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HIV-1 and IFN-I modulate the composition of the nuclear envelope proteins

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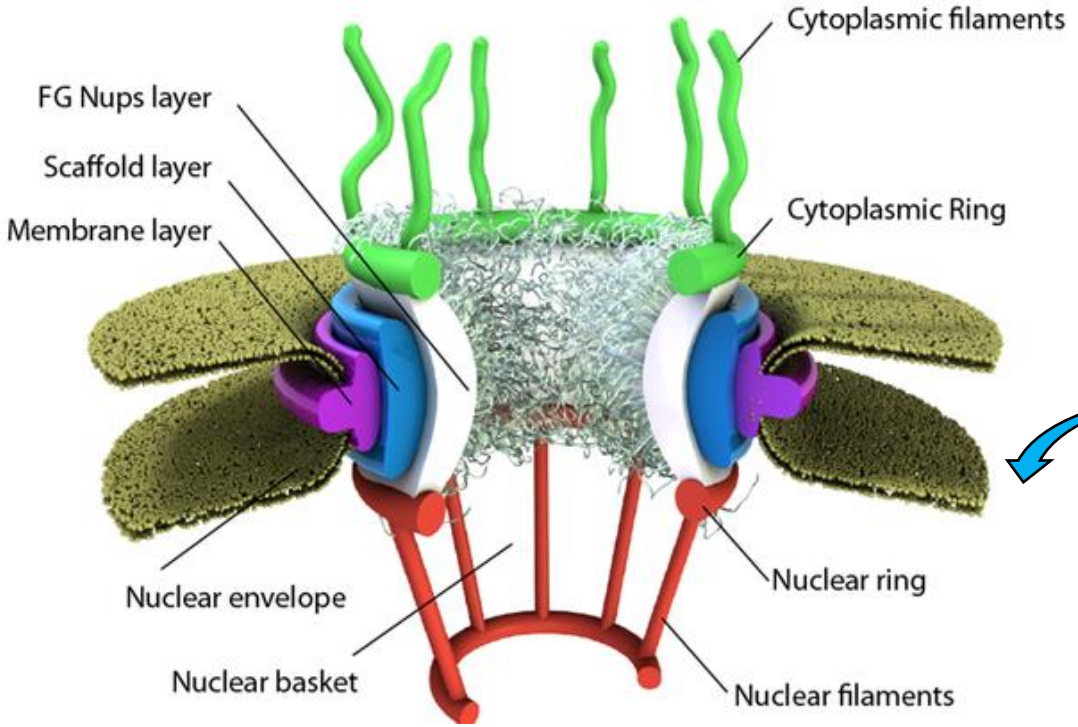
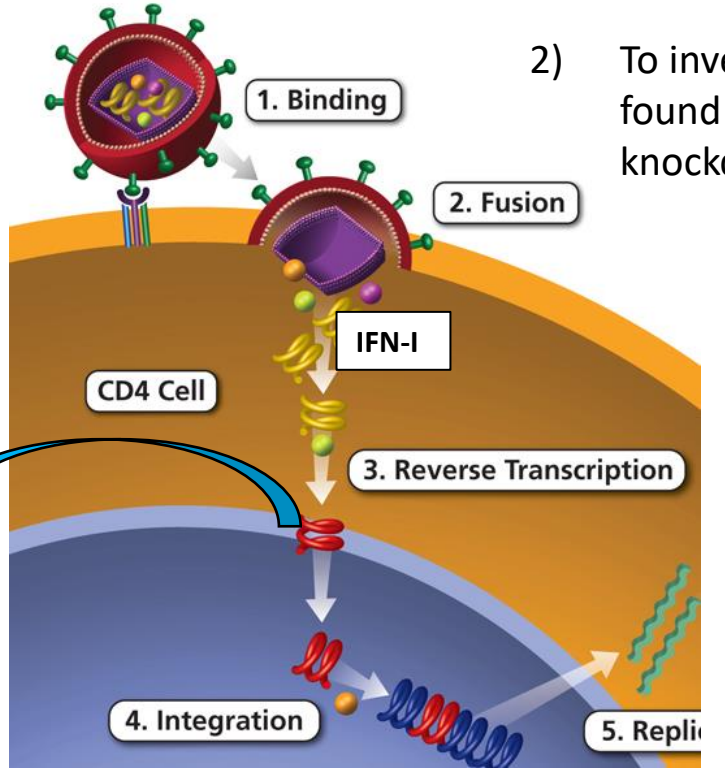
Introduction

Cellular innate immune get activated as cytoplasmic sensors detect viral genome in the cytoplasm resulting in secretion of IFN-I and expression of interferon stimulated genes (ISGs)

Nuclear transport of pre-integration complex (PIC) involves interaction with nuclear membrane proteins and nucleoporins (Nups, building blocks of nuclear pore complex (NPC))





Hypothesis: HIV-1 infection and innate immune response can change protein composition of the nuclear envelope.

