated within the medical or laboratory information system but to still ensure a well-used and sustainable system
- Biobank information management system should follow all regulations of security and efficiency
- Discussing biobanks as key resources, future development of biobanks, increasing the number of biobanks, possible fields of usage
- Common Features of Biobanks – good biobanking should be unspecified for research – collecting without bias of the expected results
- Cooperation Partners – academia, industry and both
- Challenges - to provide adequate samples - depending on the speed of sample processing, some analyses might be wrongly performed within the biobank, pre-analytical flow is important
- Discussing the translational research cycle - the biobank is essential to provide solutions
- Discussing the path to clinical implementation from translational research

- Communication strategy is essential while setting up a biobank - to convince the donors/supporters that it will be a good investment
- Discussing different stages of biobanking

3. **Minimal Requirements to Build a Biobank - Prof Dr Karine Sargsyan**

- Infrastructure – special fire security systems, calibration of all used equipment
- Biobanks in medical research - personalized medicine
- Planning – set a goal, on-time planning, project management, sustainable financial and economic concepts, cooperative approach to implementation, infrastructure planning – plan for backups, setting up a specific access policy and transparency, Quality management (certification), HR strategy, ELSI and PR strategy, risk management, exit strategy and termination concept
- Preparation of a good project management plan for the biobank – a business plan
- Space requirements – office, donor/patient area, sector FFPE storage, sector -80°C, -150°C storage, paper/chemical archive, lab tissue workplace, lab blood/fluids workplace, lab PC working place, server room
- Presenting important technical aspects of biobank - cooling source, working lighting conditions, floor bearing capacity, and balance of the heavy storage space, oxygen/nitrogen level sensors
- Ethics in biobanking
- Networking between the biobank and the analyses centers
- Importance of continuous education and training of technical and higher staff
- Communication strategy – be very open and transparent, videos, newspapers, website in many languages, open days
- Be ready to communicate the biobanking idea to anybody – group exercise in two groups – communicate the biobanking idea to a 5-year old child – presentation by Dr Milena Cavic
- Importance of SWOT analysis for a biobank

4. **Biobank and Ethics - Dr Anna Michalska-Falkowska**

- Importance of ethics in the field of biobanking – ethical, legal, public health, business and ecological points of view
- Moral dilemma – can all moral dilemmas be solved – ethical issue for sensitive groups
- A system for protecting the interests and rights of donors
- International codes of ethics
- Discussing legal aspects of biobanking – EU Directives
- Discussing legal aspects of biobanking in Austria
- Discussing legal aspects of biobanking in Poland
- Discussing the general principle of Biobanking
- Informed consent – ethical aspects – ask the patient for permission to be re-contacted after a few years for longitudinal studies if needed
- Discussing different types of Informed Consent

  - Study Specific Consent
  - Broad Consent – statement for the future use of the samples at the University of Graz, if you don't know yet what project is going to use the samples
  - Tiered Consent
  - Meta-Consent
  - Dynamic Consent interactive digital platforms – electronic consent where the donors can check all phases via a digital access – regulation tight with EU rules, performed in accordance will all GDPR rules and e-security
- Presenting the scope of information provided before consent
- Informed Consent – formal requirements
- Discussing how to create a biobank from previously collected samples

5. Management and Sustainability in Biobanks, Prof Dr Karine Sargsyan

- Strategic management – mission, vision, values
- Define the mission statement
- The vision – envision a path/program where you want to lead the biobank
- Core values - fundamental beliefs or guiding principles of an organization
- Strategic plan – a roadmap - have a plan for how to go bigger, and how to go smaller – anticipate all possible *force majeure*
- Business plan - put a business plan with a strategic plan and MVV
- Always state education in your strategic plan
- Making the plan real – do not over-aim
- Developing a biobank strategy - sample collection strategy, digitalization
- Biospecimens in a human biobank
- Expectations regarding biobanks - everyone will expect from you to be certified, ensure highest quality possible in your specific setting

6. Cost–calculation, financing and funding, Dr Anna Michalska-Falkowska

- Discussing sustainability, objectives, fundamental questions
- Cost calculation - How to calculate the biobanking cost – which cost should be compensated by the customer?
- Two methods of calculation – Bottom up-approach (BIOBANK), Top-down approach (ACCOUNTING DEPARTMENT)
- Presenting biobank cost calculators – Biobank resource center
- Models for collaboration around biobanking costs
- How to find the right sources?
- Horizon Europe R&I - Infrastructure Research and Innovation Actions, Innovation Actions – perfect for new biobanks
- Innovative Training Networks (ITN) - to increase the visibility of biobanking in countries where the public understanding is low – public support crucial for the implementation long-term sustainability
- EURAXESS networks – to gain insight in other biobanking facilities
- Package your idea into an attractive proposal - How to write a strong proposal?

