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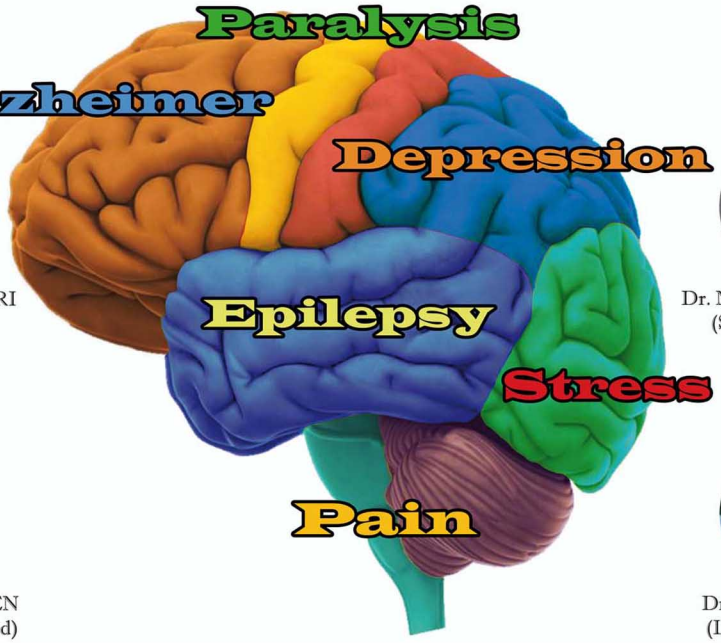

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AIM AND SCOPES
Journal of Cellular Neuroscience and Oxidative Stress is an online journal that publishes original research articles, reviews and short reviews on the molecular basis of biophysical, physiological and pharmacological processes that regulate 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)

READERSHIP

Biophysics	Biochemistry
Biology	Biomedical Engineering
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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.

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SPEAKERS

Speak No. 1

Mice microglia fluorescent Ca^{2+} imaging and TRP channels

Mustafa NAZIROĞLU
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As the brain's resident immune cells, microglia regulate phagocytosis, neuronal network maintenance, and brain development. The cytosolic free Ca2+ concentration [Ca2+]c rises, stimulating the activation and phagocytosis of microglia. Microglia that have been triggered in turn produce oxidative damage and neuronal death. This means that the $[Ca^{2+}]_c$ determination has a significant impact on oxidative stress and apoptosis in microglia and neuronal cells.

The Ca^{2+} permeable calcium channels include voltage gated and neurotransmitter gated Ca^{2+} channels. A new member of Ca^{2+} permeable calcium channels is transient receptor potential (TRP) superfamily with 28 members. The stimulators of TRP channels are very different from the voltage gated and neurotransmitter gated Ca^{2+} channels. For instance, the hot chili component (capsaicin), DNA-damage product (ADP-ribose), and cinnamaldehyde are stimulators of TRV1, TRPM2, and TRPA1, respectively (Carrasco et al. 2018). Some green fluorescent dyes, including Fluo-3 AM and Fluo-8, have long been used to study TRP channel stimulation-mediated $[Ca^{2+}]_c$ in microglia and neurons using the laser scan confocal and fluorescent microscopes (Yıldızhan and Nazıroğlu 2020). A ratiometric analysis of $[Ca^{2+}]_c$ in microglia and neurons in the neuron is induced by using Fura-2 acetoxymethyl (AM) ester. The analyses of Fura-2 AM are performed in the neurons by using a spectrofluorometer.

In conclusion, it appears that Fura-2 AM is the best ratiometric approach for the examination of TRP channels, while Fluo-3 AM and Fluo-8 are the most valuable imaging dyes for the laser scan confocal microscope.

Keywords: Fluo-3 AM; Fura-2 AM; Laser scan confocal microscope; TRP channels: Microglia.

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SPEAKERS

Speak No. 2

Behavioral assays and animal models of psychiatric disorders

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Animal models are important tools in the study of human diseases and/or disorders. They allow us to use research methods to understand underlying pathological mechanisms and screen for/identify/test new therapeutic agents. Consequently, scientists have developed several criteria to assess the validity and reliability of the behavioral assays and/or animal models of human disorders. Regarding psychiatric disorders (e.g. anxiety, depression and schizophrenia) many of the symptoms used to diagnose these disorders in humans (e.g., hallucinations, delusion, anxiety, intrusion of traumatic memories, sadness, guilt) are hard to be convincingly established in animals. Furthermore, unlike other brain diseases (e.g. Alzheimer's, Parkinson's, ALS and stroke), the exact pathological mechanisms underlying psychiatric disorders are unknown making it even harder to establish a convincing animal model. We will discuss the importance of animal models in neuroscience. An overview of classical literatures summarizing definitions of animal models, criteria to establish their validity and additional assessments to establish their reliability will be presented. We will zoom in and focus on behavioral assays and animal models relevant to psychiatric disorders. Students will be introduced to animal models of fear memory, depression, helplessness and schizophrenia as well as to some behavioral assays that are used to establish relevant behaviors. Behavioral assays and animal models of psychiatric disorders do demonstrate reasonable correlates to human symptoms (e.g. motivational, exploration, reward and cognitive deficits). Thus, they are indispensable tools to study mechanisms underlying psychiatric disorders and identify new treatments. Extra efforts are required, however, to exclude confounding factors and/or alternative interpretations of the behavioral readouts.

