MITOCHONDRIA AS A TARGET FOR DEVELOPMENT OF TERAPY FOR NEURODEGENERATIVE DISORDERS

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The socioeconomic burden of an aging population has accelerated the urgency of novel therapeutic strategies for neurodegenerative disease. One possible approach is to target mitochondrial dysfunction, which has been implicated in the pathogenesis of numerous neurodegenerative disorders. This is an important area of clinical research, with several novel therapeutics already in clinical trials and many more in preclinical stages. We are focusing on possible novel approaches, looking at mitochondrial defects which have more recently been linked to neurodegeneration. Mitochondria are vital to cellular functions by supplying energy in form of ATP and affect cell physiology via calcium, ROS and signalling proteins. Changes in mitochondrial calcium homeostasis and ROS overproduction can induce cell death by triggering mitochondrial permeability transition pore opening. One of the major triggers for PTP is mitochondrial calcium overload. We found that a novel compound, TG-2112x, can inhibit only the lower concentrations mitochondrial calcium uptake but not the uptake induced by higher concentrations of calcium. Pre-treatment of neurons with TG-2112x protected the neurons against calcium overload upon application of toxic concentrations of glutamate, mitochondrial calcium overload in familial forms of Parkinson's disease.