Antiretroviral therapy (ART) has revolutionised the care of people living with HIV. However, to be most effective, therapy is life-long from the time of diagnosis. This presents a huge burden both for health care systems in terms of delivery logistics and cumulative costs, and for patients in terms of long-term compliance, viral resistance, cumulative toxicity and ongoing stigma. The current challenge for effectively advancing the treatment of HIV-1 infection is prolonged viral reservoir control without continuous ART. A number of strategies are being investigated to permanently control HIV-1 infection, such as the "shock and kill" and "block and lock" approaches. The former attempts to reactivate or "shock" latently infected cells awake using *latency reversing agents*, then relies on an immune response or other targeted methods to "kill" the cell. This has shown limited success in clinical trials. The latter attempts to mimic the naturally occurring transcriptionally latent state of the virus via *latency inducing agents*, which "block" transcription at the virus promoter & "lock" the promoter in permanent latency through repressive epigenetic modifications. However, a critical barrier to latent reservoir control is the ability to deliver cure strategies *in vivo* to the specific cells that make up the viral reservoir.

Gene therapy aims to introduce new genetic material into target cells without toxicity to treat or prevent disease. Although this approach holds great promise to create enduring (perhaps life-long) protection for individuals living with a broad range of incurable diseases, clinical progress has been slow. One major limitation lies in development of safe and efficient gene delivery systems.

This presentation will update the progress on the "block and lock" strategy, especially with regards the induction and maintenance of viral super latency by si and sh RNAs targeting the HIV promoter both in vitro and in vivo. It will also update the current strategies for delivery of these constructs to CD4+ T cells and monocytes and macrophages using both lentiviral and nanocapsule technologies.