List of doctoral projects available for the academic year 2026/2027

Biology

Discipline	Biological sciences
Supervisor	Prof.dr hab. Andrzej Gamian (andrzej.gamian@hirszfeld.pl)
Subject	**Structural and biosynthesis studies of a new advanced glycation end product (AGE) present in human tissues**
Description	Advanced glycation end products (AGEs) are conjugates of proteins with sugars and aldehyde metabolites. They occur in a large number for example in diabetes mellitus and are also supplied with food. In a high level the AGE are pro-inflammatory factor. Monoclonal antibodies to these products recognize a hitherto unidentified antigen present in human tissues, including cancer [Sci Rep. 2021 Feb 3;11(1):2940]. The task is also to identify the structures present in the cells recognized by monoclonal antibodies by SEM and TEM electron microscopy as well as their biosynthesis. The work will concern the separation and purification of AGE, then structural investigation with mass spectrometry and NMR spectroscopic methods. The research methodology mainly includes glycobiology, immunochemical, cell biology, electron microscopy techniques. The research is important for understanding the basic cellular processes and will be used in the immunohistochemical diagnosis of diseases, including cancer.
Methods	1. Synthesis and purification of advanced glycation end-products using microwaves reactor, FPLC fractionation of high and low molecular mass compounds with their SDS-PAGE, immunoblotting analysis. 2. Monoclonal antibody purification from hybridoma cell supernatants using affinity chromatography and preparation the gold conjugates. 3. Surface electron microscopy and transmition electron microscopy identification of cellular localization of new epitope in human cells. 4. Mass spectrometry – MALDI and HPLC-MS/MS analyses.

Discipline	Biological sciences
Supervisor	Dr hab. Tomasz Goszczyński (tomasz.goszczynski@hirszfeld.pl)
Auxiliary Supervisor	Dr Bożena Szermer-Olearnik (bozena.szermer-olearnik@hirszfeld.pl)
Subject	**Metallacarborane-Based Compounds as Novel Antibacterial Agents**
Description	Boron can form extraordinary three-dimensional, σ-aromatic structures known as boron clusters. These unique entities differ markedly from compounds formed by other elements of the periodic table and are absent from biological systems. Consequently, living organisms have not evolved mechanisms capable of metabolizing boron clusters. These distinctive properties create broad opportunities for the use of boron clusters in biological chemistry, particularly in the design and synthesis of new biologically active compounds. Studies of these compounds may provide a source of new substances with anticancer and antibacterial properties. In the Laboratory of Biomedical Chemistry, we study a special subgroup of boron clusters metallacarboranes. We have obtained a library of metallacarborane derivatives, including conjugates with known organic antibiotics from various classes and with different mechanisms of action. Many of these derivatives exhibit high antimicrobial activity. The main research topic will focus on studying the interactions of these compounds with bacteria in order to identify structural motifs that promote antibacterial activity, with particular emphasis on their molecular mechanisms of action. The proposed topic is interdisciplinary: candidates will gain knowledge and skills in chemistry, biochemistry, and microbiology.
Methods	The planned methods include microbiological tests for the evaluation of antibacterial activity, including determination of MIC and MBC values, bacterial growth inhibition assays, time-kill studies, and analysis of potential synergistic effects with selected antibiotics. Mechanistic studies will include assays of bacterial membrane integrity and permeability, biofilm formation or disruption assays, fluorescence-based viability tests, and microscopic analysis of treated bacterial cells. Electron microscopy, including SEM and/or TEM, will be used to evaluate morphological changes in bacterial cells after exposure to the tested compounds. Additional methods may include fluorescence or confocal microscopy and flow cytometry. In order to assess the application potential and determine the selectivity index of the obtained conjugates, their impact on the viability of normal eukaryotic cells will be assessed using standard laboratory procedures like SRB, PrestoBlue or LDH assays. No animal experiments are planned within the project. The biological studies will involve work with bacterial cultures used as test microorganisms; therefore, infectious biological material may be used. All experiments will be conducted under appropriate biosafety conditions and in accordance with institutional procedures for work with microorganisms.

