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8th World Congress

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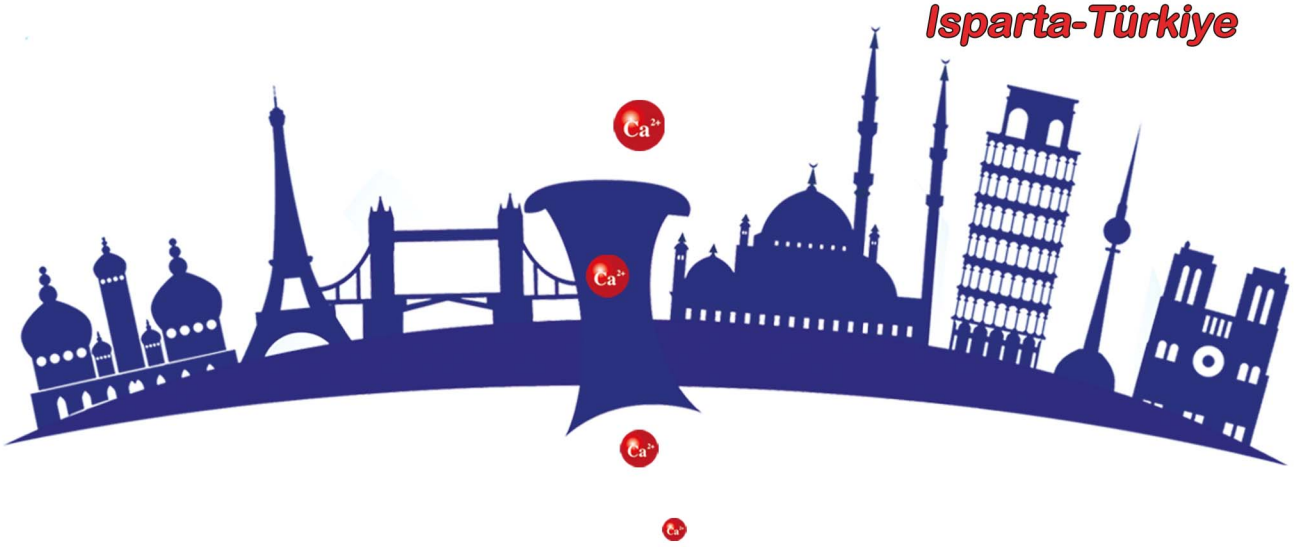
5 - 8 September 2023

Isparta-Türkiye



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AIM AND SCOPES
Journal of Cellular Neuroscience and Oxidative Stress is an online journal that publishes original research articles, reviews and short reviews on the molecular basis of biophysical, physiological and pharmacological processes that regulate cellular function, and the control or alteration of these processes by the action of receptors, neurotransmitters, second messengers, cation, anions, drugs or disease.

Areas of particular interest are four topics. They are;

A- Ion Channels (Na^+- K^+ Channels, Cl^- channels, Ca^{2+} channels, ADP-Ribose and metabolism of NAD^+, Patch-Clamp applications)

B- Oxidative Stress (Antioxidant vitamins, antioxidant enzymes, metabolism of nitric oxide, oxidative stress, biophysics, biochemistry and physiology of free oxygen radicals)

C- Interaction Between Oxidative Stress and Ion Channels in Neuroscience
(Effects of the oxidative stress on the activation of the voltage sensitive cation channels, effect of ADP-Ribose and NAD^+ on activation of the cation channels which are sensitive to voltage, effect of the oxidative stress on activation of the TRP channels in neurodegenerative diseases such Parkinson's and Alzheimer's diseases)

D- Gene and Oxidative Stress
(Gene abnormalities. Interaction between gene and free radicals. Gene anomalies and iron. Role of radiation and cancer on gene polymorphism)

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Keywords
Ion channels, cell biochemistry, biophysics, calcium signaling, cellular function, cellular physiology, metabolism, apoptosis, lipid peroxidation, nitric oxide, ageing, antioxidants, neuropathy, traumatic brain injury, pain, spinal cord injury, Alzheimer's Disease, Parkinson's Disease.

8th World Congress of Oxidative Stress, Calcium Signaling and TRP Channels

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8th World Congress of Oxidative Stress, Calcium Signaling and TRP Channels

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SPEAKERS

Keynote Speak No. 1

Decoding oxidative stress in cell death by redox lipidomics

Valerian KAGAN
Pittsburgh, USA

No abstract

SPEAKERS

Keynote Speak No. 2

How do immune cells navigate to their targets? What clinical benefit can we achieve by inhibiting neutrophil invasion

Peter A. McNaughton
London, UK

No abstract

SPEAKERS

Keynote Speak No. 3

A colorimetric method to measure oxidized reduced and total glutathione levels in tissue

Özcan EREL
Department of Clinical Biochemistry, Faculty of Medicine, Ankara Yıldırım Beyazıt University, Ankara, Türkiye

Glutathione (GSH) is the most important intracellular antioxidant molecule. Against increasing oxidants, two reduced glutathione molecules are oxidized and converted to oxidized glutathione by forming a disulfide bond. The resulting GSSG is converted back to GSH by glutathione reductase. Thus, intracellular GSH/GSSG homeostasis is maintained. Many methods have been described so far to determine oxidized and reduced glutathione levels. Most of the described spectrophotometric methods are expensive methods that use enzymes and coenzymes as reagents. In this study, a new, inexpensive, easily applicable, high accuracy, reproducibility and precision spectrophotometric method measuring oxidized and reduced glutathione levels in tissues was developed.

The newly developed method consists of two stages. In the first stage, the reduced glutathione levels in the medium were determined and expressed as native glutathione. Afterwards, the total glutathione level was determined by reducing the oxidized glutathione with sodium borohydride. Half of the difference between total glutathione and native glutathione was given as oxidized glutathione.

The newly developed method was found to be linear between 0 and 3000 µmol/L (r^2=0.99). The recovery percentages of the parameters found in the developed method were between 92 and 107%. Precisions were 3%, 2%, and 7% for total glutathione, native glutathione, and oxidized glutathione, respectively.

In conclusion, GSH and GSSG levels of tissues can be determined safely with this method, which has high accuracy, precision and reproducibility.

Keywords: Disulfide; Oxidized glutathione (GSSG); Reduced Glutathione (GSH); Thiol.

References

Erel O. and Neselioglu S. (2014). A novel and automated assay for thiol/disulphide homeostasis. Clin Biochem, 2014. 47(18): 326-332.

Senat A, Tas EE, Eroglu H, Bal C, Yavuz AF, Yucel A, Erel O, Ersoz A. (2023). A comprehensive assessment of redox balance in small for gestational age newborns and their mothers. Lab Med. 2023 Jul 27: lmad065. doi: 10.1093/labmed/lmad065. Online ahead of print.

SPEAKERS

Speak No. 1

Mitochondrial metabolism in sepsis induced organ dysfunction

Hülya BAYIR
New York, USA

No abstract

SPEAKERS

Speak No. 2

Non genomic regulation of TRPM8: from thermosensation to cancer

Dimitra Gkika, C
ANTHER Lab, UMR9020 CNRS - UMR-1277 Inserm, University of Lille, France

TRPM8, a predominant detector of cold temperatures in vivo, is also expressed in sensory fibers innervating visceral organs and in epithelia such as prostate, bladder, testis and skin. In epithelia TRPM8 was involved in carcinogenesis and seems to be one of the most promising clinical targets for prostate cancer due to the variation in its expression. In an effort to characterize physiological factors other than cold playing a putative role in TRPM8 activation/modulation, several hormones were tested in our laboratory. In this context we have recently shown that testosterone regulates directly TRPM8 activity in both prostate carcinogenesis and cold thermosensation.

In this presentation I will provide a mechanistic insight in the hormonal non genomic regulation of TRPM8 channel in two processes modulated during ageing, cold thermosensation and malignant transformation.

Keywords: Cancer; Thermosensation; TRPM8.

SPEAKERS

Speak No. 3

Nutrition and COVID-19

Cem EKMEKCIOĞLU
Wien, Austria

No abstract

SPEAKERS

Speak No. 4

TRPM7 as a novel target for neurological disorders

Zhigang XIONG
Department of Neuronal Biology, Morehouse School of Medicine, USA

Transient receptor potential melastatin 7 (TRPM7) is a non-selective cation channel broadly expressed in various cells and tissues, including those of the central nervous systems. Activation of TRPM7 is involved in a wide range of physiological processes including cell growth, proliferation, embryonic development, synaptic transmission and plasticity, etc. Dysregulation of TRPM7 has been implicated in several neurological disorders, including ischemic stroke, traumatic brain injury, spinal cord injury, seizures, amyotrophic lateral sclerosis, Parkinson's disease, and Alzheimer's disease. In addition to Ca^{2+} toxicity, zinc entry through TRPM7 channels also plays an important role in TRPM7-meiated neuronal injury. Pharmacological modulation of TRPM7 activity or down regulation of its expression has shown promise in preclinical studies. However, much remains to be learned about the precise mechanisms of TRPM7 regulation and its downstream signaling pathways in various neurological contexts. Further research into the TRPM7 as a potential therapeutic target for neurological disorders holds great promise for the development of novel and effective treatments.

SPEAKERS

Speak No. 5

TRPML1 controls mitochondrial function and cellular metabolism of TNBC cells

Yassine El HIANI
Halifax, Canada

No abstract

SPEAKERS

Speak No. 6

The interaction between hypoxia-induced NMDA receptor activation and TRPM2 channel

Mustafa NAZIROĞLU[1,2,3]
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[2]Drug Discovery Unit, BSN Health, Analyses, Innov., Consult., Org., Agricul., Trade Ltd, Isparta, Türkiye
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Hypoxia is induced by ischemic conditions. Hypoxia may cause a variety of pathological changes, such as the activation of inflammation-related cytokines, oxidative stress, and apoptosis, that eventually result in the loss of neuronal cells (Wu et al., 2021).

Activation of apoptotic (caspase-3, -8, and -9) and oxidant (mitochondrial reactive oxygen species and lipid peroxidation) signaling pathways is further induced by the hypoxia-mediated overload Ca^{2+} influx, resulting in the eventual death of neurons in the nervous system (Yıldızhan and Nazıroğlu 2021). ADP-ribose, oxidative stress (H2O2), high cytosolic Ca^{2+} concentrations, and other stimuli work together to activate TRPM2, a cationic channel/receptor (McHugh et al. 2003). N methyl-D-aspartate (NMDA) receptor is also a cationic channel/receptor. The cytosolic Ca^{2+} concentration increase when the NMDA receptor and TRPM2 channel are overstimulated. This could trigger the apoptosis and oxidative injury of neuronal cells by activating particular caspases and reactive oxygen species (Yıldızhan and Nazıroğlu 2021). The suppression of cytosolic Ca^{2+} concentration increase has thus been proposed as a therapeutic target for the management of hypoxia-induced oxidative cell damage and death. In a recent paper, we observed that NMDA receptor activation-mediated increase in cytosolic Ca^{2+} concentration stimulated TRPM2 channel-mediated increases in cytosolic Ca^{2+} concentration in hypoxia, although the inhibition of NMDA receptors through the memantine and MK-801 decreased the increases in cytosolic Ca^{2+} concentration through inhibition of TRPM2.

In the presentation, I will summarize the recent findings related to TRPM2 channel-NMDA receptor-mediated overload Ca^{2+} influx and hypoxic injuries in neuronal cells.

Keywords; High cytosolic Ca^{2+} concentration; Hypoxia; Memantine; Oxidative stress; TRPM2 channel;

References

McHugh D, Flemming R, Xu SZ, Perraud AL, Beech DJ., 2003. Critical intracellular Ca2+ dependence of transient receptor potential melastatin 2 (TRPM2) cation channel activation. J Biol Chem. 278(13), 11002-11006. https://doi.org/10.1074/jbc.M210810200.

Wu Y, Fan L, Wang Y, Ding J, Wang R. (2021). Isorhamnetin Alleviates High Glucose-Aggravated Inflammatory Response and Apoptosis in Oxygen-Glucose Deprivation and Reoxygenation-Induced HT22 Hippocampal Neurons Through Akt/SIRT1/Nrf2/HO-1 Signaling Pathway. Inflammation 44(5), 1993-2005. https://doi.org/10.1007/s10753-021-01476-1.

Yıldızhan K, Nazıroğlu M. (2023). NMDA Receptor Activation Stimulates Hypoxia-Induced TRPM2 Channel Activation, Mitochondrial Oxidative Stress, and Apoptosis in Neuronal Cell Line: Modular Role of Memantine. Brain Res. 1803:148232. https://doi.org/10.1016/j.brainres.2023.148232.

SPEAKERS

Speak No. 7

TRPC and Orai channels in ischemic heart disease

Tarik SMANI
Seville, Spain

No abstract

SPEAKERS

Speak No. 8

Oxidative stress induced ion channels couple metabolic status to resting membrane potential of the neurons in the mouse ventral cochlear nucleus

Ramazan BAL
Gaziantep, Türkiye

No abstract

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SPEAKERS

Speak No. 9

Metal oxide nanoparticles in cosmetic: possibility of inducing oxidative stress

Salina MUHAMAD[1], Mustafa NAZIROĞLU[2]
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[2]Neuroscience Research Center (NÖROBAM), Suleyman Demirel University, Isparta, Türkiye

Metal oxide nanoparticles, including titanium dioxide (TiO_2) and zinc oxide (ZnO), are becoming increasingly popular in the global cosmetic industries as they can alter and enhance product properties, including solubility and chemical reactions. Excessive use and possible inhalation of those nanoparticles may lead to health concerns, such as oxidative stress. However, most products on the market failed to list those nanosized materials, leaving consumers unaware of their existence and, more importantly, the risk. Hence, this study was conducted to examine and investigate the presence of these potentially harmful materials in popular consumer products, specifically compact powder. All selected samples were characterized using X-ray diffraction (XRD) and energy dispersive X-ray (EDX). XRD analysis revealed that those samples contain ZnO with crystallite sizes ranging from ~24 nm to ~85 nm, while TiO_2 crystallite sizes range from ~15 nm to ~90 nm. The composition was subsequently disclosed by EDX, which proved the existence of Zn, O, and Ti elements in those samples. The presence of nanosized TiO_2 and ZnO is confirmed, with a crystallite size less than 100 nm. Considering the existence of these nanoparticles in cosmetics, the possibility of inducing oxidative stress in consumers is significant, according to recent studies. The health authority should continuously regulate cosmetic manufacturers to ensure that the content is appropriately labelled. Campaigns and commercials may be put in place to inform and educate consumers about this issue.