- Presentation of SMART goals
- Acquire the biobanking ISO 20387:2018 standard before setting up the biobank, if possible, ISO 9001 as well as it is an organizational standard for quality control.

7. Biobanking networks in Europe - Prof Dr Karine Sargsyan and Dr Anna Michalska-Falkowska

- The idea behind the networks is to simplify access to information and samples, harmonize, unify, standardize, and collaborate at an international level
- European/International Biobank Networks/Societies:
  - ISBER
  - ESBB
  - the governance structure of ESBB
  - BBMRI ERIC structure and services - application to join BBMRI ERIC is performed at a national level
- BBMRI Directory - good for partner/sample search
- ISBER website
- Goal harmonization of quality on a high level
- Mining the biobanking landscape

8. Group Work Introduction to group work & start of group work - Prof Dr Sargsyan Karine, Dr Anna Michalska-Falkowska

- The participants were divided into two groups
- Each group was given the task of forming a biobank
- The presentation of the biobanks was followed by a discussion on the proposed biobanks
- STEPUPIORS team members made a great contribution during this exercise, presentations made by Dr Ana Djuric and Dr Snezana Bjelogrlic

14.3.2023.

1. Sample Management and Sample Logistics - Dr Karine Sargsyan, Dr Anna Michalska-Falkowska

- Sample management needs to be tightly regulated in order to have a high-quality biobank.
- Discussing SOPs and related biobank documentation
- Quality of the sample is always an issue
- Discussing process requirements – strategy of biobanking
- Discussing cryo tissue sample collection, cryopreservation, lab material for cryo tissue samples, cryo tissue sample handling, cryo tissue sample storage
- Special attention on safety measures for cryo tissue storage in liquid nitrogen
- Discussing sample labeling - how a tissue sample enters the biobank
- FFPE tissue sample collection, FFPE tissue sample processing, FFPE tissue sample handling, FFPE blocks

- Discussing ischemia as a critical factor for tissue sample preparation – warm ischemia, cold ischemia
- Liquid sample collections, manual liquid sample handling, fully automated liquid sample handling, liquid sample transport
- Lab Ware Requirements
- Pseudonymization should be immediate

2. Quality Standards for Biobanking – ISO and CEN-Standards - M.Sc. Andrea Wutte

- Presentation of BBMRI – Members and Observers
- Support of IT, ELSI services, public affairs
- Training possibilities – CME accreditation available
- Auditing program available
- Presentation of BBMRI ERIC's overview of biobanking procedures and standards
- Important to increase the visibility of biobanks/importance of biobanking
- Presentation of quality management services – knowledge hub, training and support, auditing, quality assurance
- Presentation of quality Policy – International Standards and Guidelines
- OECD best practice guidelines
- WHO IARC guidelines for biological resource centers
- ISO standards on a global level, each country has a national standardization body that gives a certificate.
- CEN CENELEC
- BBMRI-ERIC liaisons with International Standardization Organizations ISO 276, ISO 212, ISO 215, CEN 140
- Why standardization is important – acquire EU funds, BBMRI ERIC participates as a partner in various Horizon and other international projects
- Presentation of workflow in personalized medicine
- For biobanking, two standards are important:
  - ISO 20387:2018 Biobanking standard
  - ISO 9001:2015 General quality management standard
- ISO 19011:2018 Auditing management systems
- ISO 20387:2018 – presentation of the scope, table of content
- International standard in development ISO/DTS 23494-1
- INI – Innovative health initiative
- Presentation of Integrated Management System
- Presentation of the European Accreditation Association
- Differences between accreditation and certification
- BBMRI-ERIC quality label in the directory - How to achieve the quality label?
- Discussing the auditing process
- Useful to perform a self-assessment and apply for an audit trail

3. Data Management and Biobanking IT – M. Sc. Denis Marino

- Importance of data quality
- Presentation of IARC animation on FAIR data
- FAIR data management self-assessment – perform to see where you stand with your data management
- Discussing biobanking data origin, data managed by biobank, data quality for biobank, data quality dimension, data types, ontologies and interoperability, data quality documentation
- Biobanks are data brokers
- Presentation of The Human Exposome Assessment Platform
- Data represent real-world facts
- Discussing ALCOA principles
- Special attention on data security and data privacy
- Biological Resources Management
- IT infrastructure - users, graphical user interface
- Differences between the usage of Excel and Biobank Management Software
- Get familiar with database, typical application architecture, relational database
- IT- system selection process
- Functional vs Nonfunctional requirements
- Planning, Communication and Training for the use of IT system
- Scrum Team – manages the data and information