Discipline	Biological sciences
Supervisor	Prof. dr hab. Sabina Górska (sabina.gorska@hirszfeld.pl)
Auxiliary Supervisor	Dr Katarzyna Pacyga-Prus (katarzyna.pacyga-prus@hirszfeld.pl)
Subject	**The role of the nasopharyngeal microbiota in shaping the pulmonary immune system**
Description	The sinonasal microbiota plays a crucial role in maintaining microbial and immune homeostasis in the respiratory tract. It not only enhances immune defense in the upper respiratory tract (URT) but also influences lung immunity. Recent studies suggest a link between sinonasal microbiota dysbiosis (microbial imbalance) and airway allergic diseases, such as chronic rhinosinusitis (CRS) and asthma. However, there is still a significant gap in understanding how the sinonasal microbiota affects the development of immune responses and allergic reactions in the lungs. This project aims to determine the role of the sinonasal microbiota in modulating lung immunity and to investigate whether sinonasal dysbiosis, as observed in CRS patients, predisposes individuals to and promotes allergic airway inflammation.
Methods	Collection and characterization of patient-derived samples Shotgun metagenomic analysis *In vivo* studies using germ-free animal models and murine models of allergy Functional analyses using in vitro cultures ELISA, Western blot, RT-PCR, and related techniques
Additional information	International collaboration and mobility are key components of this project. Scientific visits to laboratories in the Czech Republic (Laboratory of Gnotobiology, CAS), collaborations with clinicians, and participation in international conferences and workshops are planned.

Discipline	Biological sciences
Supervisor	Dr hab. Anna Jarząb (anna.jarzab@hirszfeld.pl)
Subject	**Meltome Atlas development and its use in the assessment of neuronal cells sensitivity to temperature in the context of infectious fever**
Description	The project will utilize Thermal Proteome Profiling (TPP) to monitor the process of protein denaturation under temperatures, particularly in the range of infectious fever. This will be assessed by mass spectrometry based proteomics approaches and bioinformatics. We will assess the influence of temperature on the protein denaturation and signaling under elevated temperatures. The general outcome and the result of our work will be the proteomics database, which will constitute the extension for existing Meltome Atlas resource available at https://meltomeatlas.proteomics.wzw.tum.de/master_meltomeatlasapp/ [Jarzab A, et al, Nature Meth. 2020]
Methods	Methods used in the project: biochemical, microbiological, immunoenzymatic, analytical methods, mass spectrometry based proteomics, bioinformatics Organisms used in the study: mammalian cell culture on cell lines (mainly glial cells e.g. astrocytes), mice studies (alternatively)
Additional information	Project will be based on a collaboration with Technical University of Munich.

Discipline	Biological sciences
Supervisor	Prof. dr hab. Sławomir Kozieł (slawomir.koziel@hirszfeld.pl)
Subject	**Polymorphisms in Dopaminergic Genes (*DRD4, DRD2, COMT, DAT1*) and Risk-Taking Behaviour in Individuals Engaged in High-Risk Activities**
Description	This project aims to identify associations between functional polymorphisms of certain dopaminergic genes and behavioural measures of risk-taking among individuals with at least five years of continuous participation in high-risk activities such as high-mountain climbing, paragliding, parachuting, cave-diving ect. by comparison to non-risk-taking controls.
Methods	Genetic material will be collected from buccal swabs, followed by DNA extraction using commercial silica-based kits. Genotyping will be performed in the molecular genetics facility of the Hirszfeld Institute employing polymerase chain reaction (PCR) with locus-specific primers for *DRD4* VNTR (48-bp repeat), *DRD2* Taq1A, *COMT* Val158Met, and *DAT1* 40-bp VNTR polymorphisms. PCR products will be visualized by agarose gel electrophoresis and, where necessary, confirmed by capillary fragment analysis. Allele frequencies will be tested for compliance with Hardy–Weinberg equilibrium. Behavioural and psychological data will be collected using the Barratt Impulsiveness Scale (BIS-11), the Domain-Specific Risk-Taking Scale (DOSPERT), and the Balloon Analogue Risk Task (BART). Generalised Linear Models (GLM) and multiple logistic regression will be applied to test genotype–behaviour associations, adjusting for covariates such as age, sex, and years of high-risk experience. Bonferroni correction ($\alpha = 0.05/n$) and power analysis will ensure statistical reliability.

