Brief information about the project

Name of the project	AP19680470 «"Involvement of phosphoinositol diphosphate (PIP2) and Kv7 potassium channels in the regulation of hyperexcitation in an epileptic model"» (government registration № 0123PK00428).
Relevance	The problem is that pathological bursts of hyperexcitation cause neuronal death and are observed in epilepsy and a number of other neurodegenerative processes. The nature of the key ion channels involved in the generation of periodic bursts of hyperexcitation and their regulation are unknown. The mechanisms of the relationship between metabotropic receptor activity and brain electrical activity in epilepsy have not been established at present. The idea behind the project is that low-threshold Kv7 channels are the link between calcium signalling and hyperexcitation, as they are controlled not only by electrical potential but also by the natural ligand phosphoinositol diphosphate. This makes it possible to activate Kv7 channels and suppress hyperexcitation using receptors conjugated to PLC and PI3K that regulate PIP2 levels.
Purpose	The aim of the project is to elucidate the role of PLC and PI3K-conjugated receptors in the regulation of Kv7 family potassium channels and the possibility of using the PIP2-Kv7 signalling pathway to suppress hyperexcitation in epilepsy.
Objectives	1. Identify the role of potassium channels of Kv7 family in the regulation of frequency and duration of action potential bursts during hyperexcitation during epileptiform activity in rat hippocampal neuronal network. 2. Show the effect of direct Kv7 activators and inhibitors on parameters of synchronous bundle activity and Ca2+ impulses in control and epileptiform neurons. 3) Determine the effect of Kv7 channels on electrical and calcium signal parameters during transition of hippocampal neurons to synchronous epileptic activity induced by GABA(A)-dependent inhibition attenuation. 4. To record changes in parameters of synchronous pacing activity and Ca^{2+} impulses during direct inhibitors and activators of PLC and PI3K that regulate PIP2 levels. 5. To record changes in parameters of synchronous kidney activity and Ca^{2+} impulses under the action of PLC and PI3K receptor agonists that change the level of PIP2. Show that activators and inhibitors of PIP2 levels control the process of hyperexcitation in the brain by regulating Kv7 activity. 6. Study neuroprotective effect of Kv7 channel activators. Show that neuroprotective effect of Kv7 channels is due to earlier termination of action potential bundles in neurons during epileptiform activity.
Expected and achieved results	The project will demonstrate the involvement of Kv7 family potassium channels in the regulation of the frequency and duration of action potential bursts during hyperexcitation during epileptiform activity induced by abolition of GABA(A)-dependent inhibition. The role of PLC and PI3K-conjugated receptors in PIP2-dependent regulation of Kv7, hyperexcitation generation and termination will be demonstrated. It will be shown that the neuroprotective effect of Kv7 channel activators is due to earlier termination of PDS clusters and calcium pulses.
Research team members with their	Project Manager: Tussupbekova Gulmira Ablaevna Candidate of Medical Sciences, Associate Professor; Senior Researcher; h=3;

identifiers (Scopus Author ID, Researcher ID, ORCID, if available) and links to relevant profiles	Researcher ID Web of Science: GEK-6286-2022; ORCID: https://orcid.org/0000-0001-9379-4687; Scopus Author ID: 57201525842. Members of the research team: 1. Tuleukhanov Sultan Tuleukhanovich Doctor of Biology, Professor, Corresponding Member of the National Academy of Sciences of the Republic of Kazakhstan, Academician of the National Academy of Sciences of Higher School of Kazakhstan; Head of the Laboratory of Biophysics, Chronobiology and Biomedicine, CS; h-index=7; Researcher ID Web of Science: DZT-2440-2022; ORCID: https://orcid.org/0000-0002-9898-0507; Scopus author ID: 52964678500. 2. Orazova Saltanat Bolatovna, Candidate of Biological Sciences, Senior Researcher; h-index=4; ResearcherID Web of Science: P-7854-2014 ORCID: https://orcid.org/0000-0003-4380-2460; Scopus author ID: 6505619573. 3. Kenzheeva Zhanar Kuralbaevna PhD, Researcher; ResearcherID Web of Science: GBU-3166-2022 ORCID: https://orcid.org/0000-0002-0890-8035; Scopus author ID: 57330878300. 4. Kairat Bakytzhan Kairatuly Researcher; Researcher ID Web of Science: AAF-2100-2019; ORCID: https://orcid.org/0000-0003-1742-2667 Scopus author ID: 58317238000. 5. Malibayeva Araylym Erzhankyzy PhD student, Junior Researcher; h=1; ResearcherID Web of Science: DFN-8696-2022; ORCID: https://orcid.org/0000-0002-4759-9087; Scopus Author ID: 57219195116. 6. Abu Nurila Bauyrzhankyzy, Master of Pedagogical Sciences, Junior Researcher. 7. Sattigulova Zanzamgul M.S. in engineering, laboratory assistant.
List of publications with links to them	1. Zinchenko V.P.; Kosenkov A.M.; Gaidin S.G.; Sergeev, A.I.; Dolgacheva L.P.; Tuleukhanov S.T. (2021) Properties of GABAergic Neurons Containing Calcium-Permeable Kainate and AMPA-Receptors. Life 2021, Volume 11 , Issue 12, 1309. Индекс цитирования -1, Q2 IF: 3.253, Процентиль – 41%, https://doi.org/10.3390/life11121309 . 2. Ossikbayeva S., Khanin M., Sharoni Y., Trachtenberg A., Tuleukhanov S., Sensenig R., Rom S., Danilenko M., Orynbayeva Z. (2021) Curcumin and Carnosic Acid Cooperate to Inhibit Proliferation and Alter Mitochondrial Function of Metastatic Prostate Cancer Cells. Antioxidants (Basel, Switzerland), 10(10), 1591. Индекс цитирования – 6, Q1 IF: 7.675, Процентиль – 85 %, https://doi.org/10.3390/antiox10101591 . 3. Shapovalov, Y.A., Gladyshev, P.P., Tuleukhanov, S.T., Shvetsova, E.V., Abdrasulova, Z.T. Radicals in Cellular Structures// Biophysics (Russian Federation) 2020, 65(4), pp. 587–598. Индекс цитирования – 0, Q4 IF 0,520, Процентиль - 14%, DOI: https://doi.org/10.1134/S000635092004020X .. 4 Dolgacheva L.P., Tuleukhanov S.T., Zinchenko V.P. Participation of Ca2+-Permeable AMPA Receptors in Synaptic Plasticity//Biologicheskie Membrany, 2020, 37(3), pp. 175–187. Индекс цитирования-0. Q4 IF 0,141, Процентиль-4%, DOI: 10.1016/j.tins.2007.01.006.

