Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i2.4579

CLINICAL SIGNIFICANCE OF SERC-A DYSFUNCTION: IMPLICATIONS FOR BRAIN FUNCTION IN ALZHEIMER'S DISEASE

Sadia Sohail[1*], Farheen Anjum[2], Dr. Muhammad Ismail Khan[3], Fatima Bibi[4], Rohma Rehman[5], Munazza Tariq[6]

[1*]Lecturer, Department of Psychology, National University of Modern Languages, Pakistan, Email: sadiasohail86@gmail.com
[2]Lecturer, Department of Psychology, Balochistan University of Information Technology Engineering and Management Sciences (BUITEMS), Quetta, Pakistan, Email: farheen.anjum@buitms.edu.pk
[3]Department of Zoology, Islamia College Peshawar, Pakistan, Email: ismail@icp.edu.pk
[4]MS Scholar, Shaheed Zulfikar Ali Bhutto Institute of Science and Technology, Islamabad, Pakistan, Email: Fatimayounas6@gmail.com
[5]Clinical Psychologist, Department of Clinical Psychology, Riphah International University, Lahore, Pakistan, Email: rohiir320@gmail.com
[6]Clinical Psychologist, Department of Clinical Psychology, Riphah International University, Lahore, Pakistan, Email: Munazzatariq90@gmail.com

***Corresponding author:** Sadia Sohail
*Lecturer, Department of Psychology, National University of Modern Languages, Pakistan, Email: sadiasohail86@gmail.com

Abstract:

Objective: This review aims to reevaluate the molecular mechanisms of sarcoendoplasmic reticulum Ca2+-dependent ATPase (SERC-A) in Alzheimer's disease and discuss the implications of calcium regulation, particularly in relation to vascular risk and the function of voltage-gated calcium channels.

Methods: We comprehensively analysed existing literature to understand the role of calcium regulation in Alzheimer's disease, focusing on the internal instability of calcium levels and its association with vascular risk. Special attention was given to the molecular mechanisms of SERC-A and the functional aspects of voltage-gated calcium channels.

Results: The prevalence of Alzheimer's disease is influenced by various factors, collectively disrupting normal neuronal functions. Internal instability of calcium levels emerges as a significant factor, with a notable connection to increased vascular risk – a condition prevalent in individuals affected by Alzheimer's disease. This review highlights the molecular intricacies of SERC-A in the disease context and provides insights into the functional significance of voltage-gated calcium channels.

Conclusion: Understanding the regulatory mechanisms of calcium, specifically the role of SERC-A and voltage-gated calcium channels, holds clinical relevance. The irregular function of SERC-A has been implicated in diverse alterations of brain function. Insights from this review may open new

avenues for therapeutic alternatives targeting calcium dysregulation in Alzheimer's disease, providing potential interventions to address the underlying causes of neuronal dysfunction.

Keywords: Alzheimer's Disease; Calcium-Transporting ATPases; Calcium Metabolism Disorders; N-Methyl-D-Aspartate Receptor; Endoplasmic Reticulum.

INTRODUCTION:

Alzheimer's disease is the most common cause of human dementia, especially in people over the age of 60. Currently, more than 46 million people worldwide suffer from Alzheimer's disease, and it is estimated that by 2050, this number will increase to more than 131 million (Collins, Zhang, & Chatham, 2022).

This disease is due to the progressive loss of neurons in different brain parts. This causes neurological atrophy, mainly of the hippocampus, cortical and limbic structures, and pathological changes that can only be evaluated post-mortem. Many factors intervene in the onset of this disease, especially if they make it difficult for normal neuronal functions, such as vascular accidents, prolonged stressful conditions or lack of external reinforcing stimuli in learning (Walters & Usachev, 2023).

There are also environmental factors that can cause abnormalities in the cytoskeleton (colchicine, lead genotoxicity, etc.) or endocrine elements associated with sexual expression since women have a higher prevalence; in addition to age, since it appears in 50% of cases of people over 80 and 15% of those between 65 and 80 (Peters et al., 2022).

