

**Project Title:** Mechanisms of DNA Damage Resulting from PIM Kinase Inhibition and Their Consequences for Activation of the Innate Immune System and Induction of Antitumor Immune Response in Diffuse Large B-Cell Lymphoma

**Funding:** Scholarship for Doctoral Student – NCN OPUS grant no. UMO-2023/49/B/NZ5/03482 (project planned to start: Q3 2024)

Scientific Supervisor: Prof. Przemysław Juszczynski, MD, PhD

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Diffuse large B-cell lymphoma (DLBCL) is the most common B-cell malignancy in adults. Our group recently demonstrated that inhibiting PIM1/2/3 kinases in lymphomas induces cell apoptosis while also eliciting immunomodulatory effects. Genetic or chemical inhibition of PIM reduced the expression of molecules involved in developing an immunosuppressive microenvironment. During these studies, we characterized additional potentially immunogenic consequences of PIM inhibition in lymphoma cells associated with the formation of DNA breaks. These observations indicate that PIM inhibition not only directly kills cancer cells and reduces the immunosuppressive nature of the microenvironment but also engages innate immunity and enhances subsequent adaptive responses through DNA damage and the generation of "danger signals." In this project, we plan to characterize the mechanisms of DNA damage induced by PIM kinase inhibition and define and characterize the immunogenic consequences of DNA breaks induced by PIM inhibitors using in vitro models and in vivo experiments. We will investigate additional features of immunogenic cell death and determine rational combinations of PIM inhibitors that increase tumor immunogenicity. Since pan-PIM inhibitors are in the clinical development stage, these characteristics could be particularly important for DLBCL immunotherapy.

More Information: NCN OPUS Grant Summary

Requirements:

- Completed (or to be completed in the current academic year) Master's degree or equivalent in biotechnology, medicine, biomedical engineering, or a related field.
- Willingness to enroll in the 4-year Doctoral School of Translational Medicine co-conducted by the Postgraduate Medical Education Center and the Institute of Hematology and Transfusion Medicine in the 2024/2025 academic year.
- High motivation for scientific work in the field of oncohematology.
- Knowledge of cell biology, molecular biology, immunology, and cell culture.
- Previous practical laboratory experience.
- Ability to present results in English.
- Willingness to enhance qualifications.
- Creativity, independence, availability, and the ability to work collaboratively in a team.