Polskie Towarzystwo Biochemiczne

Oddział Wrocławski

Uniwersytet Wrocławski

UCZELNIA BADAWCZA
INICJATYWA DOSKONAŁOŚCI

Politechnika Wrocławska

Oddział Wrocławski Polskiego Towarzystwa Biochemicznego przy współudziale Uniwersytetu Wrocławskiego oraz Politechniki Wrocławskiej zaprasza na sympozjum pt.

Wrocław branch of the Polish Biochemical Society in cooperation with the University of Wrocław and the Wrocław University of Science and Technology invites you to a symposium entitled

„New Perspectives in Biochemistry Research”

15 czerwca 2026 o godzinie 14.00 w sali rektorskiej budynku H-14 Politechniki Wrocławskiej (ul. Wybrzeże S. Wyspiańskiego 40, 50-370 Wrocław).

June 15, 2026, at 2 p.m. *in the rector's hall of building H-14 of the Wrocław University of Science and Technology (ul. Wybrzeże S. Wyspiańskiego 40, 50-370 Wrocław)*

Scientific Program

14.00 - 14.10 OPENING

14.10 - 14.55 KEYNOTE LECTURE: Michał Grzybek "Molecular Recognition at Biological Interfaces: Understanding Receptor Activation in Metabolic and Immune Signaling" (University Hospital and Faculty of Medicine Carl Gustav Carus of TU Dresden)

14.55 - 15.15 Weronika Gajdzik-Nowak "Palmitoylation regulates membrane domain association and bilayer-organizing activity of MPP1" (University of Wrocław)

15.15 - 15.35 Priya Sagar "Biochemical Investigation of Salt-Mediated Effects on the Structure and Stability of L-α-Phosphatidylcholine" (Wroclaw University of Science and Technology)

15.35 - 15.55 Maxime Kucharski "Comparative Analysis of LNP Manufacturing Across Commercial and Custom Platforms" (Wrocław University of Science and Technology; Lipid Systems sp. z o. o.)

15.55 - 16.15 COFFEE BREAK

16.15 - 17.00 KEYNOTE LECTURE: Theresia Gutmann "Molecular Recognition at Biological Interfaces: Understanding Receptor Activation in Metabolic and Immune Signaling" (European Molecular Biology Laboratory (EMBL))

17.00 - 17.20 Izabela Krauze "Investigating the molecular basis of cytoprotective functioning of NPAS4 under Hypoxic and Oxidative Stress Conditions" (Wrocław University of Science and Technology; Wrocław Medical University)

17.20 - 17.40 Adrianna Nawrot "Acute RNA polymerase II perturbation by arsenic triggers arm-wide γH2A signaling" (University of Wrocław)

17.40 - 18.00 Nicole Horáková "Characterization of crystal-associated proteins in calcium oxalate-rich plant tissues" (Wrocław University of Science and Technology; Masaryk University)

18.00 - 18.20 Ewa Stefanik "When glycogen cannot fuel movement: a zebrafish model of McArdle disease" (University of Wrocław)

18.20 - 19.00 COFFEE BREAK/GENERAL DISCUSSION

In case of questions please contact secretary of the Wrocław branch of the Polish Biochemical Society: magdalena.chmielewska@uwr.edu.pl.

Dr. Theresia Gutmann (European Molecular Biology Laboratory (EMBL), Heidelberg, Germany)

Curriculum vitae:

- since 2026 Research Staff Scientist / Project Lead Associate at EMBL Heidelberg
- 2020-2026 Postdoc at Max Planck Institute Dresden with Tony Hyman
- 2018-2020 Wrap-up Postdoc at Helmholtz Center Munich/TU Dresden with Coskun
- 2012-2018 PhD in Biology at Dresden University of Technology with Ünal Coskun
- research stay at Helsinki University with Akseli Hemminki
- studied Biology at Humboldt University Berlin and ETH Zurich

Molecular Recognition at Biological Interfaces: Understanding Receptor Activation in Metabolic and Immune Signaling

Cell signaling relies on molecular recognition events that enable cells to sense and respond to changes in their environment. Understanding how receptor proteins recognize diverse signals and convert them into robust yet specific cellular responses remains a central challenge in biology.