Alzheimer's disease is, therefore, not an entity that a single anomalous event can explain. Still, it results from the conjunction between extrinsic factors, such as those already mentioned, and intrinsic alterations of the β-amyloid protein (Aβ).) (not in all cases), the accumulation of protein aggregates on the myelin sheaths or the nerve nuclei, the processes associated with the inflammatory cascade, the oxidative neuronal damage due to mitochondrial dysfunction, the protein alterations of the Tau molecule, the formation of tangles neurofibrillary, synaptic failure and neurotransmitter depletion, as well as autosomal dominant inheritance of apolipoprotein E allele 4 (APOE$^{\varepsilon}$4) and mutations in amyloid precursor proteins (APP) and presenilin-1 and 2; everything was correlated with cases of early familial Alzheimer's disease (Sharma et al., 2023).

In any case, the clinical manifestation of the disease is associated with a complex neurodegenerative progression that produces memory impairment and loss of other cognitive and non-cognitive processes. In general, several neurological disorders, including Parkinson's and Alzheimer's, are linked by incidence to cardiovascular alterations. Still, the molecular elements correlated between the two processes have not been adequately delineated, although Ca2+-mediated osmotic alterations after those above are mentioned alterations (Sun et al., 2023).

Therefore, cellular instability of calcium levels is associated with increased vascular risk. Its regulation opens up a wide range of treatments for kidney disease, transplantation, and heart problems. However, little is currently known about calcium regulation before and during Alzheimer's disease and whether it is related to irrigation vascularization (Zampese et al., 2022).

In this work, the molecular mechanisms of Ca2+ regulation during Alzheimer's disease are examined to establish whether ATPases, particularly Ca2+-dependent sarcoendoplasmic reticulum (SERC-A), could be a possible therapeutic target for treatment (Takenaka et al., 2023b).

Calcium As A Regulator Of Synaptic Potential:

The neuronal function begins with the emission and reception of signals propagating across the cell membrane due to changes in plasma permeability. As a result, an electrical potential develops and propagates throughout the entire presynaptic neuron until the release of chemical signals in the gap or synapse, which allows the transition of the signal to the dendritic terminals of the postsynaptic neuron, where the receivers of these signals are (Yamasaki et al., 2023).

During this process, the arrival of an action potential at the presynaptic terminal induces depolarization of the membrane in that area, which causes the opening of voltage-gated Ca2+ channels, the N-methyl-D-aspartate receptors (NMDARs) and Alpha 7, nicotinic acetylcholine receptors (nAChR); generating the concentration of Ca2+ cytosolic concentration of resting neurons, which varies from 50 to 300 nM, increases up to the order of µM in the active zone for a few microseconds (Berna-Erro et al., 2023; Yadav, Narayanasamy, & Aradhyam, 2023).
This sudden increase is necessary to synchronize neurotransmitter release in the presynaptic cleft. Therefore, to recover the resting potential, it is necessary to reduce the cytosolic Ca2+ level again, requiring the action of Ca2+ pumps such as the plasma membrane Na+/Ca2+ pump (NCX) and the plasma membrane C2+ ATPase (PMCA). It is also possible to sequester the excess ion in the lumen of the endoplasmic reticulum using pumps that use ATP to capture Ca2+ in these intracellular stores until the pre-release potential is reached (Figure 1) (Zhang et al., 2022).
Although Ca2+ pumps have a low concentration in nerve cells, they play a fundamental role in their metabolism and physiology, controlling processes that depend on the amplitude, frequency and subcellular localization of Ca2+ signals, such as neuronal plasticity, nervous impulse, neuronal aging or apoptosis. Many neurological diseases, including Alzheimer's disease, lead to alterations in Ca2+ homeostasis or deficiencies in the functioning of the pumps (Takenaka et al., 2023a).

CA2+-TRANSPORTING ATPASES AND THEIR ROLE IN DEGENERATIVE NEUROPATHIES:

Capacitive Ca2+ influx is essential for Ca2+ homeostasis. Maintains adequate and functional concentrations in the lattice endoplasmic. Therefore, this organelle is the primary cellular calcium reservoir, which enables sustained signaling through ion mobilization. Capacitive Ca2+ entry is based on a feedback mechanism activated by the decrease in Ca2+ within the endoplasmic reticulum, which triggers its entry across the plasma membrane (Pereira et al., 2022).