Keywords: Animal models; Psychiatric disorders; Fear memory; Anxiety; Depression; Schizophrenia

SPEAKERS

Speak No. 3

Calcium imaging techniques in the isolated DRG neurons

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SPEAKERS

Speak No. 4

Cholesterol as a therapeutic target for Alzheimer's disease

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Alzheimer's disease (AD) is the most common cause of dementia, currently affecting around 44 million people. AD is an age-related neurodegenerative disorder, characterized by cortical and hippocampal atrophy. AD patients present impaired short-term memory, judgement and learning. The predominant clinical feature of AD is abnormally accumulated extracellular amyloid β-protein (Aβ) plaques and intracellular neurofibrillary tangles (NFT), which are caused by the aggregation of hyperphosphorylated tau protein. Cholesterol has been reported to be accumulated in senile plaques of AD patients and AD rodent models. Genome wide association studies have reported that cholesterol homeostasis-related genes are associated with AD, such as APOE gene. Actually, cholesterol can directly interact with Aβ and high level of cholesterol promotes Aβ plaque formation. We are investigating dysregulation of cholesterol in the retina and brain of 5XFAD mice, a common model of AD. We are also examining the therapeutic potential of a small chemical in 5XFAD mice. In this talk, I will update recent progress of cholesterol studies in AD and present our findings from the 5XFAD mice.

Keywords; Alzheimer's disease; APOE gene; Cholesterol.

SPEAKERS

Speak No. 5

Principles of Ca^{2+} and Na^{+} imaging using low-affinity indicators

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Ca^{2+} and Na^{+} are the two cations that enter the cell when permeable ion channels open. Na^{+} influx produces currents that underlie action potentials and excitatory synaptic potentials in neurons whereas Ca^{2+} is principally a molecular messenger that triggers signals in the intracellular cytoplasm. Ca^{2+} influx through a specific Ca^{2+} channel can selectively bind to proteins physically interacting with the channel in nanoscale domains, but it also increases the cytosolic Ca^{2+} concentration binding to proteins in unspecific manner. The experimental measurement of Ca^{2+} and Na^{+} consists in introducing a Ca^{2+} sensitive fluorescent buffer that alters the physiological Ca^{2+} signalling and this constraint must be taken into account when designing this type of experiments.

In this lecture I will introduce the principles of Ca^{2+} and Na^{+} imaging using low-affinity indicators and the important applications to investigate the truly physiological Ca^{2+} dynamics in native systems. First, I will analyse in detail the issue of competition of the Ca^{2+} indicator with the endogenous Ca^{2+} buffers expressed by the cell and how Ca^{2+} imaging can be performed to monitor the free Ca^{2+} concentration without perturbing the physiological Ca^{2+} homeostasis. Second, I will show how the fast equilibration of low-affinity indicators can disclose the physiological kinetics of voltage-gated Ca^{2+} channels underlying neuronal excitability. Third, by combining Ca^{2+} imaging with membrane potential imaging, I will show how low-affinity indicators can unravel the occurrence protein activation at nanoscale domains. I will then extend these aspects to Na^{+} imaging showing how this type of measurement, performed at the axon initial segment, allows unravelling in detail the sequential activation of Na^{+} channels underlying the generation of an action potential.

I will finally illustrate how these techniques can be applied to preclinical research to investigate the biophysical consequences of channelopathies responsible of a variety of rare genetic diseases.

Keywords: Calcium; Ion channels; Neuronal excitability

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SPEAKERS

Speak No. 6

RT-PCR and Western blot analyses in the rodent brain samples

Denis ROUSSEAU
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No abstract.

SPEAKERS

Speak No. 7

State dependent block of voltage gated sodium and calcium channels as modern treatment for epilepsy

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Epilepsy is the fourth most common neurological disorder and affects people of all ages. Medication for epilepsy is often life-long and has a major impact on the quality of life - mostly being related to substantial adverse effects. Therefore, over 30% of people with epilepsy do not achieve sufficient seizure control whilst effective medication being available.

Ion channels are often primary targets of anticonvulsant drugs. They can either act as blockers for voltage gated sodium and calcium channels or as activators for potassium or chloride channels. Additionally, modulators of ligand gated ion channels ($GABA_A$ or Glutamate receptors) are frequently used to treat epilepsy.