Keywords: Metal oxide nanoparticles; Cosmetics; Oxidative stress.

SPEAKERS

Speak No. 10

Anti-ferroptotic drugs as a novel tool to reduce placental sFlt-1secretion: a potential treatment for preeclampsia

Sapir LIANSKI, Tehila MIZRACHI, Shirin Elhaik GOLDMAN, Debra GOLDMAN-WOHL, Simcha YAGEL, Ofer BEHARIER
Department of Obstetrics and Gynecology, Hadassah Hebrew University Medical Center, Jerusalem, Israel

We recently found that ferroptosis, a unique form of programmed cell death, causes human trophoblast injury and is associated with pregnancy complications. Hence, the development and repurposing of pregnancy-safe drugs that inhibit ferroptosis may ofer novel, promising treatment approach and significantly advance the field of obstetrics. Here we study the link between placental ferroptosis and soluble fms-like tyrosine kinase-1 (sFlt-1) secretion, a key player in the pathophysiology of preeclampsia. We use PMZ and DPY drugs found in our high throughput screening as pregnancy-safe drugs that inhibit ferroptosis.

Placental explants of normal term pregnancies, were treated with Vehicle (DMSO), RSL3 (0.4-0.8uM, ferroptosis specific inducer), Ferrostatin-1 (Fer-1, ferroptosis specific inhibitor) and PMZ and DPY for 24h. We monitored the secretion of sFlt-1 and LDH using Human VEGFR1/Flt-1 ELISA (R&D) and LDH-Cytotoxicity Assay (R&D), respectively.

Induction of ferroptosis in human placental explants, n=7 (A) results in excess secretion of sFLT-1, n=5 (B). Inhibition of ferroptotic signaling attenuates sFLT-1 secretion in placental explant of normal term, n=7 (C), and early preeclampsia, n= 3(D). Preeclamptic placental tissues were obtained from two patients with early PE (31, 30, and 28 weeks) with severe features (severe hypertension or HELLP).

We provide the first direct evidence linking placental ferroptosis and sFlt-1 secretion. These findings mark anti-ferroptotic treatment as a potential novel treatment or preventive tool for preeclampsia.

SPEAKERS

Speak No. 11

The role of computational modeling in uncovering mechanisms of oxidative stress in regulated cell death

Karolina Mikulska-Ruminska
Torun, Poland

No abstract

SPEAKERS

Speak No. 12

Genetic Biosensors and Chemogenetic Tools: Unlocking Redox Biology through Multiparametric Imaging

Emrah EROĞLU[1,2]

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[2]Molecular Biology, Genetics, and Bioengineering Program, Faculty of Engineering and Natural Sciences, Sabanci University, Istanbul, Türkiye

This lecture presents our latest advancements in developing innovative strategies for multiparametric imaging of cellular redox signaling events. By harnessing genetically encoded fluorescent protein-based biosensors for Calcium and reactive molecules such as ROS and RNS, the field of redox biology has witnessed a transformative shift. These powerful tools enable the visualization of biological processes with exceptional spatial and temporal resolution, both in vitro and in vivo. We have expanded the repertoire of genetically encodable tools and introduced novel chemogenetic enzymes that can precisely manipulate the cellular and tissue-level redox tone. The integration of diverse genetic biosensors and chemogenetic devices has paved the way for groundbreaking investigations into ROS and RNS signaling pathways through multiparametric live-cell imaging with unparalleled precision. Nonetheless, there remains untapped potential in these approaches that redox biologists have yet to explore fully. This lecture will delve into recent progress and future prospects of these toolkits, highlighting their capacity to bridge existing knowledge gaps in our understanding of redox biology.

Keywords: Chemogenetic tools; Genetically encoded biosensors, Reactive oxygen species; Reactive nitrogen species; Oxidative stress.

References

Erdogan, Y. C., Altun, H. Y., Secilmis, M., Ata, B. N., Sevimli, G., Cokluk, Z., … Eroglu, E. 2021. "Complexities of the chemogenetic toolkit: Differential mDAAO activation by d-amino substrates and subcellular targeting". Free Radical Biology and Medicine, 177(October), 132–142.

Eroglu, E., Gottschalk, B., Charoensin, S., Blass, S., Bischof, H., Rost, R., … Malli, R. 2016. "Development of novel FP-based probes for live-cell imaging of nitric oxide dynamics". Nature Communications, 7.

Eroglu, E., Saeedi Saravi, S. S., Sorrentino, A., Steinhorn, B., Michel, T. 2019. "Discordance between eNOS phosphorylation and activation revealed by multispectral imaging and chemogenetic methods". Proceedings of the National Academy of Sciences of the United States of America, 116(40), 20210–20217.

Saeedi Saravi, S. S., Eroglu, E., Waldeck-Weiermair, M., Sorrentino, A., Steinhorn, B., Belousov, V., Michel, T. 2020. "Differential endothelial signaling responses elicited by chemogenetic H2O2 synthesis". Redox Biology, 36(May), 101605.

Secilmis, M., Altun, H. Y., Pilic, J., Erdogan, Y. C., Cokluk, Z., Ata, B. N., … Eroglu, E. 2021. "A Co-Culture-Based Multiparametric Imaging Technique to Dissect Local H2O2 Signals with Targeted HyPer7". Biosensors, 11(9), 338.

SPEAKERS

Speak No. 13

Neuronal and astrocytic calcium signalling disturbances in Alzheimer's disease: toward the validation of TRPA1 as a therapeutic target

Alain BUISSON
Grenoble, France

No abstract

Young Speakers

Young Speaker 1

The Involvement of mitochondrial reactive oxygen species-mediated TRPC3 activation in itch

İpek DAĞ
Student, Faculty of Dentistry, Suleyman Demirel University, Isparta, Türkiye

Reactive oxygen species, (ROS) including hydroxyl and superoxide radicals, are mostly produced by mitochondria. Antimycin A (AA), an inhibitor of mitochondrial electron transport chain complex III, when given intrathecally to normal mice, produces mechanical hyperalgesia, demonstrating the essential function that ROS play in the sense of pain. AA also activates nociceptive vagal sensory nerves by suppressing mitochondrial electron transport chain complex III. ROS produced by mitochondrial metabolism activate the Ca^{2+}-permeable TRP channel TRPC3. However, it still has not been studied whether mitochondrial failure and the resulting ROS overproduction generated by stimulating TRPC3 contribute to the itching sensation. As a result, Kim et al. (2022) carried out a study to test whether AA could stimulate small trigeminal ganglion (TG) neurons and trigger itch through TRPC3 stimulation. They found that localized elevated mitochondrial generation of ROS is attributed to mitochondrial dysfunction induced itch via TRPC3, which may be one of the underlying mechanisms of chronic itch. I'll review recent evidence on itch and TRPC3 changes in my presentation.

Keywords: Mitochondria; TRPC3; Trigeminal ganglia; Itch; Oxidative stress

References

Kim SA, Jang JH, Kim W, Lee PR, Kim YH, Vang H, Lee K, Oh SB. (2022). Mitochondrial Reactive Oxygen Species Elicit Acute and Chronic Itch via Transient Receptor Potential Canonical 3 Activation in Mice. Neurosci Bull. 38(4):373-385. https://doi.org/10.1007/s12264-022-00837-6

Young Speakers

Young Speaker 2

The activation of TRPM8 induces hyperosmotic stimuli-induced nociception in dental afferents

Büşra OĞUZ
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When tooth dentin is exposed, it may trigger dentin hypersensitivity, resulting in unexpected, strong dental pain that often prevents patients from eating and drinking. Osmotic stimuli are known to cause dentinal fluid movement, which in turn produces dentin hypersensitivity. TRPM8 is activated by several stimuli, including hyperosmotic stimuli (Sato et al. 2013; Quallo et al. 2015). The presence of osmo-sensors on other TRP channels such as TRPM7, TRPV1, and TRPV2 in hyperosmotic stimuli-induced nociception in neurons was shown by the results of the recent studies (Lee et al. 2020).

TRPM8 channels were found to be molecularly and functionally expressed in some dental primary afferent neurons in a study by Lee et al. (2020). Hyperosmolar stimulation induced a response in neurons expressing TRPM8, and the TRPM8 antagonist (AMTB) prevented calcium transients produced by hyperosmolar sucrose solution. They concluded that TRPM8 in dental primary afferent nerve functions as a hyper-osmosensor in adult mice, contributing to oral nociception. In the talk, I will give a summary of the few reports that are available on hyperosmotic stimuli-induced nociception in dental afferents.

Keywords: Dentin; Hyperosmotic stimuli; TRPM8; Nociception.

References

Lee PR, Lee JY, Kim HB, Lee JH, Oh SB. (2020). TRPM8 Mediates Hyperosmotic Stimuli-Induced Nociception in Dental Afferents. J Dent Res. 99(1):107-114. https://doi.org/10.1177/0022034519886847.

Quallo T, Vastani N, Horridge E, Gentry C, Parra A, Moss S, Viana F, Belmonte C, Andersson DA, Bevan S. (2015). TRPM8 is a neuronal osmosensor that regulates eye blinking in mice. Nat Commun. 6:7150. https://doi.org/10.1038/ncomms8150.

Sato M, Sobhan U, Tsumura M, Kuroda H, Soya M, Masamura A, Nishiyama A, Katakura A, Ichinohe T, Tazaki M, Shibukawa Y. (2013). Hypotonic-induced stretching of plasma membrane activates transient receptor potential vanilloid channels and sodium-calcium exchangers in mouse odontoblasts. J Endod. 39(6):779-87. https://doi.org/10.1016/j.joen.2013.01.012.

Young Speakers

Young Speaker 3

Orthodontic teeth movement-induced pain and TRPV1 channel

Ayshan ALİYEVA
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Orthodontic force leads the peripheral and central nervous systems to have a variety of morphological and neurochemical responses. Exposed orofacial muscles induce mechanical hyperalgesia and uncontrolled pain, which are both caused by TRPV1. Inhibition of TRPV1 reduces the amount of facial grooming or grimacing that rats experience as a result of orthodontic force. The role of TRPV1 in other orthodontic pain modes, such as bite-evoked pain, is unclear. It's essential to comprehend TRPV1's role in bite-evoked pain given its differing contribution to spontaneous pain and bite-evoked pain under muscular inflammation.

According to the findings of Wang et al. (2019), the pain related to orthodontics is caused by trigeminal nociceptors that express TRPV1. In accordance with the study of Leite-Panissi et al. (2023) using the operant orofacial pain assessment device, rats' sensitivity to carrageenan-induced pain is mediated by TRPV-expressing neurons. According to Wang et al. (2020), orthodontic force results in transcriptome changes in the TG that reflect nerve injury, and nociceptive inputs through afferents that express TRPV1 cause additional modifications in gene expression. In my presentation, I'll give an overview of new research on the pain that orthodontic tooth movement causes in experimental animals when TRPV1 channels are activated.

Keywords; Orthodontic teeth movement; Pain; TRPV1.

References

Leite-Panissi CRA, De Paula BB, Neubert JK, Caudle RM. (2023). Influence of TRPV1 on Thermal Nociception in Rats with Temporomandibular Joint Persistent Inflammation Evaluated by the Operant Orofacial Pain Assessment Device (OPAD). J Pain Res. 16:2047-2062. https://doi.org/10.2147/JPR.S405258.

Wang S, Chung MK. (2020). Orthodontic force induces nerve injury-like transcriptomic changes driven by TRPV1-expressing afferents in mouse trigeminal ganglia. Mol Pain. 16:1744806920973141. https://doi.org/10.1177/1744806920973141.

Wang S, Kim M, Ali Z, Ong K, Pae EK, Chung MK. (2019). TRPV1 and TRPV1-Expressing Nociceptors Mediate Orofacial Pain Behaviors in a Mouse Model of Orthodontic Tooth Movement. Front Physiol. 10:1207. https://doi.org/10.3389/fphys.2019.01207.

Young Speakers

Young Speaker 4

The interaction between melatonin and TRPM2 channel in traumatic brain injury

Tarkan EŞENLI
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The most frequent cause of traumatic brain injury (TBI) is a severe blow or trauma to the head or body. TBI can also occur when something gets caught inside the brain's tissue, such as a piece of the skull or an assault rifle. The brain's cells may react negatively right away to mild brain trauma. A more serious TBI in brain may cause several adverse actions such as bleeding, tissue damage, bruises, and other forms of physical trauma. These wounds may have long-term effects or possibly be fatal.

Excessive increases in the cytosolic calcium ion (Ca^{2+}) concentration via the excessive generation of reactive oxygen species play an essential role in the induction of TBI. Ca^{2+} permeable transient receptor potential (TRP) melastatin 2 (TRPM2) is a member of the TRP superfamily. ADP-ribose and H_2O_2 are two examples of the various stimuli that can gate the TRPM2 channel. Melatonin is a strong antioxidant, and its protective role in traumatic brain injury in rodents was reported (Xie et al. 2022). It is inhibited by antioxidants, including melatonin. In the result of recent studies, the protective role of melatonin through the inhibition of TRPM2 on TBI-induced oxidative stress and apoptosis in rats was reported (Choi et al. 2015; Yürüker et al. 2015). I'll provide a summary of recent findings on the effects of TBI on experimental animals when the TRPM2 channel is activated in my presentation.

Keywords; Apoptosis; Traumatic brain injury; TRPM2 channel; Oxidative stress.

References

Choi HJ, Sun D, Jakobs TC. (2015). Astrocytes in the optic nerve head express putative mechanosensitive channels. Mol Vis. 21:749-66.

Xie LL, Li SS, Fan YJ, Qi MM, Li ZZ. (2022). Melatonin alleviates traumatic brain injury-induced anxiety-like behaviors in rats: Roles of the protein kinase A/cAMP-response element binding signaling pathway. Exp Ther Med. 23(4):248. https://doi.org/10.3892/etm.2022.

Yürüker V, Nazıroğlu M, Şenol N. (2015). Reduction in traumatic brain injury-induced oxidative stress, apoptosis, and calcium entry in rat hippocampus by melatonin: Possible involvement of TRPM2 channels. Metab Brain Dis. 30(1):223-231. https://doi.org/10.1007/s11011-014-9623-3.

