Introduction
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Measles virus (MV) belongs to the family Paramyxoviridae and has single stranded, nonsegmented RNA genome of negative polarity. The naked genomic (-) and antigenomic (+) MV RNAs are not infectious and become functional only as a ribonucleoprotein (RNP) complex. Functional complex consists of either (-) or (+) RNA (15894 nucleotides) tightly wrapped with nucleoproteins (N) and more loosely associated proteins, the phosphoprotein (P) and the large protein (L) constituting the RNA dependent RNA polymerase. The RNP is surrounded by an envelope derived from the plasma membrane of the host cell. The viral matrix protein (M) is lining the inner surface and the two viral glycoproteins viz, the fusion protein (F) and the haemagglutinin protein (H) constitute the transmembrane components.

Nucleoprotein is the most abundant of the measles virus proteins expressed during infection and carried along with the virions. Being an RNA-binding protein, it was projected to organize viral RNA in a manner suited for packaging, and conferring cognitivity with viral transcription and replication protein apart from protecting the viral RNA from cellular ribonucleases. It gets exposed to the intracellular protein during virus proliferation and is likely also to interact with many of them to exert regulatory or direct functional influences in order to maximize progression of the virus. We have studied the effects of nucleoprotein expression on human breast cancer cell line MCF7 and on human embryonic kidney cells 293T. We showed that N induces the death of human breast cancer cells which involves increase in ROS generation and procaspase-3 activation (Chapter 1). We also did proteomic studies of cells expressing N. Our proteomic results present a prima facie evidence that the MV nucleoprotein interacts with or cause differential expression of a wide range of cellular factors (Chapter 2).

The icosahedral viruses have packaging limits of nucleic acid but the measles virus that has helical nucleocapsid within a pleiomorphic virion does not pose such size limits. To rescue infectious MV from cDNA a helper cell line, designated 293-3-46 which constitutively expressed T7 RNA polymerase together with MV proteins N and P was created. Recently, a 5 plasmid cotransfection system has been developed for rescue of recombinant measles virus

By reverse genetics approach, it is possible to handle RNA viruses as their cDNA and rescue the infectious virions with defined insertion of heterologous coding
sequences fused in frame with a viral surface protein. Such recombinant virions are expected to display novel peptides as their surface constituents. As a result, the virions may acquire new cytotropic properties. Thus the viral pseudotypes may serve as vehicles for efficient and perhaps targeted delivery of nucleic acid and proteins to chosen cell types. We can engineer the attachment protein H of an attenuated measles virus and generate truly retargeted viruses that may be blind to the native receptors CD46 and SLAM, but which propagate efficiently via alternative cellular receptors.

AIDS is a growing concern all over the world. It represents the late stages of infection by a retrovirus called Human Immunodeficiency Virus (HIV). The presence of cell membrane proteins that act as virus receptors determines whether a cell can be invaded by a virus or not. We can exploit the specificity of receptor interactions in a reverse manner, namely by incorporating receptor proteins into the envelope of a virus in order to target selectively virus-infected cells that display spike proteins on their surface. HIV preferentially enters cells that express CD4 along with a co-receptor CCR5 found on the surface of macrophages and dendritic cells or co-receptor CXCR4 found on the T cells. We incorporated the T cell marker CD4 into measles viruses and tested its tropism towards the cells displaying HIV protein gp160 (Chapter 3). This is the first study of its kind employing measles virus. With the rescued recombinant viruses we would like to target HIV infected cells. This study will explore the current status and future direction of viral vectors for use against diseases like AIDS.

To carry out the above mentioned work, the following objectives were charted.

- Effect of nucleoprotein expression in MCF7 cells and 293T cells.
- Proteomic profiling of MCF7 cells expressing nucleoprotein.
- Construction of antigenomic measles virus cDNA having ORF of human CD4.
- Rescue of recombinant measles virus expressing human CD4.
- Rescue of recombinant measles virus expressing 12p peptide which specifically binds to HIV gp120.
- Testing tropism of the rescued measles viruses towards cells displaying HIV protein gp160.