Portfolio of the academic advisor of the participants of the International Olympiad of the Global Universities Association on the track of postgraduate studies in 2022-2023

	**Elena Popugaeva** Doctor of sciences (pharmacology, physiology) (the degree was awarded on the basis of the decision of the dissertation council of the Zakusov Research Institute of Pharmacology, Moscow (chairman, academician, MD S.B. Seredenin)) Senior Researcher, Laboratory of Molecular Neurodegeneration Researcher, “Digital Technologies in Biomedical Systems” Research Laboratory
University	Peter the Great St. Petersburg Polytechnic University
English proficiency	advanced
Field of study on which the postgraduate student will be enrolled	PHYSICAL SCIENCE 1.5.2. Biophysics BIOLOGY & BIOTECHNOLOGY 1.5.3. Molecular biology
List of research projects of a potential supervisor (participation / supervision)	• RSF grant No. 14-25-00024 project topic: "Investigation of the molecular mechanisms of calcium signaling in neurodegenerative diseases" (2014-2018) (main contractor). • Grant state assignment No. 17.1360.2014/K project topic: "Investigation of the role of calcium signaling in the pathogenesis of neurodegenerative diseases and the search for therapeutic agents" (2017-2019) (main contractor). • Grant of the private Russian foundation "Dynasty" project topic: "Intracellular calcium signaling and synaptic dysfunction in Alzheimer's disease" (2013-2015) (supervisor). • RFBR grant 17-04-00710 A (Competition A) project topic: "The role of neuronal calcium signaling in the loss of synapses in Alzheimer's disease" (2017-2018) (supervisor). • Grant of the President of the Russian Federation for young Ph.D. Contract No. 14.Y30.17.1043-MK project topic: "Biophysical study of the role of the sigma 1 receptor in the pathogenesis of Alzheimer's disease" (2017-2018) (supervisor). • RSF grant No. 18-74-00027 project topic: "Investigation of intracellular mechanisms of calcium dysregulation in Alzheimer's disease" (2018-2020) (supervisor).

	• RSF grant No. 20-75-10026 project topic: "Neuronal calcium signaling modulators are promising pharmacological agents for the treatment of pathogenetic forms of Alzheimer's disease" (2020-2023/25) (supervisor).
List of possible research topics	• Search, development and verification of potential pharmacological agents for the treatment of synaptic loss in the hippocampus in Alzheimer's disease • Study of the molecular mechanisms of neuroprotection
Field of study	Neurobiology, molecular biology, neurophysiology, pharmacology
Supervisor's research interests	Alzheimer's disease (AD) is the most common form of progressive dementia in the elderly, in the European Union it is observed in every 20th European over 65 years of age. The budget for the treatment of AD in Europe alone is about 120 billion USD. It is expected that by 2040 the prevalence of AD will double in Western European countries, and triple in Eastern European countries. The prevalence of AD in the Russian Federation has similar indicators. The treatment of AD is limited and inefficient. Drugs that are used to treat AD only temporarily reduce the severity of the symptoms of the disease due to the regulation of impaired neurotransmission. Acetylcholinesterase blockers, donepecil, galantamine, and rivastigmine, are used to alleviate cognitive deficits. The N-methyl-D-aspartate glutamate receptor (NMDA) blocker memantine is widely used. Memantine, acting on NMDA receptors, reduces the permeability of calcium ions into the cytosol, protecting neurons from excitotoxicity. In clinical practice, acetylcholinesterase blockers and memantine are often used together to treat mild to moderate AD. However, these drugs are not able to significantly slow down the development of the disease. Therefore, the improvement of the pharmacotherapy of AD is one of the priorities of modern pharmacology. The development of effective agents for the pathogenetic therapy of AD requires supplementing the understanding of the mechanisms underlying neurodegeneration leading to the development of dementia, with an assessment of molecular and morphological differences in changes in neurons during normal aging and during the development of dementia. The obvious multifactorial nature of the sporadic form of AD determines the need for further studies, including pharmacogenetic ones, to analyze the pathogenetic mechanisms and molecular basis of the disease, namely, to detect violations in the molecular cascades that determine the physiological functions of neurons. Thus, it seems possible to identify pharmacological targets, the regulation of which will provide a therapeutic effect.
Research highlights	Development of pharmaceutical drugs limiting synaptic loss, search for molecular targets, study of molecular mechanisms of neurodegeneration and neuroprotection