My research focuses on how molecular recognition mechanisms govern metabolic and immune signal transduction from individual receptor proteins to higher-order assemblies. In this talk, I will demonstrate how we use bottom-up biochemical reconstitution approaches to reveal the molecular mechanisms of receptor activation.

I will present how we discovered the mechanism underlying insulin receptor activation, and how these insights may inform the development of novel receptor agonists. I will further discuss the relevance of supramolecular assemblies and biomolecular condensation in cell signaling and showcase recent work on the recognition of cytosolic DNA by the innate immune receptor cGAS and how viruses subvert this process.

Dr. Michał Grzybek (Center of Membrane Biochemistry and Lipid Research, Dresden, Germany)

Curriculum vitae:

- Since 08/2021 Research Group Leader, Center of Membrane Biochemistry and Lipid Research, University Hospital and Faculty of Medicine Carl Gustav Carus of TU Dresden, Germany
- 2013–2023 Research Associate, Paul Langerhans Institute Dresden of the Helmholtz Centre Munich at the University Clinic Carl Gustav Carus, TU Dresden, Germany
- 2008–2012 Postdoctoral fellow, Max Planck Institute of Cell Biology and Genetics, Dresden, Germany
- 2003–2008 PhD studies, Department of Cytobiochemistry, University of Wrocław, Poland

Lipid Perspective of Cell Signalling

Lipids, or fats, perform numerous essential functions in living organisms. In addition to serving as a major energy source, they are fundamental structural components of biological membranes and act as signaling molecules that regulate diverse cellular processes, including growth, differentiation, and stress responses. While the importance of dietary fats for health has long been recognized, it is becoming increasingly clear that their biological effects are determined not only by their caloric value but also by their molecular composition. Different fatty acids possess distinct physicochemical properties and, when incorporated into cellular membranes, can alter membrane thickness, fluidity, lipid packing, and protein activity.

These observations have led to the emerging concept that dietary lipids can influence cellular function by remodeling membrane architecture. However, despite growing evidence linking diet-induced changes in membrane composition to cellular signaling, the mechanisms connecting dietary lipid quality, membrane organization, and organismal physiology remain poorly understood. Understanding these relationships is particularly important in light of the increasing prevalence of diet-related disorders and the growing interest in personalized nutrition.

In this talk, I will discuss how dietary lipids shape biological function across multiple levels of organization. Using *Drosophila melanogaster* as a model system, I will present examples demonstrating how the quality of dietary fats influences organismal fitness and survival. I will also discuss how specific lipid species modify membrane properties and thereby affect cellular signaling pathways and downstream cellular responses. Together, these findings highlight the intimate connection between diet, membrane biophysics, and organismal health.

Abstracts – short talks

Palmitoylation regulates membrane domain association and bilayer-organizing activity of MPP1

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[2] *Present address: Laboratory of Cancer Cell Architecture, Institute of Biochemistry and Experimental Oncology, First Faculty of Medicine, Charles University, 128 00 Prague, Czech Republic*

Membrane domains are structures necessary for lateral membrane organization, providing temporal and spatial separation of lipids and proteins involved in membrane-related cellular processes. However, the mechanisms underlying their formation remain elusive. Proteins localized within membrane domains are frequently regulated by their modification with fatty acids, among which S-palmitoylation is the most common. S-palmitoylation is a reversible post-translational lipid modification that regulates protein stability, trafficking, activity, and membrane association, and has recently been proposed as a trigger influencing membrane organization in living cells. Through modulation of protein–membrane interactions, this modification contributes to the dynamic organization of membrane domains and associated signalling platforms. MPP1, a MAGUK scaffold protein, is implicated in erythroid membrane organization and membrane domain stabilization. However, the functional significance of its palmitoylation remains poorly understood.