Stromal interaction molecules and the expression product of the Orai1 gene, a structural protein of the calcium-selective ion channel activated by calcium release 1, are the leading players in the capacitive influx of Ca2+. A stromal interacting molecule detects the contents of Ca2+ within the endoplasmic reticulum and, when it decreases, activates transcription of Orai1, which results in a calcium channel operated by intracellular stores in the plasma membrane. The final destination of the incoming Ca2+ is not the cytosol but the endoplasmic reticulum, which is filled with it very efficiently. The lattice Ca2+ ATPasethe sarcoendoplasmic (SERC-A) is the third element of the capacitive Ca2+ input, which is tightly coupled. The proximity between the intracellular stores and SERC-A promotes the rapid pumping of Ca2+ from the Ca2+-rich microdomains generated in the cytoplasmic mouth of the intracellular stores towards the endoplasmic reticulum (Figure 1) (Ousingsawat et al., 2023).

Ca2+-transporting ATPases have high affinity and are responsible for active ion transport at the expense of ATP hydrolysis in several cell membranes. Three families have been identified: sarcoendoplasmic reticulum Ca2+-ATPase (SERC-A), plasma membrane Ca2+-ATPase (PMCA), and secretory pathway Ca2+-ATPase (SPCA), as well as other family members specialized in of H+/K+, Na+/K+ ions (Rajeev et al., 2022).

SERC-A is an amphiphilic protein integrated into the membranes of the sarcoendoplasmic reticulum, which transports two Ca2+ ions from the cytoplasm to the lumen of these compartments, using the hydrolysis energy of ATP in the presence of Mg2+. This protein has been identified and first purified in the sarcoplasmic reticulum of skeletal muscle, where the SERC-A1 isoform is found. This constitutes 90% of total membrane proteins and plays a significant role in muscle contraction or relaxation, although numerous other isoforms have been described in different tissues over time (Aluja, Delgado-Tomás, Ruiz-Meana, Barrabés, & Inserte, 2022; Rieder, 2023).

