Targeting HIV replication and maturation: Role of APOBEC proteins and bevirimat

Ritu Gaur
South Asian University, India

The human immunodeficiency virus type 1 (HIV-1) Vif protein plays a crucial role during the viral life cycle by regulating virion infectivity and in vivo pathogenesis. Vif counteracts a cellular factor identified as APOBEC3G (APO3G). APO3G is a cytidine deaminase and causes editing of the viral cDNA during reverse transcription. The effect of Vif on APO3G is species specific. The Vif protein from African green monkey (Agm) simian immunodeficiency virus (SIVagm) is unable to suppress the antiviral activity of human APO3G but is active against Agm APO3G. SIVmacVif on the other hand, possesses antiviral activity against both human and Agm APO3G. In an attempt to map domains in SIVmacVif, we have constructed a series of Vif chimeras and determined their activity against human, Agm and rhesus APO3G. We found that replacing any region in SIVmacVif by corresponding fragments from SIVagmVif only moderately reduced the activity of the chimeras against Agm APO3G but in all cases resulted in a severe loss of activity against human APO3G. Further mutagenesis is ongoing in an attempt to define the residues involved in activity of SIV Mac Vif. One of the major problems faced during anti-retroviral treatment of HIV patients is evolution of drug-resistant viruses. We are currently working on a new class of inhibitors called Maturation Inhibitors, which block virus maturation into infectious particle. In collaboration with NIH (USA), we are working on the first-in-class maturation inhibitor bevirimat (BVM). BVM acts by blocking a specific step in the Gag processing cascade namely, cleavage of the capsid-spacer peptide 1 (CA-SP1) processing intermediate to mature CA. Experiments are underway to screen BVM analogs that might be more potent than parental compound.

Biography
Ritu Gaur has completed her PhD from National Institute of Immunology in 2001 and Postdoctoral studies from National Institute of Health, USA. She is currently working as an Associate Professor at South Asian University, New Delhi. Her main area of interest is HIV pathogenesis and interaction with host proteins.  
rgaur@sau.ac.in