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MECHANISTIC STUDIES OF TYPE III CRISPR-Cas ACTIVITY REGULATION AND CHARACTERIZATION OF ASSOCIATED TRANSLATION-INHIBITING EFFECTORS (Biochemistry)

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Dissertation defended:
29 January 2025

CRISPR-Cas systems are widespread in prokaryotes providing adaptive protection against viral nucleic acids. Csm complexes of CRISPR-Cas type III-A systems recognise and cleave foreign RNA. This thesis aimed to supplement the established model of Csm activity with focus on their deactivation and determine the roles of ancillary proteins. Here, fluorescence correlation spectroscopy assays showed that despite rapid RNA shredding, the terminal RNA cleavage products remain bound to the complex for the mean duration of over an hour. Retained RNA stimulate DNase activity of Cas10 subunit of the complex and upon RNA release Cas10 is inhibited. Cas10 proteins also synthesise cyclic oligoadenylate molecules which activate ancillary CARF effectors. Sequence analysis shows that CARF proteins co-opted a mRNA interferase toxin called RelE giving rise to CARF-RelE fusion proteins Cami1. Biochemical and *in vivo* toxicity assays showed that Cami1 cleave mRNA and inhibit bacterial growth when activated by cyclic tetraadenylate. Ring nuclease activity of CARF domain allows to cleave the activator. Structural studies of Cami1 proteins revealed that they are recruited to the ribosomes via ribosomal stalk protein bL12. This is the first observation of a prokaryotic ribosome toxin hijacking the ribosome stalk to facilitate binding to the ribosome.

CHARACTERIZATION OF HUMAN ENDOMETRIAL MESENCHYMAL STEM/STROMAL CELLS AND THEIR THERAPEUTIC APPLICATION IN *IN VIVO* MODELS OF FERTILITY DISORDERS (Biochemistry)

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Dissertation defended:
31 January 2025

Fertility disorders are a significant health problem. According to the latest data from the World Health Organisation (WHO), approximately one in six people of reproductive age around the world will experience some fertility disorder at least once in their life. The WHO lists infertility as the fifth leading global disability for young people. Infertility treatment is one of the fastest-growing medical specialties. Still, it is estimated that even today 30–40% of all couples remain childless for five years from diagnosis and the beginning of treatment. One of the main reasons for this, and at the same time the most challenging in the fields of reproductive medicine, is endometrial disorders related to the pathology of blastocyst implantation. In such cases, stem cell therapy is increasingly being considered. The results of the scientific research confirm the potential of using endometrial-derived mesenchymal stem/stromal cell therapy to correct fertility disorders caused by endometrial pathology, the use of these cells in other experimental models of infertility and provide a basis for creating new biotechnology solutions and developing previous ones. Moreover, the multifacetedness of the infertility problem and the necessity of the cooperation of a multidisciplinary team of specialists to achieve optimal results in the diagnosis and treatment of fertility disorders are highlighted.

DEMODIFICATION BY TudS PROTEINS: FROM INDIVIDUAL THIONUCLEOBASES TO INTACT tRNA (Biochemistry)

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Dissertation defended:
6 February 2025

One of the most abundant RNA sulfur modifications in bacteria is 4-thiouridine (s4U), commonly located at position 8 within tRNA molecules. This modification acts as a UV sensor and contributes to the thermodynamic stability of tRNA. Previous research revealed that a family of widespread bacterial proteins TudS act as thiouracil desulfidases; however, the specificity of TudS and the function of another widespread TudS-DUF1722 (RudS) fusion protein remained elusive. In this thesis, TudS and RudS were biochemically characterised, suggesting their physiological roles in thiomodified nucleotide recycling and bacterial UV-stress response. Additionally, the previously uncharacterised Domain of Unknown Function 1722 (DUF1722) within RudS was proposed to have a tRNA-binding function. The widespread prokaryotic stand-alone TudS domain proteins were identified as 4-thio-UMP desulfidases, contributing to the understudied field of modified nucleotide catabolism. Moreover, it was demonstrated that TudS supports bacterial growth by utilising exogenous 4-thiouracil-containing compounds as uracil sources, some toxic to bacteria, thereby concurrently detoxifying their environment. RudS, a fusion protein containing TudS and DUF1722 domains, was identified as a tRNA 4-thiouridine de-modifying enzyme. Proof-of-concept experiments conducted in this study indicated that RudS is involved in the prokaryotic UV-stress response and may contribute to bacterial adaptation to UV radiation.

CHEMOENZYMATIC SYNTHESIS OF NUCLEOSIDE 5'-MONOPHOSPHATES (Biochemistry)

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Dissertation defended:
21 February 2025

Nucleoside and nucleotide analogues are extensively used in biochemistry, molecular biology, and pharmacology. These compounds function as substrates or inhibitors in enzymatic reactions and have significant applications in nucleic acid research, anticancer and antiviral treatments, and RNA vaccines. In this study, a series of novel N4-amino acid-modified deoxycytidine nucleosides were synthesised, enriching the library of nucleoside analogues. Along with additional pyrimidine nucleoside analogues, the newly synthesised compounds were tested as substrates for *Drosophila melanogaster* deoxynucleoside kinase (DmdNK) and *Bacillus subtilis* deoxycytidine kinase (BsdCK). The findings revealed that wild-type DmdNK and BsdCK exhibited activity toward pyrimidine nucleosides with minor modifications at the N4/O4 and C5 positions. Nucleoside kinases, coupled with a phosphate donor regeneration system, were applied for a milligram-scale synthesis of nucleoside monophosphates, showcasing potential for scalable and eco-friendly nucleotide production. Additionally, successful application of site-directed mutagenesis demonstrated that specific mutations in the active sites of DmdNK and BsdCK enhance enzymatic activity towards N4-modified nucleosides, enabling the customisation of these enzymes for tailored applications.

ENZYMATIC DEGRADATION OF PYRIDINE AND PYRIDINOLS (Biochemistry)

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Dissertation defended:
31 March 2025

Pyridine and its derivatives are widespread environmental pollutants originating from natural and anthropogenic sources. While microbial degradation of pyridine and pyridinols is recognised, the understanding of the underlying enzymatic mechanisms remains incomplete. This thesis explores novel catabolic pathways and enzymes involved in the microbial metabolism of N-heterocyclic aromatic compounds. Four newly identified pathways provide key insights into bacterial adaptation to pyridine-based compounds, expanding our understanding of microbial detoxification. The identified biocatalysts highlight the evolutionary ingenuity of bacteria in responding to chemical diversity in their environments. Beyond fundamental research, this work highlights the biotechnological potential of microbial enzymatic diversity. The novel enzymes show promises and prospects for bioremediation, green chemistry, and synthetic biology. By elucidating novel metabolic routes, it contributes to the development of sustainable industrial processes and innovative environmental remediation strategies, bridging basic science with applied solutions for ecological challenges.

EVALUATION OF CARBONIC ANHYDRASE IX AND CCL2-CCR2 SIGNALING PATHWAY INHIBITION IN SOLID TUMORS USING *IN VITRO* CELLULAR AND *IN VIVO* MOUSE MODEL (Biochemistry)

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Dissertation defended:
30 May 2025

Despite recent breakthroughs in cancer treatment, the survival of paediatric patients presenting with advanced-stage or relapsed solid tumours remains poor. Tumours employ a variety of compensatory mechanisms to evade tumour killing. Tumour hypoxia and associated peritumoral acidosis significantly contribute to cancer progression and treatment resistance. CAIX, a hypoxia-induced enzyme, helps cancer cells overcome intracellular acidosis and survive whereas CCL2-CCR2 axis promotes immunosuppressive tumour microenvironment. Both, CAIX enzyme and CCL2-CCR2 chemokine signaling axis have become attractive targets in cancer therapy development. Our work highlights the compensatory mechanisms involved when CAIX or CCL2-CCR2 axis is inhibited in paediatric cancer solid tumour models, such as neuroblastoma and osteosarcoma. We demonstrate feasibility of combining CAIX inhibition with CCR2 antagonist in neuroblastoma xenograft model. In addition, we evaluated the CAIX inhibitor synthetic compounds' suitability and limitations for CAIX expressing tumour's recognition in vivo. Additionally, we show how hypoxic conditions alter the expression of different cellular markers and impair CCR2 antagonist effects in the experimental 143B osteosarcoma model. All these findings can serve as a foundation for future hypoxic tumour niche recognition-based therapy and diagnostics development.

STRUCTURAL AND FUNCTIONAL STUDIES OF ADSORPTION COMPLEX OF THE *KLEBSIELLA* INFECTING BACTERIOPHAGE RaK2 (Biochemistry)

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Dissertation defended:
9 June 2025

Klebsiella spp. bacteria pose a significant threat to human health, particularly in individuals with compromised immune systems. Therefore, effective strategies to combat this pathogen must be developed. *Klebsiella* genus bacteria are known to exhibit multi-antibiotic resistance and are difficult to eradicate due to their virulence factors. However, bacteriophages may offer hope to the affected patients, as their inherent nature is to 'reproduce' and 'kill' by exploiting bacterial vitality. The RaK2 virus is one of many bacteriophages capable of lysing *Klebsiella pneumoniae*. However, its uniqueness lies in its genome size (as it is classified as a jumbo phage belonging to the *Alcyoneusvirus* genus) and in the distinctive morphology of its adsorption complex. Notably, viruses within this genus remain largely understudied, particularly regarding the structure and function of their adsorption complexes. Therefore, the primary aim of this dissertation was to investigate the branched long tail fibres located within the adsorption complex of the RaK2 phage. The study encompassed a variety of experiments focused on the proteins that comprise the fibre, including the determination of their location, structure, and function. Specifically, structural modelling, phage adsorption inhibition assays, immuno-labelling, and enzymatic specificity analyses were utilised. As a result, a probable architecture of the RaK2 branched long tail fibre was proposed, and key proteins involved in initiating phage infection – gp531 and gp098 – were identified. Furthermore, the enzymatic specificity of the associated depolymerase gp531 was determined to be beta-(1,4)-glucosidase, which targets and degrades the capsular polysaccharide of *K. pneumoniae* K54 serotype.

INSIGHTS INTO TYPE III CRISPR-Cas IMMUNITY: MECHANISMS OF Csm6 DEACTIVATION AND A COMPREHENSIVE CHARACTERIZATION OF THE Lon-SAVED EFFECTOR (Biochemistry)

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Dissertation defended:
13 June 2025

Bacteria and archaea use CRISPR-Cas systems to defend themselves against viral infection. These adaptive immune mechanisms detect and neutralise invading nucleic acids. Among them, type III CRISPR-Cas systems are unique: alongside viral RNA degradation, they trigger an additional layer of defence by producing signaling molecules, cyclic oligoadenylates (cAn), which activate various downstream effectors. This thesis explores two of these effectors: the ribonuclease Csm6 and a Lon-SAVED fusion protein CalpL of the tripartite CalpL-CalpT-CalpS effector. Csm6 is activated by cA6 binding to its CARF domain, triggering HEPN domain-mediated RNA degradation. Cell metabolite analysis and biochemical assays revealed that Csm6 also degrades its own activator, cA6, creating a built-in self-limiting loop. The second part characterises the CalpL-CalpT-CalpS effector, which responds to cA4. Biochemical and *in vivo* toxicity assays showed that cA4 binding activates CalpL to cleave the anti-σ factor CalpT, marking it for degradation by cellular proteases and thereby releasing the σ factor CalpS. CalpL also degrades its own activator, functioning as a self-limiting effector. Furthermore, structural studies revealed how filament formation governs CalpL's protease and the regulatory ring nuclease activities. Together, these findings show how type III effectors integrate cAn signaling with intrinsic regulatory mechanisms.