Young Speakers

Young Speaker 5

Epilepsy and TRPV1 channels

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3.4 million people experience epilepsy worldwide. The number of epileptic seizures can be somewhat controlled with the use of contemporary antiepileptic drugs. There are a number of causes for epilepsy, including oxidative stress and changes in calcium channel function. Hippocampal neuronal calcium ion (Ca^{2+}) buildup has long been recognized as a significant factor in the etiology of epilepsy. A member of the TRP superfamily is the Ca^{2+} permeable transient receptor (TRP) vanilloid 1 (TRPV1). According to Caterina et al. (1997), capsaicin plays a significant part in the TRPV1 channel's activation. Oxidative stress also stimulates the TRPV1 channel, while capsazepine and 5'-iodoresiniferatoxin (IRTX) block it. According to Talebi et al.2022, the dentate gyrus and hippocampal regions exhibit the highest levels of TRPV1 channel expression. The theory that TRPV1 channel blockage likely explains many of the advantages associated with epilepsy, including enhanced apoptosis, antioxidant, and regulated Ca^{2+} entry, is consistently supported by the accumulating findings on the therapeutic potential of TRPV1. TRPV1 has been linked to epilepsy in a small number of recent findings, suggesting that this may be a novel target for possible medications that treat the condition (Nazıroğlu and Övey 2015; Talebi et al. 2022). As a result, oxidative stress activates TRPV1 and has epileptic effects; this effect can be mitigated by powerful inhibitors like IRTX. Additionally, it has been reported that TRPV1 antagonists changed the glutaminergic networks in the rat hippocampus, which reduced spontaneous excitatory synaptic transmission. As a result, TRPV1 inhibition in the hippocampus may potentially be a novel target for preventing epileptic seizures and apoptosis. The findings in the existing literature support a role for Ca^{2+} buildup through TRPV1 channel in the genesis of epileptic seizures.

Keywords: Apoptosis; Calcium ion; Epilepsy; Oxidative stress; Seizures; TRPV1 channel.

References

Caterina MJ, Schumacher MA, Tominaga M, Rosen TA, Levine JD, Julius D. (1997). The capsaicin receptor: a heat-activated ion channel in the pain pathway. Nature. 389(6653):816-824. https://doi.org/10.1038/39807.

Nazıroğlu M, Övey İS. (2015). Involvement of apoptosis and calcium accumulation through TRPV1 channels in neurobiology of epilepsy. Neuroscience. 293:55-66. https://doi.org/10.1016/j.neuroscience.2015.02.041.

Talebi F, Ghorbani S, Alizadeh L, Akhlaghi F, Sadat Moeeni S, Karimzadeh F. (2022). Alteration in Neuregulin 1/ERbB4 in Absence Epilepsy: Regulatory Effect on TRPV1 Expression. Basic Clin Neurosci. 13(6):777-788. https://doi.org/10.32598/bcn.2021.731.2.

Young Speakers

Young Speaker 6

The interaction between oxidative stress-induced TRP channel activation and Alzheimer's disease

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Alzheimer's disease (AD) is the major cause of dementia and is characterized by decreased thinking caused by cell degeneration in the brain. The brain has a low antioxidant level but has high oxygen consumption and polyunsaturated fatty acid content. Hence, the brain is vulnerable to oxidative stress. Based on research, the two primary causes of AD are oxidative stress and apoptotic induction due to microglia activation, so oxidative stress is one of the mechanisms that activates numerous transient receptor potentials (Thapak et al., 2020).

The presentation summarized the role of the oxidative stress-dependent activated TRPA1, TRPV1, TRPV4, TRPM2, TRPM7, and TRPM8 channels in AD (Çınar and Nazıroğlu 2023; Rather et al. 2023). ROS regulates these channels, which are important for Ca^{2+} levels, synaptic function, and inflammation, all of which are linked to the development of AD. It seems that the oxidative stress-dependently activated TRP channels have the main role in the induction of AD, although the disease was modulated by their inhibitions.

Keywords; Alzheimer's disease; TRP channel; Oxidative stress.

References

Çınar R, Nazıroğlu M. (2023). TRPM2 Channel Inhibition Attenuates Amyloid β42-Induced Apoptosis and Oxidative Stress in the Hippocampus of Mice. Cell Mol Neurobiol. 43(3):1335-1353. https://doi.org/10.1007/s10571-022-01253-0.

Rather MA, Khan A, Wang L, Jahan S, Rehman MU, Makeen HA, Mohan S. (2023). TRP channels: Role in neurodegenerative diseases and therapeutic targets. Heliyon. 9(6):e16910. https://doi.org/10.1016/j.heliyon.2023.e16910.

Thapak P, Vaidya B, Joshi HC, Singh JN, Sharma SS. (2020). Therapeutic potential of pharmacological agents targeting TRP channels in CNS disorders. Pharmacol Res. 159:105026. https://doi.org/10.1016/j.phrs.2020.105026.

Young Speakers

Young Speaker 7

Are there actions of TRPM2 and TRPV1 in the etiology of fibromyalgia?

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Increased mitochondrial intermembrane depolarization results from too much calcium ion (Ca^{2+}) entrance into the cytosol of neurons, which in turn promotes too much intracellular reactive oxygen species (ROS) generation. Because low selenium levels were found in the plasma of fibromyalgia patients, oxidative stress plays a significant role in the pathophysiology of a variety of neurological illnesses, including fibromyalgia (Fischer et al., 2020). As a cofactor of the glutathione peroxidase enzyme, selenium plays a significant role in preventing oxidative stress. In cells, selenium has both harmful and therapeutic effects. It has been determined that administering selenium in low amounts can help to maintain cellular viability.

In humans, there are six subfamilies and 28 members of the TRP channel superfamily. The majority of these channels are in charge of Ca^{2+} permeation, particularly in neuronal cells and dorsal root ganglion neurons. In the DRG neurons, there is high expression of the TRPM2 and TRPV1 channels, and they exhibit oxidative stress-dependent activation (Elma et al. 2020). Different forms of pain were associated with higher DRG TRPM2 and TRPV1 channel expression levels. Since a decade ago, there has been speculation that extracellular antioxidant delivery as well as intracellular antioxidant support may be beneficial in fibromyalgia to prevent Ca^{2+} influx mediated by TRP channels (Yüksel et al. 2017).

The regulation of TRPM2 and TRPV1 channels by selenium may provide a unique strategy to treat FM-induced pain, mitochondrial oxidative stress, and apoptosis. Future research should, however, clarify the topic.

Keywords: Apoptosis; Selenium; Fibromyalgia; TRPM2 channel; TRPV1 channel

References

Elma Ö, Yilmaz ST, Deliens T, Coppieters I, Clarys P, Nijs J, Malfliet A. (2020). Do Nutritional Factors Interact with Chronic Musculoskeletal Pain? A Systematic Review. J Clin Med. 9(3):702. https://doi.org/10.3390/jcm9030702.

Fischer SPM, Brusco I, Brum ES, Fialho MFP, Camponogara C, Scussel R, Machado-de-Ávila RA, Trevisan G, Oliveira SM. (2020). Involvement of TRPV1 and the efficacy of α-spinasterol on experimental fibromyalgia symptoms in mice. Neurochem Int. 134:104673. https://doi.org/10.1016/j.neuint.2020.104673.

Yüksel E, Nazıroğlu M, Şahin M, Çiğ B. (2017). Involvement of TRPM2 and TRPV1 channels on hyperalgesia, apoptosis and oxidative stress in rat fibromyalgia model: Protective role of selenium. Sci Rep. 7(1):17543. https://doi.org/10.1038/s41598-017-17715-1.

Young Speakers

Young Speaker 8

Dexmedetomidine, cerebral ischemia, and TRPV1 channel

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An increasing amount of research indicates that excessive reactive oxygen species (ROS) in rats with cerebral ischemia play a significant role in the physiology of cerebral ischemia and are responsible for deficiencies of intracellular free calcium (Ca^{2+}) amount (Randhawa and Jaggi 2018; Xie et al. 2021). Various channels, particularly chemical and voltage-gated channels, allow Ca^{2+} to flow through the membranes of cells. In addition to the recognized cation channels, the transient receptor potential (TRP) superfamily of channels was only recently identified. Thirty members of mammalian and nonmammalian species make up the seven subfamilies that make up the TRP superfamily.

The voltage-gated calcium channels' stimulation and inactivation processes are substantially different from those of TRP channels. For instance, ADP-ribose and oxidative damage activate the TRPM2 channel, whereas many stimuli, such as capsaicin and oxidative stress, activate the TRPV1 channel (Randhawa and Jaggi 2018). Dexmedetomidine (DEX), a drug that causes an immediate reaction and is simple to manage, is essential for long-term sedation in patients receiving emergency medical care. According to Akpnar et al. (2016), DEX has a modulator effect on the Ca^{2+} content in a number of neurons. According to the findings of a recent study, rats' hippocampal TRPM2 and TRPV1 channels were activated by cerebral ischemia, ROS, and DEX.

In summary, new research shows DEX therapy reduces intracellular Ca^{2+} signaling and oxidative damage generated by brain ischemia via blocking TRP channels. It seems that additional study will be required to determine the exact link between DEX and TRP channel activation in cerebral ischemia.

Key words: Dexmedetomidine; Cerebral Ischemia; TRPV1 channel; Oxidative stress

References

Akpınar H, Nazıroğlu M, Övey İS, Çiğ B, Akpınar O. (2016). The neuroprotective action of dexmedetomidine on apoptosis, calcium entry and oxidative stress in cerebral ischemia-induced rats: Contribution of TRPM2 and TRPV1 channels. Sci Rep. 6:37196. https://doi.org/10.1038/srep37196.

Randhawa PK, Jaggi AS. (2018). A Review on Potential Involvement of TRPV1 Channels in Ischemia-Reperfusion Injury. J Cardiovasc Pharmacol Ther. 23(1):38-45. https://doi.org/10.1177/1074248417707050.

Xie Q, Ma R, Li H, Wang J, Guo X, Chen H. (2021). Advancement in research on the role of the transient receptor potential vanilloid channel in cerebral ischemic injury (Review). Exp Ther Med. 22(2):881. https://doi.org/10.3892/etm.2021.10313

Young Speakers

Young Speaker 9

Selenium modulates experimental dementia via inhibition of TRPM2 and TRPV1 channels

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Alzheimer's disease (AD) is the most common form of dementia among elderly people. Involvements of brain amyloid plaque accumulation, Tau protein formation, and oxidative stress in the etiology of AD are well-known. An increasing amount of research indicates that excessive reactive oxygen species (ROS) in humans with dementia play a significant role in the physiology of dementia and are responsible for increases in calcium ion (Ca^{2+}) amounts (Walia et al. 2022). Various channels, particularly chemical and voltage-gated channels, allow Ca^{2+} to flow through the membranes of cells. In addition to the recognized cation channels such as voltage gated and chemical channels, the transient receptor potential (TRP) superfamily of channels was only recently identified. Thirty members of mammalian and nonmammalian species make up the seven subfamilies that make up the TRP superfamily. TRPM2 and TRPV1 are two members of the TRP superfamily.

The brain is the main target of ROS due to its low antioxidant but high polyunsaturated fatty acid content and oxygen consumption rate. Therefore, the accumulation rate of ROS is high in the brains of patients with dementia. There is an association between low blood selenium levels and dementia induction (Zhou et al. 2023). In the last decade, there has been great interest in the combination of several antioxidants, including selenium, that have proved to be effective against a wide range of ROS-induced dementias (Balaban et al. 2017). I evaluated current data on selenium through the inhibition of TRPM2 and TRPV1 channels on oxidative stress and apoptosis in the treatment of dementia.

Key words: Dementia; Selenium; TRPV1 channel; Oxidative stress.

References

Balaban H, Nazıroğlu M, Demirci K, Övey İS. (2017). The Protective Role of Selenium on Scopolamine-Induced Memory Impairment, Oxidative Stress, and Apoptosis in Aged Rats: The Involvement of TRPM2 and TRPV1 Channels. Mol Neurobiol. 54(4):2852-2868. https://doi.org/10.1007/s12035-016-9835-0.

Walia V, Kaushik D, Mittal V, Kumar K, Verma R, Parashar J, et al. (2022). Delineation of Neuroprotective Effects and Possible Benefits of Antioxidants Therapy for the Treatment of Alzheimer's Diseases by Targeting Mitochondrial-Derived Reactive Oxygen Species: Bench to Bedside. Mol Neurobiol. 59(1):657-680. https://doi.org/10.1007/s12035-021-02617-1.

Zhou J, Zhang W, Cao Z, Lian S, Li J, Nie J, Huang Y, Zhao K, He J, Liu C. (2023). Association of Selenium Levels with Neurodegenerative Disease: A Systemic Review and Meta-Analysis. Nutrients. 15(17):3706. https://doi.org/10.3390/nu15173706

Young Speakers

Young Speaker 10

The interaction between eicosapentaenoic acid-induced TRPM2 activation and cisplatin in the glioblastoma cell death

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Through repeated generations of oxidative stress, excessive glial cell activation causes glioma. Glioblastoma multiforme (GBM) is a highly proliferative form of tumor in the brains of adults, and it also comes on by overstimulating glial cells in the brain's nervous system (Schwartzbaum and Cornwell 2000). GBM cannot be totally curable.

One of the most common and effective chemotherapy drugs is cisplatin. Patients suffering from GBM obtain therapy with cisplatin. The resistance of cisplatin to tumor cell killing, however, frequently inhibits its effectiveness. As a result, crucial doses of cisplatin are given to GBM patients due to its resistance. Treatment with cisplatin induces a high level of reactive oxygen species (ROS), Ca^{2+} influx, and other variables leading to apoptosis and cell death in DBTRG glioblastoma cells. One of the main components of omega-3 polyunsaturated fatty acids, eicosapentaenoic acid, has recently been associated with beneficial health benefits (Shi et al. 2021). Eicosapentaenoic acid has been demonstrated to have synergistic effects against cisplatin-resistant tumors by activating the TRPM2 channel in several kinds of tumor cell lines, including GBM (Öcal and Nazıroğlu 2022).

I reviewed the connection between cisplatin and eicosapentaenoic acid-induced TRPM2 stimulation in glioblastoma cell death.

Key words: Eicosapentaenoic acid; Cisplatin; Glioblastoma multiforme; TRPM2 channel; Oxidative stress.

References

Öcal Ö, Nazıroğlu M. (2022). Eicosapentaenoic acid enhanced apoptotic and oxidant effects of cisplatin via activation of TRPM2 channel in brain tumor cells. Chem Biol Interact. 359:109914. https://doi.org/10.1016/j.cbi.2022.109914.

Schwartzbaum JA, Cornwell DG. (2000). Oxidant stress and glioblastoma multiforme risk: serum antioxidants, gamma-glutamyl transpeptidase, and ferritin. Nutr Cancer. 38(1):40-49. https://doi.org/10.1207/S15327914NC381_7.