Discipline	Biological sciences
Supervisor	Prof. dr hab. Jolanta Łukasiewicz (jolanta.lukasiewicz@hirszfeld.pl)
Auxiliary Supervisor	Dr Anna Maciejewska (anna.maciejewska@hirszfeld.pl)
Subject	**Immunogenicity and epitope mapping of *Pseudomonas aeruginosa* O antigens**
Description	The doctoral project will be a part of the NCN SHENG 4 project, entitled "Chemical synthesis, immunogenicity and identification of protective sugar epitopes of *Pseudomonas aeruginosa* antigens". You will be a member of interdisciplinary team with expertise in microbiology, structural analysis of carbohydrates and your PhD project will focus on glycoconjugate synthesis, antibodies selection, and antigen-antibody interactions and epitope mapping by NMR spectroscopy. *Pseudomonas aeruginosa* is an opportunistic pathogen that causes serious hospital-acquired infections in people with cystic fibrosis and severe burns. Although several vaccine candidates have entered clinical trials, the efficacy results of these preparations are insufficient and there is currently no approved vaccine against *P. aeruginosa* available. Lipopolysaccharide (LPS, O antigen) is one of the main surface antigens and virulence factors of this bacterium. When designing O antigen-based vaccines, naturally isolated or synthetic polysaccharides can be used. In both cases, the antigen is selected based on its immunogenicity, and in the latter case, based on access to developed and efficient chemical synthesis procedures. The project is based on Polish-Chinese cooperation. The Chinese team will develop methods for the synthesis of new O antigens of defined length, and the Polish team, as part of the NCN project, will describe how selected oligosaccharides in the form of glycoconjugates are processed and presented by antigen-presenting cells of the immune system. Further exploration of these processes will contribute to the design of effective glycoconjugate vaccines. We offer work in a dynamic, interdisciplinary and friendly team conducting research in the field of immunochemistry of bacterial sugar antigens. LINK TO THE WEBSITE: https://hirszfeld.pl/struktura/laboratoria/laboratorium-immunochemii-drobnoustrojow-i-szczepionek/ Principal investigator: Prof. Jolanta Łukasiewicz, Laboratory of Microbial Immunochemistry and Vaccines, jolanta.lukasiewicz@hirszfeld.pl (ORCID: 0000-0001-8081-7261). The PhD project does not involve animal experiments.
Methods	microbiology, microbial cultures in fermenters, preparative (HPLC) and analytical chemistry of carbohydrates and glycoconjugates, immunoassays, flow cytometry, surface plasmon resonance (Biacore T200), NMR spectroscopy, ESI and MALDI-TOF mass spectrometry, GC-MS, flow cytometry.
Additional information	Aims of this PhD project: (1) preparation of glycoconjugates for the purpose of obtaining antibodies directed against selected *P. aeruginosa* antigens (bacterial cultures, antigen preparations, synthesis and purification of glycoconjugates, cooperation in the isolation of antibodies – immunoenzymatic and preparative methods, in vitro studies). (2) verification of the structure of sugar antigens and their glycoconjugates using NMR spectroscopy and mass spectrometry. (3) mapping of epitopes recognised by the obtained antibodies and sera using immunoenzymatic and instrumental methods, such as surface plasmon resonance (SPR, Biacore T200) and STD (saturation transfer difference)-NMR spectroscopy. (4) participation in the preparation of reports and publications. You will be trained and gain access to variety of analytical instruments and techniques. Your professional development will be supported by scholarships, courses, and participation in scientific conferences.