EVALUATION OF THE PROPERTIES AND DELIVERY POTENTIAL OF *SACCHAROMYCES CEREVISIAE* L-BC-1 VIRUS-DERIVED NANOPARTICLES (Biochemistry)

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Dissertation defended:
25 June 2025

Virus-like particles (VLPs) are nanostructures composed of self-assembling viral proteins. For VLP synthesis in this study, we selected the L-BC-1 virus found in *Saccharomyces cerevisiae* that lacks an extracellular phase. The stability and encapsulation potential of VLPs derived from the L-BC-1 virus was evaluated to assess their suitability for the development of VLP-based delivery systems. The recombinant capsid protein Gag of the L-BC-1 virus was successfully synthesised in *Escherichia coli* and *S. cerevisiae*, forming symmetrical and spherical particles approximately 40 nm in diameter. The stability of the Gag-derived VLPs was assessed using dynamic light scattering (DLS), transmission electron microscopy (TEM), and thermal shift assays (TSA). The particles maintained a stable size for up to 24 weeks under various conditions. Structural particle degradation was observed at high temperatures, in alkaline environment or upon exposure to urea. VLPs produced in *E. coli* exhibited greater sensitivity to environmental conditions compared to those synthesised in yeast. Using passive diffusion, a small peptide nisin Z was encapsulated into the VLPs – resulting particles demonstrated antibacterial activity. Additionally, a large amount of red fluorescent mCherry protein was encapsulated via genetic fusion, and the ability of such particles to enter mammalian cells was demonstrated. It was shown that VLPs synthesised in bacteria exhibited cytotoxic effects on mammalian cells, while those produced in yeast did not. These findings provide valuable insights into the properties of the L-BC-1 virus and support its potential application in the development of delivery systems.

ADIPOSE STEM CELL SECRETOME AND BIOPRINTED TISSUES: POTENTIAL TREATMENTS OF URETHRAL FIBROSIS (Biochemistry)

Povilas Barasa

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Dissertation defended:
4 July 2025

Strictures, or critical narrowing of the urinary tract, affect between 200 and 1200 per 100 000 people. Damage to the urethra triggers uncontrolled scarring, or development of fibrosis, which leads to the narrowing of the urinary vessel. Current treatment options face significant challenges, including recurrence and limitations in available grafts. The use of stem cells or their products, such as the secretome, or their application in manufacturing artificial tissue, has attracted significant interest. In this study, we aimed to identify fibrosis markers in fibroblasts that could be modulated by human adipose stem cell conditioned medium. Our *in vitro* results suggested a profibrotic outcome when fibroblasts were treated with secretome-enriched medium. Therefore, we continued by investigating the application of stem cells in manufacturing artificial urethral tissue. Using a hydrogel-based bioprintable ink, we created artificial tissue with properties similar to natural urethra and developed protocols for differentiation of stem cells towards smooth muscle and epithelium. The efficacy of this approach was evaluated in reconstruction of the urethra in a rabbit model, and results were verified using human stem cells *in vitro*.

VIRULENCE STRATEGIES OF THE EMERGING OPPORTUNISTIC PATHOGEN *STENOTROPHOMONAS MALTOPHILIA* (Biochemistry)

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Dissertation defended:
26 August 2025

Stenotrophomonas maltophilia is a Gram-negative, multidrug-resistant opportunistic human pathogen causing hard-to-treat infections in immunocompromised patients. This study aimed to compare the virulence-associated characteristics of clinical and environmental *S. maltophilia* isolates and to identify the key traits that enable this pathogen to cause infections. We showed that the ability to grow and express virulence-related traits at human body temperature was significantly more characteristic of clinical *S. maltophilia*, and tolerance to human body temperature could be used to distinguish between clinical and environmental *S. maltophilia* isolates. We also identified and characterised previously unreported virulence traits of *S. maltophilia* that contribute to immune evasion, including the formation of a polysaccharide capsule and the secretion of proteases capable of degrading host complement system proteins. These findings deepen our understanding of the virulence strategies employed by the opportunistic pathogen *S. maltophilia*.

EXPLORATION OF ANTICANCER COMPOUNDS AND ENZYME-PRODRUG SYSTEMS (Biochemistry)

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Dissertation defended:
27 August 2025

The ongoing challenges of drug resistance and systemic toxicity in cancer treatment highlight the urgent need for more effective and selective therapeutic strategies. This thesis explores two complementary approaches: developing novel anticancer compounds and investigating enzyme-prodrug systems for targeted cancer therapy. Several water-soluble indirubin derivatives were evaluated for cytotoxicity, identifying compounds with promising anticancer activity. In parallel, a collection of modified 5-fluoropyrimidine nucleosides was proposed as prodrugs suitable for activation by specific bacterial enzymes. Two amidohydrolases, YqfB and D8_RL, were shown to catalyse the hydrolysis of N4-acylated 5-fluorocytidines, yielding the active anticancer agent 5-fluorocytidine. Three cytidine deaminases – CDA_EH, CDA_F14, and CDA_Lsp – efficiently converted various S4-/N4-/O4-modified 5-fluoropyrimidines into cytotoxic 5-fluorouridine or 5-fluoro-2'-deoxyuridine. Several novel enzyme-prodrug pairs were identified, offering high specificity and potential for clinical application. These findings contribute to developing more selective cancer therapies and support ongoing research into enzyme-prodrug systems.

REMODELING OF ARTIFICIAL LIPID MEMBRANES INDUCED BY PROINFLAMMATORY S100 FAMILY PROTEINS (Biochemistry)

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Dissertation defended:
12 November 2025

Neuronal cell death induced by cell membrane damage is one of the major hallmarks of neurodegenerative diseases. Neuroinflammation precedes the loss of neurons; however, whether and how inflammation-related proteins contribute to the loss of membrane integrity remains poorly understood. This study aimed to investigate the interactions of the proinflammatory proteins S100A8, S100A9, and the S100A8/A9 complex with an artificial lipid bilayer mimicking the neuronal plasma membrane. For the first time, it was demonstrated that direct interactions of S100A8, S100A9, and the S100A8/A9 complex with an anionic membrane compromise lipid bilayer integrity. High-speed atomic force microscopy enabled real-time observation of morphological changes induced by S100A8 and S100A8/A9, indicating that membrane disruption proceeds via a detergent-like mechanism. In contrast, conventional atomic force microscopy demonstrated that insertion of S100A9 into the membrane induces lateral expansion of lipid molecules and reduces membrane mechanical stiffness. Furthermore, it was found that changes in membrane composition significantly influenced S100 protein aggregation and the potential formation of neurotoxic assemblies. These findings not only enhance our understanding of the links between inflammation and neurodegeneration but also may facilitate the development of novel diagnostic and therapeutic strategies.

INVOLVEMENT OF THE GUT MICROBIOTA IN THE DEVELOPMENT OF FOOD ADDICTION (Biochemistry)

Solveiga Samulėnaitė

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Dissertation defended:
21 November 2025

In Western society, the high abundance of palatable foods increases the risk of food addiction characterised by compulsivity, persistence, and high motivation towards palatable foods. Although food addiction has overlapping mechanisms with drug addiction, the exact neurobiology is not yet fully understood. Recently, the gut microbiota has gained attention for its role in brain function via the gut-brain axis. Therefore, this thesis investigates the neurobiology of food addiction and the gut microbiota-brain crosstalk. Using an operant model in mice, reinforced by chocolate-flavoured pellets, we first employed a chemogenetic approach to study cognitive inflexibility linked to food addiction. Secondly, we identified common microbiota signatures in humans and mice, revealing a distinct gut microbiota profile in individuals with food addiction. This discovery led to microbiota-based interventions, showing the protective effects of potential pre- and probiotics against food addiction development. Lastly, we explored faecal microbiota transplantation and its impact on cognitive performance in mice. Overall, our findings suggest that microbiota-based therapies could prevent cognitive impairments and the development of food addiction.

MICROBIOTA-GUT-BRAIN AXIS MODULATION BY MICROBIAL METABOLITES AND MICROBIOTA-BASED INTERVENTIONS (Biochemistry)

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Dissertation defended:
8 December 2025

The microbiota-gut-brain axis is a novel scientific field that combines neuroscience and microbiology. This thesis investigated the role of the gut microbiota in CNS disorders on multiple levels. We identified reduced microbial diversity, a change in metabolic profile, and the absence of beneficial taxa in Lithuanian children with autism spectrum disorders (ASD). Faecal microbiota transfer (FMT) experiments demonstrated that ASD-associated microbiota can induce long-lasting changes in the microbial community, metabolome, and behaviour in adult mice, while maternal exposure during gestation induced sex-specific effects on offspring gut and plasma metabolome, behaviour, and hippocampus gene expression. Amino acid and in particular tryptophan metabolite changes were prominently observed in adult and maternal FMT exposure models. We characterised host indole metabolism and identified metabolites capable of crossing the blood–brain barrier. To emphasise the potential of mild microbiota-based interventions, we showed that *Akkermansia muciniphila* and galactooligosaccharides improved microbial diversity, intestinal and metabolic function, and alleviated cognitive and behavioural deficits in an Alzheimer's disease mouse model. Together, our findings provided evidence that the gut microbiota and its metabolites regulate the host's metabolic profile, brain physiology, behaviour, and indicate that microbiota-targeted interventions are promising strategies to target CNS disorders.

MODULATION OF MICROGLIA FUNCTIONS IN AGEING AND NEUROINFLAMMATION: FROM MECHANISMS TO THERAPEUTIC INTERVENTIONS (Biochemistry)

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Dissertation defended:
9 December 2025

Aging fundamentally alters microglial activity, promoting chronic neuroinflammation, metabolic changes, and reduced functional capacity, which contribute to the development of neurodegenerative diseases. This dissertation examines how aging, diet, the gut microbiota, and the endocannabinoid system interact to influence microglial functions and evaluates therapeutic interventions targeting these processes. First, using APP/PS1 mouse models of Alzheimer's disease, long-term administration of the next-generation probiotic *Akkermansia muciniphila* was shown to reduce anxiety-like behaviour, improve cognitive performance, and decrease microglial cell density in the hippocampus. To precisely analyse age-associated microglial states, an optimised protocol for isolating microglia from aging mouse brains was developed, ensuring high purity and preservation of the *in vivo* resting phenotype. In aged mice, long-term consumption of a high-fat diet induced anxiety, memory impairments, and dysbiosis, and in microglia reduced phagocytosis, increased reactive oxygen species production, and accelerated cellular senescence. Administration of prebiotics (galactooligosaccharides and fructooligosaccharides) attenuated these behavioural, microglial functional, and microbiota changes by preserving beneficial bacteria and restoring microglial activity. Finally, modulation of the endocannabinoid system was shown to regulate microglial functions in an age-dependent manner: CB1 and CB2 receptor agonists differentially affected phagocytosis and oxidative stress in young and aging cells. This work evaluates the interplay between aging, the gut microbiota, and the endocannabinoid system in the context of microglial function and regulation. Addressing these knowledge gaps is essential for the development of novel, personalised therapeutic strategies aimed at reducing age-related neuroinflammation and neurodegenerative processes.

