There are almost 40 million people throughout the world living with HIV-1. Since its discovery almost 40 years ago there is still no cure. Major reason that a cure for HIV continues to elude us is that the virus hides away in cells, forming a persistent reservoir in which the virus is dormant (i.e. latent), and in such cells the virus is not visible to the immune system and to antiretroviral therapy. Consequently, latency persists, cannot be eliminated and represent a major hurdle to finding a cure. With no vaccine on horizon, several strategies are currently proposed in order to fight latent HIV. One of them is "shock and kill" that involves induction of latent viruses (HIV reactivation, "shock") using latency-reversing agents while maintaining antiretroviral therapy ("kill") in order to prevent new spreading infection. This kind of strategy would allow latently infected cells to die from viral cytopathic effect or host immune response. However, there is increasing body of evidence showing that this strategy is not efficient enough in reactivating the virus due to blocks that are not efficiently overcome by latency-reversing agents (LRAs). In this context, we have recently identified a novel block related to limiting levels of MATR3 (a posttranscriptional factor involved in HIV RNA export) in patients cells that impede the efficient action of LRAs.

In this project we propose to further characterize this novel block and test a hypothesis that combined treatment of MATR3 with LRAs will positively impact the efficient viral reactivation. In order to increase our knowledge on this intriguing factor that is still poorly characterized we will aim to identify MATR3 nuclear interactome using mass spectrometry approach. Results obtained within this project will be very important for designing new, more potent "shock" protocols to purge the latent reservoir.