PROGRAMME

YOUNGPHARM

Satellite meeting for the Next Generation by HUPHAR

2-3 June, 2026
Matrahaza, Hungary

2nd June, 2026 Tuesday	3rd June, 2026 Wednesday
11:00 On-site registration	9:00-10:00 Elevator Speech II.
12:00-12:15 Opening & Welcome Remarks	
12:15-14:00 Early Career Researchers Talk	
14:00-14:30 Coffee Break	10:00-10:30 Break
14:30-16:30 Academia-Industry Roundtable - „Bridging Horizons”	
16:30-16:50 Break	
16:50-17:20 Elevator Speech Session I.	10:30-12:30 Career Path & Work-Life Balance Workshop
18:30-19:00 Quiz & Ice-breaker	
19:00 Networking Dinner & Wine Evening	

June 2, 2026 (Tuesday)

11:00- **Registration**

12:00-12:15 **Opening & Welcome Remarks**
Welcome Speech: Zsuzsanna Helyes, Barbara Fülöp

12:15-14:00 **T1** **EARLY CAREER RESEARCHER TALKS**
Moderator: Zsuzsanna Helyes

T1-1 [1]**Yaren ÇAKMAK,** [1]Gökçe YILDIRIM BUHARALIOĞLU **(10'+5')**

[1]Faculty of Pharmacy, Department of Pharmacology, Ege University, Turkey

Identification of androgen-regulated epigenetic regulatory enzymes in prostate cancer

T1-2 [1]**Julia Sapienza Passos**, [1]Giovanna Cassone Salata, [1]Giovanna Barros de Melo, [1]João Agostinho Machado-Neto, [2]Alyssa Panitch, [1]Luciana B. Lopes **(10'+5')**

[1]Department of Pharmacology, Institute of Biomedical Sciences, University of Sao Paulo, Brazil, [2]Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology, United States

Multifunctional nanoparticles for co-delivery of elacridar and paclitaxel for breast cancer local treatment: development, optimization, and cytotoxicity in drug-sensitive and drug-resistant cell lines

T1-3 [1,2]**Sarah K. Abbood**, [1,2]Judit Mária Kirchlechner-Farkas, [1,2]Imre Boldizsár, [1,2]Kornél Király, [1,2]Laszlo G Harsing Jr, [1,3]E. Sylvester Vizi, [1,2]Mahmoud Al-Khrasani **(10'+5')**

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research & Development, Semmelweis University, Hungary, [3]Hun-Ren Institute of Experimental Medicine, Molecular Pharmacology Res. Group, Hungary

Mimicking the spinal endogenous adrenergic system and modulating voltage-gated calcium channels is a promising strategy to halt neuropathic pain

T1-4 [1]**Gergő Bitay**, [1,2]Noémi Tóth, [1,2]Zsófia Kohajda, [1]Leila Topal, [1]Vivien Demeter-Haludka, [1]Muhammad Naveed, [1]Aiman Saleh A. Mohammad, [1,2]Norbert Jost, [1]László Virág, [1]István Baczkó, [1,2]András Varró, [1,2]Norbert Nagy **(10'+5')**

[1]Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Szeged, Hungary, [2]HUN-REN-SZTE Research Group of Cardiovascular Pharmacology, Hungary

Intensive physical training increases the risk of ventricular alternans in a canine athlete's heart model

T1-5

[1,2]**Péter Pápai**, [1,2]Ádám István Horváth, [1,2]Éva Borbély, [1,3,4]Valéria Tékus, [5,6]Anett Futácsi, [5,6]Boldizsár Czéh, [7]Ádám Dénes, [1,2,3,8]Zsuzsanna Helyes **(10'+5')**

[1]IDepartment of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Hungary, [2]National Laboratory for Drug Research and Development, Hungary, [3]HUN-REN-PTE Chronic Pain Research Group, Hungary, [4]Department of Laboratory Diagnostics, Faculty of Health Sciences, University of Pécs, Hungary, [5]Department of Laboratory Medicine, Medical School, University of Pécs, Hungary, [6]Structural Neurobiology Research Group, János Szentágothai Research Centre, University of Pécs, Hungary, [7]"Momentum" Laboratory of Neuroimmunology, HUN-REN Institute of Experimental Medicine, Hungary, [8]PharmInVivo Kft., Hungary

The cx3cr1 fractalkine receptor mediates both joint pain and destruction in a mouse osteoarthritis model

T1-6

[1,2,3]**Máté Váczy-Földi**, [1,2,3]Bettina Benczik, [1,2]Zsolt Papp, [1,2]Olivér Balogh, [1,2]Barnabás Váradi, [1,2]Dóra Bihary, [1,2]Zoltán Bereczki, [1,2,3]András Makkos, [1,2,3,4]Anikó Görbe, [3,4]Péter Bencsik, [1,2,3]Péter Ferdinandy, [1,2,3]Bence Ágg **(10'+5')**

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research & Development, Semmelweis University, Hungary, [3]Pharmahungary Group, Hungary, [4]Department of Pharmacology and Pharmacotherapy, University of Szeged, Hungary

miRNAtarget: a network-based solution and benchmarking framework for predicting transcriptome-wide concerted regulatory effects of microRNAs

T1-7

[1,2,3]Tamara Madácsy, [1,2]**Zsófia Horváth**, [1,2]Aletta Kata Kiss, [1,2]Petra Susánszki, [1,2]Tünde Molnár, [1,2]Noémi Csákány-Papp, [1,2]Marietta Görög, [1,2,3]Petra Pallagi, [1,2,3]József Maléth **(10'+5')**

[1]University of Szeged, Department of Internal Medicine, Hungary, [2]USZ-Momentum Epithelial Cell Signaling and Secretion Research Group, Hungary [3]University of Szeged, Department of Public Health, Hungary

The protective effects of methylene blue on PMCA in alcohol-related pancreatic and hepatic injury

14:00-14:30 **Coffee Break – Sponsored by Greiner Bio-One Hungary Ltd.**

14:30-16:30 **ACADEMIA-INDUSTRY ROUNDTABLE - ,,BRIDGING HORIZONS"**
Moderator: Zsófia Onódi

16:30-16:50 **Break**

16:50-17:20 **T2** **ELEVATOR SPEECH SESSION I.**
Moderator: Ágnes Király

Session introduction (3')

T2-1 [1,2]**Anita Steib**, [1,2,3]Katalin Rozmer, [1,2]Zoltán Sándor, [1,2,4]Éva Szőke, [1,2,5]Krisztina Pohóczky, [1,2,4,6]Zsuzsanna Helyes **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Hungary, [2]National Laboratory for Drug Research and Development (PharmaLab), Hungary, [3]Institute of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Pécs, Hungary, [4]Hungarian Research Network, Chronic Pain Research Group (HUN-REN PTE), Hungary, [5]Department of Pharmacology, Faculty of Pharmacy, University of Pécs, Hungary, [6]PharmInVivo Kft., Hungary

Allyl-isothiocyanate decreases the viability of human prostate adenocarcinoma cell lines independently of Transient Receptor Potential Ankyrin 1 receptor activation

T2-2 [1,2]**Artúr Tóth**, [1,2]Sára Jezsoviczky, [1,2]Andrea Kovács, [1,2]Zsombor Hegedüs, [1,2]Márk Jakab, [1,2,4]Zoltán V. Varga, [1,2,3] Péter Ferdinandy, [1,2]Zsófia Onódi **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research & Development, Semmelweis University, Hungary, [3]Pharmahungary Group, Hungary, [4]HUN-REN-SU System Pharmacology Research Group, Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary

Cardiovascular effects of anti-gout drugs: evaluation of echocardiographic differences of febuxostat and allopurinol in a mouse myocardial injury model