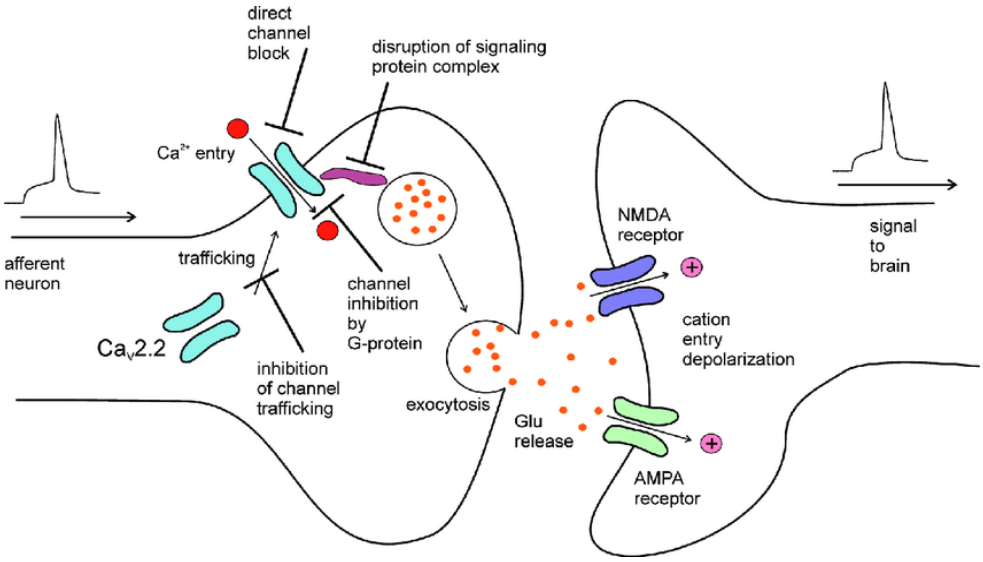


Figure 1. *Calcium as a regulator of synaptic potential*

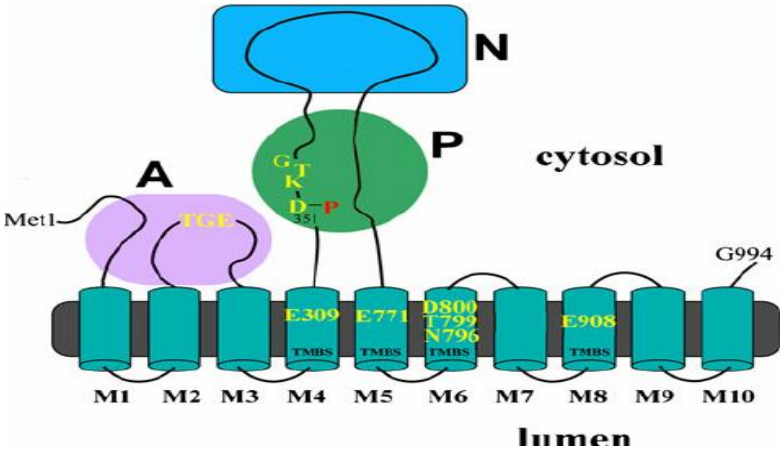
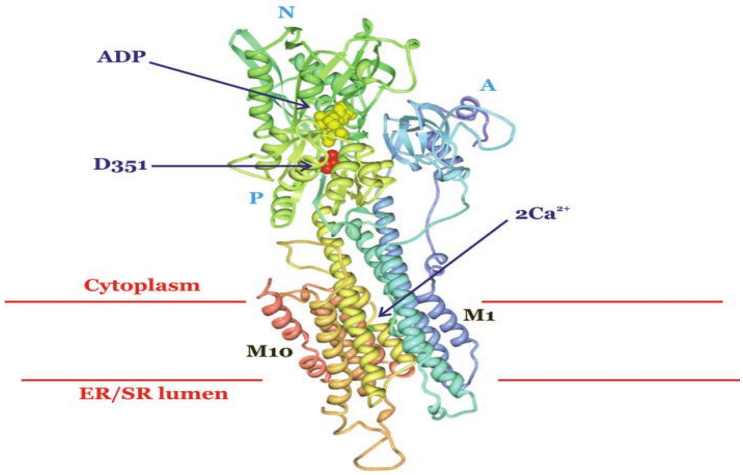


Figure 2. *The Ca2+-ATPase of the sarcoendoplasmic reticulum. A) Schematic representation of the structure of SERC-A, showing the numbered transmembrane segments, the catalytic domain, and the N and C termini for the different isoforms.*



B) Three-dimensional model of the SERC-A1.

The protein comprises approximately 1,000 amino acids with a molecular weight of 110 kDa. It has the N-terminal and C-terminal ends towards the cytoplasm (SERC-A1, 2a and 3); occasionally, the C-terminus is oriented towards the lumen (SERC-A2b), has 10 (SERC-A1, 2a and 3) to 11 (SERC-A 2b) transmembrane domains. These transmembrane domains, which also constitute the calcium