Discipline	Biological sciences
Supervisor	Dr hab. Tomasz Niedziela (tomasz.niedziela@hirszfeld.pl)
Subject	**Metabolic labeling in the structural analysis of bacterial glycans using NMR spectroscopy**
Description	Understanding of the structure of bacterial glycans at the atomic level provides insights into their immunochemical properties and biological roles. Nuclear magnetic resonance (NMR) spectroscopy is a powerful technique that provides detailed information on the structure of biomolecules at atomic-resolution. However, NMR of carbohydrates suffers from poor chemical-shift dispersion in 1D ^{1}H experiments due to spectral overlap. Heteronuclear NMR experiments, which take advantage of the larger spectral dispersion of ^{13}C and ^{15}N, have lower sensitivity due to the low natural abundance of these NMR-active nuclei. Isotopic labeling enables a significant sensitivity enhancement and fast acquisition of the NMR experiments. The distribution and the extent of isotopic enrichment of the labeled glycans can be assessed by NMR. The use of isotope labeling to obtain structural information from bacterial glycans is still limited and thus the development of metabolic labeling will be pursued.
Methods	NMR Spectroscopy will be the primary technique used for the analysis of glycans at different stages of the project. The metabolic labeling will require skills related to immunochemistry/microbiology (e.g. bacterial cultures, preparation of the glycans, HPLC). The structural analysis will be complemented by mass spectrometry techniques (ESI MS, MALDI-ToF MS). Microbiological segment will include tasks (cultures) that involve infectious material (*Bordetella pertussis*, etc.).
Additional information	Project will involve: • practical application of 1D & 2D homo- and heteronuclear techniques of NMR spectroscopy of glycans (polysaccharides, oligosaccharides) • immunochemistry and analytical techniques used in the field of complex carbohydrates (A minimal hands-on experience related to NMR applications will be favorable)

Discipline	Biological sciences
Supervisor	Prof. dr hab. Anna Pawlik (anna.pawlik@hirszfeld.pl)
Subject	**Molecular mechanisms of *H. pylori's* response to oxidative and acid stress**
Description	*Helicobacter pylori* is a bacterium of significant concern due to its high pathogenicity and widespread prevalence, yet many of its host-adaptive mechanisms remain poorly understood. The aim of this project is to clarify the complex molecular mechanisms that underlie *H. pylori's* response to the oxidative and acid stress it constantly encounters in the human gastrointestinal tract. *H. pylori* encodes a limited number of signal transduction proteins to regulate gene expression when necessary, and the molecular mechanisms that control gene induction or repression in response to acid and oxidative stress are still puzzling. Through this project, we aim to gain a deeper understanding of how *H. pylori* has adapted to its environment using a limited set of regulators. This adaptability makes it a highly effective human pathogen that can persist in its host for a lifetime unless treated.
Methods	Molecular microbiology techniques, including bacterial mutagenesis, transcriptomic, proteomic, metabolomic, ChIP-seq/qPCR, and protein-DNA and protein-protein interactions analyses, are planned to be employed. *H. pylori* is an infectious bacterium (category 2 pathogen). Work with genetically modified microorganisms (GMM II) is planned.
Additional information	Representative review literature: 1. Trastoy, R. et al. Mechanisms of Bacterial Tolerance and Persistence in the Gastrointestinal and Respiratory Environments. Clin. Microbiol. Rev. 31, (2018). 2. Flint, A., Butcher, J. & Stintzi, A. Stress Responses, Adaptation, and Virulence of Bacterial Pathogens During Host Gastrointestinal Colonization. Microbiol. Spectr. 4, (2016). 3. Krulwich, T. A., Sachs, G. & Padan, E. Molecular aspects of bacterial pH sensing and homeostasis. Nature Reviews Microbiology 2011 9:5 9, 330–343 (2011). 4. Flint, A., Stintzi, A. & Saraiva, L. M. Oxidative and nitrosative stress defences of *Helicobacter* and *Campylobacter* species that counteract mammalian immunity. FEMS Microbiol. Rev. 40, 938–960 (2016). 5. Malfertheiner, P. et al. *Helicobacter pylori* infection. Nat. Rev. Dis. Primers 9, 1–24 (2023). 6.Vannini, A., Roncarati, D., D'Agostino, F., Antoniciello, F. & Scarlato, V. Insights into the Orchestration of Gene Transcription Regulators in *Helicobacter pylori*. International Journal of Molecular Sciences 2022, Vol. 23, Page 13688 23, 13688 (2022). 7. Noszka, M. et al. Profiling of the *Helicobacter pylori* redox switch HP1021 regulon using a multi-omics approach. Nat. Commun. 14, 6715 (2023). 8. Loh, J. T. et al. Delineation of the pH-responsive regulon controlled by the *Helicobacter pylori* ArsRS two- component system . Infect. Immun.