T2-3 [1]**Enikő Rózsa**, [1,2,3]Maja Payrits, [1,4,5]Klaudia Barabás, [1]Bence Linka, [1]Kepe Eszter, [1,2,3]Zsuzsanna Helyes, [1,2,3]Éva Szőke **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy& Centre for Neuroscience, Faculty of Medicine, University of Pécs, Hungary, [2]National Laboratory for Drug Research and Development, Hungary, [3]Hungarian Research Network, Chronic Pain Research Group, Hungary, [4]Institute of Physiology, University of Pécs, Medical School, Hungary [5]Centre for Neuroscience, University of Pécs, Hungary

The role of the transient receptor potential ankyrin 1 ion channel in memory and motor coordination during aging in female mice

T2-4 [1,2]**Tudor Cristian Cozma**, [1,3]Amir Makolli, [1]Bertalan Tordai, [1]Viktória Barna, [1,4]Anett Rancz, [1]Karen Krisztina Fazekas, [1]Marie Anne Engh, [1,5,6,7]Peter Hegyi, [1,3]Renata Papp, [1,3,8,9]Péter Ferdinandy **(3'+3')**

[1]Centre for Translational Medicine, Semmelweis University, Hungary, [2]Department of Physiology, Grigore T. Popa University of Medicine and Pharmacy, Romania, [3]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [4]Department of Rheumatology and Immunology, Semmelweis University, Hungary, [5]Institute of Pancreatic Diseases, Semmelweis University, Hungary, [6]Institute for Translational Medicine, Medical School, University of Pécs, Hungary, [7]Translational Pancreatology Research Group, Interdisciplinary Centre of Excellence for Research, Development and Innovation, University of Szeged, Hungary, [8]Center for Pharmacology and Drug Development, Semmelweis University, Hungary, [9]Pharmahungary Group, Hungary

Statin treatment and sarcopenia: a systematic review and metanalysis

Moderator closing (3')

18:30-19:00 **Quiz & Ice-breaker**

19:00 **Networking Dinner & Wine Evening**

June 3, 2026 (Wednesday)

9:00-10:00 **W1** **ELEVATOR SPEECH SESSION II.**
Moderator: Barbara Fülöp

Session introduction (5')

W1-1 **[1]Dávid Vince Simon**, [1]Eszter Kepe, [2]Eszter Pákai, [2]András Garami, [1]Éva Borbély **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Hungary [2]Department of Thermophysiology, Institute for Translational Medicine, Medical School, University of Pecs, Hungary

Hemokinin-1 as a modulator of thermoregulation

W1-2 **[1,2]Márta Szabó**, [4]Tamara Szabados, [1,2]Regina Nagy, [1,2]Boglárka Frankó, [1,2,3]Áron Gyovai, [1,2,3]András Makkos, [1,2]Zoltán Bereczki, [1,2,3]Bence Ágg, [3,4]Péter Bencsik, [1,2,3,4]Anikó Görbe, [1,2,3]Péter Ferdinandy **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research & Development, Semmelweis University, Hungary, [3]Pharmahungary Group, Hungary, [4]Cardiovascular Research Group, Department of Pharmacology and Pharmacotherapy, Albert Szent-Györgyi Medical School, University of Szeged, Hungary

Identification and development or mir-450a for cardioprotection

W1-3 [1]**Dóra Biskup**, [1]Rita Börzsei, [1]Helyes Zsuzsanna, [1]Erika Pintér, [1]Csaba Hetényi **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Hungary

Estimation of target-ligand binding affinity by in silico approach

W1-4 [1,2,3,4]**Márton Kocsis**, [1,2,3,4]Anna Kulin, [1,2,3,4]Lilla Szabó, [1,2,3,4]Tamás Gergely, [1,2,3,4] Sayour Viktor Nabil, [1,2,3,4]Viktoria Tóth, [1,2]Dávid Nagy, [1,2,3,4]Tamás Kovács, [1,2,3,4]Zsombor I.Hegedűs, [1,2,3,4]Luca Varga, [1,2]Bence Ágg, [1,2,5]Péter Ferdinandy, [1,2,3,4]Zoltán V Varga **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research & Development, Semmelweis University, Hungary, [3]HCEMM-SU Cardiometabolic-Immunology Research Group, Hungary, [4]MTA-SE Momentum Cardio-Oncology and Cardioimmunology Research Group, Hungary, [5]PharmaHungary Group, Hungary

The thymus-heart axis: active thymic output is a prerequisite for immune checkpoint inhibitor-associated cardiotoxicity

W1-5 [1]**Rodrigo dos Anjos Miguel**, [1]Giovanna Barros de Melo, [1]João A Machado-Neto, [1]Glaucia Machado-Santelli, [1]Ana Paula Lepique A, [1]Luciana B Lopes, [1]Leticia V Costa-Lotufo **(3'+3')**

[1]Department of Pharmacology, Institute of Biomedical Sciences, University of São Paulo, Brazil

Polymeric nanoparticles as tools to enhance seriniquinone translational potential

W1-6 [1]**Emese Ritter**, [1,2]Kata Csekő, [3,4]Noémi Kovács, [3]Ildikó Horváth, [5]Zsombor Ritter, [3,6]Domokos Mathe, [3,6]Christer Halldin, [1,2,7,8]Zsuzsanna Helyes **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, University of Pécs, Medical School, Hungary, [2]National Laboratory for Drug Research and Development, Hungary, [3]Department of Biophysics and Radiation Biology, Faculty of Medicine, Semmelweis University, Hungary, [4]In Vivo Imaging Advanced Core Facility, Hungarian Centre of Excellence for Molecular Medicine, Hungary, [5]Department of Medical Imaging, Medical School, University of Pécs, Hungary, [6]HUN-REN TKI "NEUROINFLAMMATION PET" Research Grant Hungary Group, Hungary, [7]HUN-REN-PTE Chronic Pain Research Group, Hungary; [8]PharmInVivo Hungary Ltd, Hungary

The novel multi-target drug candidate (szv-1287) improves endotoxin-induced acute airway inflammation in mice

W1-7 [1,2]**Olivér Balogh**, [1,2]Lóránt Sagát, [3]András Horváth, [1,2,4]Péter Ferdinandy, [1,2,4]Bence Ágg **(3'+3')**

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research

& Development, Semmelweis University, Hungary, [3]Faculty of Information Technology and Bionics, Pázmány Péter Catholic University, Hungary, [4]Pharmahungary Group, Hungary

Protegan: a generative, self-supervised model with edge-level attention for network-based protein–protein interaction prediction

W1-8

[1,2,3]**Zsófia Rita Hernádi**, [2]Eszter Bálint, [2]Viktor Román, [3]Erika Pintér, [1]István Hernádi **(3'+3')**

[1]Translational Neuroscience Research Group, Szentágothai Research Center, University of Pécs, Hungary, [2]Department of Pharmacology and Drug Safety Research, Gedeon Richter Plc., Hungary, [3]Department of Pharmacology and Pharmacotherapy, University of Pécs, Hungary

Effortful choice in rats: a preclinical tool for understanding altered motivation in pharmacological anhedonia and appetite suppression

Moderator closing (7')

10:00-10:30 **Break**

10:30-12:30 **Career Path & Work-Life Balance Workshop**

Moderator: Péter Zentai – Physchologist and family therapist
Indroduction: Kata Csekő - Representative of the Young Researchers' Group
Krisztina Keresnyei - Business and team coach
Csenger Kovácsházi – Semmelweis University, Hungary
Csilla Laczka – Semmelweis University, Hungary

ORAL ABSTRACTS

YOUNGPHARM

Satellite meeting for the Next Generation by HUPHAR

2-3 June, 2026
Matrahaza, Hungary

T1-1 IDENTIFICATION OF ANDROGEN-REGULATED EPIGENETIC REGULATORY ENZYMES IN PROSTATE CANCER

[1]Yaren ÇAKMAK, [1]Gökçe YILDIRIM BUHARALIOĞLU

[1]Faculty of Pharmacy, Department of Pharmacology, Ege University, Turkey

Prostate cancer (PCa) develops through the accumulation of genetic and epigenetic alterations. Dysregulation of chromatin-modifying enzymes (CMEs) contributes to the initiation and progression of PCa. In early stages, PCa growth is highly dependent on androgen signaling, which regulates genes involved in proliferation and tumor progression. Androgen signaling has also been associated with regulation of matrix metalloproteinases (MMPs), which play critical roles in extracellular matrix remodeling, invasion, and metastasis.

