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Viral characteristics associated with the maintenance of elite neutralizing activity in HIV-1 Clade C-infected children

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About the speaker:

Dr. Kalpana Luthra is a Professor in the Department of Biochemistry, All India Institute of Medical Sciences (AIIMS), New Delhi, India. She completed her PhD at AIIMS in 1994 and joined as faculty at AIIMS in 1998. She was awarded the Fogarty fellowship in 2002 and availed training in HIV-1 antibody related work at New York University. The major focus of her work has been towards understanding the immune responses elicited by HIV-1 infected adults and children; generation of human anti-HIV-1 recombinant monoclonal antibodies as potential therapeutic reagents against HIV-1 and to map the neutralization determinants on the HIV-1C to identify Indian clade C specific epitopes for immunogen design. She is actively involved in ongoing national and international collaborative research projects in this area of research. Recently, her research group successfully generated an anti-HIV-1 broadly neutralizing antibody from an Indian paediatric elite neutralizer. This antibody is being further characterized to evaluate its potential as an anti-HIV-1 reagent. Further her team has shown that distinct circulating viruses in chronic HIV-1 infected children are associated with maintenance of elite neutralizing activity in chronically HIV-1 clade C infected monozygotic pediatric twins. Mapping the neutralizing determinants on these viral envelopes will contribute information towards an Indian clade C based immunogen design.

Abstract:

Broadly neutralizing antibodies (bnAbs) develop in a subset of HIV-1 infected individuals over 2–3 years of infection. HIV-1 infected infants develop plasma bnAbs frequently and as early as 1-year post-infection, suggesting that factors governing bnAb induction in infants are distinct from adults. We evaluated the presence of plasma bnAbs in a cohort of 51 HIV-1 clade-C infected infants to identify viral factors associated with early bnAb responses. Plasma bnAbs targeting V2-apex on the env are predominant in infant elite and broad neutralizers. Circulating viral variants in infant elite neutralizers are susceptible to V2-apex bnAbs. Interestingly, in the infant elite neutralizers with multivariant infection, potential env specific antibodies directed at two distinct viral variants, recognised/targeted epitopes on both envelopes.

In a previous study, we observed the longitudinal development of bnAbs in a pair of chronically HIV-1 clade C-infected monozygotic pediatric twins, AIIMS_329 and AIIMS_330, who acquired the infection by vertical transmission. The plasma from these twin donors, sharing a similar genetic makeup and infecting virus, showed the evolvement of bnAbs targeting common epitopes in the V2 and V3 regions of the envelope, suggesting that bnAb development in these twins may perhaps be determined by specific sequences in the shared virus that can guide the development of immunogens aimed at eliciting V2 and V3 bNAbs.

Further, we observed the evolution of a viral pool in the AIIMS_330 donor comprising plasma antibody neutralization-sensitive or -resistant diverse autologous viruses that may have contributed to the development and maintenance of elite neutralizing activity as compared to the AIIMS_329 donor plasma that showed a decline in neutralizing activity with time.