lek. Piotr Rodak
[redacted]
mail piotr.rodak@sum.edu.pl

Streszczenie rozprawy doktorskiej w języku angielskim

„Interaction and the between selective estrogen receptor modulators (SERM) FasR/FasL pathway in a model of retinal ischemia in ovariectomized rodents”

Estrogen deficiency during menopause is an important risk factor for the development of retinal neurodegenerative diseases, including optic neuropathies and ischemic retinal disorders. The aim of this dissertation was to evaluate the impact of estrogen deprivation induced by ovariectomy on the function and survival of retinal neurons, as well as to determine the neuroprotective effects of estrogen receptor modulators and inhibition of the FasR/FasL pathway in models of retinal ischemia. The study was divided into two parts. In the first part, the effects of surgically induced menopause on retinal ganglion cell function and survival were assessed in an animal model of optic nerve crush injury. Electrophysiological and histological analyses demonstrated that estrogen deficiency leads to retinal dysfunction, loss of interneurons, and increased microglial activation. Furthermore, surgical menopause increased the susceptibility of retinal ganglion cells to neurodegenerative damage. The second part of the study evaluated the neuroprotective effects of 17β estradiol, raloxifene, and the FasR/FasL pathway inhibitor (KP 7-6) in acute and chronic models of retinal ischemia. It was shown that both estrogen receptor modulation and inhibition of the FasR/FasL pathway exert anti-apoptotic effects; however, the strongest neuroprotective efficacy was observed with combined therapy. The combination of raloxifene and the Fas receptor antagonist increased retinal ganglion cell survival and preserved their function both in ovariectomized and control animals. The obtained results indicate that estrogen deficiency increases the vulnerability of retinal neurons to ischemic injury, whereas simultaneous modulation of estrogen signaling and the FasR/FasL apoptotic pathway may represent a promising therapeutic strategy for neurodegenerative retinal diseases associated with aging and menopause.