Objectives:

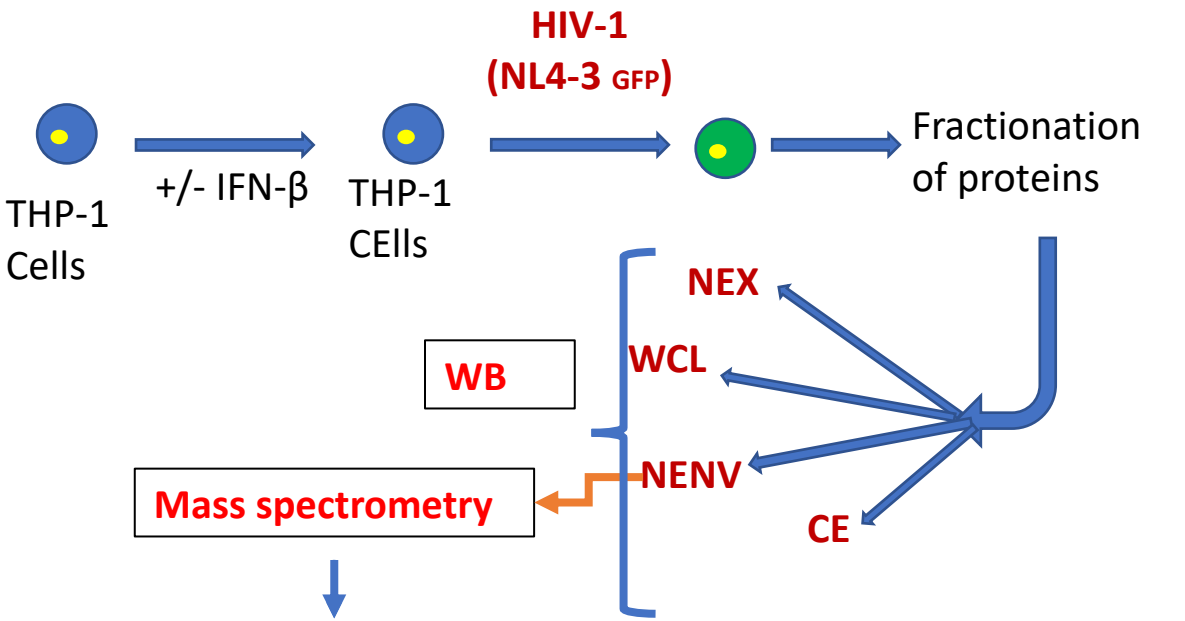
1) To identify the nuclear membrane proteins modulated upon infection of human cells with HIV-1, or treatment with IFN-I, or both.

2) To investigate the role of specific protein found to be modulated, making knockdown.