Shi HH, Chen LP, Wang CC, Zhao YC, Xue CH, Wang YM, Mao XZ, Zhang TT. (2021). Short-term supplementation of DHA-enriched phospholipids attenuates the nephrotoxicity of cisplatin without compromising its antitumor activity in mice. Food Funct. 12(19):9391-9404. https://doi.org/10.1039/d1fo02000e.

Young Speakers

Young Speaker 11

Anticancer action of bee venom melittin via TRPM2 channel stimulation

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Reactive oxygen species (ROS) that are generated in excess lead to the death of tumor cells. The TRPM2 channel is activated, which results in an increased Ca^{2+} influx. Through the activation of caspases like caspase-3, -8, and -9, TRPM2, a stimulation caused by an excessive rise in cytosolic Ca^{2+} induces tumor cell death and apoptosis (Fig. 1). Additionally, the TRPM2 stimulation generates an excessive amount of ROS production. The toxic component of bee venom known as melittin is well-known for its powerful hemolytic, antibacterial, and TRPV1 channel stimulation features (Du et al. 2011). Melittin may also have anti-tumor impacts on different types of tumor cells. By activating the TRPM2 channel in a number of tumor cell lines, including glioblastoma, melittin has been shown to have synergistic benefits against cisplatin-resistant malignancies (Ertilav and Nazıroğlu 2023).

I talked through how melittin-induced ROS and apoptosis in cancer cells relate to TRPM2 stimulation.

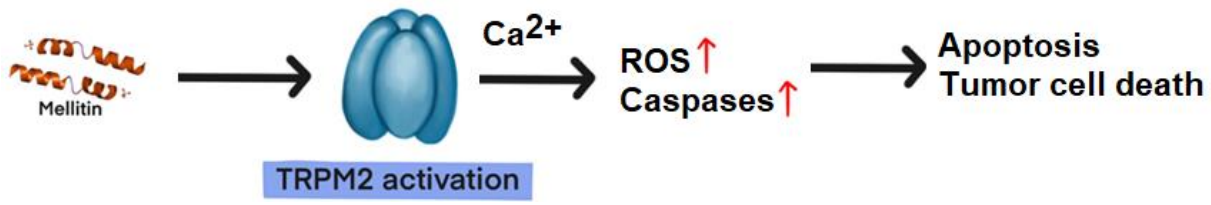

Fig. 1. Activation of TRPM2 stimulates excessive oxidative stress (ROS) and apoptosis through the activation of caspases in tumor cells (prepared by Asiye Kılıç).

Key words: Apoptosis; Melittin; Cisplatin; Tumor cells; TRPM2 channel.

References

Ertilav K, Nazıroğlu M. (2023). Honey bee venom melittin increases the oxidant activity of cisplatin and kills human glioblastoma cells by stimulating the TRPM2 channel. Toxicon. 222:106993. https://doi.org/10.1016/j.toxicon.2022.106993.

Du YR, Xiao Y, Lu ZM, Ding J, Xie F, Fu H, Wang Y, Strong JA, Zhang JM, Chen J. (2011). Melittin activates TRPV1 receptors in primary nociceptive sensory neurons via the phospholipase A2 cascade pathways. Biochem Biophys Res Commun. 2408(1):32-37. https://doi.org/10.1016/j.bbrc.2011.03.110.

Young Speakers

Young Speaker 12

NMDA receptor stimulation induces TRPM2 channel activation in hypoxia

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Several pathophysiological conditions can cause hypoxia. The negative effects of hypoxia are seen in the neurons and brain. Increasing evidence suggests that hypoxia causes excessive Ca^{2+} influx by activating NMDA receptors (Hänggi et al. 2014). ADP-ribose and H_2O_2 trigger the TRPM2 channel (Miller and Cheung 2016). An increased cytosolic Ca^{2+} concentration opens the channel. In a recent study, it was examined if the activation of the TRPM2 channel in neuronal cells was influenced by the Ca^{2+} influx caused by NMDA receptor stimulation (Yıldızhan and Nazıroğlu 2023). They discovered that the increased Ca^{2+} influx brought on by NMDA receptor stimulation stimulated TRPM2 channels. MK-801 and memantine, however, prevented the activation of the TRPM2 channels.

It appears that a therapeutic target for the management of hypoxia-induced oxidative cell damage and death has thus been recommended: the blocking of the increase in cytosolic Ca^{2+} concentration.

Key words: Hypoxia; NMDA receptors; TRPM2 channel; ADP-ribose.

References

Hänggi P, Makhro A, Gassmann M, Schmugge M, Goede JS, Speer O, Bogdanova A. (2014). Red blood cells of sickle cell disease patients exhibit abnormally high abundance of N-methyl D-aspartate receptors mediating excessive calcium uptake. Br J Haematol. 167(2):252-264. https://doi.org/10.1111/bjh.13028.

Miller BA, Cheung JY. (2016). TRPM2 protects against tissue damage following oxidative stress and ischaemia-reperfusion. J Physiol. 594(15):4181-4191. https://doi.org/10.1113/JP270934.

Yıldızhan K, Nazıroğlu M. (2023). NMDA Receptor Activation Stimulates Hypoxia-Induced TRPM2 Channel Activation, Mitochondrial Oxidative Stress, and Apoptosis in Neuronal Cell Line: Modular Role of Memantine. Brain Res. 1803:148232. https://doi.org/10.1016/j.brainres.2023.148232.

Young Speakers

Young Speaker 13

Melatonin attenuates hypoxia-induced oxidative neurotoxicity via inhibition of TRPV4 in a neuronal cell line

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Because cerebral ischemia/reperfusion damage is mainly what causes cerebrovascular disease, there is an alarming mortality rate globally. The brain and neurons suffer hypoxia in the brain as a consequence of the ischemia/reperfusion damage (Sekhon et al. 2017). More than 75% of hospital patients who suffered cardiac arrest have cerebral hypoxia as their main cause of death. Inducing hypoxia in the brain causes apoptosis, which results in neuronal and brain cell death.

TRP vanilloid 4 (TRPV4) is a member of the Ca^{2+}-permeable transient receptor potential (TRP) superfamily. GSK1016790A is an agonist that is selective for the TRPV4 channel, whereas ruthenium red is an antagonist. Additionally, a greater generation of reactive oxygen species (ROS) activates TRPV4. The pineal gland secretes melatonin, an effective and strong antioxidant. Additionally, according to Alkozi et al. (2017), the release of melatonin and GSK1016790A-mediated TRPV4 activation are closely linked. Although apoptosis and ROS were reduced by ruthenium red, stimulation of TRPV4 increased hypoxia-induced apoptosis and ROS in the neuronal cell lines (Öcal et al. 2022).

It appears that the manipulation of TRPV4 through the administration of a new Ca^{2+} channel inhibitor may control the ROS and apoptosis triggered by neuronal hypoxia.

Key words: Hypoxia; Melatonin; TRPV4 channel; Oxidative stress.

References

Alkozi HA, Perez de Lara MJ, Pintor J. (2017). Melatonin synthesis in the human ciliary body triggered by TRPV4 activation: Involvement of AANAT phosphorylation. Exp Eye Res. 162:1-8. https://doi.org/10.1016/j.exer.2017.06.018.

Öcal Ö, Coşar A, Nazıroğlu M. (2022). Amantadine Attenuated Hypoxia-Induced Mitochondrial Oxidative Neurotoxicity, Apoptosis, and Inflammation via the Inhibition of TRPM2 and TRPV4 Channels. Mol Neurobiol. 59(6):3703-3720. https://doi.org/10.1007/s12035-022-02814-6.

Sekhon MS, Ainslie PN, Griesdale DE. (2017). Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model. Crit Care. 21(1):90. https://doi.org/10.1186/s13054-017-1670-9.

Young Speakers

Young Speaker 14

Diabetic neuropathic pain and TRPM7 channel

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A metabolic chronic disease with a simply increasing worldwide incidence is diabetes mellitus. Diabetes mellitus reduces the quality of life because it can't be controlled. Diabetes-related neuropathy is one of the long-term effects of diabetes mellitus. Enhanced Ca^{2+} permeable-voltage-gated cation channel stimulation and TRP channel activations were used to control the release of insulin. The TRPM7 channel, also known as TRP melastatin 7, is a member of the TRP superfamily. Naltriben is a TRPM7 agonist. One of the TRPM7 antagonists is carvacrol (Gualdani et al. 2022). Carvacrol has been demonstrated to function as a TRPM7 antagonist in a number of neurons. The dorsal root ganglion neurons show high TRPM7 expression levels. The activation of TRPM7 in dorsal root ganglions substantially raises Ca^{2+} influx, which in turn significantly increases the production of pain (Aydın and Nazıroğlu 2023). Additionally, excess Ca^{2+} influx caused by TRPM7 activation promotes adverse reactions including apoptosis and oxidative stress in neurons, including the dorsal root ganglia (Huang et al. 2018). However, the carvacrol and antioxidant treatments' inhibition of TRPM7 moderated the negative effects in the neurons.

Although the inhibition of it with antioxidants has a protective impact against the diabetes mellitus-generated neuropathic pain, it seems that diabetes mellitus stimulates the TRPM7 channel to generate the diabetic neuropathic pain.

Key words: Diabetes mellitus; Diabetic nephropathic pain; TRPM7 channel; Calcium ion

References

Aydın B, Nazıroğlu M. (2023). Involvement of TRPM7 Channel on the Induction of Diabetic Neuropathic Pain in Mice: Protective Role of Selenium and Curcumin. Biol Trace Elem Res. 201(5):2377-2395. https://doi.org/10.1007/s12011-022-03518-7.

Gualdani R, Gailly P, Yuan JH, Yerna X, Di Stefano G, Truini A, Cruccu G, Dib-Hajj SD, Waxman SG. (2022). A TRPM7 mutation linked to familial trigeminal neuralgia: Omega current and hyperexcitability of trigeminal ganglion neurons. Proc Natl Acad Sci U S A. 119(38):e2119630119. https://doi.org/10.1073/pnas.2119630119.

Huang Y, Leng TD, Inoue K, Yang T, Liu M, Horgen FD, Fleig A, Li J, Xiong ZG. (2018). TRPM7 channels play a role in high glucose-induced endoplasmic reticulum stress and neuronal cell apoptosis. J Biol Chem. 293(37):14393-14406. https://doi.org/10.1074/jbc.RA117.001032.

Young Speakers

Young Speaker 15

Silver nanoparticles kills glioblastoma cells via the activation of TRPM2

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Due to their ability to produce reactive oxygen compounds (ROS), which correspond with both an increase in tumor cell mortality and a decrease in tumor cell proliferation, silver nanoparticles are particularly promising for the treatment of cancer. In addition, silver nanoparticles may interfere with crucial cancer hallmarks by increasing the level of apoptosis mediated by caspase activation and Ca^{2+} concentration. According to an investigation (Asharani et al. 2009), treatment with silver nanoparticles destroys a number of tumor cells. ROS activates the TRPM2 channel. In tumor cells, including glioblastoma, the silver nanoparticles caused high levels of ROS, which triggered TRPM2 channels and Ca^{2+} influx (Kabir et al. 2022; Akyuva and Nazıroğlu 2023).

Treatment of glioblastoma tumor cells is challenging, and each patient may require a unique approach. According to recent research, a subpopulation of glioblastoma tumor cells is especially vulnerable to the treatment of silver nanoparticles because they activate ROS and apoptosis. Thus, through stimulating TRPM2, silver nanoparticles appear to be a strong agent against glioblastoma tumors.

References

Akyuva Y, Nazıroğlu M. (2023). Silver nanoparticles potentiate antitumor and oxidant actions of cisplatin via the stimulation of TRPM2 channel in glioblastoma tumor cells. Chem Biol Interact. 369:110261. https://doi.org/10.1016/j.cbi.2022.110261.

Asharani PV, Hande MP, Valiyaveettil S. (2009). Anti-proliferative activity of silver nanoparticles. BMC Cell Biol. 10:65. https://doi.org/10.1186/1471-2121-10-65.

Kabir SR, Islam F, Asaduzzaman AKM. (2022). Biogenic silver/silver chloride nanoparticles inhibit human cancer cells proliferation in vitro and Ehrlich ascites carcinoma cells growth in vivo. Sci Rep. 12(1):8909. https://doi.org/10.1038/s41598-022-12974-z.

Oral Presentations

Oral Presentation 1

Modulation of the TRPA1 function and traffic by reactive oxygen species

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TRPA1 is a polymodal TRP channel with roles in pain sensation, inflammation, or thermoregulation. The channel is activated by natural compounds such as electrophile isothiocyanates, thiosulfates, or unsaturated aldehydes. In cancer, TRPA1 was reported to be overexpressed in melanoma, gastric cancer, and pancreatic adenocarcinoma (PDAC) (Takahashi et al., 2018). In PDAC cell lines, the channel is overexpressed and inhibits migration while shifting the cell cycle toward the pre-G1 phase (Cojocaru et al., 2021). TRPA1 was identified as one of the best sensors for reactive oxygen species (ROS), supporting the hypothesis that ROS may be the endogenous stimuli in some cancers (De Logu et al., 2021).

In this work, we evaluate the effect of two compounds resulting from oxidative stress: 4-hydroxynonenal (4-HNE), a product of lipid peroxidation, and H_2O_2, on TRPA1 expressed in PDAC cell lines.

Firstly, using confocal microscopy, we evaluated the TRPA1 traffic to the membrane after prolonged exposure (24 hours) to 4-HNE and H_2O_2. We measured the ratio of TRPA1 expression at the plasma membrane and ER and noticed significant changes in the presence of 4-HNE.

Secondly, we used calcium microfluorimetry to evaluate the effects of ROS on channel activation. 4-HNE strongly activated the channel. Finally, we also report a substantial change in cell cycle progression in the presence of 4-HNE, independent of TRPA1 activation. In conclusion, 4-HNE is a potent activator of TRPA1 when acutely applied to PDAC cells, and it may mediate TRPA1 traffic upon prolonged cell exposure. Although the compound arrests the cell cycle in the G2/M phase, the effect is independent of TRPA1 activation.

Keywords: Pancreatic cancer; Oxidative stress; TRPA1 channel.

References

Takahashi, N.; Chen, H.Y.; Harris, I.S.; Stover, D.G.; Selfors, L.M.; Bronson, R.T.; Deraedt, T.; Cichowski, K.; Welm, A.L.; Mori, Y.; et al. Cancer Cells Co-opt the Neuronal Redox-Sensing Channel TRPA1 to Promote Oxidative-Stress Tolerance. Cancer cell 2018, 33, 985-1003 e1007, doi:10.1016/j.ccell.2018.05.001.