channel, have a globular head consisting of two cytoplasmic domains, one of which is the catalytic domain, where there is an aspartic acid residue that is phosphorylated during activation and the ATP binding site (figure 2) (Ferrer, 2022).
Isoforms 1, 2, and 3 are produced by three highly conserved genes located on different chromosomes that, in addition, generate further diversity through alternative processing of messenger RNAs from three domains located at the COOH terminus (Yamasaki et al.).
Up to 10 SERC-A isoforms have been identified at the protein level with high tissue and developmental stage specificity. The SERC-A1 isoform is specific to adults, while the B form is specific to newborns; both differ in their C-terminal region. They are specific to fast-twitch skeletal muscle, contributing to the Ca2+ flux involved in muscle contraction or relaxation; SERC-A1a makes up 90% of the total proteins in skeletal muscle. These variants are encoded by the ATP2A1 gene located in the chromosomal region 16p12(MacLeod, 2023).
Autosomal recessive mutations in the ATP2A1 gene have been associated with Brody disease in humans, a rare inherited myopathy characterized by a detrimental increase in skeletal muscle relaxation during exercise, resulting in stiffness and cramps. Surprisingly, ataxia associated with Alzheimer's disease has similar symptomatology (Michalak, 2023; Nakamura et al., 2023).
SERC-A2b is the main isoform of nervous tissue, although it is also present in smooth muscle and non-muscle tissues such as skin. Autosomal dominant mutations are associated with Darier disease in humans, a skin disease characterized by loss of adhesion between epidermal cells and abnormal keratinization. Neuropsychiatric problems such as epilepsy, schizophrenia, bipolar disorder and depression have also been described in some families affected by this disease (Li et al., 2024).
It is striking that mRNAs generated by alternative intron recombination for the SERC-A2a isoform are much less stable than their counterparts in muscle tissue, so the calcium transport system is assumed to be much more sensitive in nervous tissue. On the other hand, decreased expression of this channel induces neuropathic pain. Inhibition of the channel causes neuronal hyperexcitation, nerve injury, endoplasmic reticulum stress, activation of satellite glial cells, and mechanical allodynia (pain due to ordinarily non-painful stimuli). Therefore, SERC-A2b activators have the potential to treat neuropathic pain (Irnaten & O'Brien, 2023; Šeflová, Cruz-Cortés, Guerrero-Serna, Robia, & Espinoza-Fonseca, 2023).
The most important thing about this proposal is that overexpression of SERC-A-2b after chronic constriction injury produces long-term relief of mechanical and thermal allodynia, accompanied by morphological and functional restoration of nervous tissue by relieving endoplasmic reticulum stress; therefore, its use in Alzheimer's disease would allow, at least partially, functional neurological recovery (Ednie, Paul-Onyia, & Bennett, 2023; Mitronova et al., 2023).

Therapeutic strategy for Alzheimer's disease based on SERC-A regulation:

Decreased Ca2+ concentration in the endoplasmic reticulum has been established as a significant cause of stress-induced apoptosis in the endoplasmic reticulum. Although several data demonstrate that Aβ influences Ca2+ homeostasis, emerging data suggest that Ca2+ stores in the endoplasmic reticulum are significantly involved in Aβ production and tau phosphorylation during AD. Unfortunately, there is currently no cure for Alzheimer's disease (Sun et al., 2023; Yu et al., 2023).
The only approved treatments are neurotransmitter modulators, consisting of cholinesterase inhibitors and the N-methyl-D-aspartate receptor antagonist, memantine. While these treatments target the symptoms of Alzheimer's disease and can provide relief and comfort to patients, they do not stop the progression of the disease itself. The one feature that has consistently been linked to the progression of dementia is the loss of neurons in the brains of Alzheimer's disease patients (MacNeil, 2023).

The brains of people suffering from Alzheimer's disease show three times fewer neurons in the hippocampus than the brains of those who do not have this alteration before the age of fifty (Hussey, Limpitikul, & Dick, 2023).
Therefore, there is a clear need for treatments that can target this mechanism of Alzheimer's disease progression. The ability of the SERC-A allosteric activator, CDN1163, to alleviate parkinsonian

akinesia in rats has recently been reported, and convincing efficacy has been reported in the transgenic mouse model for the amyloid precursor protein and for presenilin-1 (APP /PS1), with Alzheimer's disease. Both proteins are involved in the secretion of the gamma complex and the production of Aβ in response to endoplasmic reticulum stress, which also induces an inflammatory reaction related to the pathogenesis of various diseases. SERC-A gene therapy has recently alleviated endoplasmic reticulum stress in several animal models (Alvarez, Jafri, & Ullah, 2023; Takenaka et al., 2023b).

The stress above induces the folding modification of numerous proteins, resulting in immediate reactions in cellular phosphorylation patterns and subsequent changes in the expression of hundreds of target genes. The purpose of these adaptive effects is to restore cellular homeostasis, or at least try to. However, if the stress caused is prolonged, the modification of the folding of several proteins can trigger the apoptotic cell death program within the cell, which, in the case of neurons, even precedes the accumulation of Aβ and is directly related to the proinflammatory signalling. In any case, the affected pathway begins with SERC-A and ends with two neuronal death pathways (Hamilton et al., 2023).