EPIGENETIC AND MOLECULAR STUDIES OF ENDOMETRIAL-DERIVED TISSUES AND STROMAL CELLS IN THE CONTEXT OF REPRODUCTIVE SYSTEM DISORDERS (Biochemistry)

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Dissertation defended:
16 December 2025

Infertility affects up to 12% of reproductive-age couples worldwide; however, diagnostic and treatment methods for infertility still have limitations. As a crucial component for successful embryo implantation, the endometrial tissue is a suitable candidate for investigating the mechanisms underlying infertility. One-third of infertile women are diagnosed with endometriosis. Although the disease is common, 60% of patients exhibiting symptoms characteristic of endometriosis remain undiagnosed, and the time from symptom onset to final diagnosis can be as long as 11 years. This dissertation research was to study the molecular and epigenetic differences associated with reproductive disorders in female reproductive tissues and stromal cells. The research examined the expression differences of molecules important for endometrial receptivity in the endometrial tissues, stromal cells, and extracellular vesicles of healthy females and those with reproductive pathologies. We found that in the endometrium of women with reproductive disorders, the expression of miRNA-34a-3p, miRNA-125b-5p, and miRNA-223-5p was significantly decreased. The expression of pro-inflammatory genes *CSF2* and *RELA*, the angiogenesis-promoting gene *PDGFA*, and the implantation and decidualization related genes *MUC1* and *HAND2* was increased. Specific miRNAs and proteins with altered expression were identified in extracellular vesicles derived from endometriotic lesions and ovarian endometriomas, which could serve as potential biomarkers of endometriosis after validation of their reliability.

ANALYSIS OF CYTOGENETIC AND EPIGENETIC MARKERS IN LYMPHOCYTES OF PATIENTS WITH DIABETES (Biology)

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Dissertation defended:
15 January 2025

The incidence of diabetes mellitus (DM) is increasing rapidly worldwide and has reached pandemic proportions in recent years. The World Health Organisation has recognised DM as one of the leading causes of disability and death, listing it among the priority non-communicable diseases The aim is to reduce the incidence of DM and its complications through science-based recommendations. However, DM is a highly heterogeneous and complex disease, and the pathogenesis of DM and its complications is still not fully understood. There is insufficient or contradictory data regarding the impact of oxidative stress on DNA damage, epigenetic changes, the development patterns of diabetic complications, and the differences between DM types. The treatment of microvascular diabetic complications, especially diabetic polyneuropathy, is also poorly effective. In this research, DM patients were examined for diabetic neuropathy using various instrumental methods and those methods were compared with each other and between type 1 and type 2 DM. Cytogenetic (chromosomal aberrations, sister chromatid exchanges, micronuclei) and epigenetic (microRNA) analyses, oxidative blood plasma markers were analysed in DM patients and the control group, and obtained results were linked to clinical data. The effect of alpha-lipoic acid (an antioxidant used in the treatment of diabetic neuropathy) on cytogenetic and oxidative markers was also evaluated in patients with diabetes.

IMMUNE RESPONSE IN ATOPY: POLYMORPHISM OF VITAMIN D RECEPTOR AND VITAMIN D-BINDING PROTEIN GENES (Biology)

Daina Bastytė

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Dissertation defended:
21 February 2025

The pathogenesis of atopy is characterised by a complex and heterogeneous immune response. Vitamin D and single nucleotide polymorphisms (SNPs) in genes related to its metabolism, such as the vitamin D receptor (VDR) and vitamin D-binding protein (GC), are thought to play a crucial role in immune regulation. This study aims to determine the significance of VDR and GC gene SNPs for the immune response during atopy. The objectives were: (1) to examine the vitamin D levels in the group of patients with atopy and compare them with data from the control group, (2) to identify polymorphisms in the vitamin D receptor gene and the vitamin D-binding protein gene and assess their relationship with vitamin D levels in the presence or absence of atopy, (3) to determine the levels of immune markers (total IgE, blood eosinophils, T lymphocytes, and associated cytokines) during atopy and evaluate their relationship with vitamin D, and (4) to evaluate the immune marker profile while considering the variants of the vitamin D receptor and vitamin D-binding protein gene polymorphisms. Six VDR and four GC gene SNPs were analysed, revealing associations with vitamin D and immune marker levels. The study found significant relationships between specific gene SNPs and vitamin D levels in the study groups. Immune marker levels during atopy varied depending on specific gene SNPs. These findings clarify the role of vitamin D and genetic mechanisms in the pathogenesis of atopy, contributing to advancements in personalized medicine.

FACTORS SHAPING POPULATION GENETIC STRUCTURE OF COMMON ROACH (*RUTILUS RUTILUS*) AND DUCKWEED (*LEMNA MINOR*) (Biology)

Ieva Ignatavičienė

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Dissertation defended:
28 February 2025

The common roach (*Rutilus rutilus*) is a widespread fish belonging to the *Cyprinidae* family, capable of adapting to various types of water bodies, therefore fish populations are found in various freshwater bodies in Europe and most of the Asian continent. The duckweed (*Lemna minor*) is one of the most widespread species of free-floating plants in Lithuania and throughout the world, and usually reproduces vegetatively by budding, forming genetically identical clones. Using the sequences of the mitochondrial DNA (mtDNA) adenosine triphosphate 6 (ATP6) gene and the D-loop region of the common roach, as well as the nuclear ascorbate peroxidase (APx) and chloroplast microsatellite markers of duckweed, population studies were conducted in the regions of Lithuania and Latvia. The impact of anthropogenic factors such as thermal pollution or electromagnetic radiation and environmental conditions on the genetic variability of the populations of the common roach and duckweed was also assessed. The high genetic similarity between geographically distant roach populations revealed specific relationships depending on different characteristics. Also, high genetic similarity was found between geographically distant clones of small floating plants collected in stagnant water bodies. Comparing roach samples collected in 2017 and 2022 in Lake Drūkšiai, the former cooler of Ignalina NPP–, using molecular markers of the mtDNA ATP6 gene and D-loop region sequences, a significant decrease in genetic diversity was found in the roach population of this lake. Exposure of duckweed clones grown inside a Helmholtz coil to low-frequency (50 Hz) electromagnetic radiation, when the electromagnetic field density reaches 2 µT (0–11 weeks) and 300 µT (12–48 weeks), initiates changes in genetic variability in the sequences of the (ascorbate peroxidase) APx, (glutathione peroxidase) GPx and (catalase) Cat genes due to an increasing number of point mutations mainly in the promoter and intron regions.

IMPACT OF GASTROINTESTINAL CANCER THERAPIES ON THE GUT MICROBIOME: FINDINGS FROM CLINICAL STUDIES AND AN *IN VITRO* MODELLING (Biology)

Kristina Žukauskaitė

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Dissertation defended:
7 March 2025

Gastrointestinal cancers are significant contributors to global mortality and pose a major challenge to public health. A critical yet underexplored aspect of these cancers is their association with the gut microbiome, which changes during the development of gastrointestinal cancer and throughout its treatment. However, the complex interactions between cancer progression, treatment, side effects of the cancer treatment, and the gut microbiome remain largely understudied. Animal models are frequently used in cancer research but fall short due to ethical considerations and biological differences from humans, while traditional *in vitro* systems lack the complexity to replicate the dynamic interactions between host cells and the gut microbiome. Bioreactor-based *in vitro* models offer a more comprehensive platform, yet models including stool microbiome are not widely utilised, especially in examining side effects of cancer treatment. A prevalent side effect is the oralization of the gut microbiome, characterised by the invasion and colonisation of oral bacteria within the gastrointestinal tract, often resulting from long-term usage of medications or surgical interventions. In this doctoral dissertation, we aim to reduce the reliance on animal models by developing an easy-to-use *in vitro* model that includes the human stool microbiome. We chose this approach to replicate the human gut environment better, providing a more accurate platform for studying the interactions between gastrointestinal cancers, their treatments, and the gut microbiome. Research often centres on creating new cancer drugs, but in our study, we emphasise the reduction of the side effects of current treatment to improve the well-being of cancer patients. We adapted a newly developed *in vitro* model to evaluate various probiotic and prebiotic combinations that could potentially reduce post-therapy side effects of oralization.

VECTOR-BORNE PROTOZOAN AND BACTERIAL PATHOGEN OCCURRENCE AND DIVERSITY IN BATS (MAMMALIA: CHIROPTERA) AND THEIR ECTOPARASITES (Biology)

Povilas Sakalauskas

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Dissertation defended:
14 March 2025

Bats (Mammalia: Chiroptera) are known as hosts of various viruses, bacteria, and protozoan pathogens, associated with well-known disease outbreaks worldwide. While the role of bats in virus transmission has been extensively studied, there is significantly less research on their involvement in transmitting protozoan and bacterial pathogens. Meanwhile, similar studies had not been conducted in Lithuania until now. During this study, seven flea species parasitising bats and one tick species were identified for the first time in Lithuania. Using molecular methods, the prevalence of five different pathogen groups – *Bartonella* spp., *Borrelia* spp., *Rickettsia* spp., *Mycoplasma* spp., and *Babesia* spp. – was determined in bat blood and internal organ samples, as well as in ectoparasites collected from bats. The study also identified unique genotypes of *Bartonella* and *Mycoplasma* pathogens. Additionally, the results indicated that in Lithuania, bats and their ectoparasites could potentially be hosts to pathogenic bacteria for humans. The findings from this study enhance our understanding of the ecology of the pathogens studied and potential transmission routes through ectoparasites parasitizing bats.

APPLICATION OF MUSCLE STEM CELLS FOR THE TREATMENT OF EXPERIMENTAL ACUTE KIDNEY INJURY (Biology)

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Dissertation defended:
27 March 2025

Acute kidney injury (AKI) is a common clinical syndrome characterised by a sudden decline in kidney function. AKI is diagnosed in 10–15% of hospitalised patients. Renal replacement therapy is the only treatment option for patients with AKI. Mesenchymal stem cells promote kidney regeneration and are considered a promising treatment for AKI. Skeletal muscle-derived stem/progenitor cells, isolated from skeletal muscles, are multipotent, exhibit long-term proliferation, have a high regenerative capacity, and promote tissue recovery. Therefore, they were selected for this study. The aim of the study was to develop an experimental treatment for AKI using skeletal muscle-derived stem/progenitor cells, evaluate their cytokinetics, and assess their effectiveness in an AKI model. Skeletal muscle-derived stem/progenitor cells were isolated, cultured, characterised, and compared with bone marrow mesenchymal stem cells. Subsequently, the effect of skeletal muscle-derived stem/progenitor cells on kidney regeneration was investigated. Finally, the differences in effectiveness and cytokinetics between the two cell types in the AKI model were evaluated. To our knowledge, we were the first group to demonstrate that skeletal muscle-derived stem/progenitor cells are an alternative source of stem cells for AKI treatment. They offer advantages such as the abundance and accessibility of muscle tissue for cell isolation, ease of isolation and expansion, and a high proliferation rate.