Cojocaru, F.; Selescu, T.; Domocos, D.; Marutescu, L.; Chiritoiu, G.; Chelaru, N.R.; Dima, S.; Mihailescu, D.; Babes, A.; Cucu, D. Publisher Correction: Functional expression of the transient receptor potential ankyrin type 1 channel in pancreatic adenocarcinoma cells. Scientific Reports 2021, 11, 8853, doi:10.1038/s41598-021-88169-9.

De Logu, F.; Souza Monteiro de Araujo, D.; Ugolini, F.; Iannone, L.F.; Vannucchi, M.; Portelli, F.; Landini, L.; Titiz, M.; De Giorgi, V.; Geppetti, P.; et al. The TRPA1 Channel Amplifies the Oxidative Stress Signal in Melanoma. Cells 2021, 10, doi:10.3390/cells10113131.

Oral Presentations

Oral Presentation 2

Anti-cancer effects of siRNA-mediated targeting of NaV1.7 channel in pancreatic cancer cell lines

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Pancreatic cancer (PCa) is a major global health concern, being among the top causes of cancer deaths (Siegel et al., 2020). This study explores the therapeutic potential of inhibiting Voltage-gated sodium channels (NaV1.7) in PCa cells. These channels are found in various metastatic cell lines (Yang et al., 2012; House et al., 2015). By targeting these channels, we hope to offer new insights into PCa management strategies.

The study engaged human keratinocyte cell line HaCaT and pancreatic cancer cell lines PANC-1 and MiaPaCa-2. We scrutinized the influence of adult and neonatal NaV1.7 isoforms on cancer cell proliferation, invasion, and metastasis.

We found that both adult and neonatal NaV1.7 mRNA expressions were significantly elevated in PANC-1 and MiaPaCa-2 cells relative to HaCaT cells. Notably, specific siRNAs were able to downregulate these expressions, leading to a substantial inhibition of cancer cell proliferation and colony formation, without exerting any cytotoxic effect on the healthy HaCaT cell line. Importantly, combining specific NaV1.7 siRNAs with the conventional PCa drug gemcitabine augmented the drug's efficacy. The siRNAs also significantly impeded cell invasion, migration, and wound healing in cancer cells, while inducing apoptosis and G1 cell cycle arrest. The inhibition of NaV1.7 influenced protein expressions associated with pivotal signaling pathways. In conclusion, the study underscores the pivotal role of NaV1.7 isoforms in the pathogenesis and progression of pancreatic cancer, suggesting their potential as therapeutic targets in treating PCa.

Keywords: Pancreatic cancer; Voltage-gated sodium channels; NaV1.7; proliferation; invasion; siRNA

References

Siegel RL, Miller KD, Jemal A. (2020). Cancer statistics, 2020. CA: A Cancer Journal for Clinicians. 70:7–30.

Yang M, Kozminski DJ, Wold LA, Modak R, Calhoun JD, Isom LL, Brackenbury WJ. (2012). Therapeutic potential for phenytoin: targeting Na(V)1.5 sodium channels to reduce migration and invasion in metastatic breast cancer. Breast Cancer Research and Treatment. 134:603–615.

House CD, Vaske CJ, Schwartz AM, Obias V, Frank B, Luu T, Sarvazyan N, Irby R, Strausberg RL, Hales TG, Stuart JM, Lee NH. (2015). Voltage-gated Na+ channel SCN5A is a key regulator of a gene transcriptional network that controls colon cancer invasion. Cancer Research. 75: 3837-3850.

Oral Presentations

Oral Presentation 3

The effect of topiramate on oxidative and nitrosative stress, inflammation and apoptosis in non-alcoholic fatty liver disease

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Non-alcoholic fatty liver disease (NAFLD) is the most common chronic hepatic disease and is a common comorbidity of obesity (Younossi et al. 2016). Although topiramate (TPM) is a drug with anti-obesity effect (Motaghinejad et al. 2017), its effect on oxidative and nitrosative stress, inflammation and apoptosis in both healthy and NAFLD is unknown. The aim of this study was to investigate the effect of topiramate on oxidative and nitrosative stress, inflammation and apoptosis in fatty liver.

24 Wistar albino rats were divided into four groups: control, diet, TPM, and diet+TPM. Diet groups received high fat diet (HFD; %35 fat) for 6 weeks to develop NAFLD. The TPM group received 100 mg/kg/day TPM po for 21 days alongside with HFD after six weeks of HFD. Rats' liver was analyzed for malondialdehyde (MDA), glutathione (GSH) levels and glutathione peroxidase (GPx) activity, nitric oxide (NO), nitrotyrosine (NT-3), TNF-α, IL-10, caspase 3 and 9, and cytochrome c (Cyt-c).

While MDA levels increased in D, TPM and diet+TPM groups, GSH and GPx levels decreased. Caspase3–9 and Cyt-c levels were increased and IL-10 was decreased both in diet and TPM groups. When applied together these two interventions further increased Caspase 9 and Cyt-c as observed in diet+TPM group. While TNF-α levels were higher both in diet and TPM groups, statistical significance attained only in diet+TPM group. TPM also increased NO and NT-3 levels both in standard and high fat diet groups. When TPM is used in NAFLD, apoptosis and inflammation increase even more.

Considering the high prevalence of NAFLD in obesity, TPM, as an anti-obesity drug, should be cautioned.

Keywords: Non-alcoholic fatty liver disease; Topiramate; Oxidative stress; Nitrosative stress; Inflammation; Apoptosis

References

Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. (2016). Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 64(1):73–84.

Motaghinejad M, Motevalian M, Babalouei F, Abdollahi M, Heidari M, Madjd Z. (2017). Possible involvement CREB/BDNF signaling pathway in neuroprotective effects of topiramate against methylphenidate induced apoptosis, oxidative stress and inflammation in isolated hippocampus of rats: Molecular, biochemical and histological evidences. Brain Res Bull. 132:82–98.

Oral Presentations

Oral Presentation 4

pH-Control: a novel approach for manipulation of intracellular pH

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pH imbalance has been implicated in various diseases such as cancer and neurodegeneration. However, the underlying mechanisms remain unknown due to a lack of proper tools for pH manipulation in subcellular locales, specific cell types, and tissues. In our recent study, we have introduced Chemogenetic Operation of iNTRacellular prOton Levels (pH-Control) approach, enabling pH manipulation with high spatio-temporal resolution. We have fully characterized pH-Control in vitro and in cellulo. Combining pH-Control with genetically encoded pH biosensors (SypHer3s) in HEK293 cells we have shown that pH-Control is capable of changing pH in subcellular locales such as mitochondria, nucleus, and cytoplasm. Besides, we have shown that the activity of pH-Control in dorsal root ganglion (DRG) neurons decreases the membrane potential. Overall, we are convinced that pH-Control has the potential to open new lines of investigation on the role of pH in health and disease.

Keywords: pH-imbalance; Chemogenetic tools, Genetically encoded biosensors;

References

Ghaffari Zaki, A., Miri, S. M., Çimen, Ş., Akgül Çağlar, T., Yiğit, E. N., Aydın, M. Ş., … Eroglu, E. 2023. "Development of a Chemogenetic Approach to Manipulate Intracellular pH". Journal of the American Chemical Society.

Oral Presentations

Oral Presentation 5

Ca as a center of cellular energetics involved in maintaining the resting state of excitable cells

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To establish a resting state in a cell, a system of sinks constructed mostly by channels has to be perfectly balanced by a system of sources presented mostly by pumps.

An analysis of steady-state surface membrane currents produced by channels, pumps, and transporters was performed to identify attraction points of the membrane as a dynamic system. To explain the obtained results, more attention was paid to further analysis of pumps and their interaction with electrogenic transporters.

The pumps have generally low turning rate (Artigas and Gadsby 2002). They also transfer energy by huge portions that correspond to the large value (~-200 mV) of the mitochondrion inner membrane potential. Both features create problems in formation of the cell resting state. To obtain stable resting state with physiologic parameters, parallel action of many pumps and electrogenic transporters is required. Ca related ones played a central role in the process. They included the sodium-calcium exchanger and various Ca pumps. However, calcium channels and pumps are positioned along both intracellular organelles and the surface membrane. So forming energy transfer routes naturally expand into intercellular communications. Many examples like hypoxic/reperfusion injury, kinds of muscle fatigue, and nerve-glia interactions could be associated with the above mentioned processes (Dimitrov 2023).

In the sensory paradigm, Ca channels release Ca^{2+} while Ca pumps clear it. Now energy transfer is also associated with Ca pumps. Could it be that the Ca channels whose working background is unknown, are also attached to the main cell energy transfer pathway?

Keywords: Na-K-ATPase; SERCA; PMCA; NCX; Resting state; Electrogenic transporter.

References

Artigas P, and Gadsby DC. (2002). Ion channel-like properties of the Na+/K+ pump. Ann NY Acad Sci 976(1): 31-40.

Dimitrov AG. (2023) Resting membrane state as an interplay of electrogenic transporters with various pumps. Pflug. Arch. 475, 1113–1128. https://doi.org/10.1007/s00424-023-02838-4.

Oral Presentations

Oral Presentation 6

Addictive behavior towards opioids and the role of vanilloid TRP channel in its molecular mechanisms

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Substance use disorders are a medical condition that affects societies both financially and socially. About 100 substances, including opioids, are known to be open to abuse and addictive. It is known that the central nervous system (CNS) regions that these substances affect at the molecular and systemic level and form the neurobiological infrastructure of addictive behavior consist of the basal ganglia (BG), amygdala and prefrontal cortex (PFC) as well as the nucleus accumbens (NAc) and ventral tegmental area (VTA).

Transient Receptor Potential (TRP) channels are Ca^{+2} permeable ion channels expressed in many different tissues, including nerve cells and generally comprise 30 different members from 7 subfamilies. We can see that TRP Vanilloid 1 (TRPV1), a vanilloid-activated TRP channel, is expressed in CNS regions such as the PFC, BG, mesolimbic pathways, NAc and VTA. In addition, TRPV1's role in morphine tolerance and hyperalgesia leads us to investigate the role of TRPV1 in the molecular mechanisms of opioid addiction behavior.

An animal study has shown that TRPV1 channel can modulate morphine-induced conditional reward effects in NAc (Hong et al. 2017). Another study said that TRPV1 also plays a role in morphine self-administration behavior modulation (Ma et al. 2018). A patch-clamp study on morphine withdrawal animal specimens demonstrated the effects of TRPV1 activation on glutamatergic transmission in NAc (Zhang et al. 2017).

When the studies that elucidate the role of the TRPV1 channel in the neuromolecular infrastructure of opioid addiction and its effect on addictive behaviors are examined together, it suggests that it may be important as a treatment target.

Keywords: TRPV1 channel, Addiction, Opioid, Morphine, Addictive behavior, Nucleus accumbens

References

Hong, S. I., Nguyen, T. L., Ma, S. X., Kim, H. C., Lee, S. Y., & Jang, C. G. (2017). TRPV1 modulates morphine-induced conditioned place preference via p38 MAPK in the nucleus accumbens. Behavioural brain research, 334, 26–33.

Ma, S. X., Kim, H. C., Lee, S. Y., & Jang, C. G. (2018). TRPV1 modulates morphine self-administration via activation of the CaMKII-CREB pathway in the nucleus accumbens. Neurochemistry international, 121, 1–7.

Zhang, H., Jia, D., Wang, Y., Qu, L., Wang, X., Song, J., Heng, L., & Gao, G. (2017). Enhanced ability of TRPV1 channels in regulating glutamatergic transmission after repeated morphine exposure in the nucleus accumbens of rat. Brain research, 1660, 47–57.

Oral Presentations

Oral Presentation 7

Structural mechanisms of TRPM7 activation and inhibition

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The transient receptor potential channel TRPM7 is a master regulator of the organismal balance of divalent cations that plays an essential role in embryonic development, immune responses, cell mobility, proliferation, and differentiation. TRPM7 is implicated in neuronal and cardiovascular disorders, tumor progression and has emerged as a new drug target. We used cryo-EM, functional analysis, and molecular dynamics simulations to uncover two distinct structural mechanisms of TRPM7 activation by a gain-of-function mutation and by the agonist naltriben, which show different conformational dynamics and domain involvement. We identified a binding site for highly potent and selective inhibitors and showed that they act by stabilizing the TRPM7 closed state. The discovered structural mechanisms provide foundations for understanding the molecular basis of TRPM7 channelopathies and drug development.

Oral Presentations

Oral Presentation 8

Effects of differentiation on SH-SY5Y human neuroblastoma cell line for TRPM channel activation

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Transient receptor potential (TRP) cation channels have several important roles involving intracellular Ca^{2+} signaling. First, as Ca^{2+}-permeable channels that respond to various stimuli, TRP channels directly affect cellular Ca^{2+} signaling. In addition, in terms of non-selective cation channels, TRP channel activation leads to membrane depolarization and affects Ca^{2+} influx through voltage-gated and store-operated Ca^{2+} channels. Finally, Ca^{2+} modulates most TRP channel activity, acting as molecular effectors downstream of intracellular Ca^{2+} signaling. As a good representation of electrical related Ca^{2+} activity, SH-SY5Y human neuroblastoma cells are widely used in cell culture for neuronal modelling. In this study, we examined the effects of SH-SY5Y cell differentiation on TRPM channel activation. Differentiation protocols including retinoic acid, brain-derived neurotrophic factor (BDNF), cholesterol and estradiol treatments have been proposed in the literature. Here, we examined the differentiated cells by applying retinoic acid (RA) + BDNF (RB) to undifferentiated SH-SY5Y cells. We observed the changes in TRPM channel activation of these cells after the differentiation procedure in comparison with TRPM2 antibody and Ca (Fluo3AM) indicator and mitochondrial ROS (MitoSOX Red). In addition, we demonstrated the changes in CACNA2D2, CACNG5, CACNA1I gene expressions associated with calcium channels in the cultivated differentiation procedure. In conclusion, we concluded that TRPM channels should be used as a neuronal model when SH-SY5Y human neuroblastoma cells are differentiated after retinoic acid and BDNF treatment.

Keywords: Neuroblastoma; SH-SY5Y; Oxidative stress; TRPM2

Oral Presentations

Oral Presentation 9

Altered metabolism and calcium signaling in Down syndrome

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Numerous sets of microarray and RNA-seq data are publicly accessible. A meta-analysis was conducted on gene expression levels comparing individuals with Down syndrome (DS) to control subjects. The analysis revealed that in DS, more than 60% of the genes located on chromosome 21 are significantly upregulated. Among these upregulated genes in DS, several encode important components of various bioenergetic pathways and calcium signaling.