Employing a panel of functional electrophysiological assays using patch-clamping on a broad range of voltage and ligand gated ion channels, we were able to successfully screen for drugs with a beneficial action profile. In successful leads we found drugs that selectively interacted with TTX sensitive, neuronal voltage gated sodium channels. Activation and fast inactivation were unchanged, while an increased affinity in the slow inactivated state was observed. This is a modern mode of action for anticonvulsive drugs. In contrast, traditional anticonvulsant drugs often show their major effects on the fast inactivated state of voltage gated sodium channels.

Mutations of voltage gated calcium and sodium channels are important risk factors for various kinds of epilepsy. Usually the mutations cause a gain of function by influencing the biophysical properties of the channels. A modern strategy to improve efficacy of anticonvulsant drugs and reduction of their adverse effects is the development of drugs interacting with multiple disease causing targets. As promising targets one isoform of the TTX sensitive voltage gated sodium channels and a voltage gated calcium channel were identified. For the screening of larger number of compounds, automated patch-clamping was used. Before starting the screening of compound libraries, stably transfected cell lines with constant high expression levels were developed and biophysically characterized. Based on the results of these experiments an assay was developed to be able to reliably differentiate effects on ion channels in certain states and at high throughput. The strategy to identify drugs with a high affinity binding to two different targets increases the risk for unwanted side effects. It is therefore necessary to check isoform selectivity and other potential adverse effects at an early stage of development.

Keywords: Epilepsy, voltage gated sodium channels, voltage gated calcium channels, state dependent inactivation, patch-clamp technique

SPEAKERS

Speak No. 8

When inflammation strikes: a deep dive into the dorsal root ganglia

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Pain is an important physiological indicator that has a great impact on an organism's survival. The ability to perceive and react to noxious stimuli confers the capacity of animals, including humans, to avoid potentially dangerous situations. However, pain can persist beyond its alarm function, and become a problem of its own. It is estimated that 19% of adult Europeans suffer from moderate to severe chronic pain and still about half of these patients report inadequate pain management[1].

In the classical neurocentric view, the pain pathway starts when a noxious stimulus depolarizes the peripheral terminals of primary afferent neurons of the somatosensory system. The initiation of pain signals in nerve endings relies critically on a repertoire of specialized ion channels that are expressed in sensory neurons, such as TRPs, ASICs, Piezo and P2X among others. Intriguingly, emerging evidence indicates that the detection and transduction of pain stimuli is not only restricted to neuronal activity. For instance, several lines of evidence point to a key role for skin keratinocytes in the detection of thermal stimuli2. More recently, a new type of Schwann cells (a type of glia in the peripheral nervous system, best known for providing myelination of peripheral axons) was identified as mechanosensitive cells in the skin, which convey nociceptive information to the adjacent DRG neurons3. Nevertheless, the roles of non-neuronal cells in somatosensation and pain remain poorly understood. Notwithstanding the complete dominance of neuronal research for so many years, glial cells are now no longer considered simple support cells. In the past decades, it became clear that glial cells have an active role in numerous physiological and pathophysiological conditions, and the knowledge of glial cells' diverse physiological functions has increased ever since. Besides the aforementioned Schwann cells, there is a second type of peripheral glial cells that may be centrally involved in acute and chronic pain: the Satellite Glia Cells (SGCs).

In this lecture, we will discuss the molecular mechanisms underlying pain signaling and then delve into the molecular sensors that are present in this pathway. These sensors play a crucial role in detecting thermal, mechanical and chemical stimuli and are involved in a variety of pain syndromes, including neuropathic pain, migraine, inflammatory pain, among others. We will discuss the impact of peripheral inflammation on sensory neuron gene expression, and how this can lead to alterations in pain perception and the development of chronic pain conditions. We will explore the complex interplay of sensory neurons and satellite glial cells in the context of inflammation. Overall, this lecture will provide a comprehensive overview of the molecular mechanisms underlying pain signaling as well as the impact of peripheral inflammation in modulating pain perception. I will highlight and demonstrate the use of essential techniques in pain research, including calcium imaging, patch clamp, single cell sequencing and spatial transcriptomics.

Keywords; Pain, ion channels, satellite glial cells, inflammation, sensory neurons

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Oral Presentations

Oral Presentation 1

The antioxidant action of silymarin in the brain

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Reactive oxygen species (ROS) including the superoxide radical and the hydroxyl radical, which are produced in excessive amounts, cause oxidative stress. The enzymatic and non-enzymatic antioxidants were in charge of regulating the production of oxidative stress. Antioxidant enzymes that are produced by enzymes include glutathione peroxidase and catalase, among others. Several vitamins, such as vitamins C and E, as well as antioxidants, such as glutathione and alpha-lipoic acid, are examples of non-enzymatic antioxidants. Despite having low antioxidant levels, the brain has significant oxygen consumption and PUFA content. Therefore, oxidative stress mostly affects the brain.