THE ROLE OF INTESTINAL EPITHELIAL microRNAs AND GUT MICROBIOTA IN THE PATHOGENESIS OF ULCERATIVE COLITIS (Biology)

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Dissertation defended:
3 June 2025

Ulcerative colitis (UC) is a chronic inflammatory bowel disease whose pathogenesis is driven by a complex interplay between epithelial barrier dysfunction, immune dysregulation, alterations in the gut microbiota, and host genetic and environmental factors. Despite extensive research, the functional significance of specific molecular and microbial changes in UC development and progression remains incompletely understood. This dissertation investigates the role of colonic epithelial microRNAs (miRNAs) and the gut microbiota in UC pathogenesis, with particular emphasis on their interaction and combined impact on intestinal barrier integrity. Using small RNA sequencing, spatially distinct miRNA expression profiles of colonic epithelial cells located at the crypt top and crypt bottom were identified for the first time, revealing compartment-specific regulatory mechanisms. In addition, UC-associated faecal microbiota was characterised, highlighting the potential role of stable commensal bacteria in regulating epithelial responses. By applying an advanced colonic epithelial organoid model derived from UC patients and healthy controls, epithelial–microbiota interactions and global DNA methylation dynamics were analysed during long-term culture. These findings provide new insights into UC-specific molecular and microbiological mechanisms and support the development of biomarkers and innovative therapeutic strategies targeting the epithelial–microbiota axis.

BIOMARKERS IDENTIFYING MOLECULAR ENDOTYPES OF UNEXPLAINED INFERTILITY IN MENSTRUAL BLOOD EXTRACELLULAR VESICLES (Biology)

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Dissertation defended:
9 June 2025

Infertility affects approximately 17.5% of the adult population worldwide, with about one-third of cases classified as unexplained. The diagnosis of unexplained infertility remains challenging due to the lack of sensitive and specific biomarkers, as well as the absence of personalised treatment approaches. This study investigated potential biomarkers of unexplained infertility using menstrual blood samples, including menstrual blood-derived mesenchymal stromal cells, and extracellular vesicles isolated from both menstrual blood serum and stromal cells. Detected biomarkers aim to stratify patients by molecular endotypes associated with different underlying aetiologies. Such stratification could enable the development of personalised treatment strategies, potentially allowing patients to conceive without *in vitro* fertilisation. For the first time, molecular endotypes of unexplained infertility were identified and characterised. Proteomic analysis revealed consistently lower levels of proteins involved in various molecular pathways, particularly those related to cell adhesion, lipid metabolism, oxidative stress response, apoptosis, and immune function, in samples from patients with unexplained infertility. The most significant alterations were found in extracellular vesicles derived from menstrual blood serum, highlighting its potential as a valuable diagnostic source for molecular endotyping. Distinct combinations of proteins associated with specific endotypes were identified and validated in these extracellular vesicles. Importantly, various endotypes or their combinations were present in different patient, underscoring the necessity for personalised diagnostic and therapeutic strategies in the management of unexplained infertility.

AIR POLLUTION EXPOSURE-INDUCED DYSFUNCTION OF HUMAN BRAIN MICROVASCULAR ENDOTHELIUM AND IMMUNE CELLS *IN VITRO* (Biology)

Justina Pajarskienė

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Dissertation defended:
19 June 2025

This doctoral dissertation investigates the cellular and molecular responses of human brain microvascular endothelial cells and immune cells to airborne pollution particles, specifically carbon black particles (CBP) and low-density polyethylene (LDPE) micro- and nanoparticles. Using *in vitro* models of human microglia, monocyte-derived macrophages, and hCMEC/D3 endothelial cells, the study explores particle uptake, oxidative stress, inflammation, and blood-brain barrier (BBB) integrity. Results show that CBP activates NRF2 signaling but downregulates downstream antioxidant and autophagy-related proteins, suggesting impaired cellular defence. LDPE exposure reduces NRF2 levels, increasing endothelial vulnerability to oxidative stress. Additionally, CBP exposure enhances transendothelial electrical resistance (TEER) and caveolin expression without affecting tight junctions, indicating mechanical barrier obstruction. This research highlights the differential effects of particles and the importance of composition in toxicity. The findings contribute to the development of advanced *in vitro* models and provide new insights into pollution-related neurotoxicity, with potential implications for public health and regulatory strategies.

THE EFFECT OF RENAL ISCHEMIA/REPERFUSION ON MITOCHONDRIAL CARDIOLIPIN OXIDATION AND RESYNTHESIS: INVESTIGATION OF MOLECULAR MECHANISMS (Biology)

Arvydas Strazdauskas

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Dissertation defended:
25 June 2025

Cardiolipin is a mitochondrial phospholipid that is important for the structure and function of mitochondria. Ischemia/reperfusion induces oxidative stress, during which cardiolipin can be oxidized, hydrolysed and, as a result, loses its characteristic chemical properties, leading to disruption of mitochondrial functions. There is a lack of information on what changes in cardiolipin occur in the kidneys during ischemia/reperfusion. The aim of this study was to evaluate the molecular mechanisms of the effect of renal ischemia/reperfusion on structural and quantitative changes in cardiolipin. The study used two models: rat kidney ischemia/reperfusion *in vivo* and human kidney cell hypoxia/reoxygenation *in vitro* models. Chromatography-mass spectrometry analysis identified 16 different cardiolipin species in rat kidneys and human renal cells. A decrease in cardiolipin levels and an increase in the oxidation products of the dominant tetra-linoleoyl cardiolipin was observed during ischemia *in vivo*, but after ischemia/reperfusion the level of tetra-linoleoyl cardiolipin increased due to the increased expression of cardiolipin remodeling enzyme tafazzin gene. In human renal cells, hypoxia/reoxygenation *in vitro* activates the gene expression of cardiolipin synthase and the remodeling enzyme lysocardiolipin acyltransferase 1, resulting in an increase in the levels of these enzymes and the levels of cardiolipin as well, despite the increased oxidative stress during reoxygenation.

RECOMBINANT BACTERIOCINS: NOVEL NARROW SPECTRUM ANTIMICROBIAL AGENTS (Biology)

Indrė Karaliūtė

Scientific supervisor:
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Dissertation defended:
26 June 2025

Antibiotics are the most effective treatment for bacterial infections, including those caused by *Klebsiella* species. However, inappropriate and excessive use of antibiotics promotes the emergence and spread of multidrug-resistant bacteria. In some regions, resistance of *Klebsiella* to antibiotics reaches up to 70%, with associated mortality rates ranging from 40% to 70%, highlighting the urgent need for alternative antimicrobial strategies. One such alternative is bacteriocins – ribosomally synthesised peptides or small proteins that act against closely related bacterial species and exhibit a narrow spectrum of activity with a lower risk of resistance development. For this reason, recombinant bacteriocins KvarIa and KvarM were selected as potential therapeutic agents for the treatment of infections caused by antibiotic-resistant *Klebsiella* species. The aim of this study was to evaluate the efficacy of recombinant bacteriocins in treating *Klebsiella*-induced infections using experimental animal models and to assess their impact on the gut microbiota. The results demonstrated that *Klebsiella quasipneumoniae* (DSM® 28212™) colonised the murine gut only after antibiotic treatment disrupted the native microbiota, and that recombinant bacteriocin KvarIa significantly reduced *K. quasipneumoniae* levels in the intestine. In addition, the study confirmed a strong antibacterial effect of bacteriocin KvarM against *Klebsiella pneumoniae* (ATCC® 43816™) during intestinal colonisation.

THE KINETICS OF CELL-FREE DNA IN RESPONSE TO EXTERNAL AND INTERNAL FACTORS (Biology)

Ema Juškevičiūtė

Scientific supervisor:
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Dissertation defended:
26 June 2025

The general aim of the research was to determine the impact of different internal and external instances, such as increased rectal temperature, three-week sprint interval training (SIT), and muscle-damaging exercise, on cell-free DNA (cfDNA) kinetics. Using a series of experimental studies, cfDNA responses were examined under conditions of training adaptation, thermal stress, and exercise-induced muscle damage without metabolic stress. The results demonstrated adaptive changes in cfDNA following SIT in both young and older men, with reduced plasma cfDNA levels indicating a potential anti-inflammatory response, particularly in the elderly, although three weeks of training was insufficient to induce full adaptation in this group. Incremental elevation of rectal temperature was identified as an independent factor affecting cfDNA concentrations, with exertional heating inducing a greater cfDNA response than exogenous heating. In addition, cfDNA levels increased following both primary and secondary muscle damage and correlated more strongly with neuromuscular fatigue markers than with conventional indicators such as creatine kinase. Furthermore, cfDNA responded to muscle-damaging exercise in a dose-dependent manner, confirming its high sensitivity. Overall, these findings highlight cfDNA as a sensitive biomarker capable of capturing acute and delayed exercise-induced inflammatory responses and support its potential application in exercise physiology and health monitoring.

EVALUATION OF THE IMPACT OF BIOLOGICAL AND CLINICAL FACTORS ON THE OUTCOMES OF UNRELATED DONOR HAEMOPOIETIC STEM CELL TRANSPLANTATION (Biology)

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Dissertation defended:
26 June 2025

Haemopoietic stem cell transplantation (HSCT) is a widely used treatment for haematological and other severe diseases and is often the most effective or the only curative option. In the cases when patients lack an HLA (human leukocyte antigen)-identical sibling donor, HSCT is performed using stem cells from an unrelated donor (UD). However, even in fully HLA-matched patient–donor pairs, acute graft-versus-host disease (aGVHD) and other post-transplant complications may develop, highlighting the importance of additional biological and clinical risk factors. This study analysed the impact of biological factors (HLA mismatches, anti-HLA and anti-non-HLA antibodies) and clinical factors (age, comorbidities, risk scores, and others) of adult patients and their unrelated donors on HSCT outcomes. The results demonstrated that any HLA mismatch, as well as non-permissive HLA-DPB1 mismatches, were independent prognostic risk factors for an increased incidence of grade II–IV acute GVHD. Higher European Society for Blood and Marrow Transplantation (EBMT) risk scores and comorbidity index scores were identified as independent prognostic factors associated with increased transplant-related mortality and reduced overall survival. For the first time, a statistically significant association between *de novo* donor-nonspecific anti-HLA antibodies and an increased risk of grade III–IV acute GVHD following unrelated donor HSCT was demonstrated. In addition, this study is the first to identify a statistically significant association between *de novo* anti-non-HLA antibodies (interacting with granulocyte–macrophage colony-stimulating factor) and the incidence of grade II–IV acute GVHD after HLA-matched unrelated donor HSCT.

DEVELOPMENT AND APPLICATION OF GENETIC TOOLS TO INVESTIGATE THE ROLE OF Tcf21 IN HEART REGENERATION (Biology)

Miglė Kalvaitytė-Repečkė

Scientific supervisor:
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Dissertation defended:
21 August 2025

Unlike adult mammals, zebrafish (*Danio rerio*) can regenerate their hearts after injury, making them an excellent model system for studying the molecular mechanisms of natural heart regeneration. Prior studies have emphasised the vital role of the epicardium, the outermost layer of the heart, in facilitating post-injury heart regeneration. While transcription factor 21 (Tcf21) is known to play a crucial role in the development of the epicardium, our understanding of its function in the adult heart is limited, primarily due to early lethality of traditional knockout models. This study aimed to investigate the role of Tcf21 in heart regeneration of adult zebrafish. To achieve this, we engineered a conditional (floxed) tcf21 allele. By employing globally expressed tamoxifen-inducible CreERT2 recombinase, we achieved nearly complete knockout of Tcf21 in both development and adulthood. Our results indicated that the absence of Tcf21 impairs heart regeneration, leading to a higher amount of collagen and fibrin present at the injury site by 60 days post-cryoinjury. Notably, loss of Tcf21 significantly hindered the repopulation of the injury area with dedifferentiated cardiomyocytes, although it did not affect their proliferation. Additionally, we generated a transgenic zebrafish line for the inducible expression of triple-HA-tagged Tcf21, making it possible to identify its direct targets during development and regeneration. Overall, this PhD project delivered novel mechanistic insights into the epicardial regulation of heart regeneration and introduced versatile genetic tools that lay the groundwork for future studies of Tcf21-mediated processes in cardiac biology.

