University of Maribor

FRAMEWORK PROGRAMME OF EARLY STAGE RESEARCHER TRAINING[1]

1. BASIC DATA

Mentor's name and surname	**Uroš Maver**	Mentor's register number at ARIS (SICRIS):	**30850**
Mentor's e-mail:	uros.maver@um.si	Mentor's tel. no.:	+38622345823
Research programme (RP) leader's name and surname:	Uroš Maver	RP leader's register number at ARIS (SICRIS):	30850
Title of research programme:	Bio-psycho-social model of quality of life	RP's Register number at ARIS (SICRIS):	P3-0036
Research organisation (RO) of University of Maribor, where training shall be conducted:	University of Maribor, Faculty of Medicine	RO Register number at ARIS (SICRIS):	0552-2334
Research field according to ARIS classification:	1.09 Pharmacy	Research field according to EURAXESS classification	Pharmacological sciences

2. DEFINITION OF RESEARCH PROBLEM AND GOALS OF DOCTORAL RESEARCH[2]

Starting point of research task of the early stage researcher and its position in the research programme, where the mentor is included, work hypothesis, research goals and foreseen result with emphasis on an original contribution to science:

BACKGROUND

Despite considerable efforts and promising progress in developing effective and representative ADME (absorption, distribution, metabolism, excretion) models, many challenges remain in reaching a level that would allow preclinical testing without the sacrifice of numerous animals and/or without incurring enormous costs that limit the overall progress of pharmacology. In recent years, considerations of ADME have become more important, partly due to an improved

[1] *Term early stage researcher (ESR) is written in male form and used as neutral for women and men.*

[2] *Research and study programme of training have to harmonise with contents of the research programme, where the mentor is a member.*

understanding of the body's response to xenobiotics, but mainly due to an aging population and the rapidly increasing number of patients being treated with multiple medications simultaneously (polypharmacy). Clinical studies, upon which guidelines are based, are most often designed to include only one variable (the impact of a single drug on the organism) and therefore do not provide answers regarding potential complications arising from the simultaneous use of multiple drugs. While potential pharmacodynamic interactions were the focus of pharmacological research in the past, pharmacokinetic interactions are now an increasingly common cause of serious clinical complications, increased hospitalizations, and even deaths. A thorough understanding of pharmacology, particularly pharmacokinetic interactions, is becoming ever more crucial in medicine, which has highlighted the significant need for the development of complex in vitro models that would allow preclinical testing of the pharmacokinetic properties (ADME) of drugs in cases of polypharmacy. Considering the time and costs required for the development of effective and timely treatment, function-based, integrated (multi-organ connections), easy-to-fabricate and reproducible (allowing simple global standardization), and relatively inexpensive—and therefore accessible—ADME models represent the future of drug discovery and development, as well as the assessment of interactions between drugs.

LINK TO THE RESEARCH PROGRAM P3-0036

The program is focused on addressing the interaction between a broad population of people and the increasingly advanced materials they come into contact with. Since this interaction significantly affects human health, well-being, and integration into the environment, it is key to the bio-psycho-social quality of life. The program approaches the evaluation of this interaction for people in medical care (patient/healthcare provider interactions) as well as outside of it (patient/relatives), involving various “materials” that are part of the care (medications, medical devices, sensors, implants, nutrition, etc.) or in direct and indirect contact (remote care) with modern ICT solutions. These interaction areas are addressed in four work packages, one of which is: 2) Advanced in vitro tissue and disease models and regenerative medicine, into which the proposed topic for this Young Researcher (MR) Proposal directly falls. It is also worth noting that the current demographic trends and the rise of non-communicable chronic diseases are among the foundations for our focus in this second work package. Moreover, the program group is among the most pioneering in the broader community in the field of new in vitro models for tissues and diseases, with a focus on understanding their physiological and pathological characteristics, which also provides an excellent basis for this MR.

WORKING HYPOTHESIS

In the last decade, significant progress has been made in developing microphysiological systems (MPS) for pharmacokinetic applications in the area of absorption, distribution, metabolism, and excretion (ADME) of substances. Despite the progress, existing solutions still represent a compromise between providing relevant tissue anatomy/physiology and the desired target function that is being simulated. Generally, the latter property has often been assumed to automatically result from the former, and as a result, it has frequently been neglected. Artificially mimicking native tissue in all its complexity will remain challenging, at least in the near future. Therefore, to enhance the transferability of ADME models to all aspects of preclinical drug research and to standardize them, we must focus much more on replicating the appropriate function of native tissue. To this end, within the framework of the MR training, we propose a radical yet highly sensible simplification

of the overall design of ADME models. This simplification will enable the preparation of function-focused models and adds an entire layer of analytical possibilities for real-time measurements. This will allow continuous monitoring of multiple biological (viability, morphology, transport, etc.) and environmental (pH, temperature, flow, O_2 concentration, substance concentration, etc.) parameters. Additionally, the proposed approach enables on-line sampling with a resolution of a single cell (a true novelty in the literature), whereby at desired time points a minimal amount of sample is taken from the "live" model (using the BioPixlar device by Fluicell, Sweden) without significantly impacting the overall functionality of the model—thus, "non-sacrificial" sampling. By retrieving cells instead of merely sampling their products, multiomic approaches (especially at the transcriptomic and proteomic levels) can provide a new level of information about the processes occurring in the model over time (e.g., expression, health, toxicity, etc.).