Increased SERC-A activity maintains calcium in the endoplasmic reticulum and, therefore, its function despite stressors. Furthermore, SERC-A activation can sequester more cytosolic Ca2+ and prevent mitochondrial signaling-induced apoptosis. All these factors suggest that pharmacological activation of SERC-A will significantly impact the treatment of Alzheimer's disease (Hansen, 2023). This has already been tested in CSM14.1 cell lines obtained from striatal progenitor neurons of rats previously treated with thapsigargin, a known inducer of endoplasmic reticulum stress that unloads luminal deposits in the endoplasmic reticulum via specific inhibition of SERC.-TO. Pretreatment with the quinoline-amide compound CDN11163, a drug that induces SERC-A activity, demonstrated the ability to rescue cells from the apoptotic process by restarting ATPase function (Seitz et al., 2023).

This result was also obtained in HEK, HeLa and BMGK cells exposed to thapsigargin and hydrogen peroxide as inducers of endoplasmic reticulum stress when using CDN1163. Similarly, providing the drug to SERC-A mutant rats, which initially accelerated Ca2+ loss due to excitotoxicity induced by glutamate (a neurotransmitter that stimulates NMDA channels), it was possible to attenuate endoplasmic reticulum stress due to exhaustion of the ion(Nikiforova et al., 2023)

Therefore, the therapeutic strategy is clear: activation of SERC-A with CDN1163 or similar will replenish Ca2+ stores, alleviating endoplasmic reticulum stress and effectively rescuing neurons damaged from apoptosis(Enrich, Lu, Tebar, Rentero, & Grewal, 2023), (Osman, Speigel, Patel, & Hemmings, 2023).

CONCLUSION:

Stress caused by a deregulation of Ca2+ levels in the endoplasmic reticulum of neurons causes their apoptosis, which is why it is a determining factor associated with Alzheimer's disease. Therefore, stimulation of the Ca2+-dependent ATPase of the sarcoendoplasmic reticulum (SERC-A) could represent a possible therapeutic target in this disease, reducing Ca2+ levels in the cytosol of hippocampal neurons.

REFERENCES:

1. Aluja, D., Delgado-Tomás, S., Ruiz-Meana, M., Barrabés, J. A., & Inserte, J. (2022). Calpains as Potential Therapeutic Targets for Myocardial Hypertrophy. International Journal of Molecular Sciences, 23(8), 4103.
2. Alvarez, J. A. E., Jafri, M. S., & Ullah, A. (2023). Local Control Model of a Human Ventricular Myocyte: An Exploration of Frequency-Dependent Changes and Calcium Sparks. Biomolecules, 13(8), 1259.
3. Berna-Erro, A., Ramesh, G., Delgado, E., Corbacho, A. J., Ferrer-Marín, F., Teruel, R., . . . Redondo, P. C. (2023). CAPN1 (Calpain1)-Dependent Cleavage of STIM1 (Stromal Interaction Molecule 1) Results in an Enhanced SOCE (Store-Operated Calcium Entry) in Human Neonatal Platelets. Arteriosclerosis, Thrombosis, and Vascular Biology, 43(5), e151-e170.