This study aimed to identify androgen-responsive epigenetic regulatory enzymes in PCa cells and to investigate the potential role of significantly altered CMEs in regulating MMP expression.

Androgen induction in LNCaP cells was validated by measuring the mRNA levels of androgen-responsive genes KLK3, TMPRSS2, and NKX3.1 using RT-PCR. Following confirmation of androgen stimulation, transcriptional changes in epigenetic regulator enzymes were analyzed using an RT-qPCR array covering 84 CMEs representing major epigenetic classes, including DNA methyltransferases, histone acetyltransferases, methyltransferases, demethylases, phosphorylation enzymes, ubiquitination regulators, and histone deacetylases. Only four CMEs—DZIP3, HDAC4, KMT2A, and PAK1—were significantly altered, with HDAC4 showing a 2.2-fold decrease. Among the 11 HDACs represented in the array, HDAC4 was the only androgen-responsive enzyme and was selected for further validation. RT-PCR confirmed the downregulation of HDAC4 identified in the array. HDAC4 regulates transcription through histone deacetylation, its reduction results in elevated gene expression. Therefore, 23 MMPs were screened, revealing increased expression of MMP-12, MMP-26, and MMP-28 in androgen-stimulated cells.

These results demonstrate that androgen signaling in LNCaP cells selectively modulates specific epigenetic regulators and matrix remodeling enzymes, with HDAC4 and distinct MMPs standing out as potential mediators of androgen-dependent transcriptional programs. Downregulation of HDAC4 result in elevated gene expression, and our data suggest that androgen may facilitate chromatin remodeling and transcriptional activation of identified MMPs through modulation of histone acetylation.

Collectively, these findings indicate that androgen-induced downregulation of HDAC4 exerts a targeted influence on specific MMP genes in PCa cells, highlighting a potential regulatory role for HDAC4 in MMP expression. These preliminary data provide a strong foundation for future studies employing pharmacological inhibitors and overexpression strategies to dissect the underlying regulatory mechanisms, further clarifying how androgen-regulated HDAC4 modulates MMP expression implicated in cancer progression.

T1-2 MULTIFUNCTIONAL NANOPARTICLES FOR CO-DELIVERY OF ELACRIDAR AND PACLITAXEL FOR BREAST CANCER LOCAL TREATMENT: DEVELOPMENT, OPTIMIZATION, AND CYTOTOXICITY IN DRUG-SENSITIVE AND DRUG-RESISTANT CELL LINES

[1]Julia Sapienza Passos, [1]Giovanna Cassone Salata, [1]Giovanna Barros de Melo, [1]João Agostinho Machado-Neto, [2]Alyssa Panitch, [1]Luciana B. Lopes

[1]Department of Pharmacology, Institute of Biomedical Sciences, University of Sao Paulo, Brazil, [2]Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology, United States

Breast cancer treatment efficacy is often limited by the adverse effects of conventional therapies and multidrug resistance, often mediated by efflux transporters such as P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). Novel local strategies, such as intraductal drug administration, offer promise for improving drug localization and minimizing systemic toxicity. In this study, we investigated lipid-polymer hybrid nanoparticles (H-NPs) and nanostructured lipid carriers (NLCs) for the local co-delivery of the cytotoxic drug paclitaxel and the P-gp and BCRP inhibitor elacridar. The NLCs were prepared via emulsion-sonication, and the H-NPs were obtained by encapsulating paclitaxel-loaded NLCs within a poly(N-isopropylacrylamide) shell functionalized with SILY, a collagen type I–binding peptide, to enhance tissue retention. All formulations exhibited a diameter below 400 nm, low polydispersity (PDI < 0.3), and negative zeta potential (-16.0 to -8.8 mV). Elacridar was incorporated into the lipid matrix of the NLC (>80% encapsulation efficiency) and in the polymeric shell of the H-NPs (~70%). H-NPs demonstrated superior stability over 60 days. Elacridar release was faster from H-NPs (~92% at 120 h) than from NLC (75%), which is consistent with its encapsulation in the external shell. In paclitaxel-resistant MDA-MB-231 breast cancer and Kasumi-1 (leukemia cell line that overexpresses P-gp) cells, co-encapsulation improved cytotoxicity and reduced IC_{50} by up to 4.2-fold compared to nanoparticles containing only paclitaxel. In MCF-7 spheroids, co-encapsulation reduced IC_{50} values by ~1.6-fold. Fluorescence imaging confirmed enhanced penetration and distribution of encapsulated compounds, especially with NLCs, justifying their higher cytotoxicity.

T1-3 MIMICKING THE SPINAL ENDOGENOUS ADRENERGIC SYSTEM AND MODULATING VOLTAGE-GATED CALCIUM CHANNELS IS A PROMISING STRATEGY TO HALT NEUROPATHIC PAIN

[1,2]Sarah K. Abbood, [1,2]Judit Mária Kirchlechner-Farkas, [1,2]Imre Boldizsár, [1,2]Kornél Király, [1,2]Laszlo G Harsing Jr, [1,3]E. Sylvester Vizi, [1,2]Mahmoud Al-Khrasani

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Hungary, [2]Center for Pharmacology and Drug Research & Development, Semmelweis University, Hungary, [3]Hun-Ren Institute of Experimental Medicine, Molecular Pharmacology Res. Group, Hungary

Introduction: The low efficacy of current medications for neuropathic pain (NP) necessitates the development of novel therapeutics, repurposing of existing drugs, and identification of effective drug combinations to improve therapeutic outcomes. The adrenergic system is among the key modulators of spinal nociception. Phenylephrine (PE), is considered a canonical α_1-adrenoceptor (α_1-AR) agonist. However, our previous data indicate that PE facilitates the release of cytosolic noradrenaline (NA), which would be relevant to the spinal pain modulation. Pregabalin (PGB), an anticonvulsant that modulates voltage-gated calcium channels (VGCCs) containing $\alpha_2\delta$ subunit, is among the first-line treatment approaches for NP. Indeed, it has a slow onset of action and low efficacy at therapeutic doses, as reflected by the number needed to treat. Furthermore, dose escalation is limited by dose-dependent adverse effects. Therefore, investigating PGB-based drug combinations to achieve effective pain relief while minimizing unwanted side effects is of clinical value. Aims: To investigate the antiallodynic potential of intrathecally and orally administered PE, alone and in combination with PGB, in a rat model of mononeuropathic pain. Uncovering the underlying mechanisms of PE in the spinal cord in the case of a positive outcome of per se intrathecal PE. Methods: Mononeuropathic pain was induced in rats via partial sciatic nerve ligation (pSNL). Tactile allodynia was assessed by the dynamic plantar aesthesiometer. PE was administered intrathecally (1, 3, 10, or 30 nmol/rat) to evaluate dose-dependent antiallodynic effects. To assess ARs mediating PE effects, the selective α_1- and α_2-AR antagonists prazosin and idazoxan, respectively, were used. In a separate cohort, oral PE (5 mg/kg) was administered alone and in combination with oral PGB (25 mg/kg). NA release was assessed in mouse spinal tissue. Results: Intrathecal PE (30 nmol/rat) significantly attenuated tactile allodynia in a prazosin- and idazoxan-reversal manner, pointing to the α_1- and α_2-ARs involvement. As a novelty, the oral administration of the combination of PE (5 mg/kg) and PGB (25 mg/kg) produced a significant antiallodynic effect with fast onset, whereas the individual compounds failed to show an effect at the test doses. Furthermore, our results indicate that the effect of PE is indirect and depends on cytosolic NA release from spinal tissue, as demonstrated by stimulation-induced release experiments in mice. Conclusions: PE produces NA-dependent antiallodynic effects in rats with NP via activation of spinal ARs, likely by activating α_2-receptors at presynaptic regions alongside activation of α_1-receptors at inhibitory interneurons. Concurrent activation of the spinal adrenergic system with VGCS modulation represents a promising strategy for the management of NP, warranting further translational investigation. Fund: TKP 2021 EGA-25