At present, dietary antioxidant supplements are very popular, and they were widely used over all the world. Most of these supplements are obtained from plants. Silybin (silibinin) is an essential component of milk thistle (Silybum marianum). It has antioxidant and free oxygen radical scavenger activity. In the treatment of liver diseases, silybin was traditionally used by patients. Later, its protective actions on several hepatic diseases and components of metabolic syndrome (Galhardi et al. 2009). In recent data, its antioxidant and protective roles were reported in the brain. In addition, its protective action against neurodegenerative diseases such as Alzheimer's disease were also reported (Aboelwafa et al. 2020; Liu et al. 2021).

As a result, I aimed to give an overview of current literature data on the antioxidant action of silymarin in this presentation.

Key words: Antioxidants; Brain disease; Silymarin; Oxidative stress.

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Oral Presentations

Oral Presentation 2

The TRPM2 channel expression levels in brain development: A literature review

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Within the past 20 years, the prevalence of neurodegenerative illnesses has dramatically increased. Neurodegenerative illnesses are predicted to affect 2% of adults over 65 each year in the majority of global studies. Parkinson's disease (PD) is one of the neurodegenerative illnesses. Several triggers, including an increase in microglial reactive oxygen species (ROS), can cause Parkinson's disease (PD). By increasing cation channel activation in response to the excessive Ca^{2+} influx, ROS are increased. The brain and neurons are particularly vulnerable to an increase in ROS due to three factors: (1) a lack of antioxidants; (2) a high concentration of polyunsaturated fatty acids; and (3) oxygen consumption. The perinatal brain development has an impact on the rises in ROS in the brain and neurons.

The stimulation of multiple cation channels causes the Ca^{2+} influx from the outside of the neurons. Transient receptor potential (TRP) is a cation channel superfamily. TRP melastatin 2 (TRPM2) channel is a subset of the TRP superfamily (Nazıroğlu 2011). An enzyme is located in the channel's C domain. The brain and neurons experience an increased Ca^{2+} influx if the enzyme is triggered by oxidative stress and ADP-ribose. In the course of the prenatal brain's development, numerous cellular and hormonal cues alter the amounts of TRPM2's mRNA and protein expression. According to the findings of a recent study, the levels of TRPM2 expression were identified in three neuron sections of the brain (neuronal, astrocytic, and microglial) and four crucial brain regions (cortex, striatum, and cerebellum) (Ratnam et al. 2018). Additionally, it has been documented that experimental animals' growing microglia can induce PD by upregulating the amounts of the mRNA TRPM2 expression (Vink et al. 2009). I will go through the TRPM2 expression levels during brain development in the oral presentation.

The present literature results indicate that the increase of TRPM2 expression has a main role in the induction of PD and activation of microglia in the experimental animals.

Key words: Brain development; mRNA expression; Oxidative stress; Parkinson’s disease; TRPM2 channel.

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Oral Presentations

Oral Presentation 3

The cell phone and Wi-Fi radiofrequencies induce female hormone and oxidative stress changes: A literature review

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In the environmental area, people are using more non-ionizing electromagnetic frequencies associated with mobile phones and Wi-Fi. First-generation (1G) and second-generation (2G) cell phones emit frequencies between 850 and 1900 MHz, while third-generation (3G) mobile phones emit high frequencies up to 2.5 GHz. The fourth (4G) and fifth (5G) work at high frequency ranges of 2-8 GHz and 3–300 GHz, respectively. High frequencies (between 2.4 and 5 GHz) are used by the modern Wi-Fi devices (Maluin et al. 2021).

Several physiological factors such as phagocytosis and mitochondrial ATP production induce oxidative stress. The oxidative stress contains several reactive oxygen species (ROS) such as superoxide radical and hydroxyl radical. The excessive ROS generations are controlled by the enzymatic and non-enzymatic antioxidants. The enzymatic antioxidants include several enzymes such as catalase and glutathione peroxidase, although the non-enzymatic antioxidants include vitamins and thiol redox antioxidant such as glutathione, vitamin E, and vitamin C. In the results of the recent studies, it was reported that the antioxidant levels were decreased in the female reproductive system by the exposure of mobile phone and Wi-Fi frequencies (Yüksel et al. 2016; Jangid et al. 2022).

The majority of female reproductive hormones, including estrogen and follicular stimulating hormone (FSH), are necessary for female reproductive processes. Multiple environmental variables have an impact on their secretions. The release of female hormones into the blood of women and experimental animals was reduced by Wi-Fi and cell phone exposure.

The oral presentation focuses on the most current research on how exposure to mobile phones and Wi-Fi affects oxidative stress and female reproductive hormones in humans and lab animals.

Key words: Electromagnetic radiation; Female hormones; Oxidative stress; Reproduction.