Supervisor's specific requirements	Having a scholarship or grant for training and internships is a significant advantage over competitors. Highly motivated specialists who are ready to study, work and scrupulously solve scientific problems in a team and independently. Willingness to work with animals (mice). Knowledge of the basics of the Russian language is welcome. In the absence of knowledge of the Russian language, willingness to learn Russian.
Supervisor's main publications	34 publications, h-index 17 https://www.scopus.com/authid/detail.uri?authorId=18038016300
Results of intellectual activity	Based on a mouse model of Alzheimer's disease (AD), the role of neuronal store-operated calcium entry (nSOCE) in the regulation of the formation of stable synaptic contacts was studied. It has been shown that nSOCE is significantly reduced in neurons with AD compared with wild-type neurons. The possibility of restoring the percentage of stable dendritic spines in a mouse model of AD was found using overexpression of the STIM2 protein [1]. It has been shown that overexpression of the STIM2 protein in the hippocampus causes a decrease in the number of amyloid plaques in the cerebral cortex of 5xFAD transgenic mice [2]. nSOCE activity modulators have been proposed as potential therapeutic agents for the treatment of AD [3]. A positive modulator of the TRPC6-nSOCE signaling pathway, piperazine derivative 51164, has been proposed as a potential compound for the treatment of AD with impaired intracellular signaling [4]. nSOCE antagonists have been proposed as potential drugs for the treatment of AD caused by the PSEN1dE9 mutation [5]. It has been shown that the TRPC6-nSOCE agonist improves short-term memory in an in vivo model of cerebral ischemia [6]. Binding sites for compound 51164 and hyperforin in the TRPC6 active site were determined [7]. The role of CaMKIIbeta in the regulation of nSOCE activity in primary hippocampal neurons has been established [8]. Literature 1. Popugaeva, E., et al., STIM2 protects hippocampal mushroom spines from amyloid synaptotoxicity. Mol Neurodegener, 2015. 10(1): p. 37. 2. Chernyuk, D.P., et al., Hyperexpression of STIM2 protein lowers the amount of Abeta plaques in the brain of Alzheimer's disease mouse model. St. Petersburg Polytechnical University Journal: Physics and Mathematics, 2016. 2(4): p. 329-336. 3. Popugaeva, E., E. Pchitskaya, and I. Bezprozvanny, Dysregulation of neuronal calcium homeostasis in

	Alzheimer's disease - A therapeutic opportunity? Biochem Biophys Res Commun, 2017. 483(4): p. 998-1004. 4. Popugaeva, E., et al., Derivatives of Piperazines as Potential Therapeutic Agents for Alzheimer's Disease. Mol Pharmacol, 2019. 95(4): p. 337-348. 5. Chernyuk, D., et al., Antagonist of neuronal store-operated calcium entry exerts beneficial effects in neurons expressing PSEN1DeltaE9 mutant linked to familial Alzheimer disease. Neuroscience, 2019. 410: p. 118-127. 6. Sysoev Yu.I., et al., Mechanism of action of a new ethanolamine derivative - bis{2-[(2E)-4-hydroxy-4-oxobut-2-enoyloxy]-N,N-diethylethanamine} butanedionate Experimental and clinical pharmacology 2019. 82(4): p. 3-10. 7. Hunanyan et al, 2021 IJMS 8. Zernov et al 2022 IBRO neuroscience reports