T1-4 INTENSIVE PHYSICAL TRAINING INCREASES THE RISK OF VENTRICULAR ALTERNANS IN A CANINE ATHLETE'S HEART MODEL

[1]Gergő Bitay, [1,2]Noémi Tóth, [1,2]Zsófia Kohajda, [1]Leila Topal, [1]Vivien Demeter-Haludka, [1]Muhammad Naveed, [1]Aiman Saleh A. Mohammad, [1,2]Norbert Jost, [1]László Virág, [1]István Baczkó, [1,2]András Varró, [1,2]Norbert Nagy

[1]Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Szeged, Hungary, [2]HUN-REN-SZTE Research Group of Cardiovascular Pharmacology, Hungary

Regular physical training provides undeniable benefits and exerts positive effects on the cardiovascular system and overall quality of life. However, multiple cases of sudden cardiac death (SCD) among elite athletes have been reported, and the underlying mechanisms remain incompletely understood. In this study, we tested the hypothesis that intensive exercise-induced electrical remodeling facilitates the development of cardiac alternans, which may serve as a substrate for arrhythmogenesis.

A total of 24 Beagle dogs of both sexes were randomly assigned to sedentary or trained groups and underwent a 16-week vigorous treadmill running protocol. Following the training period, in vivo arrhythmia provocation, action potential measurements in left ventricular tissue slices, patch-clamp recordings from isolated left ventricular cells, and Western blot analyses were performed.

Trained animals exhibited enhanced in vivo arrhythmia susceptibility, prolonged action potentials, greater action potential and Ca^{2+} transient alternans, and increased Purkinje–ventricle action potential dispersion. Additionally, sarcoplasmic reticulum Ca^{2+} content was reduced, while Ca^{2+} buffering capacity was elevated. Western blot analysis revealed downregulation of CACNA1C (L-type Ca^{2+} channel) expression.

These findings suggest that intensive physical training promotes the development of cardiac alternans through electrical and Ca^{2+}-handling remodeling, which may contribute to the increased arrhythmia susceptibility. Overall, these results provide new insights into the mechanisms underlying sudden cardiac death in competitive athletes.

T1-5 THE CX3CR1 FRACTALKINE RECEPTOR MEDIATES BOTH JOINT PAIN AND DESTRUCTION IN A MOUSE OSTEOARTHRITIS MODEL

[1,2]Péter Pápai, [1,2]Ádám István Horváth, [1,2]Éva Borbély, [1,3,4]Valéria Tékus, [5,6]Anett Futácsi, [5,6]Boldizsár Czéh, [7]Ádám Dénes, [1,2,3,8]Zsuzsanna Helyes

[1]IDepartment of Pharmacology and Pharmacotherapy, Medical School, University of Pécs, Hungary, [2]National Laboratory for Drug Research and Development, Hungary, [3]HUN-REN-PTE Chronic Pain Research Group, Hungary, [4]Department of Laboratory Diagnostics, Faculty of Health Sciences, University of Pécs, Hungary, [5]Department of Laboratory Medicine, Medical School, University of Pécs, Hungary, [6]Structural Neurobiology Research Group, János Szentágothai Research Centre, University of Pécs, Hungary, [7]"Momentum" Laboratory of Neuroimmunology, HUN-REN Institute of Experimental Medicine, Hungary, [8]PharmInVivo Kft., Hungary

The fractalkine chemokine receptor 1 (CX3CR1) is primarily expressed on macrophages, T-cells, osteoclast precursors, and microglia. Its activation mediates inflammatory processes both in the periphery and the central nervous system and contributes to the activation and sensitization of pain-related brain areas. Although the role of neuroinflammation has been described in some pain conditions, little is known about the involvement of CX3CR1 in chronic joint pain. Therefore, we investigated the involvement of CX3CR1 in a chemically induced chronic mouse osteoarthritis (OA) model.

OA was induced by intra-articular injection of moniodoacetate (MIA) into the right knee of C57BL6/J (WT) and CX3CR1 gene-deficient ($CX3CR1^{-/-}$) mice. WT mice were treated with the selective CX3CR1 antagonist AZD8797 (2x1 mg/kg/day, i.p.) or its vehicle every day during the 21-day experimental period. Mechanonociception was assessed by aesthesiometry, weight distribution by dynamic weight bearing, knee swelling by digital caliper, bone microarchitecture by micro-CT, histopathological changes by semi-quantitative scoring and glia activation by immunohistochemistry in pain-related brain regions.

MIA induced remarkable decrease of weight bearing and paw withdrawal threshold, increase of knee swelling, alteration of tibial and femoral structures (decreased trabeculation and cortical erosions), histopathological damage (disorganized cartilage structure, hypocellularity, decreased matrix staining, disrupted tidemark integrity, synovial hyperplasia, and osteophyte formation), and changes in the astrocyte and microglia density in the periaqueductal grey. Mechanical hypersensitivity and histopathological damage were reduced, bone resorption and cortical erosions were increased in $CX3CR1^{-}/^{-}$ mice compared to WT controls, while weight bearing asymmetry and knee edema were unchanged in the whole experimental period. AZD8797 decreased weight bearing asymmetry, histopathological damage and astrocyte density, but did not influence mechanical hypersensitivity, knee edema and structural bone alterations.

CX3CR1 activation mediates chronic OA pain and cartilage destruction, mainly independently of the peripheral inflammation. The pharmacological blockade of CX3CR1 provides structural and functional protection offering a promising novel analgesic perspective with disease-modifying potential in OA.

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T1-6 MIRNATARGET: A NETWORK-BASED SOLUTION AND BENCHMARKING FRAMEWORK FOR PREDICTING TRANSCRIPTOME-WIDE CONCERTED REGULATORY EFFECTS OF MICRORNAS

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In the past decade endeavours to develop small RNA therapeutics have grown explosively, which necessitates the accurate prediction of the effects of small RNA therapeutics to ensure therapeutic efficacy and avoid off-target toxicity. This prediction task poses an even greater challenge for the combinatorial effects of multiple microRNAs.

To tackle this problem, we aimed to create a robust evaluation framework and a comprehensive benchmarking dataset for prediction tools, demonstrating its applicability through a comparative performance analysis of our network topology-based model, miRNAtarget™.

A comprehensive differential gene expression benchmark dataset was constructed using a uniform processing pipeline applied to paired small RNA-sequencing and bulk messenger RNA-sequencing data sourced from five studies publicly available in the Gene Expression Omnibus. This dataset was utilized as ground truth within a rigorous and expandable validation framework to perform a comparative performance analysis evaluating the predictive accuracy of the multi-source miRNAtarget™ model against its own single-source variants, which rely exclusively on individual databases such as TargetScan, miRDB or miRTarBase and a random classifier.