IDENTIFICATION OF EPITRANSCRIPTOMIC M^{6}A BIOMARKERS IN GLIOMA THROUGH PROFILING OF STEM CELLS AND TUMOR TISSUES (Biology)

Rugilė Dragūnaitė

Scientific supervisor:
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Dissertation defended:
26 August 2025

Research into post-transcriptional chemical modifications of RNA is relatively new, and although some knowledge about RNA modifications and their functional importance has emerged, significant results are still limited. Even with m^{6}A, the most well-studied methylation mark mechanism by which it modulates mRNAs remains unclear. The focus on mRNA modifications is particularly intriguing because of their role in protein translation, and alterations in m^{6}A levels in certain malignancies can enhance the translation of oncogenic mRNAs. In glioblastoma (GB), an aggressive and treatment-resistant primary brain tumour, the investigation of m^{6}A changes in glioma stem cells (GSCs) and tumour tissues represents a novel and important research direction, positioned at the crossroads of RNA biology, cancer stem cells, and neuro-oncology. The reversibility and targetability of m^{6}A modifications indicate their potential as therapeutic vulnerabilities, as regulating epitranscriptome modifications in GSCs may influence tumour growth and progression. For the first time, this study analysed m^{6}A-modified and stemness-related mRNA gene candidates in patients' glioma tumour tissues with different glioma grades. Also, this study provides insights into a set of selected mRNAs suitable for future investigations for the development of prognostic and diagnostic glioblastoma treatment methods targeting glioma stem cells. Furthermore, patients' m^{6}A methylation data were deposited in the public repository GEO under the accession number GSE282642. It is worth noting that it was the first methylation data placed into database. The significance of this study goes beyond glioma biology. Studying m^{6}A in glioma stem cells can shed light on how RNA modifications influence stem-like behaviour in malignancies and potentially enlighten similar mechanisms in other cancers.

INVESTIGATION OF MOLECULAR BIOMARKERS IN PROSTATE CANCER FOR PROGNOSIS AND TREATMENT PREDICTION (Biology)

Margarita Žvirblė

Scientific supervisor:
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Dissertation defended:
27 August 2025

This study comprehensively evaluated a spectrum of molecular biomarkers in prostate cancer (PCa) with the aim of determining their diagnostic and prognostic significance, elucidating associations with disease progression, and exploring their potential to improve both diagnostic accuracy and immunotherapy efficacy. The DU-145 PCa cell line model, *Bacillus subtilis* IMVB 7724 lectin, which selectively binds sialic acids, a key component of PD-L1 glycosylation, was employed to address diagnostic challenges arising from PD-L1 glycosylation. Furthermore, the effect of aerosolized atezolizumab was investigated as an innovative drug-delivery strategy for localised modulation of the tumour microenvironment. A principal objective of the study was the identification of robust, non-invasive biomarkers and their combinations capable of capturing PCa heterogeneity. Circulating sPD-L1 and sPD-1 levels were quantified in PCa patients, compared with healthy controls, and correlated with clinical parameters, including AR, PSMA, PCA3 expression, and frequencies of immunosuppressive cell populations such as Tregs and MDSCs. These analyses were aimed at uncovering causal relationships and establishing clinically relevant biomarker panels for PCa detection through liquid biopsy approaches that are readily translatable into clinical practice. Advanced histopathological imaging techniques – nonlinear multimodal optical microscopy and its modalities, including second- and third-harmonic generation – enabled high-resolution assessment of collagen remodeling, a critical component of the tumour microenvironment. Texture-based image analysis yielded quantitative metrics of collagen architecture, facilitating correlation with molecular and clinical data. Collectively, the findings of this study provide valuable insights that may inform the development of personalised diagnostic algorithms and immunotherapy strategies, improve risk stratification and prognostic assessment, and foster the discovery of novel therapeutic targets in PCa.

DEVELOPMENT OF REPRODUCTIVE TISSUE TRANSPLANTATION *IN VIVO* AND MATURATION *IN VITRO* METHODS (Biology)

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Dissertation defended:
28 August 2025

This doctoral dissertation explores the issue of fertility preservation and restoration in cancer patients, with a particular focus on still-experimental strategies – pre-transplantation manipulation of ovarian tissue (OT) and the construction of artificial ovaries. These are the first scientific studies in Lithuania to use cryopreserved human OT. The aim of this research was to develop safe and effective fertility restoration strategies by evaluating *in vivo* ovarian tissue transplantation, *in vitro* follicle activation, and artificial ovary construction models. The study applied OT cryopreservation techniques, xenotransplantation, microRNA and gene expression analyses, as well as follicle maturation and 3D structural engineering technologies to comprehensively assess the viability and functionality of OT. The results show that the applied slow-freezing and rapid-thawing protocol is effective in preserving tissue viability and functionality. Additional pre-treatment of OT with growth factor VEGF-A and antioxidant rutin before xenotransplantation did not produce a significant improvement in transplantation outcomes. Moreover, primordial follicles isolated from cryopreserved OT remained viable and successfully developed into functional higher development stage follicles within 3D structures *in vitro*, particularly when OT stromal cells were introduced into the artificial ovary model. The findings of this dissertation provide not only theoretical insights but also practical evidence supporting the clinical applicability of the slow-freezing method for ovarian tissue. One of the most significant outcomes of this work is an application of this technology in Lithuania for prepubertal girls.

INFLUENCE OF SOIL MICROBIOME COMPOSITION AND FUNCTIONALITY ON PLANTS VEGETATIVE PROCESSES (Biology)

Raimonda Mažylytė

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Dissertation defended:
29 August 2025

In recent years, a decrease in soil fertility has been recorded all over the world. The main factors reducing soil fertility are global climate change, temperature rise, changing soil moisture and water shortage, and the rapid decrease in organic and mineral substances available for plant development. With the rapid development of biotechnology, bioproducts are increasingly being used to restore degraded soil, as they improve the efficiency of plant nutrition, cause changes in vital and structural processes, and increase product yield and quality. During this project, an innovative bioproduct prototype was created to improve plant vegetative processes. It combines microorganisms isolated and selected from the rhizosphere of the roots of various agricultural plants, which secrete biologically active compounds that stimulate plant vegetative processes. During the scientific project, the composition of the most compatible selected microorganisms was determined, which is able to provide plants with an effective supply of nutrients and resistance to abiotic and biotic stresses. Laboratory-scale fermentation processes was also developed, in which several different bacterial genera are cultivated in one environment, and such results can be applied in large-scale industrial fermentation processes in the future. The biopreparations *Priestia* sp. IIIDEG4, *Paenibacillus* sp. IIIDEG36 + *Priestia* sp. IIIDEG93 and *Bacillus* sp. IJAK27 + *Pseudomonas* sp. IJAK44 + *Streptomyces* sp. IJAK91, composed during the fermentation processes, were identified as competitive microbiological products with unique properties and effective applicability in agriculture.

IDENTIFICATION AND MOLECULAR CHARACTERIZATION OF THE CAUSATIVE AGENTS OF CENTRAL NERVOUS SYSTEM INFECTIONS (Biology)

Anželika Slavinska

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Dissertation defended:
4 September 2025

In recent years, whole genome sequencing has emerged as a crucial tool in epidemiological surveillance. The molecular characterisation of disease-causing microorganisms provides valuable insights into the biology of infectious agents, their virulence, and enables the timely detection of newly emerging and antibiotic-resistant strains. This study analysed isolates of *Neisseria meningitidis* and *Listeria monocytogenes* collected in Lithuania from 2009 to 2021. A comprehensive epidemiological review was conducted, along with molecular characterisation of the isolates, determination of antimicrobial susceptibility, and whole genome sequencing of selected samples. The methods employed in this research, along with the results obtained, allowed for the identification of genomic differences between circulating strains. This provided insights into their pathogenicity, virulence, and potential for antimicrobial resistance. Notably, this is the first study to explore the relationship between Lithuanian isolates and strains from other countries worldwide through core genome and SNP analysis. The study identified new strains of neuroinfectious agents, as well as unique variants or combinations of virulence and antibiotic resistance genes. The detection of hypervirulent clones and the presence of outbreak-associated strains underscore the need to review and strengthen epidemiological surveillance strategies in Lithuania.

PREVALENCE AND GENETIC DIVERSITY OF VIRUSES TRANSMITTED BY *VARROA DESTRUCTOR* MITES AND OTHER VIRAL AND BACTERIAL PATHOGENS IN THE WESTERN HONEY BEE (*APIS MELLIFERA*) POPULATION IN LITHUANIA

Paulina Amšiejūtė-Graziani

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Dissertation defended:
26 September 2025

The Western honey bee (*Apis mellifera*) is one of the most important pollinators of flowering plants, however, its populations are increasingly threatened by viral and bacterial pathogens, as well as the ectoparasitic mite *Varroa destructor*. The aim of this study was to assess the prevalence of honey bee viruses in Lithuanian apiaries, to determine the genetic diversity of Deformed Wing Virus (DWV) variants transmitted by *V. destructor*, and to characterize the genotypes of *Paenibacillus larvae*, the causative agent of *American foulbrood* (AFB). Molecular methods were applied, including PCR, sequencing of viral genome fragments (*RdRp*, *LP*, *VP3*, *Helicase*), and MLVA/MLST genotyping of bacterial isolates. The results demonstrated that between 2012 and 2021, seven major viruses, widely distributed globally, circulated in Lithuanian honey bee colonies, among them DWV-A and DWV-B. The latter predominated and was strongly associated with mite infestation. Genetic analysis revealed high diversity within DWV variants and indicated the circulation of potential recombinant lineages. All *P. larvae* isolates were assigned to the ERIC I genotype, however, internal genetic differentiation and MLST sequence types (ST) specific to Lithuania were identified. The findings expand current knowledge on honey bee pathogen dynamics, confirm the important role of *V. destructor* in viral epidemiology, and provide a foundation for improving honey bee disease diagnostics and control strategies at both national and international levels.

PREVALENCE AND GENETIC DIVERSITY OF TICK-BORNE BACTERIAL PATHOGENS IN URBAN AND PERI-URBAN HABITATS IN LITHUANIA (Biology)

Justina Snegiriovaitė

Scientific supervisor:
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Vytautas Magnus University

Dissertation defended:
30 September 2025

Urbanisation affects all components of natural ecosystems in a complex manner, including abiotic and biotic conditions, vegetation, animal populations, and communities. The distribution of green spaces within urbanised environments often creates a fragmented, mosaic-like structure that helps maintain local biodiversity. At the same time, these spaces provide habitats where disease vectors, such as ticks and mosquitoes and the pathogens they transmit, can persist and spread. Despite existing studies on pathogen prevalence in ticks, systematic research addressing tick infection in different anthropogenic habitats in Lithuania, particularly in urban and peri-urban areas, remains very limited, and the distribution of ticks in these environments is largely unknown. This dissertation investigates the distribution and abundance of Ixodidae ticks, *Ixodes ricinus* and *Dermacentor reticulatus*, as well as the prevalence and genetic diversity of their associated pathogens in urban and peri-urban habitats in Lithuania. For the first time, the abundance and distribution of *I. ricinus* and *D. reticulatus* ticks were assessed across different urban and peri-urban habitats of Lithuania; the prevalence of bacterial tick-borne pathogens, *Borrelia burgdorferi* s. l., *Borrelia miyamotoi*, *Anaplasma phagocytophilum*, *Neoehrlichia mikurensis*, and *Rickettsia* spp., were determined in urban and peri-urban areas; the human-pathogenic bacterium *N. mikurensis* was detected, and its occurrence in *I. ricinus* ticks as well as its genetic diversity were investigated; *Borrelia lusitaniae* was identified in *I. ricinus* ticks, certain strains of this species are associated with Lyme borreliosis in humans.