Based on these findings, it can be concluded that cells of individuals with DS exhibit a pseudo-hypoxic state. The cellular metabolic and bioenergetic mechanisms in DS show pathophysiological alterations that resemble cellular responses associated with hypoxia, even though there is no disruption in the oxygen supply to the cells.

Oral Presentations

Oral Presentation 10

Molecular simulation approaches in elucidating the biophysics of divalent cation sensing

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Divalent cations are critical messengers of the internal homeostatic status of the cell. Their cues are sensed by internal molecular machines of the cell, including sensory transmembrane channels such as those of the TRP family, and the genomic material of the cell, chromatin. This collective response to divalent cations is peculiar in the sense that the mechanical trigger of an internal element to them can be highly passive, such as competition for DNA minor groove binding between a basically charged residue and a Magnesium ion, or highly well-orchestrated, such as an allosteric coupling of a Calcium ion binding site and a cation gate several nanometers away. In this talk, I will discuss our in silico approach to both cases via atomistic molecular simulations: first, the global-level opening of the CENP-A histone containing nucleosome, and second, our early strategies toward understanding the Calcium-coupling in TRPM4 channel.

Oral Presentations

Oral Presentation 11

Investigation of TNF alpha, IL6, Paraoxonase, and Superoxide Dismutase enzyme activities in Obsessive Compulsive Disorder

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The brain is exposed to the attack of reactive oxygen and nitrogen radicals due to its richness in lipid molecules and high oxygen consumption. The harmful effects of highly reactive radicals with unpaired electron balance on cells are reduced or destroyed by antioxidant enzymes and molecules, but when this balance is disrupted in favor of oxidant molecules, oxidative stress occurs. In psychiatric diseases, including obsessive-compulsive disorder, infiltration of peripheral immune cells into the central nervous system, disorders in serotonin, dopamine, glutamate metabolism, disruption of the kynurenine/tryptophan ratio and oxidative stress conditions in the cell can cause chronic inflammation (Wang et al. 2015; Marazati et al.2018). Paraoxonase (PON) is an enzyme with antioxidant and anti-inflammatory capacity that can detoxify xenobiotics such as organophosphates carried by high-density lipoproteins that protect against atherogenesis (Ozdemir et al 2019).

We wanted to examine the role of TNF-α and IL-6 pro-inflammatory cytokines, PON1 enzyme activities with antioxidant properties, and superoxide dismutase enzyme (SOD) activities, in the pathology of the disease in OCD. In our study, 100 patients diagnosed with OCD and 50 healthy people without neuropsychiatric disease constitute our control group. Serum TNF-α, IL-6 and activities of SOD were determined Enzyme linked Immunosorbent Assay. PON1 activities were assayed kinetically as the measurement of the linear increase of absorbance of p-nitrophenol. We found that TNF- α ($p<0.001$) as a pro-inflammatory cytokine was significantly increased in the OCD group, and the activities of PON1 ($p<0.05$) and SOD ($p<0.001$) were decreased.

In conclusion, we can suggest that increased pro inflammatory cytokines and the decrease in antioxidant PON1 and SOD enzymes have important roles in the pathogenesis of OCD disease.

Keywords: Obsessive Compulsive Disorder, TNF-α, IL-6, Paraoxonase 1, Superoxide dismutase

References

Wang, Qiongxin, Danxia Liu, Ping Song, and Ming-Hui Zou.(2015). Deregulated Tryptophan Kynurenine Pathway Is Linked to Inflammation, Oxidative Stress, and Immune Activation Pathway in Cardiovascular Diseases. Frontiers in Bioscience (Landmark Edition) 20:1116.

Marazziti, Donatella, Federico Mucci, and Leonardo F. Fontenelle. (2018). Immune System and Obsessive- Compulsive Disorder. Psychoneuroendocrinology 93: 39–44.

Güzel Ozdemir, Pınar, Ekrem Yilmaz, and Emine Yilmaz. (2019). Comparison of Paraoxonase, Prolidase Activities and HS-CRP, BDNF Levels in Patients with Autogenous and Reactive Subtypes of Obsessive Compulsive Disorder. Anadolu Psikiyatri Dergisi 20(4): 360–67

Oral Presentations

Oral Presentation 12

Neuroprotective effect of chrysin in PTZ-induced neurotoxicity in SH-SY5Ycells: Role of TRPM2 channel

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Chrysin (CHR) is a promising phytochemical that belongs to the flavonoid class based on its chemical structure. Experimental studies have shown that CHR has various biological effects, including anti-cancer, antioxidant, hepatoprotective, antiviral, neuroprotective, and anti-anxiety properties (Stompor-Goracy et al., 2021). In recent years, transient receptor potential (TRP) ion channels have been reported to play an important role in the pathology of neurological disorders (Yıldızhan et al., 2020). TRP Melastatin 2 (TRPM2) are oxidative stress-dependent active cation channels within the TRP superfamily and are widely expressed, including in the brain, immune system, endocrine cells, and endothelium. This study examined the protective role of CHR against neurotoxicity induced via the TRPM2 channel in SH-SY5Y cells exposed to pentylenetetrazol (PTZ). For the study, control, CHR (50 μM, 24 h) (Darendelioglu 2020), PTZ (30 μM, 24 h) (Ahlatci et al., 2022), and PTZ+CHR (CHR treatment was administered 30 minutes before PTZ incubation) groups were formed from SH-SY5Y cells. The study measured the levels of MDA, GSH, ROS, PARP-1, and TRPM2 channels in the cells using ELISA kits. The study found that administering PTZ to the human neuroblastoma cell line SH-SY5Y resulted in neurotoxicity demonstrated by decreased GSH levels and increased MDA, ROS, PARP-1, and TRPM2 ($p < 0.05$). In SH-SY5Y cells treated with CHR prior to PTZ incubation, levels of MDA, ROS, PARP-1, and TRPM2 decreased, and levels of GSH increased, compared to the PTZ group ($p < 0.05$). Consequently, we found that CHR treatment may effectively reduce PTZ-induced neurotoxicity in SH-SY5Y cells by inhibiting the activation of TRPM2 channels.

Keywords: Chrysin, Pentylenetetrazole, SH-SY5Y cell, TRPM2 channel

References

Stompor-Goracy, M., Bajek-Bil, A., Machaczka, M. (2021) Chrysin: Perspectives on Contemporary Status and Future Possibilities as Pro-Health Agent. Nutrients. 13 (6): 1-17

Yıldızhan, K., and Nazıroğlu, M. (2020) Glutathione Depletion and Parkinsonian Neurotoxin MPP +-Induced TRPM2 Channel Activation Play Central Roles in Oxidative Cytotoxicity and Inflammation in Microglia. Molecular Neurobiology., 57: 3508-3524

Ahlatci, A., Yildizhan, K., Tuluce, Y., Bektas, M. (2022) Valproic Acid Attenuated PTZ-induced Oxidative Stress, Inflammation, and Apoptosis in the SH-SY5Y Cells via Modulating the TRPM2 Channel. Neurotox Res. 40 (6): 1979-1988

Darendelioglu, E. (2020) Neuroprotective Effects of Chrysin on Diclofenac-Induced Apoptosis in SH-SY5Y Cells. Neurochem Res. 45 (5): 1064-1071

Oral Presentations

Oral Presentation 13

Meta-analysis of the effect of *Fasciola hepatica* infections on the total antioxidant capacity of the host

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Fasciola hepatica, popularly known as the liver butterfly, is a parasite of the liver parenchyma (young parasites) and in bile ducts (mature parasites) of herbivorous mammals, especially sheep and cattle, and humans (Cicek et al. 2012). In humans, fascioliasis can present with very different clinical findings, ranging from asymptomatic infections to severe liver cirrhosis and death (Cengiz et al. 2022). Oxidative stress is thought to have an important role in the pathogenesis of fascioliasis. The aim of this study is to evaluate the results of studies investigating the effect of fascioliasis infections on the total antioxidant capacity (TAC) of the host by meta-analysis.

A systematic search was conducted in Web of Science, PubMed, and Google Scholar to identify studies to be included in the meta-analysis. Statistical analysis program Jamovi (Ver. 2.4.1.0) was used for meta-analysis. The analysis was carried out using the standardized mean difference as the outcome measure. A random-effects model was fitted to the data.

A total of six studies were included in the analysis (Cicek et al. 2012; Bottari et al. 2015; Karsen et al. 2011; Kołodziejczyk et al. 2013; Nasreldin and Zaki 2020; Siemieniuk et al. 2008). The estimated average standardized mean difference based on the random-effects model was 0.77 (95% CI: -1.3 to 2.8). This value (0.77) suggests a strong association between correlation between fasciolasis and decreased TAC according to the Cohen classification.

The fact that fasciolasis causes a decrease in the antioxidant capacity of the host may cause the prooxidant-antioxidant balance to shift to the prooxidant direction. Shifting the prooxidant-antioxidant balance in favor of prooxidant causes oxidative stress in the host. In conclusion, high oxidative stress occurs in the host during *F. hepatica* infection, which causes severe liver damage.

Keywords: Fasciolasis, Oxidative stress, Meta-analysis, Antioxidant capacity

References

Bottari NB, Mendes RE, Lucca NJ, Schwertz CI, Henker LC, Olsson DC, et al (2015). Oxidative stress associated with pathological lesions in the liver of rats experimentally infected by *Fasciola hepatica*. Exp Parasit. 159: 24-28.

Cicek M, Evliyaoglu O, Boyuk A, Tekin A. (2012). Investigation of some sera biomarker levels in fascioliasis patient. Kafkas Univ. Vet. Fak. 18: 181-185.

Karsen H, Sunnetcioglu M, Ceylan RM, Bayraktar M, Taskın A, Aksoy N et al. (20119. Evaluation of oxidative status in patients with *Fasciola hepatica* infection. Afr Health Sci. 11: 14-19.

Kołodziejczyk L, Jarocka I, Skrzydlewska E. (2013). The effects of *Fasciola hepatica* infection on the total antioxidant status (TAS) and the activity of proteases and their inhibitors in rat serum. Folia Biol. 61: 227-232.

Nasreldin N, Zaki RS. (2020). Biochemical and immunological investigation of fascioliasis in cattle in Egypt. Vet World. 13 (5): 923-930.

Siemieniuk E, Kolodziejczyk L, Skrzydlewska E. (2008). Oxidative modifications of rat liver cell components during *Fasciola hepatica* infection. Toxicol Mech Methods. 18: 519-24.

Cengiz ZT, Yılmaz H, Beyhan YE, Ekici A, Çiçek M, Aydemir S. (2022). The importance of antioxidant enzymes and oxidative stress in human fascioliasis. Türkiye Parazitol Derg. 47: 38-41.

Oral Presentations

Oral Presentation 14

The effect of endoplasmic reticulum stress induced apoptosis and autophagy in myocardial hypertrophy caused by hyperthyroidism: PERK/ATF4/CHOP signaling pathway

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In this study, aimed to investigate the effect of endoplasmic reticulum stress mediated apoptosis and autophagy signaling pathways in cardiac hypertrophy due to hyperthyroidism. For this purpose, 24 Sprague Dawley adult male rats were used and rats were divided into two groups as control group and hyperthyroid group. The hyperthyroidism model was performed using L-thyroxine 0.3 mg/kg/ml/day intraperitoneal injection. Control group (received intraperitoneal injections of saline solution 1ml/daily for 8 week) and hyperthyroid group (received intraperitoneal injections of L-thyroxine 0,3 mg/kg/ml/daily for 8 week). It was determined that absolute and relative heart weights increased in the hyperthyroid group ($P<0.001$). Microscopically; it was determined that the mean myofibril thickness in the hyperthyroid group were increased statistically significantly compared to the control group ($P<0.001$). Hypertrophy and interstitial fibrosis in both longitudinal and transverse myofibrillar sections in the left ventricle were noted in a few animals in this group. Nuclei in hypertrophic myocytes were observed to be partially hyperchromatic. Myofibrillar disorganization (disarray) and endocardial fibrosis were not detected in the hyperthyroid group. Hyperthyroidism significantly increased malondialdehyde level ($P<0.001$), PERK ($P<0.01$), GRP78 ($P<0.01$), CHOP ($P<0.05$), ATF4 ($P<0.01$), Bax ($P<0.05$), LC3 I/II ($P<0.01$), Beclin ($P<0.01$), ATG5 ($P<0.05$) protein expression levels, Bax/Bcl-2 ratio ($P<0.05$) and significantly decreased glutathione level ($P<0.01$), glutathione peroxidase ($P<0.01$) and catalase enzyme activities ($P<0.05$). There was no difference in Bcl-2 protein expression levels ($P\geq0.05$).

In conclusion, these results showed that increased thyroid hormones levels lead to endoplasmic reticulum stress caused by oxidative stress in the heart, and PERK/ATF4/CHOP mediated apoptosis and autophagy may play an important role in the hypertrophy caused by hyperthyroidism.

Keywords: Hyperthyroidism, Heart, Oxidative Stress, Endoplasmic Reticulum Stress, Apoptosis, Autophagy

Oral Presentations

Oral Presentation 15

The effect of zingerone on Sirt1/Nrf2/HO-1 signaling pathway and spermatological parameters in diabetic rats*

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In this study, it was aimed to investigate the effect of zingerone, which is present in ginger and display an antioxidant capacity, on the oxidative stress, spermatological parameters, and expression levels of oxidative stress-related protein in the reproductive system of the diabetic male rats.

In the study, a total of 75 male Sprague-Dawley rats were divided into 6 groups as follows; control, zingerone 50 mg/kg (Zin50), zingerone 100 mg/kg (Zin100), diabetic (DM), diabetic+zingerone 50 mg/kg (DM+Zin50), and diabetic+zingerone 100 mg/kg (DM+Zin100). Zingerone was administered by gavage for 8 weeks. Diabetes was induced by intraperitoneally administering a single dose of 55 mg/kg streptozotocin. At the end of the animal experiment, rats were decapitated and testicular tissues were collected. In the testicular tissues; malondialdehyde (MDA) and glutathione (GSH) levels, catalase (CAT) and glutathione peroxidase (GSHPx) enzyme activity were evaluated. Also, expression levels of sirtuin 1 (Sirt1), nuclear factor E2-related factor 2 (Nrf2), and heme oxygenase-1 (HO-1), which are oxidative stress-related proteins, and the spermatological parameters were evaluated.