4. Introduction Biobank Graz (incl. movie KIMCL) Prof Dr Karine Sargsyan

- Biobank Graz largest clinical/hospital-based biobank in Europe
- Discussing collection strategy
- Biobank Graz certified by ISO 9001:2015, but not accredited by ISO 20387:2018
- Presentation of development of Biobank Graz, change of infrastructure through time
- Discussing project service
- Discussing labeling
- Presentation of storage space: paraffin sample storage, shelves, liquid storage -80ºC
- Watching the movie about Biobank Graz

5. Group Work SWOT Analysis - Prof Dr Sargsyan Karine, Dr Anna Michalska-Falkowska

The two groups of participants (same as the first course day) performed SWOT analysis on their Biobanks.


CERTIFICATE

Medical University of Graz

This certifies that

Dr Snezana Bjelogrlic

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Suzana Stojanovic-Rundic

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Katarina Mirjacic Martinovic

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Ana Vuletic

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Marija Djordjic Crnogorac

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Mladen Marinkovic

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Ana Djuric

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education


CERTIFICATE

Medical University of Graz

This certifies that

Dr Milena Cavic

has successfully completed the 2-day training course

„How to build a biobank"

Graz, Austria
March 13-14, 2023

Prof. h.c. Karine Sargsyan, MD
Managing Director International Biobanking and Education

Mag. (FH) Gabriele Hartl
Project Officer International Biobanking and Education

ИНФОРМАЦИЈЕ ЗА ПАЦИЈЕНТА

Истраживачки центар: Институт за онкологију и радиологију Србије, Пастерова 14, 11000 Београд

Главни истраживач: др сци Милена Чавић, ВНС

Главни одговорни клиничар: Доц. др сци мед Сузана Стојановић-Рундић, ВНС

Назив истраживања: **"**Испитивање клиничких и молекуларних параметара успешности примене преоперативне радиохемиотерапије у лечењу локално узнапредовалог карцинома ректума" у оквиру европског мултиинституционалног пројекта за карцином ректума (*Horizon Europe Twinning Project STEPUPIORS; Agreement No. 101079217*)

Поштовани,

Желимо да Вас информишемо о истраживању које се спроводи на Институту за онкологију и радиологију Србије. Пре него што дате свој пристанак важно је да разумете зашто се ово истраживање изводи и у чему се оно састоји. Прочитајте ове информације и, уколико желите, разговарајте и посаветујте се са члановима своје породице или другим особама. Уколико Вам је нешто нејасно или желите више информација биће нам драго да одговоримо на сва Ваша питања. Имате довољно времена да одлучите да ли прихватате да учествујете у нашем истраживању. Захваљујемо Вам што сте посветили своје време читању ових информација.

Досадашњим дијагностичким поступцима утврђено је да болујете од рака завршног дела дебелог црева, односно ректума. На основу ове дијагнозе и стадијума болести, код Вас се планира започињање лечења зрачном терапијом уз хемиотерапију сходно протоколу лечења. Циљ овог истраживања је да се испита како туморско ткиво реагује на примену зрачне терапије и хемиотерапије. Желимо да знамо да ли постоје параметри који нам и пре започињања лечења могу указати какав ће бити одговор на терапију, и на тај начин у будућности омогућити прилагођавање лечења карактеристикама сваког пацијента и његове болести. Користили бисмо мањи део туморског ткива узетог приликом колоноскопског прегледа дебелог црева у моменту утврђивања болести, што значи да неће бити потребно да се поново ради колоноскопија. Поред тога користили бисмо узорке крви (10mL - две кашичице) узете у склопу редовне контроле параметара крвне слике у пет временских момената: пре започињања лечења, током лечења, непосредно по завршетку лечења, као и на контролама 4 и 8 недеља по завршеном лечењу. Узорци ће бити чувани у склопу биобанке у Институту за онкологију и радиологију Србије под строго контролисаним условима. Биобанка је намењена преузимању, чувању, руковођењу/руковању и дељењу великог броја људских биолошких узорака који су од великог интереса за проучавање/истраживање. Крајњи циљ је допринос у напретку познавања природе болести, ранијем и тачнијем утврђивању постојања болести, спречавању настанка болести

и/или унапређењу лечења болести. Пре него што се започне било које истраживање на Вашим узорцима биће затражено одобрење Етичког комитета о оправданости датог истраживања. Постоји могућност слања узорака у иностранство ради додатних анализа.