PRETREATMENT OF BEE POLLEN AND THEIR ANALYSIS EMPLOYING CHEMICAL, BIOLOGICAL AND CHEMOMETRIC METHODS (Biology)

Vaida Damulienė

Scientific supervisors:
Assoc. Prof. Dr Vilma Kaškonienė,
Assoc. Prof. Dr Paulius Kaškonas
Vytautas Magnus University

Dissertation defended:
30 September 2025

The growing demand for functional foods has directed attention toward apitherapeutic products, particularly bee pollen, due to its abundance of bioactive compounds and health-promoting properties. This study aimed to evaluate the effects of solid-state fermentation, enzymatic hydrolysis and stepwise fermentation on bee pollen's chemical composition, antioxidant, antibacterial and anti-inflammatory activity using chemometric analysis methods and to prepare recommendations for the preparation of bee pollen with increased biological activity. Results demonstrated significant ($p \leq 0.05$) increases in phenolic content (1.24–4.96 times), antioxidant activity (1.16–6.29 times), antibacterial activity (up to 7.56 times) and anti-inflammatory activity (1.1–5.3 times). Treated pollen extracts displayed notable interaction with antibiotics against pathogenic bacteria. Analysis of polyphenolic compounds revealed increased levels of gallic acid, ferulic acid, p-coumaric acid, rutin and quercetin, and new acids – caffeic and benzoic acid – were also detected after processing. A significant increase in essential amino acids – lysine, valine, methionine and phenylalanine – was also found. It was found that stepwise fermentation, when enzymatic hydrolysis is followed by bacterial fermentation, is the most advanced method to increase the biological activity of pollen, preserve its functional properties, and promoting probiotic potential.

THE EFFECT OF TEMPERATURE MANIPULATION ON SKELETAL MUSCLE FUNCTION AND THERMAL STRESS RESPONSES IN YOUNG MALES (Biology)

Viktorija Treigytė

Scientific supervisor:
Dr Thomas Chaillou
Lithuanian Sports University

Dissertation defended:
3 October 2025

This dissertation investigated the effects of different cooling and heating methods and their duration on skeletal muscle function and thermal stress in young, recreationally active males. Temperature modulation using passive methods, such as hot or cold water immersion, or active methods, such as physical exercise, can alter core and muscle temperature, thereby influencing muscle contractile properties, fatigue development, recovery, and hormonal responses. The main objectives of the study were to compare physiological, hormonal, and perceptual responses induced by passive and active heating when core temperature elevation was closely matched but skin temperature differed. Previous studies have suggested prolactin as a potential marker of central fatigue and heat stress; however, hormonal responses to different heating modalities remain insufficiently understood. In addition, the neuromuscular and hormonal mechanisms responding to temperature changes, particularly with respect to exposure duration (acute versus prolonged) and differences between active and passive heating, have not been fully clarified. Most previous research focused on short-term (~45 min) temperature interventions, leaving the effects of intermittent or prolonged heating and cooling insufficiently explored. The findings of this dissertation address these gaps in sports science by providing new insights into the physiological, neuromuscular, hormonal, and perceptual responses to temperature modulation. The results demonstrate that different heating and cooling strategies and their duration distinctly affect muscle function, fatigue development, recovery, and thermal stress. These findings are particularly relevant for athletes and coaches aiming to optimise performance and recovery, as well as for individuals working in clinical or occupational settings where exposure to heat or cold stress is common.

DEVELOPMENT AND APPLICATION OF MOLECULAR METHODS FOR THE ENVIRONMENTAL DETECTION OF *SARCOCYSTIS* SPP. (Biology)

Agnė Baranauskaitė-Lengvinienė

Scientific supervisor:
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Dissertation defended:
3 October 2025

Currently, over 200 species of parasites within the genus *Sarcocystis* have been identified, which are capable of infecting mammals, birds, and reptiles. Although infections are frequently asymptomatic, extensive infections in intermediate hosts can result in fever, nausea, diarrhoea, miscarriage, or even death. Certain species pose a threat to human health, with infections occurring through the consumption of improperly cooked beef or pork. While human infections are often asymptomatic, mild health issues may also arise. To date, research on *Sarcocystis* parasites has predominantly involved the analysis of animal carcasses, with environmental samples being studied only sporadically. Consequently, the objective of the doctoral studies was to develop reliable extraction and molecular detection techniques for identifying *Sarcocystis* species in environmental samples, with a focus on species that utilise farm animals as intermediate hosts. During the work, a newly developed and optimised method was used to isolate *Sarcocystis* parasites from environmental samples, specifically targeting sporocysts in water, forage, and soil samples. Analysis of various water bodies revealed that the properties of a water body do not influence the detection and prevalence of *Sarcocystis* spp. in environmental water samples. A comprehensive regional study of the distribution of *Sarcocystis* species was conducted by collecting bottom sediments of water bodies in Estonia, Latvia, Lithuania, and Poland. For the first time, the diversity of *Sarcocystis* species infecting domestic animals was determined in environmental water, forage and soil samples. During the study, two zoonotic species, *S. hominis* and *S. suihominis*, were detected in environmental samples of Lithuanian for the first time.

CHARACTERISTICS OF *FESTUCA GIGANTEA* (L.) Vill.: PHYLOGENETIC ORIGIN AND RELATIONSHIPS WITH ENDOPHYTES (Biology)

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Dissertation defended:
10 October 2025

In this study, the origin of the wild allopolyploid *Festuca gigantea* genome and relations with root endophytes are examined. The phylogenetic origin study used the root cytological preparations of *F. gigantea*, diploid *Lolium* and *Festuca* species and *L. perenne* × *F. gigantea* hybrids. The FISH/GISH method enabled us to determine that two-thirds of the *F. gigantea* genome consists of *Lolium* spp. and *F. pratensis* chromosomes, as well as the chromosomal rearrangements of the *L. perenne* × *F. gigantea* hybrids: dispersive expansion of the *Fesreba* sequence across the *L. perenne* chromosomes and the presence of interstitial telomeric sequences. Endophyte isolation from root tissue was used to determine the root endophytic fungi and bacteria diversity, the distribution of *F. gigantea*, and species and their hybrids related to *Lolium* and *Festuca*. In total, 21 fungal species (60 isolates) and 26 bacterial species (59 isolates) were isolated. The most common endophytes were *Microdochium bolleyi* and *Bacillus* sp. The greatest diversity of endophytic fungi was distinguished *F. gigantea* (six species) and bacteria – *F. arundinacea* (nine species). The annual *L. multiflorum* and *L. temulentum* exhibited a significantly higher abundance of endophytes than the related perennial species. The two *Basidiomycota* species – *Coprinellus disseminatus* and *Sistotrema brinkmannii* – were exclusively found in the roots of *F. gigantea*. Inoculation of *L. multiflorum* seeds with endophytic fungi spores suspension, *Cadophora fastigiata*, *Paraphoma fimeti* and *Plectosphaerella cucumerina*, the experiment determined growth-promoting effect on plants. The obtained results complement knowledge about genome formation of allopolyploid species and about endophytic fungi as a plant growth biostimulator.

INDUCTION OF BYSTANDER EFFECT AFTER ELECTROPORATION-BASED ANTICANCER TREATMENTS (Biology)

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Scientific supervisor:
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Dissertation defended:
28 November 2025

Electroporation-based anticancer therapies, such as electrochemotherapy, calcium electroporation, and irreversible electroporation, are promising but local cancer treatment methods. A key limitation of these therapies is their unknown systemic effect on the organism. Accordingly, the objective of this dissertation was to determine if these therapies could induce the bystander effect, defined as an alteration in the viability of neighbouring cells not directly targeted by the electric field. In this study, the bystander effect was evaluated on three levels: in monolayer (2D) and spheroid (3D) cell cultures *in vitro*, and as a systemic abscopal effect *in vivo*. For the first time, this study demonstrates that electric field-based anticancer therapies induce the bystander effect. The effect was proven in both cancer (4T1) and non-cancer (CHO-K1) 2D and 3D cell cultures. It was determined that, depending on the electric field parameters used, the bystander effect can be twofold: either negative (inhibiting the viability of adjacent cells) or positive (promoting viability). The most significant scientific novelty of this research is the observation of the abscopal effect in BALB/c mice following treatment with electric field-based anticancer therapies. This is a systemic response where the local treatment of a tumour leads to the regression of other metastases distant from the treatment site. The results of this dissertation expand the possibility of using electric field-based therapies not only as a local, but also as a systemic cancer treatment method.

IN VIVO STUDIES ON THE SAFETY AND EFFICACY OF PICOSECOND LASER SYSTEMS (Biology)

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Dissertation defended:
3 December 2025

This dissertation systematically investigated the safety and efficacy of Nd:YAG picosecond laser systems generating 100 ps and 150 ps pulses *in vivo*, applied for tattoo removal and fractional laser procedures. The studies were conducted using Lithuanian White and Göttingen minipig models and included clinical evaluation in accordance with ISO 10993-23:2021, siascopy, digital image analysis, spectrophotometric measurements, as well as histological and immunohistochemical assessments (Ki-67 and p53 biomarkers). Tattoo removal experiments demonstrated that a wavelength of 1064 nm was the most effective for black pigment removal, while 532 nm was more effective for coloured pigments, including green, yellow, and blue. Treatment efficacy was primarily influenced by the number of procedures, pulse intensity, and beam diameter. Although a smaller beam diameter (2 mm) resulted in greater pigment fragmentation, it was also associated with more pronounced signs of tissue damage. Histological analysis revealed that these tissue alterations were transient, and immunohistochemical findings confirmed a physiological, reversible proliferative response without indications of cellular stress. In studies of fractional laser procedures, localised and reversible laser-induced optical breakdown (LIOB) microlesions were observed. These changes did not result in scarring or pigmentary disorders, even after twelve treatment sessions. Overall, the results demonstrate that 100 ps and 150 ps pulse durations are safe and effective when appropriate laser parameters – such as pulse energy, power density, wavelength, and beam diameter – are carefully selected, allowing an optimal balance between treatment efficacy and safety.