In this study, we investigated both the pattern and functional significance of MPP1 palmitoylation using biochemical and membrane biophysics approaches. Acyl-RAC and Acyl-PEG Exchange (APE) analyses combined with cysteine mutagenesis demonstrated that all four cysteine residues of MPP1 are susceptible to palmitoylation. Among these sites, Cys242 was identified as the predominant modification site. In addition, endogenous MPP1 displayed variable levels of palmitoylation across different cellular models, indicating that the extent of this modification may depend on cellular context. To further investigate the functional consequences of MPP1 palmitoylation, we examined the membrane behaviour of palmitoylated and non-palmitoylated MPP1 variants. Detergent-resistant membrane (DRM) fractionation experiments demonstrated slightly altered partitioning of a palmitoylation-deficient MPP1 mutant, suggesting a role for palmitoylation in membrane domain association in cells. In contrast, preliminary microscale thermophoresis (MST) experiments did not reveal substantial differences in liposome binding between bacterially expressed MPP1 and its *in vitro*-palmitoylated variant. These findings suggest that palmitoylation does not primarily regulate membrane binding affinity. To assess whether palmitoylation affects membrane properties, we analysed the influence of mammalian-derived palmitoylated and bacterially expressed

non-palmitoylated MPP1 on model lipid membranes differing in phase composition. Measurements of membrane order using C-laurdan generalized polarization (GP) revealed that palmitoylation may modulate the impact of MPP1 on lipid organization, particularly in liquid-disordered membranes. These observations are consistent with our previously published fluorescence lifetime imaging microscopy (FLIM) studies in giant unilamellar vesicles (GUVs), which demonstrated a similar effect of palmitoylated MPP1 on membrane organization, further supporting the idea that palmitoylation modulates the membrane-organizing activity of MPP1.

Together, our findings identify palmitoylation as an important regulator of MPP1 membrane-organizing activity and provide further insight into how lipid modifications contribute to membrane organization.

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Biochemical Investigation of Salt-Mediated Effects on the Structure and Stability of L-α-Phosphatidylcholine

Priya Sagar, Nina Tarnowicz-Staniak, Katarzyna Matczyszyn

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Phosphatidylcholine (PC) is a phospholipid that serves as the primary building block of eukaryotic biological membranes. It constitutes nearly 40-50% of total phospholipids in mammalian cells. While playing a crucial role as lung surfactant, it also helps in maintaining the structural and functional integrity of neuronal and mitochondrial membranes and cell signaling pathways [1]. The disruption of these structures is detrimental to human health and may arise from several genetic, physical and ionic factors. Hence, investigating the influence of physiologically relevant ions [2] (Na^+, K^+, Cl^- and CH_3COO^-) on pristine L-alpha phosphatidylcholine under in vitro conditions can provide phenomenological insights on ion-specific interactions and their role in modulating membrane structural organization. The concentration range of 0.01M, 0.03M, 0.05M, 0.07M was selected for salt investigation on dried lipid cake (20mg/ml), prepared using L-α-phosphatidylcholine in chloroform. The lipid cake hydration results in the formation of multilamellar structures known as myelin figures. The lipid hydration is influenced by factors such as the hydration gradients, ionic environment, ambient humidity, and temperature [3]. The observation of myelin figures using an Olympus BX-60 polarised light microscope for 9 minutes revealed the presence of two distinct populations of myelin tubes, depending on the origin of their nucleation and growth. The tubes originating from the central region of the lipid cake were referred to as centre tubes, while those emerging from its periphery were named as edge tubes. The final lengths and

diameters of around 700 myelin tubes from both populations were measured and recorded for quantitative analysis, using ImageJ.

The results demonstrated that NaCl and KCl produced comparatively small variations in tubular morphologies across the concentration range, with spatial differences observed between the centre and the edge tubes. In NaCl-influenced systems, centre tubes consistently exhibited longer lengths and wider diameters compared to KCl-affected systems. This enhanced growth behaviour may be attributed to the kosmotropic nature, smaller ionic size, and stronger hydration shell associated with Na^+ ions, which influence phospholipid packing, hydration-mediated interactions, and membrane organisation. Similar morphological trends were observed for KCl systems, although the overall extent of growth variation remained comparatively limited. Further ion-specific investigations at a fixed concentration of 0.05M for acetates and chlorides of sodium and potassium revealed that anion effects are more pronounced, since chloride- and acetate-based salts segregated into two distinct groups. The observed behaviour can be interpreted within the framework of the Hofmeister series [4], where ion-specific effects govern molecular organisation, hydration dynamics, and interfacial stability in phospholipid-based systems.

Overall, the study demonstrates that physiologically relevant ions significantly influence phosphatidylcholine tubular morphology. Hence, this research may contribute to the rational design of lipid-based drug delivery systems, where ionic environments influence membrane stability, drug encapsulation efficiency, permeability, and release behavior.

[1] Pohl, H.R., Wheeler, J.S., Murray, H.E., Met. Ions. Life. Sci. 2013, 13, 29-47.
[2] Gurtovenko, A. A., Vattulainen, I., J. Phys. Chem. B 2008, 112(7), 1953-1962.
[3] Benkowska-Biernacka, D., Smalyukh, I., Matczyszyn, K., *J. Phys. Chem. B 2020, 124(52), 11974–11979.*
[4] Leontidis, E., Adv. Colloid Interface Sci. 2017, 243, 8–22
[5] Alakhras, F., Holay, M., Kurnia, K. A., J. Mol. Struct. 2018, 1167, 105–115

Comparative Analysis of LNP Manufacturing Across Commercial and Custom Platforms

Magdalena Przybyło[1,2], **Maxime Kucharski**[1,2], Marek Langner[1,2]

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[2]*Lipid Systems sp. z o. o.*

The production of lipid nanoparticles (LNPs) with well-defined physicochemical properties is critically dependent on precise control of fluid dynamics and mixing regimes during the formulation process [1]. As LNP-based delivery systems continue to gain prominence in both research and clinical applications, the scalability and reproducibility of manufacturing protocols have become key challenges, particularly in the transition from laboratory-scale optimization to industrial-scale production under Good Manufacturing Practice (GMP) standards [2].

In this study, a comprehensive comparison of LNP manufacturing conditions was conducted using three distinct technological approaches: a fully automated commercial production system (Knauer), a fully custom-built platform (Liposhell extruder), and a hybrid configuration combining a custom system with commercial microfluidic mixers (Precision NanoSystems). The resulting nanoparticle characteristics— hydrodynamic size, polydispersity index (PDI), and cargo encapsulation efficiency—were evaluated as a function of total flow rate, device configuration, microfluidic mixer architecture, and lipid composition. Emphasis was placed on the influence of mixing regimes and shear conditions on formulation outcomes.

A critical aspect of the study involved assessing the impact of the quenching step using Tris buffer on formulation stability and particle integrity. This was investigated across both in-line microfluidic mixing systems and bulk-type custom preparation methods, enabling direct comparison of post-mixing stabilization strategies. Furthermore, two distinct optimization paradigms were examined: flow rate–driven optimization and mixer architecture–driven optimization, providing insight into their relative effectiveness and practical limitations.

The results reveal substantial variability in LNP characteristics depending on the selected manufacturing platform and process parameters, underscoring the complex interplay between hydrodynamic conditions and formulation composition. Notably, discrepancies were identified between optimization strategies commonly employed in academic research and those required for robust, scalable production in GMP-compliant environments. These findings highlight the importance of platform-specific process optimization and the need for standardized methodologies that bridge the gap between exploratory research and industrial implementation.

[1] Nakamura K, Aihara K, Ishida T, Importance of Process Parameters Influencing the Mean Diameters of siRNA-Containing Lipid Nanoparticles (LNPs) on the in Vitro Activity of Prepared LNPs. Biol. Pharm. Bull. 2022, 45, 497–507. https://doi.org/10.1248/bpb.b21-01016

[2] Xu S, Hu Z, Song F, Xu Y, Han X, Lipid Nanoparticles: Composition, Formulation, and Application. Mol. Ther. Methods Clin. Dev. 2025, 33, 101463. https://doi.org/10.1016/j.omtm.2025.101463

Investigating the molecular basis of cytoprotective functioning of NPAS4 under Hypoxic and Oxidative Stress Conditions

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NPAS4 (Neuronal PAS domain-containing protein 4) is a stress-responsive transcription factor belonging to the bHLH-PAS family. NPAS4, classified as an Immediate Early Gene (IEG), was shown as a cytoprotecting protein in neurological and pancreatic disorders. Its

expression was initially identified primarily in neuronal cells; however, subsequent studies demonstrated NPAS4 expression in various tissues, including pancreatic beta cells.

Although NPAS4 has been implicated in cytoprotective responses under hypoxic and metabolic stress conditions, its exact mechanisms of action remain poorly understood. We hypothesize that the cytoprotection could be achieved by involvement in endoplasmic reticulum (ER) stress regulation and non-genomic stress-associated functions. Since ER stress, oxidative stress, and hypoxia contribute to the pathogenesis of neurodegenerative diseases, ischemic injury, metabolic disorders, and cancer, understanding NPAS4-mediated cytoprotective mechanisms may have potential therapeutic relevance.

The aim of our study was verification of the connection between the cytoprotective role of NPAS4 under hypoxic and oxidative stress conditions and ER stress and unfolded protein response (UPR) signaling. Murine neuroblastoma N2A cells overexpressing YFP-tagged NPAS4 were exposed to physiological hypoxia (under hypoxia chamber), chemical hypoxia induced by deferoxamine and cobalt chloride (DFO and $CoCl_2$), and oxidative stress induced by hydrogen peroxide (H_2O_2). The expression of ER stress-associated markers was analyzed using RT-qPCR while NPAS4 localization was assessed by confocal microscopy. In addition, preliminary lipidomic analyses were performed to evaluate potential NPAS4-dependent lipidome remodeling under stress conditions.

Our results suggest that NPAS4 exerts stress-context-dependent cytoprotective effects. Under hypoxic conditions, NPAS4-associated protection appears to involve modulation of ER stress and UPR pathways. Importantly, distinct hypoxic models activated different UPR pathways: physiological hypoxia was associated predominantly with IRE1-related signaling, whereas chemical hypoxia induced stronger activation of the PERK and ATF6 pathways. In contrast, under oxidative stress conditions, NPAS4-mediated protection appeared to be less dependent on the ER stress and rather associated with antioxidant responses, including increased Sod1 expression. Confocal microscopy demonstrated elevated NPAS4 expression under both hypoxic and oxidative stress conditions. NPAS4 was predominantly localized in the cytoplasm; however, chemical hypoxia promoted its partial nuclear translocation. Furthermore, in the case of all kinds of stress, NPAS4 presented a punctate localization pattern suggesting the liquid–liquid phase separation (LLPS) process. Under severe chemical hypoxia, NPAS4 partially co-localized with stress granules, indicating a potential non-genomic role in cellular stress adaptation. Interestingly, preliminary lipidomic analyses suggest that NPAS4 may influence stress-associated lipidome remodeling.

Collectively, these findings indicate that NPAS4 may function as a novel regulator of cellular stress adaptation through both genomic and non-genomic mechanisms involving ER stress modulation, antioxidant responses, and potentially LLPS-associated processes that awaits further studies.

Acute RNA polymerase II perturbation by arsenic triggers arm-wide γH2A signaling

Adrianna Nawrot, Litwin I.