The primary outcome of this work is the construction of the benchmarking dataset and the successful application of the validation framework, which enabled a quantitative comparison of the miRNAtarget™ variants. This comparison revealed that predictive performance of miRNAtarget is dependent on the evaluation metric. When evaluating by the magnitude of predicted effect (top ten percent by absolute value of change), the single-source miRNAtarget variant relying on miRDB was the top performer (best in six out of seventeen comparisons). However, when evaluating by directional accuracy (top ten percent of most up- and downregulated predictions), the TargetScan-based variant was better (best in eight out of seventeen comparisons).

In this study, we first propose the task of predicting the transcriptome-wide mRNA expression changes induced by microRNA combinations. To advance this newly defined task, we provide the first comprehensive benchmarking framework and unified benchmark dataset for the rigorous and reproducible evaluation of prediction models. Furthermore, we present a simplistic first solution, miRNAtarget™, a network topology-based model, as a baseline, which is capable of handling a combination of microRNAs.

T1-7 THE PROTECTIVE EFFECTS OF METHYLENE BLUE ON PMCA IN ALCOHOL-RELATED PANCREATIC AND HEPATIC INJURY

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Introduction: Alcohol-related diseases can damage multiple organs, particularly the pancreas and the liver. Alcohol-induced acute pancreatitis (AP) and alcoholic hepatitis (AH) are major complications of excessive alcohol consumption. Ethanol and fatty acids impair the expression and function of the cystic fibrosis transmembrane conductance regulator (CFTR), an ion channel essential for epithelial homeostasis in both organs. This dysfunction also destabilizes the CFTR–plasma membrane Ca^{2+}-ATPase (PMCA)-calmodulin complex, resulting in impaired intracellular Ca^{2+} regulation and toxic Ca^{2+} overload that contributes to disease progression. Pharmacological strategies that restore epithelial Ca^{2+} handling may therefore offer therapeutic benefit. Methylene blue (MB), an antioxidant influencing intracellular Ca^{2+} regulation, may therefore support PMCA-mediated protection in alcohol-related pancreatic and liver injury.

Aim: We aim to investigate the potential beneficial effects of MB on PMCA and to examine its protective role in models of AP and AH.

Methods: MB effects on PMCA and CFTR were studied in human and mouse pancreatic ductal and mouse liver organoids (hPO, mPO, mLO). In vitro injury was induced by pre-treating organoids with 100 mM ethanol (EtOH) and 200 uM palmitic acid (PA) for 24 hours. Organoids were analyzed using microfluorimetry, immunofluorescence (IF), qPCR, and mitochondrial potential assays (TMRM, JC-10), while cytotoxicity was assessed with a 3D viability assay. In vivo AP was induced by EtOH and palmitoleic acid, while AH was induced by a Lieber–DeCarli EtOH diet with binge alcohol. Disease severity was evaluated by histology, Oil Red O staining, serum analysis, and ketone body measurement.

Results: MB significantly enhanced PMCA-mediated Ca^{2+} extrusion in hPOs, mPOs and mLOs after EtOH-PA exposure, accompanied by stronger apical PMCA4 localization. Mitochondrial membrane potential measurements confirmed MB's protective role in maintaining mitochondrial function. Gene expression analysis showed no significant changes in CFTR, PMCA4, or ORAI1 expression between EtOH-PA and MB treated groups. In vivo, MB reduced pancreatic injury in acute pancreatitis, lowering serum amylase and histological scores. In an alcoholic hepatitis model, MB decreased serum ALT/AST levels and hepatic lipid accumulation. Together, these results indicate that MB protects against ethanol- and fatty acid-induced pancreatic and liver injury through regulation of PMCA activity and stabilization of mitochondrial function.

Conclusion: Our findings demonstrate that MB protects pancreatic and liver tissues from ethanol- and fatty acid-induced injury by enhancing PMCA activity, reinforcing apical PMCA expression, and preserving mitochondrial function. These results highlight MB as a promising translational candidate for mitigating alcohol-induced acute pancreatitis and alcoholic hepatitis, although further studies are required to fully establish its therapeutic potential.

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T2-1 ALLYL-ISOTHIOCYANATE DECREASES THE VIABILITY OF HUMAN PROSTATE ADENOCARCINOMA CELL LINES INDEPENDENTLY OF TRANSIENT RECEPTOR POTENTIAL ANKYRIN 1 RECEPTOR ACTIVATION

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The Transient Receptor Potential Ankyrin 1 (TRPA1) agonist allyl isothiocyanate (AITC) has been demonstrated to reduce the proliferation and progression of various malignancies including glioblastoma, osteosarcoma, small and non-small cell lung cancer, but its actions on prostate adenocarcinoma (PAC) remain unknown. Therefore, here we investigated the effects of AITC on PAC cell line viability and proliferation along with its functional expression.

The viability of 22Rv1 and LNCaP PAC cell lines following AITC treatments was assessed by ATP-based luminescence assay at concentrations of 1, 2, 10, 50, 100, 200 µM. Cell proliferation was evaluated after 48 hours of AITC treatment at 1, 10, 50 µM using Luna II automated cell counter. TRPA1 mRNA expression was determined by RNAscope *in situ* hybridization on benign prostate hyperplasia, PAC tissues and cell lines, and validated by qPCR. The functionality of the ion channel was measured by fluorescent Ca^{2+}-influx assay after 100 µM AITC administration.

AITC concentration-dependently reduced the viability of 22Rv1 and LNCaP with the IC50 values of 91.6 µM and 32.8 µM, respectively. This viability decreasing effect was not reversed by the TRPA1 antagonist HC-030031 (50 µM) and A967079 (1 µM) suggesting non-TRPA1-mediated cytotoxic effect. 48 h incubation with 1 µM AITC significantly inhibited the proliferation of both cell lines.

Although TRPA1 transcripts were detected in benign prostate hyperplasia, PAC tissues and both cell lines, AITC did not induce intracellular Ca^{2+} increase demonstrating the lack of functionally active ion channel proteins. Interestingly, the non-selective TRPA1 agonists cinnamaldehyde, thymol and formaldehyde induced Ca^{2+} influx, but it was not inhibited by A967079.

In conclusion, although AITC reduces PAC cell viability and proliferation, these actions are not mediated by TRPA1 activation. Despite their mRNA expressions, no TRPA1 channel is expressed functionally on these cell lines. Future studies will investigate the Ca^{2+}-influx-inducing mechanisms and effects of cinnamaldehyde, thymol and formaldehyde in PAC cells.

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T2-2 CARDIOVASCULAR EFFECTS OF ANTI-GOUT DRUGS: EVALUATION OF ECHOCARDIOGRAPHIC DIFFERENCES OF FEBUXOSTAT AND ALLOPURINOL IN A MOUSE MYOCARDIAL INJURY MODEL

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Introduction: In the last decade, many trials have been published about cardiovascular safety of two anti-gout medications. Results are ambiguous, given that CARES trial have revealed elevated mortality in patients with febuxostat in comparison with allopurinol. Other trials have shown no alteration in cardiovascular events. Additionally, females with gout are more vulnerable to cardiovascular diseases. However, little data are in literature of sex differences of anti-gout medications.

Purpose: Our objective was to evaluate the echocardiographic and fibrotic differences of febuxostat and allopurinol in a myocardial injury mouse model.