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Oral Presentations

Oral Presentation 4

Experimental bipolar disease models: A mini review

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Bipolar disorder (BD) is a severe psychiatric illness that manifests as extreme variations in mood and energy, usually labelled as mania and depression. The disorder afflicts approximately 1-2% of people. Despite presence of several papers, the pathophysiology of the disease remains unknown. However, the proposed mechanisms in the etiology of BD are including the genetic factors, neurotransmitter changes, neurotrophic factor (BDNF) changes, inflammation, and oxidative stress (Recart et al. 2021).

There are two main groups of BDs, and they are cell culture and experimental animal models. BD's cyclical character makes it challenging to develop an appropriate model. It's also important to remember that some signs of psychiatric illness in people cannot be evaluated in animals. Animal models that replicate this complex behavioral state are frequently used to study this disease because manic episodes are essential for the diagnosis of BD. The animal and cell culture models are induced by several chemicals. The chemicals include psychostimulant (via the increase in dopamine efflux but inhibition of DA reuptake, or DA degradation by the enzyme monoamine oxidase), Ouabain (Na^+,K^+-ATPase inhibitör), and ketamine (non-competitive NMDA glutamate receptor antagonist) (Pierone et al. 2020). For testing the induction of BD in the experimental animals, open-field test is a common test (Kolar et al. 2021). The protctive actions of several antioxidants such as curcumin, quercetin, gallic acid, and alpha-lipoic acid were tested in the cell culture and animal experimental models.

During the oral presentation, I will discuss the most current studies on the BD models in the cell culture and experimental animal models. There are also genetic models for the induction of BD but I will not focus on the models in the presentation.

Key words: Bipolar disease; Mania; Oxidative stress; Open-field test.

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Oral Presentations

Oral Presentation 5

The increase of TRPM2 channel expression induces neuronal cell death and oxidative stress

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Calcium ion (Ca^{2+}) concentration is low inside of cells (50-100 nM) as compared to the outside of the cells (1-3 mM). Several physiological and neuronal factors such as muscle contraction, cell proliferation, and growth are induced by the Ca^{2+} influx. However, the excessive Ca^{2+} influx induces cell death and apoptosis via the activation of calcium channels. The excessive Ca^{2+} influx-mediated neuronal death is induced in several diseases, including the neurodegenerative diseases.

The involvements of voltage gated calcium and chemical channels on the Ca^{2+} influx in neuronal cells have been known for a long time. In addition to the well-known calcium channels, the new channel superfamily namely transient receptor potential (TRP) was discovered within last decades. The TRP superfamily contains 28 members in mammalian, and their activation and inhibition mechanisms are very different from the voltage gated calcium and chemical channels.

TRP melastatin 2 (TRPM2) is a subfamily member of the TRPs. The TRPM2 channel's protein structure consists of an enzyme (ADP-ribose pyrophosphatase) in the C domain (Nazıroğlu et al. 2020). When the enzyme is activated by oxidative stress and ADP-ribose, it causes a rise of excessive Ca^{2+} influx in the brain and neurons. The increased expression of TRPM2 channels also contributes to the rise in excessive Ca^{2+} influx. Numerous molecular pathways, including increases in the mitochondrial membrane potential and caspase (caspase-3, caspase-8, and caspase-9) activations are induced by the increased cytosolic free Ca^{2+} concentrations.

The apoptotic and neural death pathways are subsequently stimulated by the activations of molecular pathways. A new study found that the increases of TRPM2 expression levels were found in the apoptotic neuronal cells (An et al. 2019). Furthermore, it has been documented that a rise in TRPM2 expression caused neurons to death by necrosis, autophagy, and apoptosis (Shi et al. 2021). I will go over the rise in oxidative stress and neuronal cell death which are induced by TRPM2 channel expression in the oral presentation.

According to evidence from the most recent research, the induction of neuronal cell death and oxidative stress in the neurons depends critically on the upregulation of TRPM2 expression.

Key words: Apoptosis; Oxidative stress; Neurodegenerative diseases; TRPM2 channel.

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Oral Presentations

Oral Presentation 6

The apoptotic and oxidant actions of chloroquine in retina

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Retinopathy is a disorder, and it is induced by oxidant and apoptotic alterations. Chloroquine is an antimalarial drug, and it induces retinopathy. Although retinal damage is usually reversible, permanent damage, including the vision loss can occur under certain conditions. the retinal pigment epithelium (RPE) is a cell types of the eye. Chloroquine-induced maculopathy primarily affects the cells of RPE.

Apoptosis is a programmed cell death, and it is induced activation of several factors, including caspase and cytochrome c activations. Apoptosis is a physiological process, but its excessive induction induces several adverse actions, including vision lost. In the retina the apoptosis levels are affected by the treatment of chloroquine. In addition, the caspase activations such as caspase -3 in the retina cell line increased after the chloroquine treatment (Yoon et al. 2010).