RESEARCH OBJECTIVES

1. **Develop a MPS concept platform (including an "extension" for on-line sampling):**
    - **Objective 1:** Establish the basic framework of an MPS suitable for constructing an integrated ADME platform.
2. **Validate the new sampling analysis approach via non-sacrificial on-line sampling over time:**
    - **Objective 2:** Demonstrate that continuous sampling on the same model in a non-sacrificial manner is possible.
3. **Develop a simplified integrated ADME model for at least one mode of drug administration (e.g., transdermal or oral) and demonstrate the key advantages of integrated ADME models:**
    - **Objective 3:** Show the ease of construction and use of the model (and consequently better potential for standardization).
    - **Objective 4:** Prove the uncompromised functionality of the model for the chosen target function (e.g., the absorption process or a specific phase of metabolism).

For each objective, we plan to publish at least one scientific contribution in first-quartile journals in the fields of pharmacy, biomaterials, biomedical engineering, materials science, and/or other related areas.

EXPECTED ORIGINAL CONTRIBUTIONS

1. **Innovative Integration of MPS and Non-Sacrificial Sampling:** We are developing a unique concept of a microphysiological systems (MPS) with an integrated "extension" for on-line sampling that enables continuous monitoring and analysis of functional and environmental parameters without compromising the integrity of the model.
2. **Completely New Sampling Methodology with a Resolution of "Few Cells":** We present a concept/platform that allows non-sacrificial sampling with a resolution of "a single cell," thereby enabling detailed multiomic analyses (transcriptomics, proteomics) for dynamic monitoring of biological processes over time.
3. **Simplified and Standardized Design of Integrated ADME Models:** Aiming to improve usability and reproducibility, we are developing a function-focused, simple, and cost-effective model that mimics the key physiological processes of absorption, distribution,

metabolism, and excretion (ADME), facilitating easier global standardization of preclinical testing.

4. **Emphasis on Pharmacokinetic Interactions in the Context of Polypharmacy:** Our approach allows for detailed investigation of pharmacokinetic interactions during the simultaneous use of multiple drugs, which is crucial for understanding and preventing serious clinical complications, thereby directly contributing to enhanced treatment safety and efficacy.

3. STUDY PROGRAMME

Foreseen study programme, to which early stage researcher shall be enrolled in academic year 2026/2027:

Biomedical Technology, Faculty of Medicine

4. DESCRIPTION OF WORK AND TASKS

WORK METHODS

The work will be divided into several parts:

1. **Literature Review.**
2. **Biomedical-Technological Part:** Preparation of a basic MPS system, including scaffolds that will serve as the supporting material for the growth of various cell types.
3. **Cellular Biology Part:** Isolation and cultivation of cells, as well as the preparation of functional ADME models using a combination of multiple cell types; ensuring an adequate supply of nutrients.
4. **Characterization:** Thorough evaluation of the structural, morphological, physiological, and other properties of the prepared scaffold materials with and without incorporated cells.

METHODS and ANALYTICAL TECHNIQUES (used for different parts)

1. Systematic reviews, critical evaluation of articles and clinical studies, and tracking of clinical guidelines and trends in the broader field of tissue engineering for various tissues/organs (e.g., skin, liver, kidneys, etc.).
2. Use of computer programs for data processing.
3. 3D printing, microfluidic printing, spin-coating, and electrospinning.
4. Immunohistochemical staining, assessment of cytotoxicity and cellular proliferative capacity, flow cytometry, fluorescence and confocal microscopy, and molecular analyses (multi-omic analysis).
5. Atomic force microscopy, IR spectroscopy, UV/VIS spectrophotometry, determination of mechanical properties, ICP-OES, and nanoCT.

5. REQUESTED LEVEL OF EDUCATION

Masters (2. Bologna level)

6. REQUESTED FIELD OF EDUCATION

Pharmacy, Medicine, Natural Sciences

7. KLASIUS SRV

18202

8. KLASIUS P

0988

9. REQUESTED KNOWLEDGE

Basic sciences, Chemistry, Biology, Physics

10. REQUESTED SPECIAL REQUIREMENTS

Curiosity, enthusiasm, high work ethic, communicative, individual and teamwork

11. REQUESTED LANGUAGES

Slovenian, English

12. REQUESTED WORK EXPERIENCE

Finished master thesis with laboratory experience in pharmaceutical/biomedical analysis

13. FORESEEN POSTDOCTORAL TRAINING

- Postgraduate, Doctoral Programme Biomedical Technology
- Duration of study: 3 years
- Number of credits (ECTS): 180 ECTS
- Professional degree awarded: Doctor of Science in Biomedical Technology

Mentor's signature:

Uroš Maver Digitally signed by Uroš Maver Date: 2026.02.11 14:05:07 +01'00'

Research programme leader's signature:

Uroš Maver Digitally signed by Uroš Maver Date: 2026.02.11 14:05:15 +01'00'

Darja Farasin Digitalno podpisal Darja Farasin Datum: 2026.02.11 14:18:28 +01'00'

Jelka Rakun Digitalno podpisal Jelka Rakun Datum: 2026.02.11 15:44:14 +01'00'

Name and surname of Dean or authorised person[3]:
Prof. Iztok Takač, MD, PhD

Signature of dean or authorised person:

Iztok Takač Digitalno podpisal Iztok Takač Datum: 2026.02.12 08:14:48 +01'00'

Place and date:

Maribor, 11. 02. 2026

Stamp:

[3] The training program is signed by the dean of the member where the ESR's employment and training will take place.