Discipline	Biological sciences
Supervisor	Dr hab. Joanna Rossowska (joanna.rossowska@hirszfeld.pl)
Subject	**Extracellular vesicle-associated immune checkpoint receptors as mediators and biomarkers of immune suppression in NSCLC**
Description	Immune checkpoint inhibitors have substantially improved treatment outcomes in non-small cell lung cancer (NSCLC), yet clinical benefits remains limited. Extracellular vesicles (EVs) released by tumor and immune cells may reflect dynamic tumor-immune interactions and contribute to immune escape by transferring checkpoint-related molecules. The aim of this project is to identify EV-associated immune-regulatory profiles linked to immune dysfunction in NSCLC and to determine their biological relevance. To address this, patient-derived EVs will be profiled for checkpoint-related molecules in order to identify patterns associated with patient response to treatment and distinct states of antitumor immune activity. The most relevant EV-associated immune checkpoint pathways will then be examined in functional assays and NSCLC cell models. Better characterization of EV-associated immune regulatory pathways may improve understanding of response variability in NSCLC and contribute to a more rational selection of treatment strategies.
Methods	The project will include analysis of EVs from NSCLC patients and NSCLC cell lines, in vitro studies with human tumor cell lines, and immune cell-based functional models. Methods will include EV isolation and characterization, multiparametric flow cytometry, bead-based assays, Western blot, ELISA. Patient-derived EVs will be profiled for checkpoint-related molecules and markers of cellular origin. Functional assays will be used to assess the effects of selected EV populations on immune cell activity. Mechanisms will be investigated in NSCLC cell models, including genetically modified cell lines. No animal experiments are planned. The project will involve human biological material and genetically modified cell lines. Work with infectious material is not planned.

Discipline	Biological sciences
Supervisor	Prof. dr hab. Jakub Siednienko (jakub.siednienko@hirszfeld.pl)
Auxiliary Supervisor	Dr Justyna Łopatecka (justyna.lopatecka@hirszfeld.pl)
Subject	**The role of the AREL1 E3 ubiquitin ligase in host innate immune responses to microbial infections**
Description	The project aims to characterise the role of AREL1 in the regulation of innate immune responses and immunomodulation during microbial infections and inflammatory signalling. AREl1 belongs to the family of E3 ubiquitin ligases, proteins which regulate the stability and activity of signalling molecules through ubiquitination. Although AREL1 has been associated with apoptosis and cellular stress response, its function in antimicrobial and PRR pathways remains poorly understood. The study will use CRISPR/Cas9-generated knockout cell lines to unravel molecular mechanisms. The results will clarify how AREL1 modulates inflammatory pathways and may reveal new targets for immune-mediated diseases.
Methods	The research project focused on AREL1 would employ the following techniques: use of the guide-it CRISPR/Cas9 Gesicle Production System to generate AREL1 knockouts in multiple cell lines, microbial infection and ligand stimulation assays, RNA isolation, reverse transcription and RT-qPCR, protein quantification by ELISA and Western Blotting, functional assays to detect bioactive Type I Interferon (IFN) levels, confocal microscopy and immunofluorescence imaging, electrophoretic mobility shift assay (EMSA), co-immunoprecipitation, and statistical analysis of experimental data. The project includes tests on animals and work with infectious biological material. Research will involve activating the immune response using live viruses.
Additional information	The selection of AREL1 is based on our previous studies on other E3 ligases where we demonstrated their involvement in antiviral immunity, supporting the rationale that ubiquitin-dependent regulation is a critical mechanism in host antiviral defence (Siednienko J. et al., 2012). Available knowledge on AREL1 remains limited, with fewer than 20 PubMed- indexed publications and no studies directly addressing its role in antiviral responses.