	5. Zinchenko V.P., Gaidin S.G., Teplov I.Yu, Kosenkov A.M., Sergeev A.I., Dolgacheva L.P., and Tuleuhanov S.T. Visualization, Properties, and Functions of GABAergic Hippocampal Neurons Containing Calcium-Permeable Kainate and AMPA Receptors Biochemistry (Moscow), Supplement Series A: Membrane and Cell Biology, 2020, Vol. 14, No. 1, pp. 44–53. Индекс цитирования -1, Q4 IF 0,694, Процентиль – 19%, DOI: https://doi.org/10.1134/S1990747820010109 6. Gaidin, S.G., Zinchenko, V.P., Teplov, I.Y., Tuleukhanov, S.T., & Kosenkov, A.M. (2019). Epileptiform activity promotes decreasing of Ca2+ conductivity of NMDARs, AMPARs, KARs, and voltage-gated calcium channels in Mg2+-free model. Epilepsy research, 158, 106224. Индекс цитирования – 6, Q3, IF 2.991, Процентиль-62%, https://doi.org/10.1016/j.eplepsyres.2019.106224 . 7. Teplov I.Yu., Tuleukhanov S.T., Zinchenko V.P. Regulation of action potential frequency and amplitude by T-type Ca2+ channel during spontaneous synchronous activity of hippocampal neurons. Biophysics, 2018, Vol. 63, No. 4, pp. 566–575. ISSN 0006-3509. Индекс цитирования - 4, Q4 IF 0,520, Процентиль - 14%, DOI:https://dx.doi.org/10.1134/s0006350918040206. 8. Maiorov, S.A., Kairat, B.K., Gaidin, S.G. et al. Activation of the Cannabinoid Receptors Suppresses Hyperexcitation of Rat Hippocampal Neuronal Networks In Vitro. Biochem. Moscow Suppl. Ser. A 17, 169–175 (2023). https://doi.org/10.1134/S1990747823030078 9. Майоров С.А., Кайрат Б.К., Гайдин С.Г., Косенков А.М., Зинченко В.П. Активация каннабиноидных рецепторов подавляет гипервозбуждение нейрональных сетей гиппокаммпа крысы in vitro // Биологические мембраны: Журнал мембранной и клеточной биологии, 2023, Т. 40, № 3, стр. 194-202. https://doi.org/10.31857/S0233475523030076 https://sciencejournals.ru/view-article/?j=biomem&y=2023&v=40&n=3&a=BioMem2303007Maiorov 10. Maiorov S. and Kairat B.K., Berezhnov A.V., Zinchenko V.P. and Gaidin S.G., Kosenkov A.M. Peculiarities of Ion Homeostasis in Neurons Containing Calcium-Permeable Ampa Receptors. Available at SSRN: https://ssrn.com/abstract=4586624 or http://dx.doi.org/10.2139/ssrn.4586624 11. Қайрат Б.Қ., Төлеуханов С.Т., Зинченко В.П. Кальций-өткізуші каинатты рецепторлардың синапстық берілістегі рөлі // Вестник КазНМУ.- 2020 г. -№ 1.- С.206-212. Режим доступа: URL https://cyberleninka.ru/article/n/kaltsiy-tkizushi-kainatty-retseptorlardy-sinapsty-berilistegi-r-li/viewer 12. Қайрат Б.Қ., Төлеуханов С.Т., Зинченко В.П. Кальций-өткізуші АМРА-рецепторлардың синапстық берілістегі рөлі // ҚазҰМУ хабаршысы. - 2020. - №4. – Б. . 245-252. Режим доступа: URL https://www.elibrary.ru/item.asp?id=45612359 13. Қайрат Б.Қ., Төлеуханов С.Т., Зинченко В.П. Нейрондардағы кальций гомеостазы мен кальций сигнализациясының ерекшеліктері // ҚазҰМУ хабаршысы. - 2021. - №1. – Б. 208-214. Режим доступа: URL https://www.elibrary.ru/item.asp?id=46130762 14. Кайрат Б.К., Гайдин С.Г., Зинченко В.П., Майоров С.А., Ларюшкин Д.П., Косенков А.М. Метод витальной идентификации

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