https://clinicalinfo.hiv.gov/en/glossary/life-cycle

Mohammad Azimi, 2013

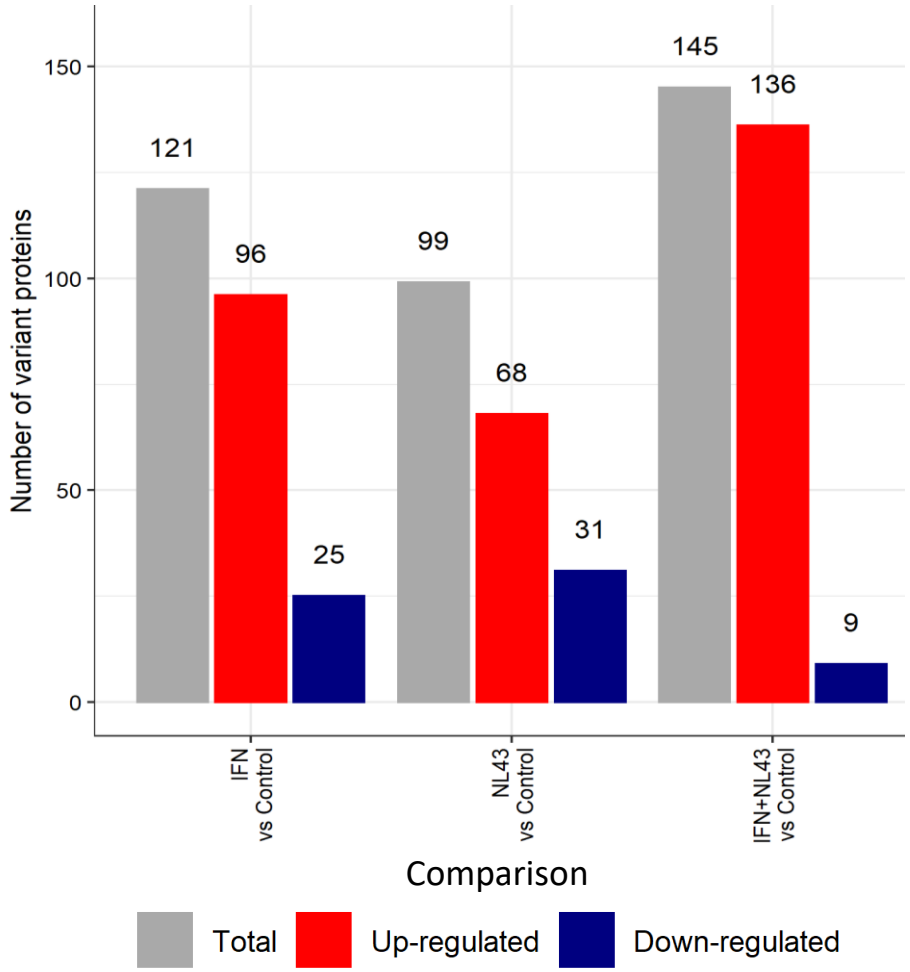
Methodology



Nuclear envelope extracts were extracted from THP-1 cells after 24h IFN-I treatment and 12h NL43GFP vector infection. Samples were subjected for label free quantitative mass spectrometry.