RESISTANCE TRAINING AS A MEANS TO IMPROVE COGNITIVE MOTOR FUNCTIONS AND BRAIN HEALTH IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENTS (Biology)

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Scientific supervisor:
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Dissertation defended:
5 December 2025

This dissertation examined the effects of a 12-week progressive resistance training programme on cognitive functions, balance control, and brain health in older adults with different levels of risk for mild cognitive impairment (MCI). The study included 74 participants aged over 60 years and employed a randomised controlled trial design combined with neuroimaging techniques, including structural magnetic resonance imaging and proton magnetic resonance spectroscopy (^{1}H-MRS). The results showed that resistance training induced small improvements in executive functions, particularly inhibitory control, with more pronounced effects observed in participants at higher risk of MCI compared to those at lower risk. Significant improvements in balance control were found only in the high-risk MCI group under more demanding dual-task conditions. The 12-week intervention was insufficient to induce significant changes in cortical thickness or neurometabolite concentrations in key brain regions, although trends suggested potential neuroprotective effects in sensorimotor and prefrontal areas. Overall, the findings contribute to a better understanding of the effects of resistance training on cognitive and motor functions in older adults with varying levels of MCI risk and highlight the potential of strength-based exercise as a non-pharmacological strategy to support healthy cognitive aging.

EXPLORING THE RELATIONSHIPS BETWEEN HORMONAL CONTRACEPTIVES AND EMOTIONAL FUNCTIONING: A PSYCHOPHYSIOLOGICAL APPROACH (Biophysics)

Ingrida Zelionkaitė

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Dissertation defended:
2 July 2025

In recent years, the effects of hormonal contraception (HC) have received increasing scientific attention, with a growing focus not only on its physiological impact but also its potential implications for mental health. Worsening mental health, which may be linked to alterations in emotional functioning, is among the most frequently reported reasons for discontinuing the HC use. This dissertation explored the association between HC use and emotional processing. The study included naturally cycling (NC) women in either the follicular or luteal phase, as well as women using oral contraceptives (OCs) or a hormonal intrauterine device (IUD). Data were collected using psychological questionnaires, self-report ratings, electroencephalography (EEG), and eye-tracking. The findings revealed no associations between HC use and self-reported emotional or psychological parameters (such as alexithymia or emotion regulation habits). The evaluation of and reactivity to emotional images did not differ between NC and OC women, suggesting similar emotional perception and reactivity across these groups. However, EEG analyses showed that IUD-users exhibited greater attentional and cognitive control engagement during a cognitive emotion regulation task compared to NC and OC women. Eye-tracking data further revealed that OC-users spent less time looking at human faces in neutral and erotic images compared to NC women. In summary, while general emotional functioning does not differ among women with different hormonal statuses, specific components such as attention and cognitive control may be modulated.

LINKS BETWEEN SEX, WOMEN'S HORMONAL STATUS AND SPATIAL ABILITIES: INTERPLAY OF COGNITIVE, NEUROPHYSIOLOGICAL, SOCIAL, AND EMOTIONAL FACTORS (Biophysics)

Rimantės Gaižauskaitė

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Dissertation defended:
29 August 2025

Research on gender differences in spatial abilities can contribute to a better understanding of how these abilities are related to sex hormones and women's hormonal status, revealing broader mechanisms of the functioning of the central nervous system. The dissertation examined the relationship between sex and women's hormonal status in spatial abilities while assessing cognitive, neurophysiological, social, and emotional factors. The study included men and women with a natural menstrual cycle (in the follicular or mid-luteal phases), women using oral hormonal contraception (OC), and those using a hormonal intrauterine device (IUD). Data were collected through psychological questionnaires, electroencephalography (EEG), and tasks assessing visual working memory and spatial abilities (mental rotation and cross-section tasks). The results showed that neither sex nor women's hormonal status was significantly related to measures of visual working memory or resting-state EEG. No gender differences were found in the mental rotation task; however, men outperformed women in the cross-section task (except for women using an IUD), and this difference was partly explained by emotional arousal. In summary, the study demonstrated that the associations between sex, hormonal status, and spatial abilities are subtle and depend on social, emotional, and individual factors. The findings highlight the necessity of considering a broader spectrum of variables when comparing cognitive functions across sexes or groups with different hormonal statuses.

NANOMATERIALS FOR BIMODAL IMAGING (Biophysics)

Marijus Plečkaitis

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Dissertation defended:
24 October 2025

Early diagnosis and intervention of cancer tumours are essential factors in improving patient survival. Since individual imaging methods used in clinical practice are often not effective enough for early cancer detection, researchers are developing various bimodal or multimodal imaging contrast agents that enable the combination of different imaging techniques, compensating for the limitations of some methods with the advantages of the other ones. Thus, the aim of this dissertation was to evaluate the potential of different bimodal nanomaterials for cancer diagnostics. Magnetic iron oxide nanoparticles decorated with gold nanoclusters (MN-AuNCs) and rare-earth-doped upconverting nanoparticles coated with maghemite nanocrystals were studied during the experiments. These nanoparticles were biocompatible *in vitro* with cells, and although they did not demonstrate specificity for only cancer cells, they combined optical and magnetic resonance imaging. Moreover, under light exposure, MN-AuNCs generated reactive oxygen species capable of inducing cancer cell death, thus, the integration of bimodal imaging capabilities with therapeutic properties makes MN-AuNCs a promising theranostic nanomaterial. The third type of nanomaterial we investigated was molecular TPPS4 aggregates; in an acidic environment, they self-assembled into a unique sea-urchin-like structure with a tubular central core and long branching filaments. TPPS4 aggregates exhibited fluorescence as well as second- and third-harmonic generation properties and therefore can also be classified as bimodal imaging nanomaterials.

NEUROCOGNITIVE CORRELATES OF INTERNET USE: PSYCHOLOGICAL MEASURES AND ELECTROPHYSIOLOGICAL SIGNATURES FROM RESTING-STATE AND TASK-BASED EEG IN A SAMPLE OF HEALTHY REGULAR INTERNET USERS (Biophysics)

Dovilė Šimkutė

Scientific supervisor:
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Dissertation defended:
4 December 2025

Problematic Internet Use (PIU) emerges amid ubiquitous connectivity yet remains conceptually heterogeneous and underrecognised. This thesis examines PIU as a continuum in a non-clinical sample, integrating psychological, behavioural, and EEG indices to identify markers across increasing levels of internet use. Participants completed self-reports (assessing psychological distress, interoception, and personality), performed an auditory equiprobable Go/NoGo task, and underwent EEG during task and resting-state (to assess ERPs, alpha asymmetry, and microstates). Network analysis of interoception–personality–internet use linked lower interoceptive awareness to higher internet use, with neuroticism bridging bodily awareness and excessive engagement. Behavioural Go/NoGo task indices did not differentiate between internet use severity, but ERPs showed domain-specific associations: a reduced N1 (Gaming), a shorter Go-N1 (total platform use), and a longer NoGo-P3 (Information Search). Resting EEG indicated greater left parietal activity and increased microstate E occurrence/coverage with increasing severity of internet use. Together, results indicate a shift toward externally driven, bottom-up attention and weakened embodied regulation within increasing internet use. Findings advance early detection targets to prevent maladaptive use from escalating.

BLOODSUCKING DIPTEROUS INSECTS (CULICIDAE, CERATOPOGONIDAE): THE BIOLOGY AND THEIR ROLE IN TRANSMISSION OF BLOOD PARASITES (Ecology and environmental)

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Dissertation defended:
10 January 2025

The objective of this dissertation was to evaluate the role of mosquitoes (Culicidae) and biting midges (Ceratopogonidae, Culicoides) in the transmission of avian blood parasites (Haemosporida (Apicomplexa) and Trypanosomatidae (Euglenozoa)). The dissertation consists of an introduction, a literature review, research methods, results, their conclusions, a list of references, and a summary. During this research, *Culex pipiens* mosquitoes were proven to be likely natural vectors of *Plasmodium matutinum* lineage pLINN1 as in mosquito salivary glands sporozoites of *P. matutinum* pLINN1 were microscopically detected for the first time. Molecularly, *P. ashfordii* (pGRW02) was detected in a bloodsucking insect (*Ochlerotatus sticticus*) for the first time. Previously, it was reported only in birds. *Trypanosoma trinaperronei* was found in *C. pipiens* mosquitoes for the first time. Hibernating *C. pipiens* were uninfected with haemosporidian parasites and thus can be recommended for experimental research using the natural population of wild-caught (laboratory non-reared) insects. For the first time, sporozoites of five genetic lineages of haemosporidian parasites were found in *Culicoides kibunensis*, five lineages in *C. pictipennis*, four lineages in *C. segnis*, and one in *C. festivipennis* and *C. reconditus* biting midges. For the first time, sporozoites of genetic lineages hCUKI1, hCULPIC02, hROFI1, hSYAT01, hSYAT13, hSYAT16 of *Haemosporida* spp. were found in salivary glands of *Culicoides* spp.

TAXONOMIC INVENTORY OF LEAF-MINING NEPTICULIDAE, ANALYSIS OF MINES, AND NEW SPECIES (Ecology and environmental)

Viktorija Dobrynina

Scientific supervisors:
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Dissertation defended:
9 May 2025

The family Nepticulidae comprises some of the smallest moths in the order Lepidoptera and represents a phylogenetically primitive yet highly specialised group. Their larvae exhibit an endobiotic, leaf-mining lifestyle within plant assimilative tissues, which, together with reduced body size, has limited dispersal abilities and promoted rapid speciation. The aim of this dissertation was to conduct a comprehensive taxonomic inventory of Nepticulidae and related leaf-mining moth families, to supplement their ecological and morphological characterisation, and to describe new species. The study was based on published global bioinventory data and extensive analysis of collection material from Lithuania, Armenia, Georgia, Ukraine, and Central and South America. An assessment of research productivity demonstrated that RGRI values of biodiversity inventory publications vary over time and are strongly influenced by factors such as open access, international collaboration, ecological focus, and article titles. Updated global estimates identified approximately 1,000 Nepticulidae species, alongside 197 Opostegidae and 170 Tischeriidae species, with 131 researchers contributing to the global inventory. Taxonomic activity peaked during 1981–1990 and 2011–2021. Morphological and ecological analysis of Nepticulidae leaf mines identified six diagnostic groups, with most species exhibiting serpentine mines characterised by dark frass arranged in a continuous line. Thirty-two species were recorded for the first time in the Caucasus, including eight species new to science, accounting for roughly one-quarter of Armenia's known Nepticulidae fauna. Several newly discovered species displayed unique genital structures previously unknown in pygmy moths. Molecular analyses supported species delimitation, revealed cryptic taxa, and confirmed the taxonomic status of newly described species, highlighting the value of integrative taxonomy in Nepticulidae research.

ACCUMULATION OF FECAL INDICATOR AND POTENTIALLY PATHOGENIC BACTERIA IN MACROPHYTE WRACK ON COASTAL SANDY BEACHES (Ecology and environmental)

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Scientific supervisor:
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Klaipėda University

Dissertation defended:
29 May 2025

This thesis presents an extensive study concerning the presence of faecal pollution-related bacteria and potentially pathogenic *Vibrio* bacteria in beach wrack, water, and sand. The study took place in four recreational beaches located in the south-eastern part of the Baltic Sea. In addition to *in situ* investigations, a systematic review of scientific literature, published during the period of 1969–2022, was performed to analyse interactions of potential pathogens and macrophytes or their wrack. The review revealed that different macrophyte groups supported different quantities of faecal indicator bacteria (FIB) and *Vibrio*; red macroalgae supported the highest quantities of potentially pathogenic bacteria, primarily *Vibrio*. The review identified a research gap regarding potentially pathogenic *Vibrio* bacteria in beach wrack. Through *in situ* research, noticeable changes in the structure of the microbial community within the water containing the wrack and within the wrack on the coast were observed, indicating that the presence of the wrack had an impact on microbial dynamics. Beach wrack was found to support significantly higher FIB levels compared to areas with no wrack. Increased FIB levels in water with wrack were related to increased cDOM and turbidity. Moreover, the environment with wrack was found to contain a higher relative abundance of enteric potential human pathogens, as well as a greater abundance and occurrence of ubiquitous potential pathogens, such as *Vibrio vulnificus*, *V. cholerae*, and *V. alginolyticus*. Environmental factors, such as relative abundance of *Vertebrata fucoides*, chlorophyll a, oxygen, temperature, and cDOM, significantly influenced the abundance and presence of *V. vulnificus* and *V. cholerae*.

