Project summary

The project "Impact of immune exhaustion and methylome changes on HIV reservoir across key viral subtypes" aims to understand how immune exhaustion and changes in the methylome affect the latent HIV-1 reservoir, depending on the viral subtype. The latent reservoir of HIV-1 refers to infected cells that harbor the virus in a dormant state, making it a significant barrier to curing HIV. This research is crucial since different subtypes of HIV-1 may influence the size of this reservoir, as well as the progression of immune exhaustion and changes in the methylome, which involves chemical modifications to DNA that affect gene expression without altering the DNA sequence itself.

The primary objective of this study is to explore the variations in the latent HIV-1 reservoir among different subtypes, specifically subtypes B and A6. Subtype B is the most common in Western Europe and North America, while subtype A6 is rapidly spreading in Eastern Europe. By investigating these differences, the study aims to identify whether specific subtypes are associated with larger reservoirs or distinct patterns of immune exhaustion and methylome alterations.

The research involves analyzing blood samples from HIV-1 infected patients. These samples will be used to measure the size of the HIV-1 reservoir using advanced digital droplet PCR technology. Additionally, the study will perform detailed flow cytometric immunophenotyping to identify which immune cells are most affected by exhaustion and whether these exhausted cells can potentially convert to other cell types that might help to rebuild the immune response.

Understanding the methylome alterations is another critical aspect of the research. Previous studies have shown that HIV-1 infection induces significant changes in the host's DNA methylation patterns, affecting genes involved in immune responses and HIV pathogenesis. This project will investigate these changes across different HIV-1 subtypes to determine if there are specific methylation patterns associated with particular subtypes.

This research is particularly timely and relevant given the changing landscape of HIV molecular epidemiology. The influx of subtype A6 variants, partly due to migration and local transmission, necessitates a deeper understanding of how these variants impact HIV progression and treatment outcomes. The study's findings could inform the development of more effective, subtype-optimized HIV cure strategies and improve the management of the disease.

The expected outcomes of this project include a comprehensive understanding of how different HIV-1 subtypes influence the latent reservoir, immune exhaustion, and methylome changes. This knowledge could pave the way for new therapeutic approaches that target the latent reservoir more effectively and help design personalized treatment plans based on the viral subtype. Additionally, establishing reliable HIV-DNA based reservoir testing in Poland will contribute significantly to the global effort to cure HIV.

In summary, this project addresses a critical gap in HIV research by examining the interplay between viral subtypes, immune exhaustion, and methylome alterations. The results will provide valuable insights that could enhance HIV cure strategies and improve patient outcomes across diverse populations.