HIV-1/AIDS since the pandemic onset in 1981 remains a major public threat with 36.3 million deaths and more than 38 million people living with HIV-1. Despite of a tremendous effort being made to combat the virus - we still do not have a cure. No vaccine exists but there is a potent antiretroviral therapy (ART) to control viral infection. However, ART does not cure the infection because virus become dormant (latent) and as such hides away from medications and immune recognition. Therefore, whenever the treatment is interrupted, latent virus wakes up and attacks human body. Thus, if cure ever is going to be reached, latency must be first eliminated. Different strategies are being indeed investigated to combat latency such as the so-called "shock-and-kill" approach that aims to wake up the virus ("shock" phase) to unmask it and makes it visible to the immune recognition and elimination ("kill" phase). However, here again the virus wins the battle as unfortunately current "shock-and-kill" therapy is inefficient.

Latency is a very complex phenomenon repressed not only by transcriptional but also less-characterized post-transcriptional mechanisms. Unfortunately, current "shock-and-kill" does not act on these post-transcriptional steps and this could be the reason why we cannot eliminate latency. As such, we need more basic studies to understand the post-transcriptional mechanisms controlling latency. Our previous studies and preliminary data highlight the existence of a novel post-transcriptional block in latently-infected cells from patients that hampers viral reactivation from latency.

The aim of this project is to further characterize this block using novel technologies such as CRISPR/Cas9 and next-generation sequencing to shed light on the molecular mechanisms underlying post-transcriptional processes controlling HIV-1.

Results obtained within this research project will be important for proposing future therapies targeted on post-transcriptional steps to improve current inefficient "shock-and-kill" approaches to hopefully reach a cure.