Several metabolic processes, including the production of several reactive oxygen species (ROS), cause oxidative stress. The increased production of ROS causes negative effects in a variety of cells, including RPE cells. The excessive ROS production causes photoreceptor degeneration. It then results in permanent eyesight loss. Because the eye is exposed to environmental stimuli like light, oxygen, and ultraviolet radiation, several eye cells, including RPE cells, are extremely susceptible to the generation of ROS. The increased oxygen requirement of retinal cells makes the cells more vulnerable to ROS damage. It is well known that RPE cells from people with various eye diseases generate more ROS than healthy cells do (Zhou et al. 2021). Additionally, excessive ROS production causes the chloroquine's apoptotic effect in the eye (Nguyen et al. 2022). Therefore, this indicates that chloroquine treatment may involve oxidative stress-induced RPE cell damage. I will address the most recent research on the apoptotic and oxidative effects of chloroquine in the retina during the oral talk.

In summary, the accumulation data indicate that the treatment of chloroquine induces oxidative stress and apoptotic actions by the increase of ROS generation.

Key words: Apoptosis; Chloroquine; Oxidative stress; Retina.

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Oral Presentations

Oral Presentation 7

The diabetes mellitus-induced oxidative retinopathy is induced by the activation of TRPM2 channel

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Retinopathy, which is caused by the microvascular complication of diabetes mellitus (DM), causes blindness in people between the ages of 20 and 65 (Chang et al. 2022). Increases in mitochondrial membrane depolarization are induced by Ca^{2+} influx. Reactive oxygen species (ROS) production rises as a result of increased mitochondrial membrane depolarization, which triggers apoptosis and death in the retina and optic nerve. Continuous oxidative damage, the loss of retinal cells, and optic nerve fibers in DM patients result in optic nerve injury and vision problems. Although the presence of ROS plainly shows that mitochondria are involved in the development of DM-mediated retinopathy, the potential mechanisms and therapeutic options for DM-induced optic nerve damage are still unknown.

TRP melastatin 2 (TRPM2), a transient receptor potential (TRP) subfamily member, is stimulated by oxidative stress and DNA damage-induced ADP-ribose. The generation of ROS is common in many organs, including the retina, in DM patients. Through the activation of TRPM2, the excessive ROS production in turn caused excessive Ca^{2+} influx in the retinal tissue and cells (Meléndez García et al. 2016). Therefore, the Ca^{2+} influx and TRPM2 activation in mice's optic nerve were modulated by antioxidant treatments like selenium and resveratrol (Daldal and Nazıroğlu 2022). During the oral presentation, I will go over the most current studies on the Ca^{2+} influx and TRPM2 activation in the DM-induced retinopathy.

In conclusion, the accumulating results show that the activation of the TRPM2 channel causes the DM-induced oxidative retinopathy.

Key words: Diabetes mellitus; Oxidative stress; Retinopathy; TRPM2 channel.

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Oral Presentations

Oral Presentation 8

NLRX1 ligand, docosahexaenoic acid, ameliorates LPS-induced inflammatory hyperalgesia in mice by decreasing TRAF6/IKK/IkB-a/NF-kB signaling pathway activity

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The nucleotide-binding oligomerization domain-like receptor X1 (NLRX1) has been associated with various anti-inflammatory mechanisms (Sambra et al. 2021). We investigated whether the NLRX1 ligand docosahexaenoic acid (DHA) ameliorates lipopolysaccharide (LPS)-induced inflammatory hyperalgesia by interacting with tumor necrosis factor receptor-associated factor 6 (TRAF6)/inhibitor of κB (IκB) kinase (IKK)/IκB-a/nuclear factor-κB (NF-κB) signaling pathway in the central nervous system (Allen et al. 2011).

Reaction time to thermal stimuli within 30 seconds was measured in male mice injected with saline, lipopolysaccharide (LPS), and/or DHA after 6 hours using the hot plate test. Co-immunoprecipitation and immunoblotting studies were performed to determine activation of the TRAF6/IKK/IκB-a/NF-κB pathway in the brains and spinal cords of LPS-treated animals (Senol et al. 2021).

Latency to the thermal stimulus was reduced by 30% in LPS-injected endotoxemic mice compared with saline-injected mice. Treatment with DHA improved latency compared with endotoxemic mice. In the brain and spinal cord of LPS-injected mice, treatment with DHA also prevented the increase in the expression and/or activity of (1) IKKa/IKKβ, IKKγ, and K63 U in the NLRX1-immunoprecipitated tissues, (2) IKKa/IKKβ, K63 U, and K48 U in the IKKγ-immunoprecipitated tissues, and (3) IκB-α, NF-κB p65, and interleukin-1β associated with decreased IκB-α expression.

In conclusion, inhibition of IKK/IκB-a/NF-κB signaling by dissociation of NLRX1 from TRAF6 in response to LPS treatment may contribute to the protective effect of DHA against inflammatory hyperalgesia.