4. Collins, H. E., Zhang, D., & Chatham, J. C. (2022). STIM and orai-mediated regulation of calcium signaling in age-related diseases. Frontiers in Aging, 3, 876785.
5. Ednie, A. R., Paul-Onyia, C. D., & Bennett, E. S. (2023). Reduced O-GlcNAcylation diminishes cardiomyocyte Ca2+ dependent facilitation and frequency dependent acceleration of relaxation. Journal of Molecular and Cellular Cardiology, 180, 10-21.
6. Enrich, C., Lu, A., Tebar, F., Rentero, C., & Grewal, T. (2023). Ca2+ and Annexins–Emerging Players for Sensing and Transferring Cholesterol and Phosphoinositides via Membrane Contact Sites Cholesterol and PI (4, 5) P2 in Vital Biological Functions: From Coexistence to Crosstalk (pp. 393-438): Springer.
7. Ferrer, B. J. (2022). Structural and Biophysical Investigation of Calmodulin Binding to the Third Domain of Human Prp40a. Vanderbilt University.
8. Hamilton, S., Terentyeva, R., Veress, R., Perger, F., Nichtova, Z., Martin, B., . . . Terentyev, D. (2023). Ryanodine receptor hyperactivity promotes mitochondrial dysfunction via calpain-dependent OPA1 proteolysis. Biophysical Journal, 122(3), 378a.
9. Hansen, M. S. H. (2023). Calcium dependent arrhythmia mechanisms in CPVT and ischemia-reperfusion.
10. Hussey, J. W., Limpitikul, W. B., & Dick, I. E. (2023). Calmodulin Mutations in Human Disease. Channels, 17(1), 2165278.
11. Irnaten, M., & O'Brien, C. J. (2023). Calcium-Signalling in Human Glaucoma Lamina Cribrosa Myofibroblasts. International Journal of Molecular Sciences, 24(2), 1287.
12. Li, R.-l., Zhuo, C.-l., Yan, X., Li, H., Lin, L., Li, L.-y., . . . Liu, L.-l. (2024). Irisin attenuates vascular remodeling in hypertensive mice induced by Ang II by suppressing Ca2+-dependent endoplasmic reticulum stress in VSMCs. International Journal of Biological Sciences, 20(2), 680.
13. MacLeod, K. T. (2023). Changes in cellular Ca2+ and Na+ regulation during the progression towards heart failure. The Journal of Physiology, 601(5), 905-921.
14. MacNeil, E. K. (2023). Ca2+-dependent inactivation of a neuronal Ca2+ channel is regulated by intracellular Ca2+ handling.
15. Michalak, M. (2023). Calreticulin: Endoplasmic reticulum Ca2+ gatekeeper. Journal of Cellular and Molecular Medicine.
16. Mitronova, G. Y., Quentin, C., Belov, V. N., Wegener, J. r. W., Kiszka, K. A., & Lehnart, S. E. (2023). 1, 4-Benzothiazepines with Cyclopropanol Groups and Their Structural Analogues Exhibit Both RyR2-Stabilizing and SERCA2a-Stimulating Activities. Journal of Medicinal Chemistry, 66(23), 15761-15775.
17. Nakamura, J., Maruyama, Y., Tajima, G., Hayakawa, S., Suwa, M., & Sato, C. (2023). Ca2+ Dependent Formation/Collapse of Cylindrical Ca2+-ATPase Crystals in Scallop Sarcoplasmic Reticulum (SR) Vesicles: A Possible Dynamic Role of SR in Regulation of Muscle Contraction. International Journal of Molecular Sciences, 24(8), 7080.
18. Nikiforova, A. B., Baburina, Y. L., Borisova, M. P., Surin, A. K., Kharechkina, E. S., Krestinina, O. V., . . . Kruglov, A. G. (2023). Mitochondrial F-ATP Synthase Co-Migrating Proteins and Ca2+-Dependent Formation of Large Channels. Cells, 12(19), 2414.
19. Osman, V., Speigel, I., Patel, K., & Hemmings, H. C. (2023). Isoflurane alters presynaptic endoplasmic reticulum calcium dynamics in wild-type and malignant hyperthermia-susceptible rodent hippocampal neurons. Eneuro, 10(8).
20. Ousingsawat, J., Talbi, K., Gómez-Martín, H., Koy, A., Fernández-Jaén, A., Tekgül, H., . . . Kunzelmann, K. (2023). Broadening the clinical spectrum: molecular mechanisms and new phenotypes of ANO3-dystonia. Brain, awad412.
21. Pereira, A. C., De Pascale, J., Resende, R., Cardoso, S., Ferreira, I., Neves, B. M., . . . Morais, S. (2022). ER-mitochondria communication is involved in NLRP3 inflammasome activation under stress conditions in the innate immune system. Cellular and Molecular Life Sciences, 79(4), 213.
22. Peters, E. C., Gee, M. T., Pawlowski, L. N., Kath, A. M., Polk, F. D., Vance, C. J., . . . Pires, P. W. (2022). Amyloid-β disrupts unitary calcium entry through endothelial NMDA receptors in mouse cerebral arteries. Journal of Cerebral Blood Flow & Metabolism, 42(1), 145-161.

