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Construction of new infectious molecular clones (IMC) expressing Renilla Luciferase (IMC-LucR) for HIV neutralization assay standardization

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Standardized assays to assess vaccine and antiviral drug efficacy are key to the HIV field. The main requirements for immunological assays (e.g., antibody neutralization and antibody-dependent cellular cytotoxicity (ADCC) are the use of natural HIV target cells such as peripheral blood mononuclear cell (PBMC), and the use of HIV-1 infectious molecular clones (IMC) that i) express a reporter gene, ii) are representative of different genetic clades and iii) are engineered to express heterologous envelope gene representating different genetic clades. Thus far, only a clade B laboratory-adapted strain IMC was developed using these approaches; moreover, only a portion of the gp160 coding sequence is swapped. Here we described the construction of three native IMC expressing the Renilla Luciferase (LucR) gene from a Circulating Recombinant Form CRF01_AE, a clade B and a clade C; all three infect cell lines as well as primary cells. Each of these constructs was engineered to swap the full envelope gene, allowing gp160 to be expressed in its native form. Our data showed infection in TZMbl cells - one of the most common cell line used for infection neutralization assays - and a majority of them infected PBMC also. Neutralization data was also generated and differences where observed when compared with the commonly used pseudovirus assay. In addition, some envelopes showed different neutralization profiles when expressed in homologous- vs heterologous-HIV chimeric clade. These data highlight the importance of using infectious molecular clones as reagent in neutralization assay for assessing HIV-1 vaccine immunogen efficacy.

Biography

Dr. Agnès-Laurence Chenine obtained her Ph.D. in 2000 from Luminy University in Marseille-France where she studied HIV infection of the intestinal tract and generated CD4-independent IMC. She was a postdoctoral fellow at the Dana-Farber Cancer Institute and then an Instructor in Medicine at Harvard Medical School focusing on mucosal transmission and HIV/parasite co-infection in a non-human primate model. In 2008, she joined the Military HIV Research Program (MHRP) as a leading scientist in the department of Molecular Virology & Pathogenesis. One of her focus is to generate IMC from different HIV-1 subtypes and from acute vs chronic to complement MHRP research capability in HIV vaccine development.