Keywords: lipopolysaccharide, inflammatory hyperalgesia, NLRX1, TRAF6/IKK/IκB-a/NF-κB signaling pathway, docosahexaenoic acid

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Oral Presentations

Oral Presentation 9

Hypericum perforatum, sciatic nerve injury, and TRPV1 channel

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Hypericum perforatum (St. John's wort) is a medical plant. The main constituents of Hypericum perforatum are hypericin, flavonoids and hyperforin, and their action pathways are unclear and likely multifunctional. Hypericum perforatum extract is traditionally used in the treatment of depression. The recent data indicated protective action of wound and nerve healing, including the sciatic nerve injury.

The sciatic nerve injury is induced by trauma of the nerve, and it results in symptoms like numbness, loss of muscle strength, and pain. In the etiology of sciatic nerve injury, the excessive reactive oxygen species (ROS) production and excessive Ca^{2+} influx have important roles (Yang et al. 2011).

The Ca^{2+} influx is induced by the stimulations of several channels such as chemical gated, voltage gated calcium channels, and also transient receptor potential (TRP) cation channels. The TRPV1 subfamily is activated by ROS. Recent data found that activation of TRPV1 channels contributed to rodent sciatic nerve damage (Ren et al. 2015; Uslusoy et al. 2017). However, sciatic nerve injury-induced injury, pain, and apoptosis were modulated by blockade of the channels (Ren et al. 2015; Uslusoy et al. 2017). It was also reported that the sciatic nerve injury-induced excessive Ca^{2+} influx and pain were decreased by treatment of Hypericum perforatum (Uslusoy et al. 2017). In the oral presentation, I will review recent studies of Hypericum perforatum on the TRPV1 channels in the sciatic nerve injury.

Keywords: Hypericum perforatum; Oxidative stress; Sciatic nerve injury; TRPM2.

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Oral Presentations

Oral Presentation 10

Recent developments in the experimental animal depression models

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Depression is a serious public disease problem with an alarming increase in incidence. Within 2021, the incidence of depression was predicted as 30-40% in the world. In addition, depression is one of the most general coexisting in patients with severe physical disorders such as cancer, cardiovascular, and neurological diseases. The coexisting depression induces a major negative action on the life quality in the patients. In addition, there is associated with limited success to medical treatment. The disease also requires huge amounts of healthcare expenditure (Arioz et al. 2022).

In experiments on depression, experimental animals like rabbits, mice, and rats are frequently utilized. As a result, they have been utilized for a while since animal brains function similarly to human brains. In addition, the management of the animals in the laboratory conditions is easy as compared to the big animals. The inductions of all symptoms and properties of neuropsychiatric disorders in the animals are difficult (Acikgoz et al. 2022). However, the animal models are adding great support to understanding the disease etiology and adding the development of drug treatments (Homberg 2013). Although the presence of disadvantages and controversial disadvantages of the animal models, there are many papers on depressed behavioral tests using rats and mice, and their numbers are growing.

As a result, I wanted to give an overview of the research on a number of depressive behavioral tests that have been utilized in the past and present in this presentation.

Key words: Depression; Mice; Rat; Stress.

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Oral Presentations

Oral Presentation 11

Involvement of TRP channels in the etiology of neurodegenerative disease

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Several diseases, including Alzheimer's disease (AD) and Parkinson's disease, are among the neurodegenerative disorders (PD). Over the past ten years, neurodegenerative disorders have become much more common. According to accumulating evidence, neurological disorders affect 2% of those over 65 each year. Free reactive oxygen species (ROS) are generated by a number of physiological activities, including phagocytosis and mitochondrial ATP generation, in the brain and neurons. The causes of the neurodegenerative disorders are not entirely known. However, increased ROS production triggers the development of neurodegenerative disorders including AD and PD (Braidy et al. 2021). Thus, it has been observed that a number of antioxidants play a protective effect in the treatment of AD in humans, experimental animals, and cell lines (Lee et al. 2021; Çınar and Nazıroğlu 2022).

A member of Ca^{2+} permeable cation channels is transient receptor potential (TRP) superfamily. TRP superfamily includes 28 members within six subgroups such as TRP vanilloid (TRPV), TRP canonical (TRPC), and TRP melastatin (TRPM). In addition to a variety of chemical, mechanical, and thermal stimuli, pH, osmolarity, and second messengers, TRP channels are activated by ROS (Braidy et al. 2021). By increasing the TRP channel activation in response to the excessive Ca^{2+} influx, ROS generations are increased. Eleven members of 28 TRP channels are activated by ROS. Numerous neurological conditions, including AD and PD, have been linked to TRP channels. With a particular emphasis on the recently discovered functional roles of oxidative stress-dependent activated TRP channels in neurodegenerative diseases connected to the disruption in Ca^{2+} homeostasis, I will concentrate on the most recent involvement of TRP channels.

The current literature data indicate that the stimulation of oxidative stress-dependent activated TRP channels such as TRPM2 and TRPV1 has a main role in the etiology of neurodegenerative diseases, although the inhibition of the channels acted therapeutic action in the diseases.