Methods: C57BL/6 mice from both sexes were used in present study. After an acclimatization period, baseline echocardiographic measurements were carried out, followed by the randomization into the following five treatment groups: vehicle control, isoprenaline (ISOP)-only, febuxostat-only, febuxostat plus isoprenaline and allopurinol plus isoprenaline. In the first two weeks, animals were only received per os daily treatment with 10 mg/ body weight kg (BWkg) febuxostat and 20 mg/BWkg allopurinol. Then, echocardiographic data were acquired, followed by myocardial injury induction with 200 mg/BW kg ISOP, and followed by another ultrasonographic imaging. In the next three weeks, the animals were treated two times weekly with ISOP 100 mg/BW kg for myocardial injury maintenance, alongside the daily per os regimen. After a total of five weeks of treatment, following the last echocardiography, mice were sacrificed for histological analysis. Long and short axis M-modes were acquired for ultrasonographic assessment. Fibrosis was assessed by picrosirius red staining and image analysis software.

Results: Diminished relative wall thickness (RWT) was observed in febuxostat plus ISOP treatment group (RWT= 0.493±0.053), in comparison with ISOP-only group (RWT=0.662±0.026) in females. Febuxostat also resulted in higher end-systolic and end-diastolic values. Additionally, significant decline in fractional shortening was observed in febuxostat plus ISOP group (FS before/after induction: 27.244±3.666 / 19.512±5.047), meanwhile such alteration was not present in the allopurinol plus ISOP group (FS: 24.887±5.735 / 25.295±7.346). On the other hand, males with febuxostat plus ISOP were presented with enhanced wall thickening (RWT=0.557±0.119) in comparison with febuxostat-only group (RWT=0.403±0.059). Febuxostat treatment in comparion with ISOP-only group in females did not alter fibrosis, meanwhile it was enchanced in males.

Conclusion: Our study revealed key differences of febuxostat effects on diametric data: in females it diminishes wall thickening, resulting in dilated cardiomyopathy, meanwhile in male more pronounced wall thickness was observed with more pronounced fibrosis. In future studies, mechanism of cardiovascular effects of febuxostat on females will be investigated.

T2-3 THE ROLE OF THE TRANSIENT RECEPTOR POTENTIAL ANKYRIN 1 ION CHANNEL IN MEMORY AND MOTOR COORDINATION DURING AGING IN FEMALE MICE

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Transient Receptor Potential (TRP) ion channels are non-selective cation channels expressed on peripheral sensory nerve endings and sensory neurons. Previous studies have shown that TRP Ankyrin 1 (TRPA1) receptor has a prominent role in pain sensation. Furthermore, our research group has previously demonstrated the involvement of the TRPA1 ion channel in age-related cognitive decline in male mice, manifested as a slower rate of memory loss in knockout animals. In our current study, we aimed to investigate the age-dependent changes in cognitive abilities and motor functions in TRPA1 knockout and wild-type female mice.

In our *in vivo* experiments, motor coordination and muscle strength were assessed using the Double horizontal bars test (DHB), the Static Rod test (SR) and the Rotarod test. Memory performance was evaluated with the Y-maze and Novel Object Recognition tests (NOR). In parallel with the behavioral assessments, we monitored the estrous cycle of the animals by performing vaginal smears at the same time each day.

We found that aging did not result in differences in muscle strength or motor coordination between wild-type (WT) and knockout (KO) animals (DHB, SR, Rotarod). We also demonstrated that spontaneous alternation in 12-month-old mice was significantly lower compared to young animals (Y-maze). Furthermore, in NOR short-term memory performance wild-type mice showed age-related decline, whereas the KO group performed better than the age-matched WT controls. We observed that at 3 months of age there was no difference in the estrous cycle between WT and KO groups, however, by 12 months of age most WT mice had become acyclic, while the KO mice continued to display regular estrous cycles. These findings suggest that the TRPA1 ion channel contributes to the development of dementia, the deterioration of motor coordination, and the decline in muscle strength during aging. Therfore, its inhibition may be beneficial in alleviating these age-related impairments.

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T2-4 STATIN TREATMENT AND SARCOPENIA: A SYSTEMATIC REVIEW AND METANALYSIS

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Statin-associated muscle symptoms are frequent side-effects of statins, ranging from mild discomfort to severe weakness. A significant proportion of statin-treated patients are at increased risk for sarcopenia, questioning safety of statins in this category. Therefore, we aimed to investigate whether statin treatment is associated with physical traits recognized in sarcopenia through systematic review and metanalysis.
A systematic search of MEDLINE, Embase, and Cochrane databases was conducted on 19/11/2025, adhering to our Cochrane protocol. 75 articles comparing statin against not-statin treated subjects were included, regardless of dominant comorbidity. Primary outcomes, the most often encountered across modern definitions of sarcopenia, were hand grip strength, walking speed and chair stand test. Secondary ones were timed up-and-go test, stair climb test, peak knee force and Short Physical Performance Battery. A random-effects model was employed to calculate difference of means (MD) with 95% confidence intervals (CI), accounting for inter-study heterogeneity.
None of the main outcomes were statistically or clinically significant differences: hand grip strength, (MD) 0.10 kg [95% CI: −0.90, 1.09], walking speed (MD) 0.00 m/s [−0.05, 0.04], and chair stand test (SMD: −0.01 [−0.41, 0.39]) showed virtually no change with statin therapy. Post-hoc analysis was performed for 6-minute walking test; in a MD plot consisting of 6373 patients, a statistically significant increase in walking performance (MD: 20.72 [6.32, 35.12] m) was reported for the statin-treated group. Subgrouping by comorbidities, chronic heart failure patients displayed highest benefit with intervention (MD: 53.52 [21.37, 85.68] m). All but one study showed risk of bias ranging from low to high, and level of evidence for most outcomes was low.
We conclude statin treatment is not associated with sarcopenia. Moreover, chronic heart failure patients appear to have some benefit with respect to 6-minute walk test. According to current evidence, prescribing statins for patients susceptible to sarcopenia appears to be safe.

W1-1 HEMOKININ-1 AS A MODULATOR OF THERMOREGULATION

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Hemokinin-1 (HK1) is a neuropeptide of the tachykinin family known to exert several functions in the central nervous system[1]; however, its role in thermoregulation has not been previously described. Based on its stable expression in the hypothalamus[2]—a key region in temperature regulation—HK1 represents a strong candidate for a regulatory role in thermal homeostasis. Therefore, our study aimed to elucidate its potential involvement in thermoregulatory mechanisms.

Experiments were conducted on adult male HK1 gene-deficient (KO) and C57Bl/6 (wildtype, WT) mice. We compared core temperature responses following cold and heat exposure, as well as after intraperitoneal administration of low (120 µg/kg) and high (5 mg/kg) doses of lipopolysaccharide (LPS). This experimental process was based on a well-known model, our research group used in previous studies[3].

Our findings show that under physiological conditions, there was no difference between KO and WT groups in response to either cold or heat exposure. However, under pathophysiological stress, i.e., systemic inflammation, we found significant differences. In the late phase of the multiphasic febrile response following low-dose LPS, the temperature rise was significantly attenuated in the KO group. Furthermore, in response to high-dose LPS, HK1 deficiency prevented the development of hypothermia.

These results demonstrate that HK1 may have both pyrogenic and cryogenic properties. Further studies are needed to elucidate the precise mechanisms underlying its role in thermoregulatory responses.

W1-2 IDENTIFICATION AND DEVELOPMENT OR MIR-450A FOR CARDIOPROTECTION

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Acute myocardial infarction (AMI) remains one of the leading causes of death worldwide, however effective pharmacotherapy is not available to protect the heart against ischaemia-reperfusion (I/R) injury. MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression at the post-transcriptional level and have emerged as promising multitarget therapeutic candidates in ischaemic heart disease. Using a translational porcine model of AMI, we previously identified cardioprotective miRNA candidates termed ProtectomiRs. Among these, miR-450a was selected for further development. The present study aimed to validate the cardioprotective effect of miR-450a across species and to explore the potential molecular pathways underlying its action.