The result of this study showed that GSH level, GSHPx and CAT enzyme activity, and Sirt1, Nrf2, and HO-1 protein expression levels were significantly decreased in the diabetic rats compared to control groups ($P<0.001$). Furthermore, spermatozoon motility and density decreased significantly, and the abnormal spermazotoon rate increased significantly in the diabetic rats compared to the control group ($P<0.001$). It was determined that GSH level, GSHPx and CAT enzyme activity, and Sirt1, Nrf2, HO-1 protein expression levels, and spermatozoon motility significantly increased, lipid peroxidation and abnormal sperm rate significantly decreased in the zingerone-treated rats compared to diabetic rats ($P<0.001$). There was no significant increase in spermatozoon density in the zingerone-treated rats compared to diabetic rats($P>0.05$).

In conclusion, zingerone supplementation displayed a positive effect on the reproductive system by reducing oxidative stress and increasing the expression levels of Sirt1, Nrf2 and HO-1 protein in diabetic rats.

Keywords: Oxidative stress, Reproduction, Antioxidant, Diabetes.

*This study was produced from Edanur GÜLER EKMEN''s PhD thesis and supported by the Scientific Research Projects Coordination Unit of Firat University (VF.22.02).

Oral Presentations

Oral Presentation 16

Oxidative Stress in Neurocysticercosis

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Neurocysticercosis is caused by Taenia solium larvae. It is estimated that as many as 3 million people worldwide are currently affected by seizures caused by neurocysticercosis (Carmen-Orozco et al. 2021). While neurocysticercosis may present with non-specific clinical symptoms, a chronic inflammatory process is triggered in the host after a while. Activated neutrophils and monocytes release reactive oxygen species such as hydrogen peroxides, hydroxyl radicals, and superoxide radicals, which can damage the tissues surrounding the inflammatory area, and this creates oxidative stress in cells. In a study, oxidants such as malondialdehyde, protein carbonyl and nitrite were found to be significantly higher in the cerebrospinal fluid of children with neurocysticercosis compared to controls, while antioxidants such as superoxide dismutase, glutathione peroxidase, ceruloplasmin, ascorbic acid, copper and zinc were found to be significantly lower (Prasad et al. 2012). Rodriguez et al. (2008) found that lipid peroxidation levels in the cerebrospinal fluid of patients with neurocysticercosis were higher than in controls. This indicates the occurrence of oxidative damage in patients with neurocysticercosis. Oxidative stress caused by neurocysticercosis can cause neurodegenerative diseases and especially meningitis.

Keywords: Taenia solium, Oxidative stress, Cysticercosis, Meningitis

References

Carmen-Orozco RP, Davila-Villacorta DG, Delgado-Kamiche AD, Celiz RH, Trompeter G, Sutherland G, et al. (2021). Changes in inflammatory gene expression in brain tissue adjacent and distant to a viable cyst in a rat model for neurocysticercosis. PLoS Negl Trop Dis. 15: e0009295.

Prasad R, Anil OP, Mishra SP, Mishra RS, Upadhyay, Singh TB. (2012). Oxidative stress in children with neurocysticercosis. Pediatr Infect Dis J. 31: 1012-5.

Rodriguez U, Rios C, Corona T, Talayero B, Ostrosky-Wegman P, Herrera LA. (2008). Lipid peroxidation in the cerebrospinal fluid of patients with neurocysticercosis. Trans R Soc Trop Med Hyg. 102: 1025-31.

Oral Presentations

Oral Presentation 17

The interaction between spinal cord injury and TRPV1 channel

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Many functions, notably cellular survival, apoptosis, physiological signaling, and excessive reactive oxygen species (ROS) generation, depend on cytoplasmic free Ca^{2+} balance. There is increasing evidence that the physiology of spinal cord injury (SCI) is significantly influenced by changes in cytoplasmic free Ca^{2+} concentration. Several membrane cation channels are responsible for regulating the cytoplasmic free Ca^{2+} concentration. A family of non-selective cation channels also called transient receptor potential (TRP) channels provides an essential part in DRG neurons. After traumatic events, the dorsal root ganglia (DRG) express a substantial quantity of calcium permeable cation channels, also called TRP vanilloid 1 (TRPV1) (Carrasco et al. 2018). It is currently proven that the TRPV1 channels in DRG neurons play a role in oxidative stress-induced cell death following mechanical trauma.

The results of the recent studies indicated that SCI-mediated excessive Ca^{2+} influx induces an increase of the mitochondrial membrane depolarization. In turn, it induces excessive generation of apoptotic and oxidant factors. The apoptotic factors include caspase -3 and -9 activations, although the oxidant factors include lipid peroxidation, mitochondrial and cytosolic ROS productions (Carrasco et al. 2018; Turtle et al. 2018). The oxidant and apoptotic actions of SCI were attenuated by the treatment of antioxidants such as Hypericum perforatum and melatonin.

I reached the conclusion that antioxidants considerably reduced the levels of oxidative stress, apoptosis, and Ca^{2+} entry via TRPV1 channel that SCI generated. The specific link between TRPV1 channel activation and SCI, however, is still unknown

Key words; Dorsal root ganglion; Spinal cord injury; TRPV1 channel; Oxidative stress.

References

Carrasco C, Naziroğlu M, Rodríguez AB, Pariente JA. (2018). Neuropathic Pain: Delving into the Oxidative Origin and the Possible Implication of Transient Receptor Potential Channels. Front Physiol. 9:95. doi: 10.3389/fphys.2018.00095

Turtle JD, Strain MM, Reynolds JA, Huang YJ, Lee KH, Henwood MK, Garraway SM, Grau JW. (2018). Pain Input After Spinal Cord Injury (SCI) Undermines Long-Term Recovery and Engages Signal Pathways That Promote Cell Death. Front Syst Neurosci. 12:27. doi: 10.3389/fnsys.2018.00027.

Oral Presentations

Oral Presentation 18

The antioxidant administration modulates traumatic brain injury through the modulation of TRPV1 channel

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The most prevalent form of traumatic brain injury (TBI) is a severe hit or trauma to the head or body. TBI can also result from an object entering the tissue of the brain, such as an assault weapon or broken piece of the skull. The brain's cells may suffer an instant effect from mild traumatic damage to the brain. A more serious TBI may cause bleeding, tissue damage, bruises, and other physical harm to the brain. These injuries may lead to long-term problems or even death.

Disturbances in the cytosolic calcium ion concentration play an essential role in the development of TBI. TRP vanilloid 1 (TRPV1) is a member of the TRP superfamily. Capsaicin and oxidative stress are two examples of the various stimuli that can gate the Na^+ and Ca^{2+}-permeable TRPV1 channels. Excessive Ca^{2+} entry, inflammation, and oxidative stress play major roles in the etiology of TBI (Yang et al. 2019; da Silva Fiorin et al. 2020).

Apoptosis, mitochondrial oxidative stress, and excess Ca^{2+} entry was recently described as being caused by oxidative stress in experimental TBI. However, antioxidants like N-acetylcysteine and selenium can prevent TBI-induced oxidative stress and apoptosis in the hippocampal neurons by preserving intracellular Ca^{2+} hemostasis, activating TRPV1 channels, and suppressing the mitochondrial oxidative stress pathway (Nazıroğlu et al. 2014; Yang et al. 2019).

I have come to the conclusion that TRPV1's oxidative failure affects the human body by activating the second messengers, which could result in the pathophysiology of TBI. It appears that additional study remains required to determine the exact link between TRPV1 channel activity and TBI.

Key words; Antioxidants; Apoptosis; TRPV1 channel; Traumatic brain injury; Oxidative stress.

References

da Silva Fiorin F, do Espírito Santo CC, do Nascimento RS, Cassol G, Plácido E, Santos ARS, Marques JLB, Brocardo PS, Fighera MR, Royes LFF. (2020). Capsaicin-sensitive fibers mediate periorbital allodynia and activation of inflammatory cells after traumatic brain injury in rats: Involvement of TRPV1 channels in post-traumatic headache. Neuropharmacology. 176:108215. doi: 10.1016/j.neuropharm.2020.108215.

Nazıroğlu M, Senol N, Ghazizadeh V, Yürüker V. 2014. Neuroprotection induced by N-acetylcysteine and selenium against traumatic brain injury-induced apoptosis and calcium entry in hippocampus of rat. Cell Mol Neurobiol 34(6):895-903.

Yang DX, Jing Y, Liu YL, Xu ZM, Yuan F, Wang ML, Geng Z, Tian HL. (2019) Inhibition of Transient Receptor Potential Vanilloid 1 Attenuates Blood-Brain Barrier Disruption after Traumatic Brain Injury in Mice. J Neurotrauma. 36(8):1279-1290. doi: 10.1089/neu.2018.5942.

Oral Presentations

Oral Presentation 19

The effect of lavandula stoechas essential oil on nerve regeneration in rats with sciatic nerve injury*

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This study, it was aimed to investigate the contribution of oral use of Lavandula Stoechas essential oil to regeneration in sciatic nerve crush injury by utilizing its antioxidant properties (Bouyahya et al., 2017, Cherrat et al., 2014, Mushtaq et al., 2018)

44 Wistar Albino male rats (4 of which were in the preliminary study) were used. Rats were randomly divided into four groups. Crush damage was created on right sciatic nerves. Groups;

Group 1: The control group, the intact left sciatic nerves of the group 2 that did not receive systemic treatment were used.

Group 2: Daily drinking water was given after damage

Group 3: Daily olive oil was given after the damage

Group 4: Daily 100 mg/kg Lavandula Stoechas essential oil +olive oil was given after the damage

Group 5: Daily 250 mg/kg Lavandula Stoechas essential oil +olive oil was given after the damage

On days 0, 7, 14, 21 and 30, the Sciatic Functional Index test was performed on groups (Bain et al., 1989) Electromyography analysis was performed on rats at the end of the 30th day and the experiment was terminated (Oğuzhanoğlu et al. 2000). General histopathological appearance, axon number and axon diameter were evaluated with oil red o staining on the sciatic nerve tissues taken. Nerve Growth Factor immunoreactivities in the tissue were determined by immunofluorescence. Electron microscopic examinations were performed on sciatic nerve tissues.

In conclusion it has been shown that a 30-day treatment of 250 mg/kg lavandula stoechas essential oil diluted in olive oil contributes to nerve regeneration. It was observed that 100 mg/kg Lavandula Stoechas essential oil treatment diluted in olive oil and olive oil treatment given to create a positive control contributed to regeneration in very low amounts.

Our findings suggest that in crush injury model, which is known to increase the severity of damage due to oxidative stress, the antioxidant property of Lavandula Stoechas essential oil supports regeneration by reducing oxidative stress.

Keywords: Crush injury; Lavandula Stoechas essential oil; Sciatic nerve

*This project was supported by Erciyes University Scientific Research Projects (BAP) Unit (Project code: TDK-2022-11522)

References

Bain J, Mackinnon S, Hunter DJP, surgery r. Functional evaluation of complete sciatic, peroneal, and posterior tibial nerve lesions in the rat 1989;83:129-136.

Bouyahya A, Et-Touys A, Abrini J, Talbaoui, Fellah A., Bakri H., Dakka Y., Nadia J. Lavandula stoechas essential oil from Morocco as novel source of antileishmanial, antibacterial and antioxidant activities 2017;12 p.:179-184.

Cherrat L, Espina L, Bakkali M, Pagán R, Laglaoui , Technologies E. Chemical composition, antioxidant and antimicrobial properties of Mentha pulegium, Lavandula stoechas and Satureja calamintha Scheele essential oils and an evaluation of their bactericidal effect in combined processes 2014;22 p.:221- 229.

Mushtaq A, Anwar R, Gohar UF, Ahmad, M., Marc Vlaic, R.A., Mureşan, C.C., Irimie, M., Bobescu, E., Biomolecular Evaluation of Lavandula stoechas L. for Nootropic Activity. Plants, Basel, Switzerland. 2021 ; p.:10.

Oğuzhanoğlu A, Kurt T, Sahiner T. Nerve conduction parameters during ischemia reperfusion in the rat sciatic nerve. Electromyography and clinical neurophysiology. 2000;40: 487-490.

Oral Presentations

Oral Presentation 20

The effect of melatonin and treadmill exercise on social isolation stress related to hippocampal BDNF, GFAP and SNAP25 gene expression levels in adult rats

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The melatonin and exercise cognitive functions have effects on the brain of rats in conditions such as chronic stress. In the presented study, our aim was to investigate the effect of combined with melatonin and exercise on the social isolation (SI) stress in adulthood.

This study, 4 months old Wistar albino male rats (n=30) were divided into 5 groups: control (C); social isolation (SI); social isolation + Melatonin (SIM); social isolated +exercise group (SIE); social isolation + Melatonin + exercise (SIME) group. Social isolation protocol was applied during 4 weeks by placing the rat alone in a cage. Melatonin (0.4 mg/ml, i.p.), was treatment of the experimental animals for 2 weeks. The rats were given exercise for 30 minutes a day for 2 weeks. Following the experimental protocol, were investigated serum corticosterone levels by ELISA method and hippocampal BDNF, GFAP and SNAP25 gene expression level by RT-PCR.

The melatonin and exercise administration did not cause a statistically significant difference on SI stress in serum corticosterone levels. BDNF was found to be down-regulated in S and SIE, but this result was not seen melatonin administered. There was no a statistically significant difference in GFAP and SNAP25 gene expression levels.

Our data suggest that melatonin prevents down-regulation of BDNF in the hippocampus of SI stress, but it showed that treadmill exercise did not have the same effect. We think that further research, that the with different exercise types, is need to understand the mechanisms underlying the combination of melatonin and exercise.

Keywords: Melatonin; Exercise; Social isolation; Hippocampus

This study was supported by Adiyaman University (grant number, TIPFMAP/2022-0003).

References

Nowacka-Chmielewska M, Grabowska K, Grabowski M, Meybohm P, Burek M, Małecki A. (2022). Running from Stress: Neurobiological Mechanisms of Exercise-Induced Stress Resilience. Int J Mol Sci. 23(21):13348. https://pubmed.ncbi.nlm.nih.gov/36362131/

Stefanovic B, Spasojevic N, Jovanovic P, Ferizovic H, Dronjak S. Melatonin modulate the expression of α1- and β2-adrenoceptors in the hippocampus of rats subjected to unpredictable chronic mild stress (2018). Bratisl Lek Listy. 119(7):429-433. https://pubmed.ncbi.nlm.nih.gov/30160132/

Oral Presentations

Oral Presentation 21

Anti-oxidant effects of melatonin on sepsis-induced oxidative stress in liver tissue of rats

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Sepsis is systemic response of the body against a microorganism, the cytokine storm that occurs with the stimulation of the inflammation induces oxidative stress (Kumar, 2020). The liver has an important role in the detoxification process in sepsis causes lead to death as a result of accumulation of toxic agents and reactive oxygen species. Several studies have reported that Melatonin has anti-oxidant effects on lipid peroxidation and oxidative stress (Chen et al., 2017). In this study, we aimed to investigate the effects of melatonin on lipid peroxidation (Thiobarbituric acid reactive substances (TBARS)), anti-oxidant enzymes chains and Chitinase-3 like protein1 (YKL-40) as a potential marker of sepsis (Steletou et al., 2023) in liver tissue in rats with sepsis induced with lipopolysaccharide (LPS).