Discipline	Biological sciences
Supervisor	Dr hab. Marta Sochocka (marta.sochocka@hirszfeld.pl)
Auxiliary Supervisor	Dr Karolina Filik-Matyjaszczyk (karolina.filik-matyjaszczyk@hirszfeld.pl)
Subject	**Antibacterial molecules based on phage receptor-binding proteins and antibody Fc fragments – characterization and evaluation of biological activity**
Description	Antibiotic resistance is a major global health threat, driving the need for new antimicrobial strategies. This project explores a novel approach combining bacteriophage receptor-binding proteins (RBPs) with antibody fragments. RBPs provide highly specific recognition of bacterial strains, while antibody fragments can engage immune cells such as macrophages to enhance pathogen clearance. The concept is to create molecules that both target bacteria precisely and stimulate immune-mediated phagocytosis. The research aims to develop a modular platform using the SpyCatcher system to link phage-derived proteins with antibody Fc fragments irreversibly. These components will be produced via genetic engineering and assembled into functional constructs, allowing flexible combinations to identify the most effective designs. Methodology includes in vitro functional assays such as flow cytometry and microscopy to assess phagocytosis, Gentamycin Protection Assay to evaluate bacterial killing, and cytokine profiling to measure immune activation. The significance of this work lies in its potential to generate innovative therapeutics against multidrug-resistant bacteria, offering a new direction for treating infections that are currently difficult to cure.
Methods	Protein overexpression in bacterial and mammalian expression systems; purification of the proteins using FPLC; protein sample analysis (SDS-PAGE, WB, etc.) Optimization of conjugation of recombinant proteins using SpyTag/Spy Catcher technology. ELISA tests (such as with bacterial cells). Cell culture – aseptic work, maintenance of the cell lines, cell line differentiation, functional assays, etc. Flow cytometry – study of phagocythosis, complement deposition, ROS production, binding kinetics. Microbiological methods – bacteria cultivation (including pathogens), quantification, aseptic work, etc.

Medicine

Discipline	Medical sciences
Supervisor	Dr hab. Monika Jasek (monika.jasek@hirszfeld.pl)
Subject	**Mechanisms regulating *ALCAM* alternative splicing and their role in bladder cancer metastasis**
Description	The growing body of evidence supports the concept that the involvement of Activated Leukocyte Cell Adhesion Molecule (ALCAM) in cancer metastasis may be influenced by the mechanism of ectodomain shedding, which has been suggested to be controlled by the availability and/or activity of proteases (sheddases), and also by alternative splicing (AS). Two ALCAM isoforms have been confirmed on both mRNA and protein level: ALCAM Iso-1 - the full-length isoform (consisted of 16 exons), and Iso-2, which lacks exon 13 encoding part of the stalk region of protein. A 10-fold increase in ALCAM Iso-2 shedding, mediated by MMP14, compared to Iso-1, mediated by ADAM17, has been observed. The increased shedding of ALCAM Iso-2 leads to reduced cell-cell adhesion *in vitro* and provides a mechanism by which ALCAM Iso-2 can promote metastasis *in vivo*. The mechanism regulating *ALCAM* alternative splicing is still unknown. In addition, other mechanisms (besides AS) that may alter ectodomain shedding have yet to be fully elucidated. Therefore, the objective of the doctoral project is to examine the mechanisms that regulate *ALCAM* alternative splicing and ectodomain shedding in the context of bladder cancer (BC).
Methods	METHODS: 1) minigene constructs for functional studies of single nucleotide variants (SNVs); 2) high resolution melting (HRM) analysis or allelic discrimination method for genotyping; 3) droplet digital PCR (ddPCR) for expression of ALCAM isoforms and expression of sheddases on mRNA level; 4) immunohistochemistry for study of ALCAM membranous and sheddases expression; 5) western blot for analysis of ALCAM in lysates from cultured cells and tissues; 6) ELISA or ProQuantum High-Sensitivity Immunoassays for shed ALCAM. MATERIAL: cell lines, tumor and non-tumor tissue samples from patients with bladder cancer, full venous blood and urine samples.