ProtectomiR candidates were identified in a clinically relevant porcine AMI model and subsequently validated in neonatal rat cardiomyocytes (NRCM) and AC16 human cardiomyocyte cells exposed to simulated I/R conditions. The effect of miR-450a mimic was assessed over a concentration range of 0.75-100 nM using cell viability measurements. To investigate the underlying molecular mechanisms, predicted target genes of miR-450a were identified using miRNAtarget™ software, followed by Gene Ontology (GO) and KEGG pathway enrichment analyses.

miR-450a demonstrated a dose-dependent cardioprotective effect in both NRCM and AC16 cells under simulated I/R. A concentration of 25 nM significantly increased cell viability, and protective effect was also observed at lower concentrations. Bioinformatic analysis identified SMAD2, DAPK2 and SOD2 among the strongest predicted targets, linking miR-450a to TGF-β signalling, apoptosis and redox regulation. Pathway enrichment analysis further highlighted mTOR and phosphatidylinositol signalling pathways, suggesting modulation of key survival networks.

In conclusion, miR-450a induces cardioprotective effects in both rat and human cardiomyocytes through the regulation of key cardioprotective signalling pathways. These findings support the further development of miR-450a as a potential cardioprotective therapeutic candidate.

W1-3 ESTIMATION OF TARGET-LIGAND BINDING AFFINITY BY IN SILICO APPROACH

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Reliable thermodynamic data of target-ligand binding are essential for successful drug design and molecular modelling projects, especially in the early (screening) stages of drug design for identifying effective ligands. The binding affinity between the target and ligand is expressed by the binding free energy (ΔG_b), which is composed of the binding enthalpy (ΔH_b) and entropy (ΔS) based on the equation $\Delta G_b = \Delta H_b - T\Delta S$ (where T is the thermodynamic temperature). These parameters can be determined experimentally or predicted computationally.

Our research group aimed to develop a simple, fast, and cost-effective computational method for estimating binding enthalpy (ΔH_b) and binding free energy (ΔG_b), using a combination of semi-empirical PM7/1SCF calculations, implicit COSMO, and predicted explicit interfacial water structures, and ligand-based descriptors. This method was validated using a diverse dataset comprising 43 systems, including small molecules and peptides as ligands.

As a case study, our validated protocol was applied to predict the binding data of somatostatin receptor complexes. Somatostatin receptors are drug targets in Alzheimer's disease, Cushing's disease, type 2 diabetes, neuroendocrine tumours, acromegaly, pain-related conditions, and depression. Our predicted binding affinities correlated well with the experimentally determined data.

In summary, this method can significantly support the identification of effective ligands and accelerate the early stages of drug design.

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W1-4 THE THYMUS-HEART AXİS: ACTİVE THYMİC OUTPUT İS A PREREQUİSİTE FOR IMMUNE CHECKPOİNT INHİBİTOR-ASSOCİATED CARDİOTOXİCİTY

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Introduction: While immune checkpoint inhibitors (ICIs) have redefined cancer management, however their clinical utility is severely capped by fatal cardiovascular complications. The prevailing consensus attributes this cardiotoxicity exclusively to the dysregulation of peripheral T-cells. We challenge this view by proposing an upstream etiology: the thymus. We propose that anti-PD-1 therapy compromises central tolerance mechanisms, effectively priming the immune system for myocardial injury.

Purpose: We have investigated whether a functional thymus is required for the development of ICI-mediated cardiac dysfunction. Furthermore, we evaluated whether inducing thymic involution through either naturally with biological aging or pharmacologically via 5-Azacytidine (AZA), confers cardioprotection against immunotherapy-induced injury.

Methods: We employed a comparative murine model involving young (12-week) and aged (16-month) C57BL/6J cohorts subjected to anti-PD-1 regimens. To isolate the role of thymic output, we induced pharmacological atrophy in young mice using AZA. Cardiac performance was assessed via high-resolution echocardiography, complemented by myocardial gene expression analysis and deep analysis of thymic and splenic microenvironments via RNAseq, flow cytometry and RNAscope.

Results: Administration of anti-PD-1 precipitated significant systolic impairment in young mice, a cardiotoxic effect that was notably absent in the aged cohort. Mechanistically, young thymuses exhibited profound transcriptional alterations indicative of impaired T-cell selection and regulatory T-cell reduction. In the heart, this resulted in a pro-inflammatory milieu characterized by upregulated *Cxcl9*, *Cxcl10*, and *Ifng*, occurring even in the absence of fulminant myocarditis. Moreover, pharmacological suppression of thymic activity with AZA successfully preserved systolic function and dampened myocardial inflammatory signaling, effectively replicating the protective phenotype observed in aging.

Conclusions: These findings expand the peripheral-centric model of immunotherapy complications, identifying the thymus as a key driver of ICI-induced cardiotoxicity. We demonstrate that anti-PD-1 lowers tolerance thresholds centrally, fueling a heart-specific inflammatory loop. Consequently, thymic activity represents a novel biomarker for cardiovascular risk stratification, and its therapeutic modulation offers a promising new way to decouple potent anti-tumor immunity from life-threatening cardiotoxicity.

W1-5 POLYMERIC NANOPARTICLES AS TOOLS TO ENHANCE SERINIQUINONE TRANSLATIONAL POTENTIAL

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Seriniquinone (SQ) is a selective cytotoxic drug candidate against melanoma cells that uniquely targets dermcidin, a cell survival- and migration-related protein, triggering endoplasmic reticulum stress, loss of cell adhesion, autophagy, and apoptosis. However, SQ is extremely poor water-soluble, which has so far hampered *in vivo* studies, and previous efforts, such as chemical optimization and incorporation into lipid-based nanocarriers, have not succeeded. In this work, we encapsulated SQ into poly(lactic-co-glycolic) acid (PLGA) nanoparticles (NPs) and evaluated their biological activity against melanoma *in vitro* models. NPs were produced by single emulsion-solvent evaporation and characterized via electron microscopy. Encapsulation efficiency and *in vitro* release at plasmatic and lysosomal pH values were quantified by high performance liquid chromatography. Cytotoxicity and uptake were evaluated in SK-MEL-28 and SK-MEL-147 melanoma monolayers by clonogenic assay, flow cytometry, and confocal microscopy. Homotypic and heterotypic spheroids (co-cultured with THP-1-derived macrophages) were used to assess cell viability by ATP quantification, and NP-mediated drug penetration with rhodamine B as a fluorescent probe. Spherical NPs (260–280 nm) with ~83% encapsulation efficiency were obtained, with no visible SQ precipitate under the microscope. SQ release was slow at pH 7.4 (~16% over 96 h) but markedly accelerated under acidic conditions (up to 70% at pH 4.5). In monolayers, NPs increased SQ cell association by clathrin-mediated endocytosis, and showed a reservoir-like behaviour, enhancing long-term cytotoxicity. In homotypic spheroids, IC_{50} values increased by 3.7 to 14.7-fold relative to monolayers, reflecting their higher complexity compared to monolayers. However, in SK-MEL-28 spheroids, encapsulated SQ showed a 2-fold lower IC_{50} than free SQ, and fluorescent probes confirmed NP penetration and broader drug distribution. In SK-MEL-147 spheroids, NPs induced an additional ~25% reduction in viability at the highest concentrations tested, likely due to solubility improvement. In heterotypic spheroids, macrophages were located both peripherally and centrally within non-viable tumour regions. When compared to homotypic spheroids, IC_{50} values increased by 2.2–2.7-fold, although NPs still reduced IC_{50} by up to 50% across models. PLGA nanoparticles successfully addressed the key pharmaceutical barrier of SQ: its poor water solubility. More than that, the nanoparticle system effectively unlocked SQ therapeutic potential by heightening cellular uptake and tumour penetration, while potentiating its antimelanoma activity in *in vitro* models of increasing complexity. The formulation therefore provides a practical and translational route for the long-standing challenge of SQ *in vivo* delivery, now advancing to evaluation in syngeneic, immunocompetent melanoma mice models.