Key words: Alzheimer's disease; TRP channels; Oxidative stress; Parkinson's disease.

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Oral Presentations

Oral Presentation 12

Effects of angiotensin converting enzyme on oxidative parameters

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Oxidative stress in a biological system; It is defined as the disproportion between all antioxidants and free radicals or prooxidants in the system. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are byproducts of various cellular processes, including aerobic metabolism. For example, RNS nitric oxide (NO·) is produced from l-arginine by nitric oxide synthase and then reacts with superoxide (O_2·-) to form peroxynitrite. The ROS/RNS are highly reactive due to their unpaired valence electrons (Kükürt et al., 2021).

The renin-angiotensin-aldosterone system (RAS) is a powerful system that regulates fluid-electrolyte balance and systemic blood pressure. Renin is synthesized, stored and secreted from the juxtaglomerular in the kidneys. After secretion, renin acts on angiotensinogen, a plasma protein, to form angiotensin I (Ang I). Ang I is also converted to angiotensin II (Ang II) by angiotensin converting enzyme (ACE). Ang II causes oxidative stress by promoting the formation of superoxide species in a biological system (Guang et al., 2012). Ang II causes ROS/RNS production by stimulating membrane-bound nicotinamide adenine dinucleotide phosphate (NADPH) oxidase Ang II' The reduction of ACE2 to Ang 1-7 reduces oxidative stress as it inhibits NADPH oxidase and hence Ang II-induced ROS/RNT synthesis. Ang II stimulates the activation of NADPH oxidase, increases the expression of NADPH oxidase subunits and induces ROS formation in vascular smooth muscle cells, endothelial cells and fibroblasts. ACE2 reduces Ang II to Ang 1-7 and inhibits ROS synthesis and reduces oxidative stress (Baser et al., 2020).

In this presentation, current literature information about the effect of ACE on Oxidative Stress will be presented.

Keywords: Oxidative stress; Antioxidant; Angiotensin; Reactive oxygen species.

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Oral Presentations

Oral Presentation 13

Importance of Dopamine Gene Receptors (DRD1-DRD5) as Biomarkers for Neuroinflammatory Diseases

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Dopamine has an important effect on the motor pathways, neuroendocrine secretion, motivation, emotional behavior, emotions, and cognitive functions including working memory and learning, which play an essential role in the central nervous system. Dopamine is a modulatory neurotransmitter that affects learning, motor performance, and reward. Autism, schizophrenia, Parkinson's disease, and other neuropsychiatric illnesses have all been linked to imbalances or defects in the dopaminergic system. (Michael Post et al., 2021).

Recent studies on neuroinflammation have revealed that dopamine can act as a potent inflammatory agent within the central nervous system Mast cells, which contain dopamine within their secretory granules, may exhibit suppression, while mast cell activation results in dopamine depletion. Dopamine and its agonists have been reported to affect immune responses, including cytokine production (Huck et al., 2015). It has been discovered that dopamine suppresses systemic inflammation and inhibits the production of proinflammatory cytokines through DRD1 (Torres-Rosas et al., 2014). Dopamine exerts its effects by binding to dopamine receptors on the cell surface. At least five distinct subtypes of dopamine receptors exist, termed DRD1-DRD5 (Meredith et al., 2005).

This review aims to elucidate the roles of dopamine receptor genes in inflammatory activations in diseases characterized by neuroinflammation and the presence of pro-inflammatory molecules such as cytokines, chemokines, and reactive oxygen species.

Keywords: Dopamine, Neuroinflammation, Biomarker, Nervous system, Immune cells.

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Poster Presentations

Poster No, 1

Stem cell reprogramming therapy and effects for brain tumor microenvironment: An Expanded Review

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Processes known as stem cell reprogramming describe efforts to transform an adult cell into an induced pluripotent stem cell (iPSC) that has received attention in recent years. These studies result in a stem cell type that has the potential to develop into any cell type in the body system, such as embryonic stem cells. This transformation occurs by the incorporation of certain genes or proteins into the adult cell that reprograms it to become pluripotent. Also called the tumor microenvironment, this cell influences the actions and responses of Cancer stem cells (CSCs) by providing signals that promote self-renewal and survival. For example, CSCs can interact with immune cells and then release factors that suppress the immune response and promote tumor growth and the microenvironment can also promote the formation of blood vessels that deliver oxygen and nutrients specifically to the tumor and ultimately to its surroundings. Normal brain tissue can make it vulnerable to invasion. The increase in tumor volume means that waste is removed from the environment and can form secondary tumors (Dzobo et al., 2023).

Finally, this review highlights potential stem cell reprogramming and brain tumor microenvironment-centered theories currently under investigation.

Keywords: Tumor, Stem cell, Brain tumors, Tumor Microenvironment, Brain tissue.

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