Adult Wistar albino rats was divided into 4 groups as; Control, LPS (10 mg/kg i.p.), Melatonin (10 mg/kg i.p. x3), Melatonin+LPS. Rats were decapitated 6 hours after LPS in-jection and liver tissues were taken and homogenized. Glutathione reductase (GR), Glutathi-one peroxidase (GSH-Px), Superoxide dismutase (SOD) and YKL-40 levels were investigat-ed by ELISA method. Statistical analysis was performed with one-way ANOVA and Tukey test was used.

Our findings; In the LPS group, GR, GSH-Px, SOD levels were significantly lower and TBARS levels were significantly higher than the other groups, also YKL-40 levels were decreased compared to the control.

Our results show that melatonin improves the reduce the oxidative stress in liver tis-sue which damaged by sepsis.

Key words: Oxidative stress; Melatonin; Sepsis; Anti-oxidant; Liver; YKL-40

References

Kumar V. Toll-like receptors in sepsis-associated cytokine storm and their endoge-nous negative regulators as future immunomodulatory targets. Int Immunopharmacol. 2020;89(Pt B):107087.

Chen G, Deng H, Song X, Lu M, Zhao L, Xia S, You G, Zhao J, Zhang Y, Dong A, & Zhou H (2017). Reactive oxygen species-responsive polymeric nanoparticles for alleviating sepsis-induced acute liver injury in mice. Biomaterials, 144, 30–41.

Steletou E, Metallinou D, Margeli A, Giannouchos T, Michos A, Kanaka-Gantenbein C, Papassotiriou I, & Siahanidou T (2023). Serum YKL-40 as a Potential Biomarker for Sep-sis in Term Neonates-A Pilot Study. Children (Basel, Switzerland), 10(5), 772.

Oral Presentations

Oral Presentation 22

The Implications of Combined Metformin and Atorvastatin Treatment on Oxidative Stress/ Antioxidant Status in the Gastrocnemius Muscle of Treadmill Exercised STZ-Diabetic Rats

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In patients with uncontrolled type 1 diabetes (T1DM), hyperglycemia increases reactive oxygen radical (ROS) production and oxidative stress (OS), especially in skeletal muscle. Excess OS damages striated muscle tissues and reduces physical activity, resulting in a decline in the patient's quality of life. Regular physical activity is thought to enhance the respiratory capacity of muscles. It can also mitigate the harmful impact of diabetes by facilitating the adaptation of the body to exercise. This process involves the activation of antioxidant systems and related mechanisms to counteract the rise in ROS production. On the other hand, some studies suggest that exercise could potentially increase OS. Metformin and atorvastatin are frequently-used drugs to regulate disease and prevent cardiovascular complications in T1DM. In addition, they have some impact on oxidative stress and skeletal muscle functions. Currently, there is no research on the effects of the simultaneous use of these medications on T1DM patients who exercise.

This study aimed to explore the impact of administering metformin and atorvastatin in combination on skeletal muscle oxidant/antioxidant parameters in T1DM rats undergoing moderate intensity treadmill training. Male Wistar rats were divided into six groups for this study: a sedentary control group (naive; N) and five "treatment group having exercise" (C), diabetes (D), diabetes with metformin (MET), diabetes with atorvastatin (ATO), and diabetes with metformin and atorvastatin (MET+ATO). Diabetes was induced by administering Streptozotocin (STZ) at a dose of 45 mg/kg intraperitoneally. The study included rats whose glucose levels in the tail vein blood were greater than 250 mg/dL after ten days. The exercise groups of rats engaged in treadmill running for five days per week, while the administration of drugs was conducted seven days per week. At the end of the fourth week, samples of the rats' gastrocnemius muscle were obtained while under ketamine anaesthesia (100 mg/kg; i.p.). Superoxide dismutase (SOD) activity, reduced glutathione (GSH), and malondialdehyde (MDA) levels were assessed as indicators of oxidative stress/antioxidant status. Analyses of total oxidative capacity (TOS) and total antioxidant capacity (TAS) were conducted to determine the oxidative stress index (OSI).

At the end of the study we have found a significant increase in tissue MDA levels (marker of oxidative stress) while a significant decrease in GSH levels from group D. There was not any significant effect of drugs on these parameters. OSI decreased by combined use of drugs, however, metformin alone was found more effective.

This study is a part of a project going on in our laboratory. After getting all results of the project, a better evaluation of the effects of the drugs combination would be possible.

Keywords: Diabetes; Metformin; Atorvastatin; Exercise training; Oxidative stress

This study was supported by the project numbered TDK-2021-9350 from the Scientific Research Projects Unit of Van Yuzuncu Yıl University and the project numbered 222S871 from the Scientific and Technological Research Council of Türkiye (TUBITAK).

Poster Presentations

Poster No, 1

Orai1 is regulated by miRNAs in vascular restenosis

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The main cause of restenosis is attributed to the excessive proliferation and migration of vascular smooth muscle cells (VSMC). Orai1 is one of the main molecular components of Store-Operated Calcium Entry (SOCE), playing a key role in VSMCs proliferation during neointima formation in the process of restenosis (Shawer et al., 2021). Recent studies have demonstrated the implication of microRNAs (miRNAs) in VSMCs proliferation (Efovi & Xiao, 2023), however, the role of these miRNAs as regulators of SOCE during vascular remodeling has not been described.

Experiments were conducted in an animal model of rat carotid angioplasty to characterize neointima formation. The neointima development after balloon injury of rat carotid arteries was confirmed by haematoxylin and eosin staining, and αSMA staining of tissue sections up to 3 weeks after surgery. Injured arteries showed significant higher expression of Orai1, as compared to non-injured arteries, indicating their possible participation in the neointima layer formation. Microarray of miRNAs analysis of the injured carotids compared to control carotids showed significant increase in the expression of miR-18a-5p, miR-20a-5p, miR-20b-5p and miR-17-5p, which was validated by RT-qPCR. These miRNAs belong to widely studied miR-17-92 cluster involved in different cell proliferation. Furthermore, in silico analysis has identified these miRNAs as potential targets of Orai1.

In conclusion, our data demonstrate that Orai1 upregulation during neointima formation in VSMCs is associated with miRNAs dysregulation, indicating that SOCE associated genes might finely regulated by miRNAs during restenosis.

Keywords: miRNAs; Orai1; carotid lesion; Smooth muscle proliferation; store-operated calcium entry

References

Efovi, D., & Xiao, Q. (2023). Noncoding RNAs in Vascular Cell Biology and Restenosis. Biology, 12 (1).

Shawer, H., Norman, K., Cheng, C. W., Foster, R., Beech, D. J., & Bailey, M. A. (2021). ORAI1 Ca2+ Channel as a Therapeutic Target in Pathological Vascular Remodelling. Frontiers in Cell and Developmental Biology, 9.

Poster Presentations

Poster No, 2

Administration of dinutuximab beta to insulinoma INS-1 cells under cytotoxic conditions causes cell dysfunction and increases insulin secretion by increasing Ca^{2+} levels and reducing K^+ channel proteins

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One of the most widely recognized pancreatic tumors is insulinoma. It originates from beta cells in the islet of Langerhans in the pancreas. (Service et al. 1991; Pelengaris and Khan, 2001). Dinutuximab is a monoclonal antibody used to treat beta neuroblastoma. This antibody has been approved for use in Europe for high-risk neuroblastoma patients (EMA 2021). The aim of this study is to investigate the effects of DB on pancreatic beta-cell tumors at the molecular level.

Insulinoma INS-1 cells were used in the study. DB (Qarziba®), available from EUSA Pharma, was used for the experiments. Streptozotocin (STZ) was used induce to cell cytotoxicity. DB was applied to the cells before or after the STZ application. KCND3, KCNN4, KCNK1, and PTHrP gene expression levels by q-RT-PCR and protein levels by western blotting were analyzed. Analysis of glucose-stimulated insulin secretion was performed. Ca^{2+} and CA19-9 levels were determined by the ELISA kit.

Decreased KCND3, KCNK1, and PTHrP protein levels increased KCND3, KCNN4, KCNK1, and PTHrP gene expression levels were observed in the STZ+DB group. Cell dysfunction was detected in the STZ+DB group according to insulin secretion analysis. Ca19-9 and Ca^{2+} levels were increased in the STZ+DB group. As a result, K^+ channels may be inactive with the decrease of K^+ channel proteins, Ca^{2+} channels may be opened, and Insulin secretion from pancreatic beta cells can increase. The increase in Ca19-9 level in the STZ+DB group which is cell dysfunction suggests that CA19-9 is associated with beta cell function.

Keywords: Insulinoma; Dinutuximab beta; K^+ channel proteins; Ca^{2+}, Ca19-9

References

Servıce FJ, Mcmahon MM, O'brıen PC, Ballard DJ. (1991). Functioning Insulinoma—Incidence, Recurrence, and Long-Term Survival of Patients: A 60-Year Study. Mayo Clinic Proceedings. 66:711–719.

Pelengaris S, Khan M. (2001). Oncogenic co-operation in beta-cell tumorigenesis. Endocrine Related Cancer. 8:307-314.

EMA. (2021). Qarziba (Dinutuximab beta) Summary of Product Character- istics. Available at: https://www.medicines.org.uk/emc/product/9441/ smpc#gref

Poster Presentations

Poster No, 3

SOD, GSH, and MDA levels in the hela cell line as a result of the combination cisplatin and ε-viniferin

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Cervical cancer is the fourth most common cancer worldwide, after breast, colorectal, and lung cancers. More than 85% of cervical cancer cases and deaths occur in developing countries. This study investigated the effects of combinations of Cisplatin (CDDP), an anticancer drug, and *ε*-Viniferin, a phenolic compound with antioxidant effect, on Hela cervical cancer cells. Glutathione (GSH) and malondialdehyde (MDA) levels, which are oxidative stress markers, and superoxide dismutase (SOD) activity were measured.

The IC_{50} value calculated from the MTT assay performed to determine the cytotoxic effects of CDDP and *ε*-Viniferin in Hela cells were 28 μM and 21 μM, respectively. Different percentages of combination were created from the obtained IC_{50} doses, and the combination index was calculated. In the study, 10% (2.1 μM *ε*-Viniferin+0.75 μM CDDP) and 20% (4.2 μM *ε*-Viniferin+5.6 μM CDDP) that were synergistic and 40% (8.4 μM *ε*-Viniferin+11.2 μM CDDP) that were found to be antagonistic were selected. The SOD activity in the combination groups (10%, 20%, 40%) was 0.805±0.02, 1.12±0.24, 1.783±0.44, respectively, compared to the control (1.550±0.10). The GSH level in the combination groups (10%, 20%, 40%) was 0.847±0.03, 0.836±0.19, 1.353±0.30, respectively, compared to the control (1.378±0.09). The MDA level in the combination groups (10%, 20%, 30%) was 3.358±0.35, 3.794±0.46, 4.307±0.59, respectively, compared to the control (0.461±0.1).

In conclusion, according to the MDA values, which are markers of oxidative stress, ε-Viniferin further potentiated the effects of CDDP in the combination groups. Thus, ε-Viniferin shows pro-oxidant effect by increasing cellular lipid peroxide levels.

Keywords: Hela cell line; Cisplatin; ε-Viniferin; Glutathione; Superoxide dismutase; Malondialdehyde

This work was funded by a grant from the Anadolu University (Project No:2107S122)

Poster Presentations

Poster No, 4

Effects of eugenol on pancreas damage in diabetic rats

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Eugenol is a phenolic compound that has been demonstrated to have several bioactivities (anti-oxidant, anti-microbial, anti-inflammatory, anti-tumor, and anti-mutagenic) (Ma et al. 2021). However, there is limited literature information on the effects of eugenol on the pancreas damage in diabetic rats (Kokabiyan et al. 2023; Mnafgui et al. 2013). The aim of this study was to determine the effect of eugenol on pancreatic damage in streptozotocin-induced diabetic rats. For this purpose, 60 Sprague-Dawley adult male rats were used, and the rats were divided into six groups. No application was made to the control group. The solvent group was given one ml of corn oil by gavage once a day for four weeks. The eugenol group was given 80 mg/kg of eugenol by gavage once a day for four weeks. A single dose of 55 mg/kg streptozotocin was administered intraperitoneally to the diabetic group. To the diabetic group fed with eugenol a single dose of 55 mg/kg intraperitoneal streptozotocin was administered, and eugenol at a dose of 80 mg/kg was administered by gavage once a day for four weeks. To the diabetic group administered metformin and insulin received streptozotocin at 55 mg/kg intraperitoneally in a single dose, metformin at 250 mg/kg dose by gavage, and insulin at 4 IU/kg dose subcutaneously once a day for four weeks.

It was determined that malondialdehyde level, GSH.Px enzyme activity significantly increased, and GSH level significantly decreased ($P<0.001$) in the diabetic group. However, while malondialdehyde level and GSH.Px enzyme activity decreased ($P<0.001$) in the diabetic group fed with eugenol, no difference was observed in GSH levels ($P > 0.05$) compared to the diabetic group. While there was no significant difference in serum glucose levels ($P >0.05$), a significant increase in final body weight ($P<0.05$) was detected in the eugenol-fed diabetic group compared to the diabetic group.

In conclusion, eugenol inhibits lipid peroxidation and regulates the antioxidant enzymes of the pancreas in diabetic rats. The results suggested that eugenol played an important role in pancreatic damage in diabetic rats because of its antioxidative effects.

Keywords: Eugenol, Diabetes, Pancreas, Oxidative Stress, Antioxidant

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References

Ma L, Liu J, Lin Q et al. (2021). Eugenol protects cells against oxidative stress via Nrf2. Experimental and Therapeutic Medicine. 21 (2): 107.

Kokabiyan Z, Yaghmaei P, Jameie SB, Hajebrahimi Z. (2023). Effect of eugenol on lipid profile, oxidative stress, sex hormone, liver injury, ovarian failure, and expression of COX-2 and PPAR-α genes in a rat model of diabetes. Molecular Biology Reports. 50:3669–3679

Mnafgui K, Kaanich F, Derbali A et al. (2013). Inhibition of key enzymes related to diabetes and hypertension byEugenol in vitro and in alloxan-induced diabetic rats. Arch Physiol Biochem. 119(5): 225–233

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