**Subject:** Evaluation of P2X7 purinergic receptor as a trigger of brain metabolic abnormalities and

neuronal degeneration in a mouse model of Parkinson’s disease

**Proposed Supervisor:** Prof. Agata Adamczyk, PhD, DSc

**Research Funding:** Grant No. 2023/50/E/NZ4/00550, titled Evaluation of P2X7 purinergic

receptor as a trigger of brain metabolic abnormalities and neuronal degeneration in a mouse

model of Parkinson’s disease,

**Principal investigator:** Dr. Anna Wilkaniec.

**Objective of the Study**

Parkinson's disease (PD) pathology is characterized by the formation of insoluble alpha-synuclein (α-Syn) aggregates known as Lewy bodies and the selective loss of dopaminergic neurons in the substantia nigra. The pathogenesis of PD remains poorly understood, and no effective causal treatments are currently available. PD etiology is thought to result from an interplay of factors such as oxidative stress, disrupted mitophagy, mitochondrial damage, and metabolic disturbances. Recent studies have highlighted the purinergic P2X7 receptor (P2X7R) as a key player in PD pathogenesis. Our previous research showed that exogenous α-Syn binds directly to P2X7R in neuronal cells, inducing calcium influx, oxidative stress, and mitochondrial dysfunction. **This study hypothesizes that dysfunctions in P2X7R contribute significantly to α-Syn-induced metabolic disturbances, leading to dopaminergic neuron death observed in PD.** This project is the first to explore the role of P2X7R as a molecular mediator of extensive metabolic changes triggered by α-Syn. The research will exploit a well-characterized preclinical mouse model of PD based on direct intrastriatal injection of oligomeric α-Syn, along with primary neuronal cultures. The study will alsoemploy P2X7R knockout (P2X7RKO) mice. All experiments will use advanced, sensitive techniques, including enzymatic assays, bioluminescence, fluorescence-based methods, confocal microscopy, magnetic resonance imaging (MRI), RT-PCR, and Western blotting.

**Research Tasks**

1. Investigating the role of P2X7R in oxidative stress induction and redox metabolism changes in vivo.
2. Analyzing the involvement of P2X7R in regulating mitochondrial unfolded protein response (mtUPR).
3. Examining the impact of P2X7R on mitochondrial autophagy.
4. Assessing P2X7R’s role in α-Syn-induced metabolic alterations.
5. Evaluating structural and metabolic brain changes mediated by P2X7R in vivo.
6. Investigating the contribution of P2X7R to brain morphological changes in PD.
7. Analyzing the effects of P2X7RKO on behavioral changes in the PD mouse model.

**Job Responsibilities**

* Planning and conducting experiments.
* Creative work, including analyzing current literature and initiating modifications during project execution.
* Analyzing and interpreting the obtained data.
* Maintaining research documentation in compliance with FAIR principles.
* Presenting findings at lab and institutional seminars, as well as at national and international conferences.
* Preparing scientific publications.

**Requirements**

* Laboratory experience in neurobiology and molecular biology.
* Proficiency in English, both written and spoken.
* Excellent organizational skills and attention to detail.
* Ability to work both independently and as part of a team.

**Additional Advantages:**

* A track record of scientific publications in internationally recognized JCR-listed journals.
* Active participation in national or international conferences and symposiums.

**We Offer:**

* A research scholarship of up to PLN 5,000/month for up to four years.
* Innovative research challenges and unique opportunities to develop research skills.
* Independence and freedom in task execution.
* Mentoring and support for career development.
* A friendly, inspiring, and supportive working environment within a large Department of Cellular Signal Transduction team.
* Opportunities to present findings at scientific conferences.
* Support for publishing and promoting research outcomes.
* Benefits packages, such as a Multisport Plus card and preferential access to group insurance.

**Required Documents**

* A motivation letter detailing scientific interests, research experience, and reasons for joining the project.
* A signed CV in PDF format.
* At least one recommendation letter from a current or former supervisor/mentor.