Ово истраживање су одобрили Медицински факултет у Београду, Научни и Етички одбор Института за онкологију и радиологију Србије. Истраживање је некомерцијално и спроводиће се у Институту за онкологију и радиологију Србије. Ово истраживање има за циљ да допринесе бољем разумевању резултата лечења рака завршног дела дебелог црева, односно ректума, применом преоперативне радиохемиотерапије.

Учествовањем у овој студији нећете бити изложени никаквом ризику. Бићете лечени и контролисани стандардним методама које се спроводе и мимо овог испитивања. Важно је да нагласимо да ће се лечење Ваше болести спроводити на потпуно исти начин без обзира на то да ли пристанете или не да учествујете у овом истраживању. За пристанак нећете добити новчану компензацију, али се надамо да ће истраживање довести до нових научних сазнања од којих ће користи имати пацијенти у будућности и друштво у целини.

У случају да се одлучите да повучете пристанак за учешће у овом истраживању, то можете учинити кад год желите, без последица по Ваше даље лечење. Сви до тог момента обрађени подаци ће остати у бази истраживача, а Вама ће бити враћен преостали део узорка ткива тумора који буде доступан у том тренутку. Преостали обрађени узорци ткива и крви могу бити уништени на Ваш захтев. Захтев за повлачење пристанка можете послати у слободној форми главном одговорном клиничару (контакт на дну стране) или заштитнику права пацијената ИОРС-а (zastita.podataka@ncrc.ac.rs).

Учествовање у овом истраживању је добровољно. Ваши лични и медицински подаци биће стриктно чувани и третирани у складу са лекарском тајном као строго поверљиви. За анализу ће се користити подаци о полу, старости и стадијуму рака завршног дела дебелог црева, као и остали подаци из медицинске документације, и гарантује се анонимна анализа података. Узорцима вашег туморског ткива и крви биће додељен број и истраживачи који учествују у експерименталном раду неће имати приступ вашим поверљивим подацима. Уколико постоји поље у оквиру којег не желите да узорци Вашег ткива и крви буду анализирани то нам можете рећи. Резултати истраживања ће бити објављени у облику научног рада у медицинским часописима и презентовани на медицинским састанцима. У стручним радовима нећете бити идентификовани и Ваш идентитет биће у потпуности заштићен. Сво особље укључено у ово истраживање подлеже законској обавези одржавања поверљиве природе ових докумената.

Хвала Вам што сте пажљиво прочитали ове информације.

Информисани пристанак

_____	_____	_____
Име и презиме учесника/пацијента (штампаним словима)	Датум рођења (дд/мм/гггг)	Редни број

Свеобухватно сам обавештен(а) о поступку, циљу и начину спровођења овог испитивања.

Прочитао(ла) сам детаљно и јасно разумео(ла) претходно наведене информације за пацијента. У току разговора са _____, могао(ла) сам да поставим питања и добијем задовољавајуће одговоре.

Јасно ми је да је учешће у овом истраживању потпуно добровољно и да ћу моћи да повучем пристанак за учествовање у било ком тренутку, без да наводим разлоге за то, као и да таква одлука неће утицати на било који начин на моје даље лечење.

Разумем да ће моји лични подаци, узорци и проистекли подаци у истраживању бити деидентификовани и шифрирани.

Имао(ла) сам довољно времена да размислим о пристанку.

☐ **Добровољно пристајем да учествујем као испитаник у <u>овом</u> истраживању**.

☐ **Добровољно пристајем да се мој узорак чува у <u>биобанци</u> Института и користи за <u>будућа</u> адекватно одобрена научна истраживања.**

Добио(ла) сам један примерак информације за пацијента и један примерак обрасца сагласности. Други примерак остаје у истраживачком центру, као део медицинске документације.

_____ _____

(Место и датум) (Потпис пацијента)

_____ _____

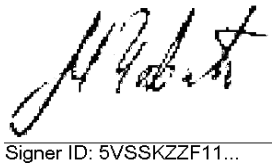
(Место и датум) (Потпис ординирајућег лекара)

Date: 09/06/2023	**Client:** Institute of Oncology and Radiology of Serbia

Reference Document:	Installation certificate
Project title:	NorayBanks Academic
Project code:	Z025 BO

Description of material, documentation delivered and/or service performed:

- Installation of NorayBanks in pre-production and production environments; latest version, v.3.60.2308.2209, tested and validated.

By Noray Bioinformatics, S.L.U.	**By the client:**
	 Signer ID: 5VSSKZZF11...
Signed: Imanol Carnero	Signed:

General remarks: