Humboldt Kolleg

EXCELLENCE IN SCIENCE AND GLOBAL CHALLENGES TODAY

EXZELLENZ IN DER WISSENSCHAFT UND GLOBALE HERAUSFORDERUNGEN HEUTE

Topics:

(United Nations Sustainable Development Goals to Transform our World)

- **Good Health and Well-Being**
- **Quality Education**
- **Affordable and Clean Energy**
- **Climate Action**

24-27 June 2026

Sofia, Bulgaria

Hall “Prof. Marin Drinov”, Bulgarian Academy of Sciences
Conference Hall of Sofia University “St. Kliment Ohridski”

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Maya Zaharieva

Program

24.06.2024

14:00 – 16:00 REGISTRATION
In front of hall "Prof. M. Drinov", BAS

16:00 – 16:30 OPENING
Hall "Prof. M. Drinov"

Chair: Ilza Pajeva

- President of the Humboldt Union in Bulgaria
- **German officials**
- **Bulgarian officials**

16:30 – 17:00

Yuri Kalvachev (Bulgaria) *President of the Humboldt Union in Bulgaria*
Bulgarian Research Landscape

17:00 – 17:40

Maria Endreva (Bulgaria) *Ambassador-scientist of the Foundation*
Presentation of the programs of the Alexander von Humboldt Foundation

17:40 – 18:00

Questions and Answers

18:30 – 20:30 Reception
National Archaeological Museum

25.06.2026

09:00 – 12:30
SESSION: *Good health and well-being*
Hall "Prof. Marin Drinov", BAS

Chair: Radka Argirova

09:00 – 09:30

Ulrike Holzgrabe, Ute Hellmich, Mitali Sarkar-Tyson (Germany, Australia) *(keynote lecture)*
Addressing virulence factors - an alternative treatment of infections

09:30 – 09:45

Rayna Nenova, Radka Argirova, Kalin Kalinov, Ana Dobreva, Dimitar Peshev, Aleksandra Nikolaeva Rangelova-Haralampieva, Ivan Iliev, Neli Vilhelmova-Ilieva (Bulgaria)
Blocking ocular herpes simplex virus-1 entry by bioactive compounds from oil-bearing Rosa damascena Mill

09:45 – 10:00

Trifon Valkov, Georgi Dimitrov, Radka Argirova (Bulgaria)
Risikoanalyse von Masernausbrüchen in Bulgarien und Rumänien für den Zeitraum 2000 bis 2023: Eine vergleichende Studie

10:15 – 10:30

Slavena Davidova, Maya Zaharieva, Galina Sachanska, Hristo Najdenski (Bulgaria)
Identifying the prevalence of Listeria monocytogenes in minced meat at different storage temperatures through artificial contamination

10:30 – 10:45 Coffee break

Chair: Radka Argirova

10:45 – 11:00

Violeta Ivanova, Ilina Poparova, Eugenia Russinova, Kiril Mishev (Bulgaria, Belgium)
The role of endomembrane trafficking complexes in plant hormone receptor dynamics

11:00 – 11:15

Simona Galabova, Irina Vaseva, Dominique Van Der Straeten (Bulgaria, Belgium)
Comparative analyses of Arabidopsis thaliana signaling mutants and transgenic lines subjected to moderate drought and recovery

11:15 – 11:30

Parashkev Katevski, Petko Alov, Maria Angelova, Elina Beleva, Boian Lazov, Antonia Diukendjieva, Dessislava Jereva, Iglika Lessigiarska, Ilza Pajeva, Tania Pencheva, Stefan Tsakovski, Peter Vassilev, Ivanka Tsakovska (Bulgaria)
Development of computational tool for predicting toxic effects of chemicals

11:30 – 11:45

Georgi Dimitrov, Radka Argirova, Trifon Valkov (Bulgaria)
Long-term cancer survival after COVID-19: Nationwide evidence in patients with solid malignancies

11:45 – 12:00

Iva Nenkova, Maria Kamusheva, Hristo Varbanov, Maya Zaharieva (Bulgaria)
Acute myeloid leukaemia: multidisciplinary insights into access, care, and therapeutic development

12:00 – 12:15

Georgi Ivanov, Nikolay Tzvetkov (Bulgaria)
In search of novel MAO-B/alpha-Synuclein inhibitors

12:15 – 12:30

Ivan Bogdanov, Nikolay Tzvetkov (Bulgaria)
From small molecules as factor XIIIa inhibitors towards target diversity

12:30 – 14:00 Lunch

Restaurant Victoria – Tsar Osvoboditel blvd, 7

14:00 – 16:00

SESSION: *Quality education*

Conference Hall of Sofia University "St. Kliment Ohridski"

Chair: Maria Endreva

14:00 – 14:30

Dennis Pausch (Germany) (*keynote lecture*)
How to Read Ancient Historiography? Potentials and Risks of Emotional Immersion

14:30 – 14:45

Maja Debska (Poland)

Der Sound der Geschichte – Techno als Gedächtnismedium und als literarische Form

14:45 – 15:00

Maria Bakalova (Bulgaria)

Transcribing Danish intonation with tobi – basics, specifics, and challenges

15:00 – 15:15

Zozan Tarhan (Bulgaria)

Der heutige Zustand und die Zukunft der Altorientalistik weltweit und in Bulgarien

15:15 – 15:30

Kalina Kupczynska (Poland)

Geschichtscomics, multidirektionale Erinnerung und Geschichtspolitik - Chancen und Herausforderungen für die Geschichtsvermittlung

15:30 – 16:00 Coffee break

16:00 – 17:15

Presentation of the programs of DFG

Conference Hall of Sofia University "St. Kliment Ohridski"

Chair: Yuri Kalvachev

16:00 – 16:45

Jörn Achterberg, Stephanie Lass, Julia Ilina, Djawed Nauroozi (Germany)

Presentation of German Research Foundation programs

16:45 – 17:15

Questions and Answers

18:30 – 21:00 Dinner

Restaurant La Branche, Crystal Palace, Shipka Street 14, Sofia, 1504, Bulgaria

26.06.2026

09:00 – 12:30

SESSION: *Climate action and Affordable and clean energy*

Hall "Prof. Marin Drinov", BAS

Chair: Petar Petrov

09:00 – 09:30

David Scheschkewitz (Germany) *(keynote lecture)*

Low-valent main group species as game changers in homogeneous catalysis?

09:30 – 09:45

Sonja Zrilic, Snejana Zaric (Serbia)

Hydrogen bonds of coordinated amino acids and water: different types and their relevance

09:45 – 10:00

Antonio Ljulj, Anamarija Jurjević, Elena Erlić, Lara Vincelj, Lea Ulm, Valerije Vrček (Croatia)

Anticancer drugs in the environment

10:00 – 10:15

Erik Dimitrov, Krum Alexandrov, Yavor Hristov, Aleksander Forys, Maria Petrova, Natalia Toncheva-Moncheva, Emi Haladjova, Iva Ugrinova, Barbara Trzebicka, Stanislav Rangelov (Bulgaria, Poland)

Cyclic polymer brushes - tunable platforms for drug and gene delivery

10:15 – 10:30

Stiliyana Stoyanova, Oumayma Mlida, Antonio Da Costa, Anthony Ferri, Evgeni Ivanov, Rumiana Kotsilkova, Fahmi Bedoui (Bulgaria, France)

Electrospun polymer nanofibers with multi-walled carbon nanotubes and graphene for piezoelectric applications

10:30 – 11:00 Coffee break

11:00 – 12:30

SESSION: *Climate action and Affordable and clean energy*

Hall "Prof. Marin Drinov", BAS

Chair: Silviya Boycheva

11:00 – 11:15

Tsanislava Genova, Alexandra Zhelyazkova (Bulgaria)

Optical clearing for OCT teeth imaging

11:15 – 11:30

Nikoleta Kircheva, Vladislava Petkova, Stefan Dobrev, Valya Nikolova, Silvia Angelova, Todor Dudev (Bulgaria)

Metal selectivity in some protein phosphatases: insights from a theoretical study

11:30 – 11:45

Lidia Zaharieva, Diana Rüesch, Søren W. Svenningsen, Fadhil Kamounah, Michael Pittelkow, Liudmil Antonov, Jan Helbing (Bulgaria, Switzerland, Denmark)

Light-driven long-range proton transfer: optimization and mechanisms

11:45 – 12:00

Alina Kumanova, Vera Deneva, Sofia Slavova, Nikolay Vassilev, Daniela Nedeltcheva-Antonova, Luidmil Antonov (Bulgaria)

Tautomeric and complexation properties of Avigan in solution

12:00 – 12:15

Dobromir Kalchevski, Stefan Kolev, Teodor Milenov (Bulgaria)

A complete model of the [1,5]-sigmatropic conversion of chorismate to 4HB and pyruvate by chorismate lyase

12:15 – 12:30

Marianna Vasilaki, N. Ilieva, G. Gocheva, S. Iliev, J. Petkova, A. Ivanova (Bulgaria)

A Trojan Horse Strategy: Molecular dynamics, design and evalution of folate-conjugates for targeted drug delivery of doxorubicin

12:30 – 14:00
Restaurant Victoria – Tsar Osvoboditel blvd, 7

14:00 – 16:00
SESSION: *Affordable and clean energy and Climate action*
Hall "Prof. Marin Drinov", BAS

Chair: Albena Paskaleva

14:00 – 14:15
Veronika Petkova, Hristo Rasheev, Alia Tadjer (Bulgaria)
Modeling of anode materials in sodium-ion batteries

14:15 – 14:30
Stoyan Gramatikov, Georgi Vayssilov (Bulgaria)
Computational modeling of the interaction of organic structure directing agents with silicate and borosilicate zeolite frameworks

14:30 – 14:45
Denis-Răducu Nichita, Mihai Dima, Petru Vaideanu, Monica Ionita (Romania, Germany)
A weakened AMOC warms winters and drives summer multidecadal variability

14:45 – 15:00
Galina Dimitrova, Anguel Demerdjiev, Dimitar Tonev, Ventzislav Rusanov, Nikolay Goutev (Bulgaria)
Evaluation of radiation fields in a TR-24 cyclotron facility

15:00 – 16:30
Discussion: Young researchers – potential candidates for AvH fellows with German professors (Selection committee members)
Moderator: Nikolay K. Vitanov

16:30 – 19:00 CITY TOUR – Social Program

19:00 – 21:00 - Dinner
Restaurant Shtastliveca San Stefano Plaza Sofia

27.06.2026

9:00 – 12:00
SESSION: *Good health and well-being*
Hall "Prof. Marin Drinov", BAS

Chair: Maya Zaharieva

9:00 – 9:30
Radka Kaneva, Kalina Mihova, Martin Georgiev, Tzvetana Kerelska, Daniela Kostova, Delyan Georgiev, Svetomir Hitov, Kamen Yonchev, Ivanka Dimova, Kristina Stefanova, Kristiana Vitanova, Simona Stankova, Konstantin Paramov, Veselina Levakova, Valentin Dichev, Nikolay Mehterov, Yordan Sbirkov, Mihail Petrov, Victoria Sarafian, Mariana Murdzheva, Vanio Mitev (Bulgaria)
Foundations for Precision Medicine: Preliminary results of the Bulgarian Genome Project

9:30 – 9:45

Lora Veleva, Stoyan Pavlov (Bulgaria)

Automated evaluation of gene expression in chromogenic in situ hybridization images using spectrum-normalized pseudo-channel

9:45 – 10:00

Desislava Tsoneva, Diana Buzova, Stefani Todorova, Yavor Enchev, Jan Frohlich, George Chaldakov, Anton Tonchev, Jan Cerveny, Manlio Vinciguerra (Bulgaria, Czech Republic, Italy)

Plasma histone monomers as novel diagnostic markers in adult glioblastoma

10:00 – 10:30 Coffee break

10:30 – 10:45

Aleksandar Atemin, Aneliya Ivanova, Teodora Dyankova-Danovska, Sonya Uzunova, Georgi Danovski, Rumen Stamatov, Petar-Bogomil Kanev, Radoslav Aleksandrov, Stoyno Stoynov (Bulgaria)

Effect of PCNA protein depletion on replication stress

10:45 – 11:00

Aneliya Ivanova, Aleksandar Atemin, Sonya Uzunova, Petar-Bogomil Kanev, Stoyno Stoynov (Bulgaria)

Dynamics of the replication fork stalling and restart in BRCA2/PALB1 deficient cells

11:00 – 11:15

Plamen Angelov, Yordanka Sapundzieva, **Denitsa Bachvarova** (Bulgaria)

In the search of novel antibacterials – mimicking the pseudomonas metabolites

11:15 – 11:30

Andreas Kontny, Andon Mladenov, Tetsumori Yamashima, Anton Tonchev **(**Bulgaria, Japan)

Ultrastructural and molecular mapping of 4-Hydroxynonenal (HNE)-induced degeneration in the murine cornea and retina

11:30 – 11:45

Veronika Petkova (Bulgaria)

Bulk transcriptome analysis of thyroid cancer and nodous goiter reveals key roles of immune system and epigenetic regulation

11:45 – 12:00

Closing remarks

12:00 – 14:00 Lunch

Restaurant Victoria – Tsar Osvoboditel blvd, 7

Book of Abstracts

(abstracts are ordered according to the Program)

ADDRESSING VIRULENCE FACTORS – AN ALTERNATIVE TREATMENT OF INFECTIONS

Ulrike Holzgrabe[a], Ute A Hellmich[b], Mitali Sarkar-Tyson[c]

[a]Institute of Pharmacy, University of Wuerzburg, Ulrike.holzgrabe@uni-wuerzburg.de; [b]Institute of Organic and Macromolecular Chemistry, University of Jena, ute.hellmich@uni-jena.de; [c]Marshall Centre for Infectious Diseases, School of Biomedical Sciences, University of Western Australia, Perth, mitali.sarkar-tyson@uwa.edu.au

Infectious diseases are a main cause of morbidity and mortality worldwide, especially due to increasing antibiotic resistance in almost all bacteria. Hence, the development of new drugs with new modes of action is of paramount importance. Alternative to the development of inhibitors of the bacterial protein and DNA synthesis, targeting virulence factor is an emerging strategy, as almost no evolutionary pressure is caused. Immunophilins, in particular the macrophage infectivity potentiator (Mip) protein, belonging to the superfamily of peptidyl-prolyl *cis-trans* isomerase (PPIase) enzymes, have been demonstrated to be necessary for virulence in a broad-spectrum of pathogens, especially of Gram-negative bacteria such as *Burkholderia pseudomallei*, *Legionella pneumophila*, *Chlamydia trachomatis*, *Neisseria speciies*, and *Coxiella burnetti* as well as *Trypanmosoma cruzei*. Compounds derived from the pipecolic moiety of Rapamycin are potent PPIase inhibitors and reduce the infectivity of each microorganism. Hence, they were used to develop MIP inhibitors of the above-mentioned microorganisms by means of structure-based design [1-4].

References:

[1] Scheuplein NJ, Bzdyl NM, Lohr T, Kibble EA, Hasenkopf A, Herbst C, Sarkar-Tyson M, Holzgrabe U. J Med Chem. 66:8876-8895:2023.

[2] Lohr T, Scheuplein NJ, Jenkins C, Norville I, Erk C, Stapf M, Kirchner L, Sarkar-Tyson M, Holzgrabe U. Arch Pharm (Weinheim). 2024; 357: e2400032.

[3] Lohr T, Herbst C, Bzdyl NM, Jenkins C, Scheuplein NJ, Sugiarto WO, Whittaker JJ, Guskov A, Norville I, Hellmich UA, Hausch F, Sarkar-Tyson M, Sotriffer C, Holzgrabe U. ACS Infect Dis. 2024; 10: 3681-3691.

[4] Pérez Carrillo VH, Whittaker JJ, Wiedemann C, Harder JM, Lohr T, Jamithireddy AK, Dajka M, Goretzki B, Joseph B, Guskov A, Harmer NJ, Holzgrabe U, Hellmich UA. J Med Chem. 2025, 68:5926-5941.

BLOCKING OCULAR HERPES SIMPLEX VIRUS-1 ENTRY BY BIOACTIVE COMPOUNDS FROM OIL-BEARING *Rosa damascena* Mill.

Rayna Nenova[a], Radka Argirova[b], Kalin Kalinov[a], Ana Dobreva[a], Dimitar Peshev[c], Aleksandra Rangelova-Haralampieva[d], Ivan Iliev[e], Neli Vilhelmova-Ilieva[d]

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Globalization facilitates the spread of emerging infectious diseases, which are challenging to treat due to a lack of specific drugs, or significant side effects, and the rapid onset of drug resistance. For centuries, *Rosa damascena* Mill. essential oil has been prized for its healing properties, which arise from a unique complex of natural constituents.

As HSV-1 is a causative agent of multiple ocular pathologies, we established an in vitro model of HSV-1 ocular infection in rabbit retinal cells (RRC) to evaluate the antiviral activity of rose oil and rose water across key stages of viral replication. The main chemical constituents of the rose oil were identified and quantified by gas chromatography with flame ionization detector.

Using a cytopathic effect (CPE) inhibition assay, neither product significantly inhibited the viral replication cycle. However, an endpoint dilution method revealed that both significantly blocked viral adsorption (rose water: $\Delta lg = 2.25$; rose oil: $\Delta lg = 2.0$) and, when used as a pretreatment, protected healthy cells from subsequent infection (rose oil: $\Delta lg = 2.5$; rose water: $\Delta lg = 2.0$).

Molecular docking simulations revealed that geraniol, citronellol, and nerol—the main constituents of rose oil—bind to the HSV-1 glycoprotein D (gD) interface for host cell receptors (nectin-1 and HVEM), suggesting a mechanism for the observed adsorption inhibition. These findings identify a promising, natural foundation for novel antiviral therapies against ocular HSV-1.

RISIKOANALYSE VON MASERNAUSBRÜCHEN IN BULGARIEN UND RUMÄNIEN FÜR DEN ZEITRAUM 2000 BIS 2023: EINE VERGLEICHENDE STUDIE

Trifon Valkov[a], George Dimitrov[b] und Radka Argirova[c]

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Masern sind eine hochansteckende, aber durch Impfung vermeidbare Infektionskrankheit. Laut dem ECDC-Bericht vom 16. Februar 2024 „Masern auf dem Vormarsch in der EU/im EWR: Überlegungen für die Reaktion des öffentlichen Gesundheitswesens" sind dringende Maßnahmen erforderlich, um der zunehmenden Ausbreitung von Masern und der unzureichenden Impfquote in der EU entgegenzuwirken. Hauptziel dieser Studie ist eine vergleichende Analyse des Masernausbruchsrisikos in zwei Nachbarländern mit intensiven Wirtschaftsbeziehungen – Bulgarien und Rumänien. Unsere Forschung ist Teil eines größeren Projekts zur Bewertung des Masernausbruchsrisikos in Bulgariens Nachbarländern, um einen umfassenderen Einblick in die potenziellen Bedrohungen der nahen Zukunft zu gewinnen.

Es wurden Daten zur Impfquote und zur demografischen Entwicklung in Bulgarien und Rumänien über einen Zeitraum von 50 Jahren erhoben. Mithilfe eines mathematischen Modells werden die Impfquote und die demografischen Parameter jährlich geschätzt. Dies ermöglicht es uns, die Anzahl der empfänglichen Personen mit zufriedenstellender Genauigkeit über einen Zeitraum von mindestens 20 Jahren zu berechnen. Kern des Modells ist die Berechnung eines jährlichen Risikoindex, definiert als das Verhältnis aller empfänglichen Personen zur Gesamtbevölkerung. Die Risikoindexkurven für Masernausbrüche in Bulgarien und Rumänien wurden für den Zeitraum von 2000 bis 2023 berechnet. Die Kurve für Bulgarien zeigt einen besorgniserregenden Anstieg nach 2015, mit besonders alarmierenden Werten, die für 2017 und später prognostiziert werden. Auch die Ergebnisse für Rumänien sind nach 2016 besorgniserregend. Im Jahr 2023 erreicht der Risikoindex für Bulgarien 7,55 %, während er in Rumänien 8,1 % beträgt.

Der Vergleich der Ergebnisse des Risikoindex mit realen Daten zu Masernausbrüchen zeigt, dass der Risikoindex ein guter Indikator für das Risiko eines Masernausbruchs ist. Er kann den Gesundheitsbehörden helfen, potenzielle Masernausbrüche vorherzusagen. Wichtig ist, dass die Impfquote parallel zur demografischen Entwicklung überwacht wird, die selbst Fachleuten entgehen kann.

IDENTIFYING THE PREVALENCE OF LISTERIA MONOCYTOGENES IN MINCED MEAT AT DIFFERENT STORAGE TEMPERATURES THROUGH ARTIFICIAL CONTAMINATION

Slavena Davidova[a,b], Maya Zaharieva[a], Galina Satchanska[b,c], Hristo Najdenski[a]

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The present study evaluated the ability of *Listeria monocytogenes* to survive and multiply in minced meat at different storage temperatures, as well as the presence of key virulence genes (*hly* and *prfA*) in the isolates studied. The focus is on the risk of contamination of meat products by psychrotrophic pathogens that can grow during refrigeration. An experimental study was conducted by artificially contaminating a minced meat mix purchased from a grocery store. DNA from seven isolates of *L. monocytogenes* was isolated and analyzed for the presence of *hly* and *prfA* by conventional PCR and digital droplet PCR (ddPCR). The samples were incubated at 4°C and 10°C for different time intervals, and growth was monitored by determining colony-forming units (CFU/ml). The results showed that *L. monocytogenes* grew at both temperatures, with higher CFU/ml values observed at 10°C. An increase in the bacterial population over time was observed under both conditions, with the most intensive growth between 48 and 72 hours at 10°C. Contaminated samples were also analyzed by ddPCR to precisely quantify *L. monocytogenes* across different dilutions and cultivation temperatures. The data confirm the psychrotrophic nature of *L. monocytogenes* and the role of *hly* and *prfA* as virulence markers. The results highlight the importance of cold storage control to limit the risk to public health.

THE ROLE OF ENDOMEMBRANE TRAFFICKING COMPLEXES IN PLANT HORMONE RECEPTOR DYNAMICS

Violeta Ivanova[a], Ilina Poparova[b], Eugenia Russinova[b,c], Kiril Mishev[a]

[a]Department of Molecular Biology and Genetics, Institute of Plant Physiology and Genetics, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria; [b]Department of Plant Biotechnology and Bioinformatics, Ghent University, 9052 Ghent, Belgium; [c]Center for Plant Systems Biology, VIB, 9052 Ghent, Belgium

Plant hormone signaling relies on the precise spatial receptor localization within the endomembrane system. The brassinosteroid receptor BRI1 represents a well-established model for studying how intracellular trafficking influences signal perception and output. Brassinosteroids (BRs) are essential plant hormones that regulate growth, development, and stress responses through their binding to the receptor kinase BRI1. It is known that the biologically active pool of BRI1 is located at the plasma membrane, while receptor internalization leads to reduced sensitivity to hormonal stimulus. The BR receptor pool is highly dynamic, with the majority of BRI1 continuously cycling between the plasma membrane and endomembrane compartments, while only a minor fraction is targeted to the vacuole for degradation. In addition to canonical trafficking pathways, autophagy represents a key mechanism for receptor desensitization, particularly under stress conditions. To gain insight into the mechanisms governing BRI1 trafficking, we investigate the role of vesicle trafficking regulators, including components of the exocyst complex – a conserved tethering complex involved in intracellular vesicle transport – in shaping BRI1 receptor dynamics in *Arabidopsis thaliana*. To dissect the role of exocyst-mediated trafficking in BRI1 regulation, we generated *Arabidopsis thaliana* lines expressing fluorescently tagged BRI1 in mutant backgrounds of key exocyst subunits - SEC8, SEC15, EXO84, and EXO70. Live-cell imaging revealed differences in BRI1 localization in exo70a1 and exo84b mutants. Pharmacological treatments further identified EXO70B1 as an important regulator of BRI1 recycling. Moreover, under conditions that induce autophagy, such as salt stress and nitrogen deprivation, EXO70B1 had a role for efficient targeting of BRI1 to autophagosomes. Taken together, these findings demonstrate that the exocyst complex plays a multifaceted role in controlling BRI1 trafficking, linking receptor localization, recycling, and degradation to the modulation of brassinosteroid signaling under both optimal and stress conditions.

COMPARATIVE ANALYSES OF *ARABIDOPSIS THALIANA* SIGNALING MUTANTS AND TRANSGENIC LINES SUBJECTED TO MODERATE DROUGHT AND RECOVERY

Simona Galabova[a], Irina I. Vaseva[a], Dominique Van Der Straeten[b]

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Drought stress is a major limiting factor in plant productivity and survival, and *Arabidopsis thaliana* serves as a model for understanding the complex regulatory networks involved in stress tolerance. Comprehensive evaluation of the variation in gene expression across diverse genotypes under water scarcity and during recovery is essential for identifying potential mechanisms of drought resilience. Therefore, the main research focus was put on transcriptional profiling of key antioxidant and osmoprotectant genes under moderate drought stress and after recovery. We analyzed *A. thaliana* ethylene-signaling mutants *ein2-1*, *ein3eil1* and *ctr1-1* and transgenic lines exhibiting tissue-specific ethylene desensitization in particular root cell types: epidermis and lateral root cap *(pA14:EBF2, pLRC1:EBF2)*, the quiescent center *(pQ6:EBF2)*, endodermis *(pE30:EBF2)*, pericycle *(pS1:EBF2)*, cortex *(pCOR:EBF2)*, and vasculature *(pS2:EBF2)* [1]. Expression levels of *APX1*, *APX3*, *SOD1*, *PER44*, *PER57*, *MSD1*, *FSD1*, *P5CS1*, *CAT1* and *CAT2* were quantified using RT-qPCR.

Under dehydration, highly genotype-specific transcriptional changes were observed, with significant upregulation of drought-specific *P5CS1* splice form (up to 67-fold in *pLRC1:EBF2*) and *CAT2* (up to 189-fold in *pS1:EBF2*). Other genes, such as *SOD1*, were downregulated across most genotypes. The recovery phase triggered a distinct shift in the transcriptional profiles, with genotype-specific spikes in expression, particularly of *PER57*, *PER44* and *P5CS1* in lines such as *pQ6:EBF2* and *pA14:EBF2*, contrasting with significant downregulation in other lines, such as *pS1:EBF2* and *pCOR:EBF2*.

These results demonstrate that tissue-specific ethylene signaling plays an important role in modulating the antioxidant response during drought and recovery. By identifying tissue-specific responses, this study provides a framework for future research into the molecular signals coordinating plant resilience and recovery.

Acknowledgements: This research was funded by the Bulgarian National Science Fund; grant number KP-06-N71/12/10 July 2024.

References:

[1]. Vaseva II, Qudeimat E, Potuschak T, Du Y, Genschik P, Vandenbussche F, Van Der Straeten D. 2018. *Proceedings of the National Academy of Sciences,* 115, 17, E4130-E4139.

DEVELOPMENT OF COMPUTATIONAL TOOL FOR PREDICTING TOXIC EFFECTS OF CHEMICALS

Parashkev Katerski[a], Petko Alov[a], Maria Angelova[a], Elina Beleva[a], Boian Lazov[a], Antonia Diukendjieva[a], Dessislava Jereva[a], Iglika Lessigiarska[a], Ilza Pajeva[a], Tania Pencheva[a], Stefan Tsakovski[b], Peter Vassilev[a], Ivanka Tsakovska[a]

[a]Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, pkaterski@biomed.bas.bg; [b]Faculty of Chemistry and Pharmacy, Sofia University "St. Kl. Ohridski"

The increasing regulatory demands under the European Union REACH legislation have accelerated the need for efficient, cost-effective, and animal-free approaches for chemical hazard assessment, particularly through *in silico* methodologies. In this study, we present the development of an integrated, web-based computational platform, **CompuToxPredictor**, designed to predict physicochemical, toxicokinetic, and toxicological properties of chemicals to support regulatory assessment.

To address human health and environmental safety, the platform integrates molecular modeling and machine learning approaches for toxicity prediction.

The platform incorporates multiple Quantitative Structure-Activity Relationship (QSAR) models, including in-house and refined models for key endpoints such as melting point (graph convolutional neural network), water solubility (random forest regression), and passive membrane permeability (PAMPA, multiple linear regression).

Docking protocols have been developed to identify potential binders to nuclear receptors (PPARγ and ERα), representing molecular initiating events associated with endocrine disruption. For environmental assessment, random forest classification and regression models have been built using large, curated datasets for aquatic organisms across multiple trophic levels. In addition, the developed interspecies Quantitative Structure-Activity-Activity Relationship (QSAAR) models enable reliable cross-species extrapolation.

The CompuToxPredictor platform is publicly accessible at www.computox.bas.bg and provides a freely available, user-friendly tool for *in silico* chemical hazard assessment.

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LONG-TERM CANCER SURVIVAL AFTER COVID-19: NATIONWIDE EVIDENCE IN PATIENTS WITH SOLID MALIGNANCIES

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The long-term effects of SARS-CoV-2 infection and COVID-19 vaccination on cancer prognosis remain insufficiently characterized, particularly regarding survival outcomes and interactions with systemic anticancer therapies in patients with solid malignancies.

We conducted a nationwide retrospective real-world cohort study using data from the Bulgarian Ministry of Health's United Information Portal. Adult patients (n = 1,797) with solid malignancies who survived hospitalization for COVID-19 between March 2020 and June 2022 were followed through November 2025. Overall survival (OS) was analyzed according to vaccination status, vaccine platform (mRNA vs vector-based), primary tumor site, and oncologic treatment modality. Multivariable regression and propensity score matching were used to adjust for demographic and clinical confounders. The study followed ESMO-GROW methodological guidance.

After a median follow-up of 48.6 months, mRNA vaccination was independently associated with reduced long-term mortality compared with vector-based vaccination or no vaccination (median OS: 43.6 vs 34.9 vs 34.5 months; OR 0.41, 95% CI 0.28–0.61; $P < 0.0001$). The survival benefit was most pronounced among patients receiving immune checkpoint inhibitors, particularly in lung cancer, where combined mRNA vaccination and immunotherapy was associated with improved outcomes (18.9% vs 31.1%; OR 0.45, 95% CI 0.20–0.98; $P = 0.036$). Findings remained consistent across multivariable and propensity score–matched analyses.

In this large nationwide cohort with nearly five years of follow-up, mRNA-based COVID-19 vaccination was independently associated with improved long-term survival among patients with solid malignancies who survived COVID-19 hospitalization. These results support durable protective effects and suggest a potential immunomodulatory interaction between vaccination and immune checkpoint inhibition.

ACUTE MYELOID LEUKAEMIA: MULTIDISCIPLINARY INSIGHTS INTO ACCESS, CARE, AND THERAPEUTIC DEVELOPMENT

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Acute myeloid leukemia (AML) is a rare hematological malignancy associated with high morbidity and mortality, posing a significant challenge to modern medicine. It is the most common type of leukemia in adults, accounting for approximately 80% of cases, and predominantly affects individuals over 45 years of age. Despite its relatively low incidence (around 4.2 per 100,000 individuals annually), AML remains a clinically complex disease, with accurate prognostic assessment continuing to be a major challenge. This study provides a multidisciplinary analysis of AML, including evaluation of access to therapy and investigation of novel therapeutic approaches based on natural compounds and metal complexes.

A comparative analysis of orphan drug reimbursement policies in Bulgaria, Romania, and Greece (2000-2024) indicates progress in aligning national legislation with the European regulatory framework and improvements in healthcare infrastructure, including expert centers, patient registries, and neonatal screening programs. However, equitable access to therapy remains unmet, with significant disparities observed, including longer access timelines in Bulgaria and Romania compared to Greece, and lack of updated national plans. In parallel, the antineoplastic activity of curcumin and cannabidiol was investigated in the HL-60 cell line, alone and in combination with standard chemotherapeutic agents (daunorubicin), with a focus on key signal transduction pathways and pro-inflammatory factors involved in leukemogenesis. Additionally, new Pt–NHC complexes were synthesized and characterized using multinuclear NMR spectroscopy, ESI-HRMS, elemental analysis, and solubility studies.

The results highlight both progress in legislative harmonization and persistent inequalities in access to therapy. Preliminary findings suggest a potential synergistic antineoplastic effect of curcumin and cannabidiol in HL-60 cells, while the newly synthesized Pt–NHC complexes represent a promising class for future investigation. Overall, these findings support the development of more effective and less toxic therapeutic strategies and emphasize the need to improve equitable access to AML treatments.

IN SEARCH OF NOVEL MAO-B/ALPHA-SYNUCLEIN INHIBITORS

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Neurodegenerative disorders such as Parkinson's disease (PD) are defined by the progressive loss of dopaminergic neurons and the pathological accumulation of alpha-synuclein (α-syn), along with disturbances in monoaminergic neurotransmission. Monoamine oxidase B (MAO-B) is a well-established enzymatic target involved in dopamine metabolism and oxidative stress regulation [1–4], whereas α-syn serves as a key disease-modifying target linked to protein misfolding, aggregation, and neurotoxicity [4]. Inhibition of MAO-B decreases dopamine breakdown and reduces the accumulation of reactive oxygen species (ROS) [1], while modulation of α-syn–associated pathways interfere with protein aggregation, toxicity, and pathological propagation [4]. Addressing both mechanisms is expected to target complementary pathological processes involved in neurodegeneration and may help slow disease progression [4].

The present study focuses on the design of novel indazole-5-carboxamide derivatives [2,3], acting as dual MAO-B/α-syn inhibitors, using an integrated approach that combines molecular docking, molecular dynamics simulations, virtual screening, chemical synthesis, and in vitro physicochemical and biological evaluation. The integration of these methodologies provides a systematic framework for the identification and optimization of small molecules with potential relevance to neurodegenerative disease research.

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FROM SMALL MOLECULES INVESTIGATED AS FACTOR XIIIA INHIBITORS TO BIOLOGICAL TARGET DIVERSITY

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Activated factor XIIIa (FXIIIa) is a key enzyme in the final stage of the blood coagulation cascade [1]. Our previous efforts were directed towards investigation of small-molecular inhibitors of activated factor XIII (FXIIIa) [2]. However, the intended approach has predestined drawback regarding the necessity of compound's pure water solubility. Therefore, our further studies were shifted towards other promising molecular targets of interest such as those, related to neurodegenerative diseases (NDs) including Parkinson's disease, depression and dementia. This study investigates small molecules with potential activity against ND-related targets using a combination of structure-based molecular docking and ligand-based target prediction, with a focus on monoamine oxidase B (MAO-B).

Two compound sets were analyzed: (i) reference compounds with established profiles, including donepezil, safinamide, and the investigational NTZ-1091 [3,4]; and (ii) novel scaffolds synthesized by our group. Ligand-based prediction was used to identify potential targets, followed by docking studies against monoamine oxidase A and B (MAO-A/B) as a new starting point of our investigations.

The identification of the human MAO-B enzyme as a potential secondary target (off-target) is supported by literature evidence demonstrating that structurally optimized small molecules can achieve high potency and selectivity toward this enzyme. Overall, combining structure and ligand-based target prediction approaches could provide a good starting point for subsequent compound optimization and experimental validation.

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HOW TO READ ANCIENT HISTORIOGRAPHY? POTENTIALS AND RISKS OF EMOTIONAL IMMERSION

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How were the works of ancient historians read by their contemporary audiences? Did they enjoy being captivated by the often highly emotional accounts, thereby becoming almost eyewitnesses of past events, as is has been described as an ideal in some of the works on rhetoric and literary theory from antiquity? Did they believe that this kind of 'multisensorial' or 'holistic' experience could help them to learn more from history and to gain a better understanding of the lives of persons long dead? Or, on the contrary, did they want to maintain a sober attitude and a critical distance from the emotions described, in order to better analyse the historical processes, as demanded, for example, by Polybius?

Both approaches have been put forward and criticised several times by writers and readers of ancient historiography alike from the time of Classical Athens to Imperial Rome. This lecture will give an overview of this debate and its key arguments. In a second step, it will explore the extent to which our approach to history today – in which not only emotions but also (digital) methods of immersion play an increasingly important role – can benefit from the debate that took place in antiquity.

DER SOUND DER GESCHICHTE – TECHNO ALS GEDÄCHTNISMEDIUM UND ALS LITERARISCHE FORM

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Der Beitrag verortet sich im Spannungsfeld kultur- und literaturwissenschaftlicher Germanistik und widmet sich der Frage, wie sich popkulturelle Phänomene wie der Berliner Techno in historische und literarische Deutungszusammenhänge integrieren lassen. Ausgangspunkt ist die These, dass Techno seit der Wiedervereinigung nicht nur als Musikgenre, sondern als kulturelles Gedächtnismedium fungiert, das gesellschaftliche Transformationsprozesse nach 1989 widerspiegelt und mitprägt. Im März 2024 wurde Techno in das bundesweite Verzeichnis des immateriellen Kulturerbes Deutschlands aufgenommen.

Zunächst wird die Genese der Technokultur in Berlin rekonstruiert und gezeigt, warum gerade diese Musikform zum Symbol und Begleiter der Umbrüche wurde – nicht zuletzt, weil sich die Dynamiken der Wiedervereinigung auch in den Räumen der Clubkultur vollzogen. Daran anschließend wird die Einbettung von Techno in den literarischen Diskurs untersucht. Anhand von Rainald Goetz' *Rave* und Thomas Meineckes *Himmelblau* wird das Verhältnis von Literatur und Technomusik beschrieben und nach der Bedeutung dieser Verbindung für die Poetik der Texte gefragt: Wodurch zeichnet sich die Musikalität eines Techno-Textes aus? Welches politische Potenzial liegt in dieser intermedialen Beziehung?

Der Beitrag macht deutlich, dass die Germanistik vor der Herausforderung steht, fluide, performative und stark gegenwartsbezogene Kulturformen methodisch zu erfassen. Zugleich zeigt er das Potenzial solcher Ansätze: Techno lässt sich als Medium des kollektiven Gedächtnisses verstehen, das neue Perspektiven auf Geschichte, Identität und Literatur eröffnet.

TRANSCRIBING DANISH INTONATION WITH TOBI – BASICS, SPECIFICS, AND CHALLENGES (IN ENGLISH)

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The present report aims to provide insight into the basics of transcribing Danish semi spontaneous utterances (in the form of short monologues based on map tasks contained in the DanPASS corpus) within the ToBI framework. As such a transcription has not yet been proposed in full for Danish, the task of transcribing Danish utterances with ToBI presents a set of challenges stemming from both the specifics of Danish prosody and the semi-spontaneous nature of the chosen empirical material. The report seeks to illustrate some of these challenges and propose possible solutions.

DER HEUTIGE ZUSTAND UND DIE ZUKUNFT DER ALTORIENTALISTIK WELTWEIT UND IN BULGARIEN

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Fast 170 Jahre nach der Geburt der Assyriologie und 150 Jahre nach der bahnbrechenden Edition der Keilschrifttafel des Sintfluttexts von George Smith können wir uns die Frage stellen, in welchem Zustand die Assyriologie/Altorientalistik sich heute befindet und welche Perspektive sie für die Zukunft hat. Kurz gesagt wird sich der Vortrag folgender Frage widmen: Was wurde in den letzten 170 Jahren erreicht und was gilt es noch zu erreichen?

Die Entzifferung der Keilschrift ermöglichte uns völlig neue Einblicke in die mesopotamische Geschichte, weit über das hinaus, was uns zuvor die klassischen Quellen und die Bibel geboten haben. Die stetige Arbeit von Generationen von Altorientalisten ermöglichte es, die Keilschrift zu entziffern, zahlreiche neue Sprachen zu entdecken, die mesopotamische Kultur zu studieren, die mesopotamische Wissenschaft zu verstehen, sowie die mesopotamische Literatur zu rekonstruieren. Während viele Sammlungen oder Archive bereits publiziert und detailliert untersucht wurden, gibt es dennoch zahlreiche unedierte Keilschrifttexte. Zudem gibt es fortlaufend neue Texte aus den Ausgrabungen. Anhand eines Archivs aus Assur, das derzeit von der Vortragenden ediert wird, wird aufgezeigt, wie moderne Keilschrifteditionen erstellt werden. Der gegenwärtig erreichte Stand der Texteditionen und unseres Wissens über die altorientalischen Sprachen macht heute historische, literaturhistorische oder vergleichende Studien möglich, die vor einigen Jahrzehnten noch undenkbar gewesen wären. Im Zentrum des Vortrags stehen der heutige Zustand der Altorientalistik, die traditionellen Wege der Erschließung von Keilschrifttexten und die Rolle digitaler Hilfsmittel. Einen weiteren Schwerpunkt des Vortrags bildet die heutige und zukünftige Entwicklung der Altorientalistik in Bulgarien.

GESCHICHTSCOMICS, MULTIDIREKTIONALE ERINNERUNG UND GESCHICHTSPOLITIK CHANCEN UND HERAUSFORDERUNGEN FÜR DIE GESCHICHTSVERMITTLUNG

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Faktenbasierte Geschichtsdarstellungen in der Comicform haben keine lange Tradition. In der Geschichte des Mediums etabliert sich erst in den 1980er Jahren die Tendenz, „historical stories, fact-based educational narratives, and committed political expression“ (Witek 1989) in nichtfiktionalen (oft autobiografischen) Comics zum Ausdruck zu bringen. Allerdings, bereits in den 1940er entwickeln sich - zuerst in den USA - die nichtfiktionalen Comics, die die Geschichte zu didaktischen Zwecken erzählen (Dolle-Weinkauff 2017). Das Potenzial, historische Inhalte narrativ zu vermitteln, wird mit der wachsenden Anerkennung des Mediums seit dem Erfolg von Art Spiegelman's MAUS (1986) entdeckt und gewürdigt. Die Entwicklung des Comics zu einem Medium der Geschichtsvermittlung erfolgt u.a. durch dessen Miteinbeziehung in den Bildungsauftrag von Museen und Gedenkstätten (Bock/Gundermann 2023; Gundermann 2025).

In meinem Beitrag möchte ich auf die rezente Erfolgsgeschichte der Geschichtscomics rekurrieren, die in Zusammenarbeit mit deutschen und polnischen Gedenkstätten entstanden sind bzw. entstehen. Folgende Fragen stehen dabei im Vordergrund: Welche geschichtspolitischen Inhalte lassen sich in Comicproduktionen aus polnischen und deutschen Holocaust-Gedenkstätten (Buchenwald, Dachau, Museum des Warschauer Ghettos, Lodzer Dialogzentrum) erkennen? Inwieweit resonieren die gebotenen historischen Darstellungen mit dem Konzept der multidirektionalen Erinnerung (Rothberg 2009)? Welche Chancen und Herausforderungen für die Geschichtsvermittlung in jeweiligem Land (Deutschland/Polen) bringt der Boom der Geschichtscomics?

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LOW-VALENT MAIN GROUP SPECIES AS GAME CHANGERS IN HOMOGENEOUS CATALYSIS?

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Homogeneous catalysis in industry has been dominated by scarce and hence expensive platinum group metals for more than half a century due to their propensity for reductive elimination and oxidative addition, key elementary steps of catalytic cycles involving the formal transfer of two electrons from substrate to catalyst and vice-versa. In view of increasing requirements on the sustainability of industrial processes, two possible abundant and cheap substitutes move increasingly into focus: (a) main group elements and (b) lighter transition metals such as iron, nickel and cobalt. Both alternatives face considerable challenges before they can efficiently compete with platinum group metals in terms of activity and selectivity. While main group elements are often characterized by one preferred oxidation state of marked stability and thus irreversible bond activation,[1] the lighter transition metals typically prefer one-electron redox processes.[2]

The lecture will discuss strategies to overcome these limitations, predominantly focusing on low-valent molecular species with elements from Group 14 of the Periodic Table. It will provide a status report on the considerable advances in bond activation, discuss the importance of reversibility of key elementary steps on route to catalytic cycles and provide insight into the application of such systems as non-innocent ligands to improve the performance of first row transition metals in homogenous catalysis of selected benchmark reactions.

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HYDROGEN BONDS OF COORDINATED AMINO ACIDS AND WATER: DIFFERENT TYPES AND THEIR RELEVANCE

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There are three conventional hydrogen bonds that coordinated amino acids can form with a water molecule, NH/O via α-amino group, O1/HO via α-hydroxyl O1 oxygen, and O2/HO via α-carbonyl O2 oxygen, and additionally, $C^{\alpha}H/O$ hydrogen bond. [1-2] We calculated interaction energies for rigid systems with linear hydrogen bonds, electrostatic potentials in the vicinity of the hydrogen bond, performed energy decomposition analysis (EDA) and quantum theory of atoms in molecules (QTAIM) analysis for each hydrogen bond. We examined the influence of complex charge, metal oxidation state, coordination and atomic number in order to identify the trends associated with these factors. The Cambridge Structural Database (CSD) search demonstrated the significance of each interaction type in experimental crystal structures. The NH/O hydrogen bond exhibits the strongest interaction energies, however, the distribution of hydrogen bond lengths and angles indicates that this interaction is frequently bent because the water is often bifurcated in these crystal structures, similarly to the much weaker O1/HO interaction. In contrast, O2/HO hydrogen bond is generally more linear even though it is weaker than NH/O. Finally, CSD analysis suggests that $C^{\alpha}H/O$ hydrogen bonds remain relevant as a secondary interaction of bifurcated water molecules, contributing to the orientation of the water molecule despite being weaker and surrounded by the stronger hydrogen bonds discussed here.

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ANTICANCER DRUGS IN THE ENVIRONMENT

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Cytostatics cyclophosphamide and ifosfamide are among the oldest and most widely used drugs in the treatment of various cancer types. After entering the body, they are excreted as metabolites or unchanged compounds and as such have been detected both in hospital wastewater and communal water treatment plants. During the treatment of wastewater these drugs undergo chlorination and hydrolysis, however little is known about the ecotoxicological profiles of the products formed in these reactions.

We have combined NMR spectroscopy and computational chemistry to investigate the reaction mechanisms, and the products of the chlorination and hydrolysis reactions. NMR was used to monitor the reactions and to identify the products, while calculations were used to explore the reaction pathways and mechanisms. An optical fibre connected to UV diodes was introduced into the NMR spectrometer to directly observe the effects of UV irradiation on both the parent compounds and the chlorinated products. Finally, the ecotoxicological profile of all identified compounds and their mixtures was investigated using test organisms *Daphnia magna* and green algae.

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CYCLIC POLYMER BRUSHES - TUNABLE PLATFORMS FOR DRUG AND GENE DELIVERY

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Cyclic polymer brushes represent a novel class of macromolecular architectures with great potential in nanomedicine. Their unique topology – comprising a hydrophobic cyclic backbone densely grafted with hydrophilic side chains – combines structural compactness, enhanced stability, and high functional tunability. This work aims to explore the synthesis, self-assembly, and biomedical applications of amphiphilic cyclic polymer brushes as innovative platforms for drug and nucleic acid delivery, as well as for the construction of a novel type of spherical nucleic acids (SNAs). The polymers are synthesized via controlled radical and ionic polymerizations, followed by efficient "click" coupling reactions to yield well-defined cyclic brush structures with adjustable composition, molecular weight, and grafting density. Their amphiphilic character enables spontaneous formation of nanosized self-assembled structures or unimolecular micelles in aqueous media, suitable for encapsulation or complexation of hydrophobic drugs and/or nucleic acids. The cationic analogues are expected to be able to coordinate DNA/RNA into stable polyplexes with high transfection potential, while direct conjugation of oligonucleotides onto hydrophobic cycles affords organic-core SNAs combining the intrinsic advantages of spherical nucleic acids - such as rapid cellular internalization, nuclease resistance, and non-immunogenicity - with tunable physicochemical properties of polymeric carriers. This interdisciplinary approach, integrating polymer chemistry, supramolecular science, and molecular biology, aims to develop novel biocompatible nanocarriers with improved pharmacokinetics and therapeutic efficacy.

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ELECTROSPUN POLYMER NANOFIBERS WITH MULTI-WALLED CARBON NANOTUBES AND GRAPHENE FOR PIEZOELECTRIC APPLICATIONS

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The incorporation of carbon-based nanofillers into electrospun PVDF fibers holds great potential to enhance their piezoelectric performance, making them attractive for energy harvesting and sensing applications. The carbon nanofillers are known to promote the formation of the electroactive β-phase in PVDF fibers, which is crucial for their piezoelectric performance. In this study the effect of annealing of electrospun PVDF nanocomposite fibers with graphene nanoplatelets (GNPs), multi-walled carbon nanotubes (MWCNTs), and their combination (hybrid) is investigated. The combination of annealing and nanofiller-induced nucleation significantly improved the crystallinity of the fibers. Structural analysis showed a pronounced α→β phase transition in 1.5 wt.% hybrid compositions (β/α ratio up to 7.8), exceeding mono-filler systems (4.7 for GNP/PVDF; 3.0 for MWCNT/PVDF). Piezoresponse force microscopy (PFM) confirmed high β-phase content at the nanoscale, revealing consistent piezoelectric response in fibers with coercive voltage decreasing from ±40 V to ±20 V due to dispersed nanofillers. These results demonstrate that combining hybrid carbon fillers with controlled annealing enables tunable crystalline structures and enhanced electromechanical performance in electrospun PVDF nanofibers.

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OPTICAL CLEARING FOR OCT TEETH IMAGING

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Optical Coherence Tomography (OCT) is increasingly being adopted in dentistry as a powerful imaging tool. Its capability to produce detailed cross-sectional and three-dimensional representations of dental structures, without exposing patients to ionizing radiation is a major leverage over the traditional dental X-ray. Its non-destructive nature makes it particularly valuable for identifying early-stage caries, monitoring enamel demineralization, and detecting structural abnormalities. Modern swept-source OCT systems can capture volumetric data quickly, achieving axial and lateral resolutions of approximately 7.4 μm, which supports precise visualization of enamel, dentin, and the dentin–enamel interface [1].

Researchers have explored various strategies to enhance OCT performance, including the use of optical clearing agents (OCAs). By minimizing refractive index differences at the tooth surface, these substances reduce scattering and allow light to penetrate deeper into the tissue. Among these, natural oils have attracted attention as safe, affordable, and biocompatible alternatives [2].

Incorporating suitable OCAs into dental OCT imaging improves both contrast and imaging depth, making it easier to observe subsurface lesions and subtle microstructural changes. As a result, OCT becomes an even more effective diagnostic tool, offering clinicians a reliable, non-invasive method for detecting and tracking dental conditions while potentially decreasing dependence on traditional radiographic imaging. This advancement supports earlier intervention and promotes more conservative treatment strategies.

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METAL SELECTIVITY IN SOME PROTEIN PHOSPHATASES: INSIGHTS FROM A THEORETICAL STUDY

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Metal ions play a crucial role in maintaining the structural integrity and catalytic function of many metalloproteins involved in cellular regulation and signaling. Protein phosphatases such as PH domain and leucine-rich repeat protein phosphatase 2 (PHLPP2) and protein phosphatase Mg^{2+}/Mn^{2+} dependent 1A (PPM1A) are key participants in phosphorylation-dependent pathways, which are directly relevant to biomedical processes like cancer signaling. However, the mechanisms that determine metal selectivity in their active sites are not yet fully understood. The performed theoretical study applies density functional theory (DFT) calculations to explore how two structurally different phosphatases select for specific metals: PHLPP2, which has a single Zn^{2+} binding site, and PPM1A, which features a binuclear Mn^{2+} catalytic center. The calculations, performed at the B3LYP/6-31+G(3d,p) level of theory, evaluate the thermodynamics of metal substitution in coordination environments relevant to biology. The findings reveal significant differences between the two proteins. The Zn^{2+} site in PHLPP2 is highly stable and strongly resists substitution by other divalent metal ions, which could be attributed to its structural protection by the protein matrix, and limited solvent accessibility [1]. In contrast, the binuclear Mn^{2+} center in PPM1A is more flexible and could easily undergo metal exchange, especially when exposed to common biological cations. Overall, this research highlights the value of DFT calculations for predicting metal selectivity in metalloproteins and offers new thermodynamic insights into the process of metal-coordinated enzyme activity regulation in biological systems.

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LIGHT-DRIVEN LONG-RANGE PROTON TRANSFER: OPTIMIZATION AND MECHANISMS

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The design of molecular switches has traditionally relied on external stimuli such as pH variation, ion binding, redox processes, or UV irradiation, typically involving elementary structural changes like bond isomerization or non-covalent interactions. In contrast, this work explores a novel switching concept based on long-range intramolecular proton transfer, where proton motion itself acts as the driving force for molecular reconfiguration. Such systems, known as proton cranes, enable controlled structural changes through proton relocation across extended molecular distances.

We investigate the switching mechanism of 8-(benzo[d]thiazol-2-yl)quinolin-7-ol [1] using time-resolved vibrational spectroscopy supported by density functional theory calculations. Upon photoexcitation, the enol tautomer undergoes an ultrafast excited-state intramolecular proton transfer, forming a transient intermediate. This is followed by rotation of a conjugated side arm, enabling proton transfer over a larger molecular distance. Relaxation to the ground state yields the keto tautomer, completing the switching cycle.

The switched state consists of two interconverting keto forms, representing a metastable configuration that gradually reverts to the initial enol structure over seconds under ambient conditions. These results provide insight into proton-driven switching mechanisms and offer strategies for tuning the dynamic behavior of conjugated proton crane systems.

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TAUTOMERIC AND COMPLEXATION PROPERTIES OF AVIGAN IN SOLTION

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Avigan is the commercial name of a substance also known as favipiravir – a prominent antiviral medication. Its tautomeric properties and complexation potential have been investigated by using DFT quantum-chemical calculations and molecular spectroscopy (UV-Vis absorption, fluorescence and NMR) [1].

According to the obtained results, the tautomeric equilibrium is shifted predominantly towards the enol tautomer as more stable in most of the organic solvents. In the presence of water, the keto form is favored due to the specific solute-solvent interactions.

The addition of alkali-earth-metal ions leads to deprotonation and complexation simultaneously, formatting 2:1 ligand:metal complex. According to the theoretical investigation the metal ion is captured in the cavity between the carbonyl groups because of the size-fit effect.

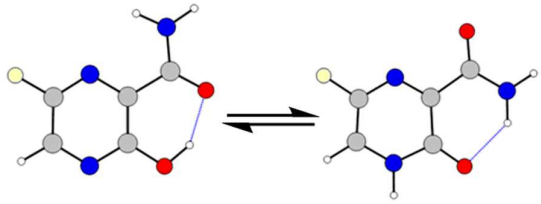

Fig.1 Tautomeric equilibrium of Avigan.

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A COMPLETE MODEL OF THE [1,5]-SIGMATROPIC CONVERSION OF CHORISMATE TO 4HB AND PYRUVATE BY CHORISMATE LYASE

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A theoretical model was created of the enzymatically catalyzed [1,5]-sigmatropic conversion of chorismate to 4-hydroxybenzoic acid and pyruvate. The substrate protein is known as chorismate lyase (UbiC). The studied process is the initial step in the formation of coenzyme Q10, which is in turn critical for the ATP cycle in *Escherichia coli*. As of the moment, there are very few known sigmatropic rearrangements in biology. Only three of them have been confirmed as enzymatically catalyzed [1]. This research should be of significant importance for rational design of proteins and biochemical systems, as a whole.

The studied process has been modeled with QM/MM Metadynamics. The MM region includes the whole enzyme, suspended in a water buffer. The QM region consists of the reagent. The SCF level of theory is DFTB3+D3(BJ) with γ correction. The protein MM field is Amber ff14SB. The water model is OPC3. Equilibration has been carried out in two steps – a longer pure MM, followed by a shorter QM/MM. The transition state (TS) and the free energy profile were found. The reaction mechanism was confirmed as sigmatropic. The intermolecular interactions were visualized and characterized on the basis of electronic density difference. The catalytic activity was explained on the basis of electronic effects within the occupied active site.

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A TROJAN HORSE STRATEGY: MOLECULAR DYNAMICS, DESIGN AND EVALUATION OF FOLATE-CONJUGATES FOR TARGETED DRUG DELIVERY OF DOXORUBICIN

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Neoplasia represent a major global health threat that leads to mortality worldwide, underscoring the crucial need for implementing pioneer strategies that can overcome the limitations and constraints of conventional chemotherapy [1]. Targeted drug delivery is a rapidly evolving approach that seeks to optimize therapeutic efficacy, while mitigating unwanted side effects, stemming from non-specific delivery of chemotherapeutics. The design of drug delivery systems (DDSs), implemented within an active targeting context, utilizes a Trojan horse strategy that relies on binding the chemotherapeutic agent to a small vector-ligand that possesses the ability to specifically bind to cancer cell hallmarks, recognizing their cellular components. Folate receptor-α (FRα), a high-affinity membrane protein involved in endocytic uptake for DNA synthesis and proliferation, is overexpressed in many cancer cells but limited in normal tissues, making it a suitable target for folate-based drug delivery [2].

In this current study, a series of folate-based peptide-spaced conjugates are investigated at physiological conditions by two-step atomistic molecular dynamics to assess their implementation as targeting constructs for receptor-specific delivery of the chemotherapeutic doxorubicin. The simulated models scale from a single conjugate in saline up to the construct in the presence of FRα in a salinized lipid bilayer mimicking a neoplastic cell membrane. Spontaneous binding is observed across all studied conjugate-receptor-membrane systems, but the time, position, and persistence depend strongly on the targeting ligand, delineating a unique fingerprint of each vector. The effect of loading the chemotherapeutic doxorubicin as bioactive cargo on the binding efficiency of the vector molecules is traced and the importance of optimizing the carrier composition for efficient binding is highlighted. The observed trends provide clues for construction of prospective biocompatible folate-based conjugates for active targeting delivery of doxorubicin.

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MODELING OF ANODE MATERIALS IN SODIUM-ION BATTERIES

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Hard carbon (HC) is one of the most promising anode materials for sodium-ion batteries due to its disordered structure, composed of randomly oriented and curved graphitic domains, defects, and nanopores that facilitate sodium-ion insertion. Although it is known that, in addition to carbon, HC contains significant amounts of O, less N, and traces of S, the role of functional groups remains insufficiently understood.

In this work, the influence of functional groups on sodium behavior during charge and discharge is investigated. Density functional theory (DFT) is employed to determine the most probable mechanisms of decomposition of functional groups across different temperature ranges. Rhombic models with long diagonal up to 15 Å, corresponding to experimentally observed graphitic domains in hard carbon, are used. The free energy of thermal decomposition of various functional groups is calculated.

The results provide new insight into the role of oxygen in HC and support the rational design of next-generation anode materials for sodium-ion batteries.

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COMPUTATIONAL MODELING OF THE INTERACTION OF ORGANIC STRUCTURE DIRECTING AGENTS WITH SILICATE AND BOROSILICATE ZEOLITE FRAMEWORKS

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In the present work we focused on the analysis of the interaction of the OSDA with zeolite framework, which is expected to affect the final stage of the zeolite synthesis. This interaction is also particularly important in the processes of zeolite growth using seeds and for interzeolite transformations due to stabilization of the framework of the newly formed zeolite material. We selected octyl trimethyl ammonium chloride (OTMAC) as OSDA, which was studied by Ma et al.[1] for synthesis of several zeolite framework with borosilicate composition using different parent zeolites as seeds. In order to contribute in explanation of the formation of specific zeolite frameworks starting from parent seeds with different framework, we initially modeled interaction of OTMAC with completely silica frameworks. Since silica framework is neutral, the channels of the as-synthesized zeolite material include both the organic part of the OSDA, ammonium cation, and compensating chloride anion, to preserve the neutrality of the whole system. The interaction energy (IE) could give a quantitative assessment of the influence of the OTMAC agents on the framework stability. For the purpose of the modeling, one auxiliary model was built – an octyl trimethyl ammonium ion ($OTMA^+$) and a chlorine anion (Cl^-), optimized in the unit cells of each modeled zeolite types.

Using the calculated interaction energies per OSDA molecule in the zeolite channels, IE/m, the most favorable is the interaction with MTT, MRE, CHA and TON and weakest is the interaction with FAU framework. The comparison of the IE/T calculated values lead to similar conclusion - the most exothermic are interactions of the OTMAC with ITH, MTT, CHA, and TON zeolite frameworks. The least favorable OSDA-zeolite interaction is calculated for MOR and FAU frameworks. Since in the seed-directed synthesis Ma et al.[1] included in the initial synthetic gel B_2O_3 together with the silica source, SiO_2, the obtained materials are borosilicates. By this reason, we constructed borosilicate models by substituting Si T-atoms by boron. Similarly to aluminosilicate zeolites, borosilicate frameworks are negatively charged due to 3+ oxidation state of boron in them and the charge compensation of the framework is accomplished by ammonium cations $OTMA^+$. The IE values clearly show that the interaction of OTMAC with borosilicate having ITH framework is the most exothermic, followed by structures with MTT and TON.

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A WEAKENED AMOC WARMS WINTERS AND DRIVES SUMMER MULTIDECADAL VARIABILITY

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The Atlantic Meridional Overturning Circulation (AMOC) is a key regulator of global climate and has been a subject of major scientific interest. Observational studies have raised concerns about its ongoing weakening and potential collapse this century. While climate models generally show an overall cooling over Europe as a result of this weakening, confirmation based on observations is lacking due to difficulties in assessing causality in data. Here, we overcome this problem by developing a causality-first approach which allows us to track each link in the causal chain of AMOC's historical impact over Europe in reanalysis data. First, arguments are given for the causal link between AMOC and its SST fingerprint. Then, decomposing the SST fingerprint of AMOC into a decreasing centennial trend (the weakening of the AMOC) and a multidecadal oscillation (AMO), we find that the trend component impacts only the winter climate, while AMO mainly summer. In winter, the weakening of AMOC warms north-central Europe and increases precipitation in the northern part in a dipolar structure. In summer, the positive phase of AMO warms and dries south-eastern Europe, while bringing low temperatures and precipitation extended over the north-western part. Whether the AMOC weakening cools Europe, as most models suggest, appears to depend on the ocean-land temperature difference. As the AMOC weakens further, the ocean may become cooler than the land, making a European cooling response more likely. These quantitative results can be an observational benchmark for future model simulations, inform policy making, and national security.

EVALUATION OF RADIATION FIELDS IN A TR-24 CYCLOTRON FACILITY

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The Institute for Nuclear Research and Nuclear Energy, Bulgarian Academy of Sciences (INRNE-BAS), is currently designing a new accelerator facility based on a TR-24 cyclotron [1]. This development requires a preliminary assessment of the radiation shielding. In this study, Monte Carlo simulations were performed using the FLUKA code [2,3] to evaluate the radiation fields generated by secondary neutrons from an ^{18}F production target, as well as by beam losses within the cyclotron vacuum chamber. To account for beam-loss effects, a simplified cyclotron model was implemented in the bunker geometry previously developed in our earlier studies [4].

The simulations yielded the distributions of radiation fields inside and outside the shielding bunker during cyclotron operation. In addition, the effect of a sacrificial layer of low-sodium concrete in the bunker walls was investigated. The results indicate a significant reduction in dose rates inside the cyclotron bunker after an irradiation session for ^{18}F production.

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FOUNDATIONS FOR PRECISION MEDICINE: PRELIMINARY RESULTS OF THE BULGARIAN GENOME PROJECT

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Precision medicine aims to tailor prevention, diagnosis, and treatment strategies to individual biological variability. The lack of population specific referent data in Bulgaria is limiting the applicability of existing genomic knowledge into clinical practice.

The Bulgarian Genome Project was established to address this gap by generating a comprehensive reference of genetic variations within the Bulgarian population. Using high-throughput sequencing technologies and integrative bioinformatics approaches, the project seeks to characterize population-specific genomic variations and enable the translation of these insights into clinical and public health applications. Here, we present preliminary results from the pilot cohort, focusing on key areas. We identify population-enriched and novel genetic variants, highlighting the distinct genetic landscape of Bulgarians in comparison to the international reference datasets. We explore variants associated with common complex diseases, such as cardiovascular and oncological diseases, providing early insights into population-specific risk profiles. We examine pharmacogenomic markers relevant to drug metabolism and response, underscoring opportunities for more effective and safer therapeutic strategies in clinical practice.

These efforts align with the initiative Genome of Europe (GoE), which aims to integrate national genomic datasets into a federated framework for research and healthcare innovation. The GoE Project will contribute to improving the representation of current European populations with 100 000 genomes. It is supported by the development of interoperable Genome Data infrastructures (GDI) that enable secure, privacy-preserving data sharing and cross-border analyses without requiring centralization of sensitive genomic data.

The findings demonstrate both the scientific value and clinical potential of population-specific genomic resources, but also highlight key challenges, such as data interpretation, ethical and legal issues, and the integration into healthcare systems.

AUTOMATED EVALUATION OF GENE EXPRESSION IN CHROMOGENIC IN SITU HYBRIDIZATION IMAGES USING SPECTRUM-NORMALIZED PSEUDO-CHANNEL

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In a primate model of temporary global cerebral ischemia, the inferior subventricular zone (SVZi) adjacent to the temporal horn of the lateral ventricle displays a unique transcriptomic profile. Chromogenic RNA in situ hybridization (CISH) is the standard technique for validating the RNA-sequencing-derived gene expression changes. However, manual analysis of CISH images is time-consuming and highly susceptible to individual biases. Alternatively, fully automated, high-throughput image analysis pipelines are constrained by the need for consistency in sample preparation and image acquisition conditions, which can limit their broader utility. In the present study, we have developed an ImageJ-based algorithm for image normalization to address the variations in the staining and the imaging setup. As proof of concept, we used NBT/BCIP CISH images of genes that are upregulated after ischemia in the primate brain. The spectral response of the pseudo-filter (defined as sensitivity 1 in the boundaries of 540 nm – 660 nm, and 0 otherwise) was fitted as a weighted linear combination of the relative sensitivity spectra of Zeiss Axiocam Mrc rev.3 (extracted from the camera documentation).

$$PseudoCh = 0 + \beta_R * R + \beta_G * G + \beta_B * B + \varepsilon$$

To create the pseudo-filtered NBT-formazan images, the model coefficients were applied as weights to ensure accurate quantification. As a normalization strategy, a modified optical density (OD) transformation was implemented that uses the topological estimate of the illumination field instead of the maximal or modal grey value as an approximation for incident light intensity. This approach allows to correct for aberrations in the light source between images as well as considers the OD of the local environment of each pixel. For spatial analysis, the ependymal layer and the subependymal region were defined using a semi-automated workflow: manual tracing of the ventricular surface, followed by Euclidian distance mapping for consistent spatial segmentation.

PLASMA HISTONE MONOMERS AS NOVEL DIAGNOSTIC MARKERS IN ADULT GLIOBLASTOMA

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Glioblastoma (GB) presents significant diagnostic challenges, as traditional approaches often fail to fully capture the tumor's molecular heterogeneity. Circulating histones and nucleosomes are potential biomarkers for cellular turnover and chromatin remodeling. However, while histone signatures are established in pediatric neuro-oncology, the specific circulating histone profile in adult GB has not been defined. In this study, we aimed to characterize the plasma histone profile in adult GB patients compared to healthy controls.

Plasma samples from 44 adult GB patients and 30 healthy controls were analyzed. ELISA quantified histones H3.1 and H3.3, while imaging flow cytometry measured individual monomers (H2A, H2B, H3, H4), macroH2A1 variants, and multi-histone complexes.

GB patients exhibited elevated histone monomers H2A and H3 (with no significant alteration in H3.1/H3.3 levels), macroH2A1.1 and macroH2A1.2, alongside reduced H4 levels. Unlike pediatric gliomas, no significant differences were found in histone complexes. MacroH2A1.2 abundance was increased in female GB patients and negatively correlated with age in male GB patients, suggesting demographic-specific epigenetic modulation.

These findings demonstrate that adult GB follows a unique "monomer-dominant" histone release pattern, which may be utilized for the detection and monitoring of adult glioblastoma in a minimally invasive manner.

EFFECT OF THE PCNA PROTEIN DEPLETION ON REPLICATION STRESS

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Replication forks encounter various impediments, which induce fork stalling and threaten genome stability, yet the precise dynamics of fork stalling and restart at the single-cell level remain elusive. Herein, we devise a live-cell microscopy-based approach to follow hydroxyurea-induced fork stalling and subsequent restart at 30 s resolution. We measure two distinct processes during fork stalling. One is rapid PCNA removal, which reflects the drop in DNA synthesis. The other is gradual RPA1 accumulation up to 2400 nt of ssDNA per fork despite an active intra-S checkpoint. Restoring the nucleotide pool enables a prompt restart without post-replicative ssDNA and a smooth cell cycle progression. ATR, but not ATM inhibition, accelerates hydroxyurea-induced RPA1 accumulation nine-fold, leading to RPA1 exhaustion within 20 min. Fork restart under ATR inhibition led to the persistence of ~600 nt ssDNA per fork after S-phase, which reached 2500 nt under ATR/ATM co-inhibition, with both scenarios leading to mitotic catastrophe. MRE11 inhibition had no effect on PCNA/RPA1 dynamics regardless of ATR activity. E3 ligase RAD18 was recruited at stalled replication forks in parallel to PCNA removal. Our results shed light on fork dynamics during nucleotide depletion and provide a valuable tool for interrogating the effects of replication stress-inducing anti-cancer agents.

DYNAMICS OF THE REPLICATION FORK STALLING AND RESTART IN BRCA2/PALB1 DEFICIENT CELLS

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The BRCA2 protein plays a central role in maintaining genome stability during DNA replication, particularly under conditions of replication stress. Replication forks can stall when they encounter DNA damage, difficult-to-replicate regions, nucleotide depletion, or other sources of stress. BRCA2 is recruited to stalled replication forks through its interaction with PALB2. At these sites, BRCA2 and PALB2 promote the loading and stabilization of RAD51 onto single-stranded DNA. The resulting RAD51 nucleoprotein filament protects nascent DNA from degradation and facilitates repair through homologous recombination. Current evidence suggests that BRCA2 and PALB2, via RAD51, shield newly synthesized DNA strands and prevent excessive nucleolytic resection. To address this, we analysed the dynamics of replication fork stalling and restart by quantifying the kinetics of recruitment and removal of RPA1 and PCNA. in PALB2/BRCA2 deficient cells.

IN THE SEARCH OF NOVEL ANTIBACTERIALS – MIMICKING THE *PSEUDOMONAS* METABOLITES

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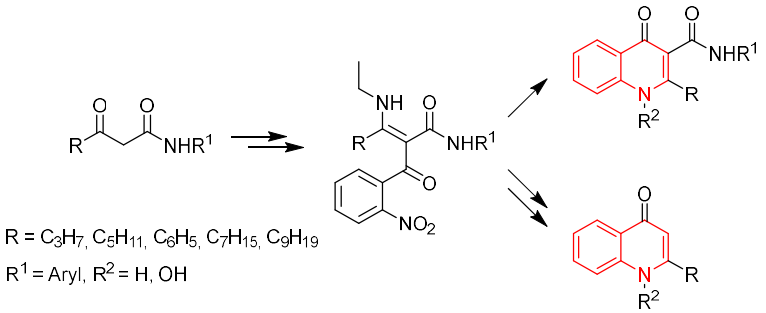
2-Alkyl-4(1*H*)-quinolones represent an important class of secondary metabolites produced by bacteria of the genus *Pseudomonas*, functioning both as antibiotics and as quorum-sensing signaling molecules [1, 2]. A practical synthesis of one such natural compound (Pseudane IX or 2-nonyl-4-quinolone) and its *N*-oxide has been developed.



Scheme 1. A novel approach to the synthesis of natural 4-quinolones and their derivatives.

To this end, an original enamine-based domino approach was employed, utilizing *β*-ketoamide precursors under mild reaction conditions. The use of various amides of 3-oxododecanoic acid in a shortened three-step variant of the method provided access to a series of novel 3-carboxamide derivatives of bacterial metabolites. Some of the newly obtained compounds were evaluated for antibacterial activity and exhibited broad-spectrum activity against strains of *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*. The obtained results reveal opportunities for structural modification of the quinolone core and provide a basis for the search for new antibacterial agents.

References:

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ULTRASTRUCTURAL AND MOLECULAR MAPPING OF 4-HYDROXYNONENAL (HNE)-INDUCED DEGENERATION IN THE MURINE CORNEA AND RETINA

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4-Hydroxynonenal (HNE), a highly reactive product of lipid peroxidation, is implicated in the pathogenesis of various oxidative stress-related disorders. Naturally HNE occurs during oxidative stress because of (not only) ischemia or inflammation. More important is the uptake through everyday food exposed to heated oils with large quantities of unsaturated fatty acids (e.g. food fried in olive oil). While its effects on the brain and liver are well-documented, its specific impact on the ocular environment - specifically the structural integrity of the cornea and retina - remains poorly defined. This study investigates the cytotoxic effects of systemic HNE exposure on the murine visual system. Mice were treated with HNE, sacrificed and with fixative perfused. Eye samples were then analyzed using cutting edge scanning electron microscopy and immunofluorescent labeling. We found alterations in the tear film on the anterior ocular surface, throughout the anterior corneal epithelium and in the ciliary marginal zone of the retina.