23. Rajeev, P., Singh, N., Kechkar, A., Butler, C., Ramanan, N., Sibarita, J.-B., . . . Nair, D. (2022). Nanoscale regulation of Ca2+ dependent phase transitions and real-time dynamics of SAP97/hDLG. nature communications, 13(1), 4236.
24. Rieder, P. (2023). Glial Ca2+ signaling in the spinal cord and the myelin-protective effect of the GABAb receptor in oligodendrocyte precursor cells.
25. Šeflová, J., Cruz-Cortés, C., Guerrero-Serna, G., Robia, S. L., & Espinoza-Fonseca, L. M. (2023). Mechanisms for cardiac SERCA activation by its substrate and a synthetic allosteric modulator using fluorescence lifetime imaging. PNAS nexus, pgad453.
26. Seitz, A., Busch, M., Kroemer, J., Schneider, A., Simon, S., Jungmann, A., . . . Ritterhoff, J. (2023). S100A1′ s single cysteine is an indispensable redox-switch for the protection against diastolic calcium leakage in cardiomyocytes. bioRxiv, 2023.2009. 2001.555853.
27. Sharma, A., Sari, E., Lee, Y., Patel, S., Brenner, M., Marambaud, P., & Wang, P. (2023). Extracellular CIRP Induces Calpain Activation in Neurons via PLC-IP3-Dependent Calcium Pathway. Molecular Neurobiology, 60(6), 3311-3328.
28. Sun, C.-C., Lee, S.-Y., Chen, L.-H., Lai, C.-H., Shen, Z.-Q., Chen, N.-N., . . . Chiu, W.-T. (2023). Targeting Ca2+-dependent pathways to promote corneal epithelial wound healing induced by CISD2 deficiency. Cellular Signalling, 110755.
29. Takenaka, M., Kodama, M., Murayama, T., Ishigami-Yuasa, M., Mori, S., Ishida, R., . . . Iino, M. (2023a). Screening for novel RyR2 inhibitors by ER Ca2+ monitoring. bioRxiv, 2023.2008. 2021.553510.
30. Takenaka, M., Kodama, M., Murayama, T., Ishigami-Yuasa, M., Mori, S., Ishida, R., . . . Iino, M. (2023b). Screening for Novel Type 2 Ryanodine Receptor Inhibitors by Endoplasmic Reticulum Ca2+ Monitoring. Molecular Pharmacology, 104(6), 275-286.
31. Walters, G. C., & Usachev, Y. M. (2023). Mitochondrial calcium cycling in neuronal function and neurodegeneration. Frontiers in cell and developmental biology, 11, 1094356.
32. Yadav, M. P., Narayanasamy, S., & Aradhyam, G. K. (2023). Structural Plasticity Allows Calumenin-1 to Moonlight as a Ca2+-Independent Chaperone: Pb2+ Enables Probing Alternate Inhibitory Conformation. Biochemistry.
33. Yamasaki, E., Thakore, P., Ali, S., Sanchez Solano, A., Wang, X., Gao, X., . . . Earley, S. (2023). Impaired intracellular Ca2+ signaling contributes to age-related cerebral small vessel disease in Col4a1 mutant mice. Science Signaling, 16(811), eadi3966.
34. Yamasaki, E., Thakore, P., Ali, S., Solano, A. S., Wang, X., Gao, X., . . . Earley, S. Defective Ca2+-dependent activation of TRPM4 channels contributes to age-related cerebral small vessel disease in Col4a1 mutant mice.
35. Yu, W., Zhang, Q., Qiu, Y., Chen, H., Huang, X., Xiao, L., . . . Tong, X. (2023). CDN1163 alleviates SERCA2 dysfunction-induced pulmonary vascular remodeling by inhibiting the phenotypic transition of pulmonary artery smooth muscle cells. Clinical and Experimental Hypertension, 45(1), 2272062.
36. Zampese, E., Wokosin, D. L., Gonzalez-Rodriguez, P., Guzman, J. N., Tkatch, T., Kondapalli, J., . . . Rizzuto, R. (2022). Ca2+ channels couple spiking to mitochondrial metabolism in substantia nigra dopaminergic neurons. Science Advances, 8(39), eabp8701.
37. Zhang, L., Au-Yeung, C.-L., Huang, C., Yeung, T.-L., Ferri-Borgogno, S., Lawson, B. C., . . . Thomas, V. (2022). Ryanodine receptor 1-mediated Ca2+ signaling and mitochondrial reprogramming modulate uterine serous cancer malignant phenotypes. Journal of Experimental & Clinical Cancer Research, 41(1), 1-20.