Discipline	Medical sciences
Supervisor	Dr hab. Łukasz Łaczmański (lukasz.laczmanski@hirszfeld.pl)
Subject	**Molecular tumor-stage specific responses characteristic of the three-dimensional Bladder Cancer cell line models to bacterial metabolites**
Description	Current evidence indicates dysbiosis of urinary tract and gut microbiota in bladder cancer (BCa) patients, but the molecular mechanisms remain unclear. This project aims to determine whether bacterial metabolites contribute to BCa progression and induce phenotypic and transcriptomic changes in 3D cell-models. Public data from urine tract and stool will be reanalyzed to identity microbes and metabolites associated with BCa. Findings will be integrated with literature to prioritize metabolites with known physiological concentrations but unclear roles in BCa. Selected metabolites will be tested in 3D BCa models co-cultured with stromal cells, assessing viability, proliferation, apoptosis, cell-cycle, hypoxia. Isolated from cultures RNA will be analyzed by ONT direct RNA sequencing enabling comprehensive transcriptomic profiling, including differential gene expression, alternative splicing, and epigenetic modifications.
Methods	The project will use a combination of in silico and in vitro methods. Publicly available whole-metagenome shotgun sequencing datasets from urine, bladder tissue, and stool samples of BCa patients will be reanalyzed to characterize microbiome composition and function. The analysis will include raw read preprocessing, host read removal, taxonomic profiling, functional profiling to characterize possible secondary metabolites, and integration with a systematic literature review of BCa-associated microbiome-derived metabolites. Based on metagenomic functional profiles and published metabolomic ranges, bacterial metabolites will be selected according to the following criteria: 1) there is no described mechanisms of action in BCa cells, 2) their concentration in urine, tissue or stool is known, 3) bacteria which is involved in production or processing of this metabolite is detected in patient samples. Experimental work will be performed in three-dimensional cell culture models generated from purchases BCa cell lines (derived from the same sex and representing different tumor grades) co-cultured with stromal cells. The spheroids will be exposed to selected purified bacterial metabolites at physiologically relevant concentrations. Phenotypic effects will be assessed by assays of cell viability and proliferation, apoptosis, cell-cycle distribution, hypoxia-related marker expression. Phenotypic readouts will be collected at two temporal windows: (1) early (at 6–24 h) and (2) later responses (at 48–72 h) after metabolite addition, to capture both immediate signaling events and downstream effects on growth and invasion. If significant phenotypic effects are observed, total RNA will be isolated and subjected to Oxford Nanopore direct RNA sequencing. Bioinformatic analyses will include bulk RNA-seq, differential genes expression analysis, alternative splicing analysis (e.g. isoform usage and splice-junction switching), and epitranscriptomic profiling of selected RNA modifications using dedicated long-read pipelines. Where relevant, additional analyses will be performed to explore changes in poly(A) tail length and their relationship to transcript stability and abundance. Results will be integrated with with publicly available BCa transcriptomic datasets, such as TCGA-BLCA and other RNA-seq cohorts or spheroid studies. The key transcriptomic findings will be validated at the RNA and protein level using RT-qPCR, Western blotting, flow cytometry and/or immunofluorescence for selected marker genes and pathways, prioritized based on their differential expression, splicing patterns and putative mechanistic relevance to metabolite action in BCa cells. No tests on animals will be performed. No infectious materials or viable pathogenic microorganisms will be used. The project will use only public sequencing data, commercially available human cell lines, stromal cells, and purified metabolites.

Discipline	Medical sciences
Supervisor	Dr hab. Łukasz Łaczmański (lukasz.laczmanski@hirszfeld.pl)
Auxiliary Supervisor	Dr Dariusz Martynowski (dariusz.martynowski@hirszfeld.pl)
Subject	**Enhancing the therapeutic potential of anti-SLAMF7 antibody in multiple myeloma treatment**
Description	This PhD project focuses on the development of a modified CAR-T receptor targeting SLAMF7 for the treatment of multiple myeloma. The construct includes an antibody against SLAMF7, and the goal is to improve its performance using structure-based design. We will apply molecular modeling with AlphaFold 3 and refine selected variants through molecular dynamics simulations. Both SLAMF7 and the anti-SLAMF7 antibody will be expressed and purified for kinetic studies. By characterizing binding affinities of selected antibody mutants, we aim to identify variants with enhanced interaction properties. The project combines computational and experimental approaches to optimize CAR-T therapy.
Methods	Bioinformatics, Molecular biology, Protein expresion and purification, Binding kinetics (SPR).