PHTHALATE ESTERS IN BOREAL ESTUARINE SYSTEMS: SOURCES, DISTRIBUTION AND FATE (Ecology and environmental)

Elise Marie Clemence Lorre

Scientific supervisor:
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Klaipėda University

Dissertation defended:
6 June 2025

Using the Curonian Lagoon as a model ecosystem, this study provides a comprehensive evaluation of the occurrence, distribution, and fate of phthalate esters (PAEs) in boreal estuarine systems. The main objective was to identify the key factors controlling PAE dynamics in estuarine environments. The results showed that estimated PAE inputs to the lagoon were generally lower than outputs to the Baltic Sea, indicating that the lagoon acts as a convergence and transformation zone before releasing PAEs to the sea. However, the lagoon's role varied seasonally and was strongly influenced by meteorological conditions such as ice cover and wind patterns. Riverine input from the main tributary was identified as the dominant source of PAEs, while wastewater treatment plant discharges contributed relatively little. Atmospheric deposition was also considered a potentially important but insufficiently studied source. A central focus of the study was the role of suspended particulate matter (SPM) in PAE transport and distribution. Although often neglected in routine monitoring, SPM proved to be a key vector, particularly for PAEs of higher molecular weight. Particle-bound PAEs were transferred to bottom sediments through sedimentation, confirming sediments as the main long-term reservoir of these compounds. It was estimated that several tonnes of PAEs had accumulated in surface sediments over more than five years, highlighting their persistence in the aquatic environment. This accumulation poses potential ecological risks, as elevated PAE levels may adversely affect aquatic organisms. Comparisons with the Szczecin and Vistula lagoons revealed similar long-term contamination trends, supporting the representativeness of the Curonian Lagoon as a model for boreal estuarine systems. In addition, the study applied novel methodological approaches that improved analytical accuracy and provided new insights into PAE degradation and pollutant fate in aquatic ecosystems.

DUST POLLUTION AS AN INDICATOR OF INDOOR ENVIRONMENT QUALITY (Ecology and environmental)

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Dissertation defended:
20 June 2025

This dissertation addresses the critical yet understudied issue of indoor dust pollution, focusing specifically on heavy metals (HMs) within educational environments in Vilnius, Lithuania. The author thoroughly explores the presence, sources, and health implications of indoor dust contamination, emphasising the vulnerability of children who spend significant periods in school settings. By conducting extensive sampling across 24 general education institutions, the research provides detailed quantitative analyses of metal concentrations, linking these indoor pollutants with external sources such as outdoor particulate matter and soil contaminants. Notably, the dissertation uses advanced methods, including Positive Matrix Factorization (PMF) and geospatial mapping, to identify and clearly illustrate the pathways through which external pollutants migrate indoors. This methodological approach strengthens the findings and offers robust evidence of the significant health risks posed by HM exposure, including both carcinogenic and non-carcinogenic impacts. One of the most compelling aspects of this research is the integration of epidemiological data with rigorous health risk modeling. The findings highlight alarming levels of contamination, particularly of heavy metals such as lead, arsenic, zinc, and copper, suggesting urgent interventions are required to protect the health of schoolchildren. The dissertation effectively fills a research gap by providing localised data from Lithuanian schools, contributing valuable insights into global discussions on indoor environmental quality and child health. Coupled with clear recommendations for mitigation, its detailed exploration of contamination sources makes it essential reading for policymakers, school administrators, public health officials, and environmental researchers concerned with indoor air quality and public health protection.

SURFACE-GROUNDWATER INTERACTIONS, HYDROLOGICAL REGIME AND LAND USE: IMPACTS ON STREAM FUNCTIONING FOR SALMONID SPAWNING AND INCUBATION PHASES (Ecology and environmental)

Rudy Benetti

Scientific supervisor:
Prof. Dr Marco Bartoli
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Dissertation defended:
26 June 2025

The Baltic Sea supports populations of Atlantic salmon (*Salmo salar*) and sea trout (*Salmo trutta*), which historically relied on Lithuanian rivers for spawning and juvenile development. Understanding how anthropogenic factors, particularly hydrological extremes and catchment land use, influence these habitats is essential for effective conservation and restoration. This thesis applies a multiscale approach to identify key environmental drivers and threats affecting salmonid spawning habitats in three Lithuanian rivers: the Blendžiava, the Smiltaitė, and the Šventoji. At the watershed scale, land cover was strongly associated with physicochemical water quality responses during hydrological fluctuations. The Blendžiava Stream, characterised by well-developed riparian zones and agricultural land with covered soils, showed consistently high oxygen levels, even during droughts. In contrast, the Smiltaitė Stream, influenced by urbanised areas and uncovered cultivated soils, exhibited elevated nutrient levels and high trophic status. The Šventoji River maintained low suspended solid concentrations year-round due to extensive forest cover, whereas flood events in the Blendžiava watershed mobilised large sediment loads. At the spawning-site scale, intragravel water showed elevated conductivity and ammonium, indicating eutrophic conditions, particularly in the Smiltaitė. During late incubation, oxygen and temperature dropped below levels required for larval survival in all rivers. Low flow conditions intensified nutrient accumulation, organic matter deposition, and biofilm growth, reducing oxygen delivery to eggs. Egg pocket structure and upwelling groundwater improved intragravel circulation, oxygen supply, and waste removal, facilitating larval emergence, especially in fine-sediment systems. Mesocosm experiments demonstrated increasing oxygen consumption and ammonium release during incubation, alongside enhanced nitrification–denitrification processes. Overall, the multiscale framework revealed critical periods when ecological thresholds are exceeded, offering valuable insights for habitat assessment, conservation planning, and salmonid spawning habitat restoration.

THE EFFECT OF HABITAT CONDITIONS ON PLANT TRAITS, REPRODUCTIVE SUCCESS AND POPULATION STRUCTURE OF *CEPHALANTHERA LONGIFOLIA*, *CEPHALANTHERA RUBRA* AND *CARDAMINE BULBIFERA* (Ecology and environmental)

Laurynas Taura

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Dissertation defended:
28 October 2025

This dissertation examines three endangered woodland plant species in Lithuania: *Cephalanthera longifolia*, *C. rubra*, and *Cardamine bulbifera*, focusing on the effects of habitat on population structure, plant traits, and reproductive success. A standardised trait-based approach combined single-census assessments, observations of natural fruit set (2021–2023), and pollination experiments (2022). The results show that *C. longifolia* is expanding and successfully colonising a wide range of habitats, whereas *C. rubra* is rare, restricted to four localities, and more sensitive to habitat changes. In *C. longifolia* populations, individual density was higher in open habitats, with vegetative individuals predominating. *C. bulbifera* populations were dominated by juvenile and immature individuals, indicating prevalent vegetative reproduction; the highest densities occurred in broadleaved forests, while hornbeam forests supported more mature individuals. Natural fruit set was consistently low in both *Cephalanthera* species, with lower-positioned flowers setting fruit more frequently. Fruit set was negatively affected by bryophyte cover and June temperature, while soil pH showed a positive correlation. Pollination experiments demonstrated high fruit set under assured pollination, confirming self-compatibility and excluding resource limitation as the cause of low natural fruiting. Overall, the study shows that population structure primarily reflects current habitat suitability rather than long-term population trends. The findings provide practical recommendations for conservation management, including habitat modification and targeted hand pollination, and highlight the value of single-census assessments alongside long-term studies.

THE EFFECT OF PROBIOTICS ON THE GROWTH, ANTIOXIDANT ACTIVITY, AND PRODUCTIVITY OF ROOT CROPS AND BERRY PLANTS (Ecology and environmental)

Božena Ignotienė

Scientific supervisors:
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Dissertation defended:
30 October 2025

The dissertation analyses the effects of probiotics ProbioHumus and NaturGel, based on effective microorganisms (EM), on root vegetables (carrots) and berries (strawberries, black currants), as well as on soil agrochemical properties in both organic and conventional cultivation systems. The research was conducted using laboratory cultivation, small plot methods, and field trials under real farm conditions. Plant biochemical parameters such as monosaccharide content, total antioxidant activity (measured by spectrophotometry), and vitamin C (measured by HPTLC) were evaluated. Soil agrochemical properties after probiotic application were also analysed. The results showed that probiotics, especially ProbioHumus, significantly improved plant morphometric parameters, yield, and biochemical indicators such as antioxidants and monosaccharides, particularly under conventional conditions. Although nitrate accumulation was not significantly affected, the nitrate content in carrots grown in organic fields was considerably lower than in conventional ones. In strawberries, vitamin C content nearly doubled after ProbioHumus treatment, and anthocyanin concentration increased significantly in black currants. Additionally, soil agrochemical properties improved significantly, including increases in total nitrogen, nitrate nitrogen, and organic carbon content. These findings indicate that probiotics are an effective and sustainable tool that can reduce the need for chemical fertilisers, improve crop productivity and nutritional value, and enhance soil quality in both organic and conventional farming systems.

DIVERSITY AND DISTRIBUTION OF CHIRONOMIDAE (INSECTA: DIPTERA) IN THE ŠVENTOJI AND ŽEIMENA RIVERS SUB-BASINS (Zoology)

Laurynas Stasiukynas

Scientific supervisors:
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Dissertation defended:
29 September 2025

Lithuania is characterised by a dense river network that plays an important role in maintaining and protecting biodiversity. The hydrological, physical, and chemical properties of rivers, such as water temperature, pH, substrate type, dissolved oxygen concentration, electrical conductivity, and salinity, directly influence the composition and functioning of biological communities in river ecosystems. However, the diversity of aquatic macroinvertebrates, particularly non-biting midges (Diptera: Chironomidae), and their relationships with environmental factors have remained poorly studied in Lithuania. Chironomidae represent one of the most abundant and ecologically diverse insect groups in freshwater ecosystems. They play a key role in the decomposition of organic matter, contribute significantly to macroinvertebrate community structure, and are widely recognised as valuable bioindicators of environmental conditions. Despite their ecological importance, comprehensive studies of chironomid communities in Lithuanian rivers have been lacking. This dissertation presents the first systematic analysis of Chironomidae diversity and distribution in six rivers of eastern Lithuania (the Dubinga, the Kiauna, the Luknelė, the Plaštaka, the Skerdyksna, and the Šešuola). The study evaluates the influence of ecological, physical, chemical, and hydrological factors, including river damming, on chironomid community structure. By comparing free-flowing and dammed river sections under varying environmental conditions, the research provides new insights into the drivers shaping chironomid assemblages. The results contribute substantially to national faunistic knowledge and improve the understanding of Chironomidae community patterns in river ecosystems. Furthermore, the findings highlight the potential of chironomids as effective bioindicators for assessing river ecological status and evaluating the impacts of human activities on freshwater ecosystems in Lithuania.