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W1-6 THE NOVEL MULTI-TARGET DRUG CANDIDATE (SZV-1287) IMPROVES ENDOTOXIN-INDUCED ACUTE AIRWAY INFLAMMATION IN MICE

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SzV-1287, a novel drug candidate patented by our research group for the treatment of neuropathic pain, has successfully completed Phase Ia clinical trials. It irreversibly inhibits the enzyme copper-containing amine oxidase 3 (AOC3), also expressed in the lung and produces tissue irritants activating Transient Receptor Potential Ankyrin1 (TRPA1), a receptor involved in airway inflammation. It also exerts direct TRPA1 and Vanilloid 1 (TRPV1) antagonist activity and additionally, its metabolite, oxaprosin is a cyclooxygenase inhibitor. We investigated the effect of SzV-1287, comparing with the reference compound selective AOC3 inhibitor LJP-1207 or dexamethasone (DEXA) in a mouse model of acute airway inflammation.

Pneumonitis was induced by intratracheal administration of 0.25 mg/kg endotoxin (lipopolysaccharide: LPS; E. coli O111:B4; in 60 µl phosphate buffer saline (PBS)) in female and male C57BL/6J mice. Treatment groups were randomized into i) PBS+vehicle (Kolliphor ip.), ii) LPS+vehicle, iii) LPS+SzV-1287 (20 mg/kg ip.), iv) LPS+LJP-1207 (20mg/kg ip.), or LPS+DEXA (5 mg/kg i.p.). Respiratory functions were measured by restrained plethysmography in conscious mice 24 h after induction, and lungs were then excised under anaesthesia. Lung inflammation was assessed by gadolinium-based magnetic resonance imaging and by histopathological analysis of hematoxylin-eosin and CD68-immunostained lung sections.

LPS-induced body weight loss was prevented by SzV-1287 and unaltered by LJP-1207. Inflammation resulted in a significantly decreased tidal volume, minute ventilation, functional residual capacity, peak inspiratory, expiratory and tidal-mid expiratory flow, as well as an increased gadolinium uptake which were counteracted by SzV-1287 and DEXA. LPS-evoked perivascular edema was alleviated by both SzV-1287 and LJP-1207, whereas CD68+ macrophage infiltration was reduced only by SzV-1287.

The multi-target drug SzV-1287 improves acute airway inflammatory parameters more effectively than the selective AOC-3 inhibitor reference compound, which can partially be contributed to its additional TRPA1/V1 ion channel and COX inhibition. Thus SzV-1287 represents a promising new therapeutic potential for this indication.

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W1-7 PROTEGAN: A GENERATIVE, SELF-SUPERVISED MODEL WITH EDGE-LEVEL ATTENTION FOR NETWORK-BASED PROTEIN–PROTEIN INTERACTION PREDICTION

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The exploration of possible protein–protein interactions (PPIs) remains a central yet challenging task of drug target discovery due to the time and cost restrains of existing experimental methods. Consequently, numerous *in silico* prediction tools have been proposed to accelerate the selection of the most likely candidate protein pairs. In our prior work (Balogh et al., 2022, DOI: 10.1186/s12859-022-04598-x), we introduced a conditional generative adversarial network model for the efficient prediction of PPIs, relying solely on the topology of PPI networks (interactomes). This model combined the principles of systems biology and the neural architectures used for image-to-image translation in computer vision, handling the adjacency matrix of the interactome similar to an image.

Here, our aim was to expand our model architecture with transformer-inspired encoder blocks that use the attention mechanism of language models from natural language processing, in order to further improve the performance of our model.

ProteGAN, the next iteration of our model now includes several encoder blocks before the convolutional u-net part, providing context-aware information about the input subgraphs through the use of edge-level attention. Furthermore, reconstruction loss was added and the network preprocessing Python code was streamlined, adding support for node2vec embedding and network topology analytics. Version 12 of the STRING (Search Tool for the Retrieval of Interacting Genes/Proteins) database was used as the primary source of interactomes for the fine-tuning of ProteGAN, with other sources such as BioGRID and HuRI utilized only for evaluations. As for performance metrics, we focused on improving the area under the precision-recall curve (AUPRC), and the precision in the top 500 predictions (P@500), an important metric for real-life applicability.

Our evaluations on the available PPI networks reveal the importance of utilizing intuitive and simple image preprocessing techniques from the field of computer vision along with powerful, state of the art neural architectures from the field of natural language processing. On the *H. sapiens* interactome of the STRING database, utilizing the common 0.7 confidence threshold, our old model achieved AUPRC: 0.092 and P@500: 0.260, while utilizing image preprocessing techniques and adding encoder blocks improved them to AUPRC: 0.415 and P@500: 0.966.

In conclusion, here we introduce ProteGAN, a generative adversarial network outfitted with transformer-inspired encoder blocks for the prediction of PPIs based on the topology of the interactome. ProteGAN shows considerable performance improvements compared to our previous model and the importance of utilizing simple yet effective preprocessing techniques instead of fully relying on machine learning. As such, ProteGAN could be a valuable tool for the high throughput prediction of candidate PPIs, contributing to a more efficient drug target identification process.

W1-8 EFFORTFUL CHOICE IN RATS: A PRECLINICAL TOOL FOR UNDERSTANDING ALTERED MOTIVATION IN PHARMACOLOGICAL ANHEDONIA AND APPETITE SUPPRESSION

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Anhedonia and reduced motivation are negative psychiatric symptoms, which are assessed in rodent behavioural essays with usually low predictive validity on the human therapeutic responses to drugs. Here we developed and validated a modified Effort Expenditure for Reward Task (EEfRT) for rats, a new translational paradigm originally designed to quantify motivational states and assess pharmacological effects on them. In this task, animals choose between a high-effort/high-reward (HEHR) option and a low-effort/low-reward (LELR) alternative, allowing detailed evaluation of effort-based decision making. To validate the paradigm, first, we divided rats into high-preference (HP) and low-preference (LP) groups based on their baseline performance in the EEfRT. Then, in HP rats, pharmacological anhedonia was induced using the dopamine-depleting agent tetrabenazine, and this deficit was reversed by the dopamine reuptake inhibitor bupropion. In LP rats, natural low motivation was improved following bupropion treatment alone. Cross-validation analyses showed no correlation between EEfRT performance and anxiety measures or food preference, suggesting that the EEfRT paradigm selectively captures motivational dimensions of behaviour. In a subsequent drug-repurposing study, we examined how commonly used GLP-1 receptor agonists influence EEfRT performance. All GLP-1 receptor agonists consistently reduced food intake, confirming their expected appetite-suppressing effects. Exenatide decreased the effort animals exerted for food rewards, while liraglutide and semaglutide did not alter effort expenditure, indicating distinct effects among GLP-1 agonists on motivation. Findings highlight that GLP-1 agonists differ in their impact on reward-related behaviours, beyond appetite suppression. Importantly, the EEfRT proved sensitive to GLP-1–induced reductions in motivational drive, validating the task as a translational tool for detecting drug-related changes in effort-based decision making. The differential effects of individual GLP-1 agents further suggest that these compounds may modulate effortful food choice through distinct motivational pathways, rather than solely via appetite suppression. These insights open the possibility that GLP-1 receptor agonists could be strategically tested in psychiatry to target motivational alterations in comorbid conditions frequently accompanying obesity, such as depression or negative symptoms in schizophrenia. Our next goal is to use this paradigm across various psychiatric disease models to determine how behavioural disturbances associated in those models may respond to pharmacological treatments and result in overlapping or distinct patterns of motivational perturbations.