Anuja Krishnan, PhD

Virology

Profile: Dr. Anuja Krishnan did her postgraduation from All India Institute of Medical Sciences (AIIMS) and PhD from National Institute of Immunology (NII). She has over 12 years of experience (post PhD) in virology. During her post doc at Delhi University she worked on target-specific virosome based drug delivery vehicle. She was awarded the Indo US Science and Technology Forum (IUSSTF) visiting scientist award for which she worked at Albert Einstein College of Medicine, New York, towards elucidating the intracellular receptor for Ebola virus which were published in high impact factor journals. She has over 10 years of experience in working at Delhi University, Institute of Molecular Medicine (IMM) and now at JH-IMM. In addition she has teaching experience at above institutes. She has been granted projects from DBT and DST. She has earned accolades including Indo US Science and Technology Forum fellowship, DST Fast Track Young Scientist, DBT Rapid grant Young Investigator (RGYI), Society of Young Scientist award (AIIMS).

Her current work involves uncovering the mechanisms by which viruses exploit their host cells to gain entry into the host cell. Apart from understanding the basic biology the long term goal is to identify critical host factor in virus infection which could provide the means for the rational design of novel intervention strategies. Her research interest also includes studying molecular epidemiology of Indian centric viruses (dengue, chickungunya, rotaviruses etc).

Research Interest: The central theme of her research is to understand the viral and host factors that determine the disease outcome. The other area involves understanding immune correlates of protection and pathogenesis in dengue disease with research involving human population.

The following research projects are being pursued to address the above goals:

I. Molecular trigger in Dengue virus-mediated fusion

Membrane fusion is an essential step during the entry of enveloped viruses into their host cell. This process is mediated by viral fusion proteins that are associated with the viral membrane and primed to undergo structural rearrangements that drive fusion. The aim of this project is to identify trigger residues of envelop (E) protein of Dengue virus involved in the fusion of viral membrane with host membrane. This is being done by using viral like particle (VLPs) and pseudotype virus assay system. *In-vitro fusion* with membrane model system, liposome, is being investigated by fluorescence dequenching. Mutational analysis of E protein is being pursued to decipher the trigger residues involved in the fusion process.

II. Assembly and release of paramyxovirus (es) from host cells

The aim of this study is to understand the mechanisms of assembly and release of paramyxoviruses using viral like particle system. Knowing the central role of matrix protein in budding process we are trying to delineate regions of matrix protein critical for the budding activity through mutation studies. Such a study should help design strategies which would focus on inhibiting viral release process resulting in containment of viral spread.

III. Antibody response in dengue virus infected patients

Human antibody response for dengue is a double edged sword as there are implications that though it can resolve infection if reinfected with same serotype, but reinfection with another serotype can actually enhance the disease thus requiring a balanced neutralizing response to all 4 serotypes for vaccine development. The strategy for developing dengue vaccines is based on the assumption that a neutralizing immune response directed to a single strain will protect against most if not all strains of DENV within the serotype. However, recent studies show that strain variation in genotype from same serotype influences dengue virus neutralization. Thus there is a huge gap in understanding of the properties of antibodies that protect or possibly enhance disease. The primary goal of this project is to expand our knowledge on quantity and quality (neutralization vs enhancement) of antibody response to natural dengue virus infection and see its association if any with the severity of the disease.

IV. Host factor in virus infection

As obligate intracellular parasites, viruses have developed numerous ways of hijacking cell processes to facilitate the completion of their life cycle. If it were possible to identify key aspects of the virus's control over host cell metabolism, antiviral therapies that interfere with this control program could be used as antiviral agents. One of our project aims to work out a detailed transcriptional profile of host genes at different time points of infection reflecting particular stage of infection. Tracing the course of infection would elucidate reprogramming of host regulators depending on its requirement for that stage of infection. The identification of host factors that interact with viral proteins or orchestrate essential steps in the virus life cycle can suggest targets for antiviral drugs.

Publications

Shipra Gupta, Anuja Krishnan, Sumit Sharma, Praveen Kumar, Satinder Aneja and Pratima Ray Changing pattern of prevalence, genetic diversity and mixed infections of viruses associated with acute gastroenteritis in pediatric patients in New Delhi. **J. Med Virol** (In Press)

Selvapandiyan A, Ahuja K, Puri N, Krishnan A. Implications of co-infection of Leptomonas in visceral leishmaniasis in India. **Parasitology**, Oct 23:1-6, 2015.

Anuja Krishnan, Emily Happy Miller, Andrew S. Herbert, Melinda Ng, Esther Ndungo, Sean P.Whelan, John M. Dye and Kartik Chandran. Niemann-Pick C1 (NPC1)/NPC1-like1 chimeras define sequences critical for NPC1's function as a filovirus entry receptor. **Viruses,** *4*, 2471-2484, 2012.

Emily Happy Miller, Gregor Obernosterer, Matthijs Raaben, Andrew S Herbert, Maika S Deffieu, Anuja Krishnan, Esther Ndungo, Rohini G Sandesara, Jan E Carette, Ana I Kuehne, Gordon Ruthel, Suzanne R Pfeffer, John M Dye, Sean P Whelan, Thijn R Brummelkamp and Kartik Chandran. Ebola virus entry requires the host-programmed recognition of an intracellular receptor. **EMBO J***. :* 31: 1947-60, 2012.

Krishnan, A., S. K. Verma, P. Mani, R. Gupta, S. Kundu and D. P. Sarkar. A histidine switch in hemagglutinin-neuraminidase triggers paramyxovirus-cell membrane fusion. **J. Virol**, 83:1727-1741, 2009

Alone, V, P., G. Malik, A. Krishnan and L.C. Garg. Deletion mutations in N-terminal a1 helix render heat labile enterotoxin S subunit susceptible to degradation. **Proc. Natl. Acad Sci** 104 (41): 16056-16061, 2007.

Verma, S. K, P. Mani, N. R. Sharma, A. Krishnan, V. K. Valluripalli, S. Bathular, Reddy, A. Chaudhuri, R. P. Roy, and D. P. Sarkar. Histidylated Lipid-modified Sendai Viral Envelopes Mediate Enhanced Membrane Fusion and Potentiate Targeted Gene Delivery. **J Biol Chem** 280: 35399-35409, 2005.

Patra, K. A., R. Mukhopadhyay, R. Mukhija, A. Krishnan, L. C. Garg and A. K. Panda. Optimization of inclusion body solubilization and renaturation of recombinant human growth hormone from *Escherichia coli*. **Protein Expression and Purification**, 18, 182-192, 2000.