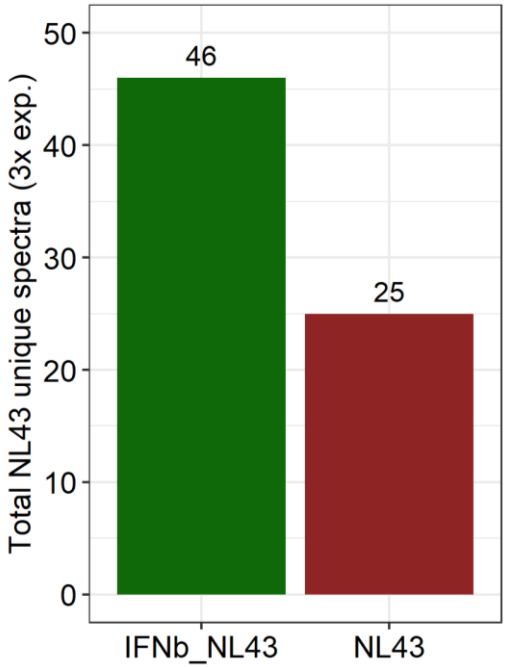
Result

Result 1. Modulated proteins with HIV-1 infection or IFN-I treatment or both

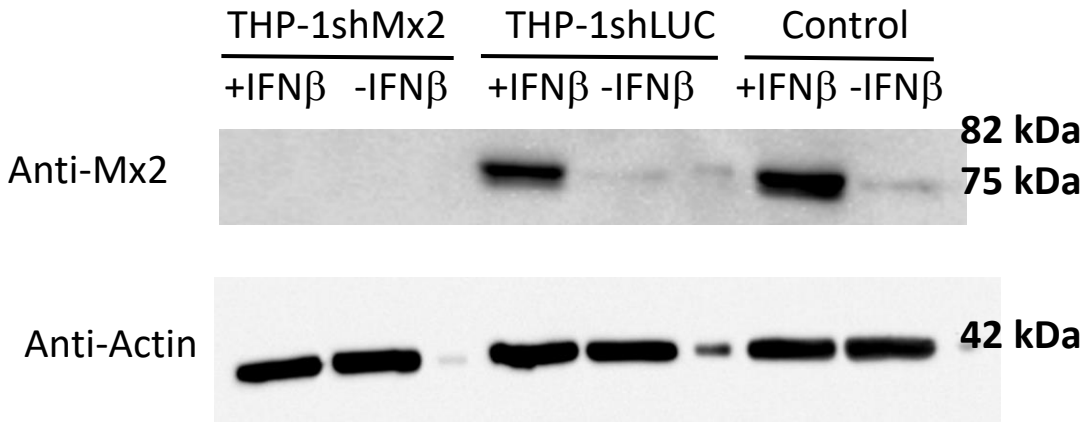


We also quantified the HIV-1 peptides detected in the infected samples. Surprisingly, more HIV-1 peptides were detected upon IFN-I treated samples. To investigate it further we knockdown the MX2 gene which is known to interact with HIV-1 capsid (CA) protein at the nuclear pore complex. To investigate if the MX2 is the reason behind HIV-1 peptides accumulation in the nuclear membrane.

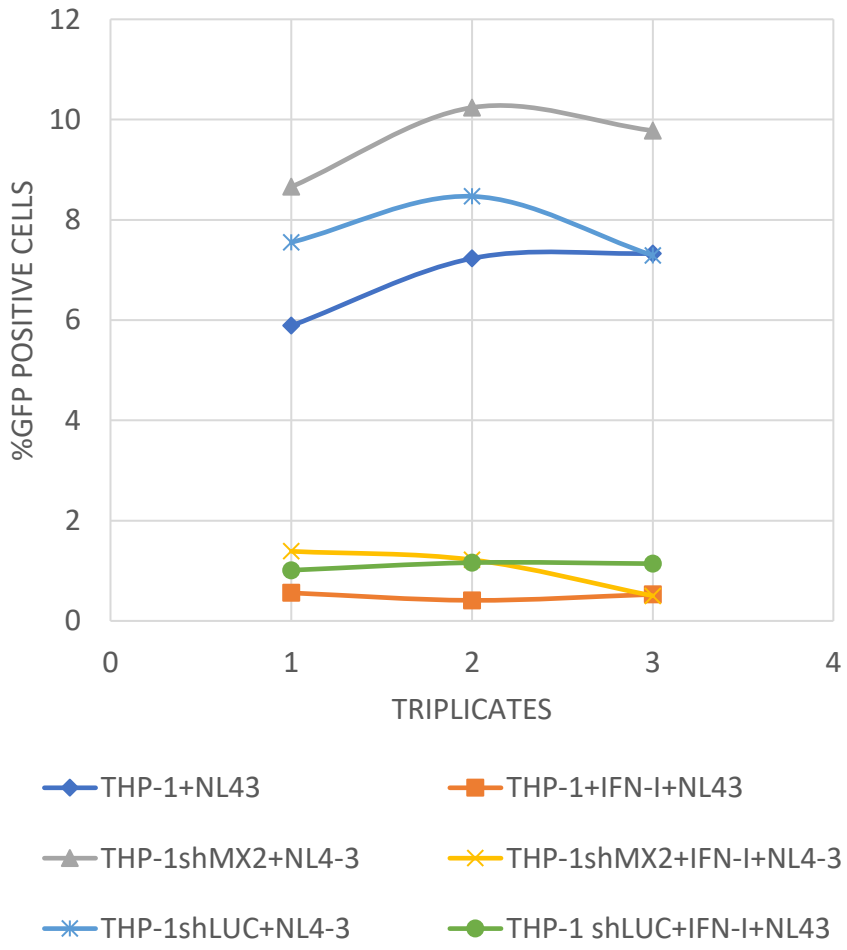
Result 2. MX2, an ISG was knockdown using shRNA technique.



Result 3. MX2, an ISG was knockdown using shRNA technique.



Result 4. THP-1shMX2 cells infected with NL4-3GFP



Inference

1. Many proteins were modulated with IFN treatment and HIV-1 infection in the presence and absence of IFN-I treatment
2. Preliminary FACS results suggested that MX2 knockdown has effect on HIV-1 infection as infection is increased on MX2 knockdown cells in compare THP-1 wild type cells.

Future Plans

Immunofluorescence assay to investigate if there is any difference in CA distribution in THP-1 shMX2 cells in compare to wild type cell in order to find the cause behind the more HIV-1 peptide detection in the IFN-I treated samples.

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