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Much of what we know about DNA damage signaling comes from studies using engineered double-strand breaks and global replication stress, whereas far less is known about how genome surveillance pathways respond to naturally occurring genotoxins. Arsenic provides a compelling context for this question. The WHO lists arsenic among the chemicals of major public health concern, and inorganic arsenic is a confirmed carcinogen whose genotoxic effects are still commonly framed in terms of ROS, oxidative DNA damage, and replication-associated DNA breaks. Here we show that short-term arsenic exposure in budding yeast induces a rapid chromosome-arm–spanning γH2A response that is largely replication-independent, arises under low oxidative stress, and occurs without detectable DNA double-strand breaks. Genetic RNAPII inactivation recapitulates this γH2A landscape, indicating that acute transcriptional shutdown is sufficient to trigger this chromosome-scale checkpoint response. Consistently, arsenic reduces RNAPII chromatin occupancy and promotes Rpb1 loss, while an arsenic-containing probe captures purified RNAPII in vitro, supporting RNAPII as an upstream arsenic target. In human cells, short-term arsenic induces ATR activation and γH2AX under low ROS, and transcriptional inhibition elicits a similar γH2AX response that is non-additive with arsenic. Together, these findings reframe early arsenic genotoxicity while pointing more broadly to acute RNAPII perturbation as a trigger of chromosome-scale checkpoint signaling.

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Characterization of crystal-associated proteins in calcium oxalate-rich plant tissues

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[2]*Department of Geological Sciences, Masaryk University, Brno, Czech Republic*

Despite the widespread occurrence of calcium oxalate in plants, the molecular mechanisms underlying its formation, including the processes that guide nucleation, polymorph development, and spatial arrangement remain poorly understood. It is also unclear how these biomineralization events relate to cellular ion balance, how associated macromolecules contribute to crystal organization, or how trace ions influence crystal stability and structure, highlighting the need for protein level investigations.

SDS-PAGE was used to separate crystal associated proteins extracted from calcium oxalate rich plant tissues, allowing visualization of distinct protein profiles. Protein bands of interest were excised from gels and subjected to in gel digestion to generate peptides suitable for mass spectrometric analysis. LC-MS/MS was then used to perform high resolution peptide separation and fragmentation, enabling proteomic profiling of the crystal associated fractions. Mass spectrometry-based protein identification was carried out by matching detected peptide spectra to plant protein databases using established search algorithms. Together, these approaches enabled the characterization of proteins potentially involved in calcium oxalate biominerals.

In proteomic analysis of calcium oxalate rich fractions are expected to reveal proteins associated with crystal formation and organization. Distinct protein patterns may indicate molecules involved in stabilizing or shaping crystals. Differences between tissues could suggest how local cellular conditions influence crystal development. Some proteins may interact with ions, potentially affecting crystal structure.

This study aims to show that calcium oxalate crystal formation is influenced by specific proteins rather than occurring purely physically. Identified proteins may contribute to crystal development, organization, and stability. Overall, the work will provide insights into the molecular mechanisms of plant biomineralization.

When glycogen cannot fuel movement: a zebrafish model of McArdle disease

Ewa Stefanik[1], Małgorzata Daczewska[1], Magda Dubińska-Magiera[1], Damian Lewandowski[1], Barbara Budzyńska[2], Marta Migocka-Patrzałek[1]

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Glycogen phoshorylase (PYGM) is a key enzyme in the first step of glycogenolysis. It is responsible for converting glycogen into glucose, the primary energy source for skeletal muscle activity. Mutations in this gene lead to McArdle's disease. Patients affected by this condition are unable to engage in excessive physical exertion due to the lack of energy. To investigate structural and functional consequences of glycogen phosphorylase deficiency, we generated a zebrafish (Danio rerio) line with CRISPR/Cas9-mediated knock-out of the pygm gene (pygm+/-). We hypothesize that zebrafish can closely mimics human McArdle disease.

Detailed morphological analyses revealed abnormalities in skeletal muscle organization in pygm+/- individuals, including disturbed myofibrillar alignment, altered muscle fiber integrity, and changes in overall body posture. These structural alterations were accompanied by significant biochemical changes in glycogen storage and behavioural

impairments. The observed phenotype closely reflects key clinical features of McArdle disease, particularly exercise intolerance resulting from compromised muscle performance. Our findings demonstrate that pygm+/- zebrafish provide a robust platform for studying the structural basis of muscle dysfunction and its functional consequences in vivo.

This model offers a valuable opportunity to further dissect disease mechanisms and evaluate potential therapeutic interventions targeting muscle performance and metabolic adaptation.

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