Thesis Title: Variable expression of Human Cytomegalovirus (HCMV) tegument genes among immunocompromised individuals and their response to different antiviral agents

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Abstract of the thesis:

Human cytomegalovirus (HCMV) is a widespread virus that often goes unnoticed in healthy adults but can cause serious illness in those with weakened immune systems. This broad investigation was conducted in metropolitan hospitals near Kolkata and found that 51.57% of hospitalized neonates and 49.20% of immunosuppressed renal transplant recipients tested positive for HCMV. Many patients showed persistent HCMV infection after antiviral therapy. The study also investigated specific clinical manifestation Choroidal neovascularization (CNV) can lead to partial or complete blindness associated with HCMV-infection to understand the immunological alteration.

It was found that HCMV-induced CNV progression was prominent in the presence of AT2R-dependent angiogenesis, while in the absence of HCMV, AT1R-dependent CCL-5-mediated angiogenesis was documented. Significant increases in CCL-19, CCL-21 chemokine responses, and CCR-7 chemokine receptor activation were observed in HCMV-induced CNV patients compared to HCMV non-induced CNV groups. These findings suggest that ocular HCMV latency poses a significant risk factor for the progression of retinal neovascularisation through a distinct NFkB non-canonical immunological signalling pathway.

In a study of renal transplant patients, a significant number of persistent infectivity of HCMV was observed after the antiviral therapy. The research aimed to understand the impact of latent HCMV infection on renal rejection in an Eastern Indian cohort. Among HCMV-positive transplant patients, 16.45% experienced early rejection, while 27.84% experienced late rejection due to persistent HCMV infection. Clinical parameters revealed that rejection due to latent HCMV cases were associated with serious health complications.

The current synthetic medications have limitations such as toxicity, processing challenges within the body, and susceptibility to viral resistance. In this study, bioactive extracellular enzyme laccase isolated from mushrooms was tested with ganciclovir, a common antiviral drug used against HCMV. The study found that laccase has promising antiviral effects and can effectively inhibit HCMV replication by targeting novel inhibitory sites on the UL54 protein. Laccase has also been observed to act synergistically with ganciclovir to inhibit HCMV replication. The in silico analysis has also indicated that the laccase enzyme's novel binding site on HCMV DNA polymerase can effectively obstruct a crucial structural component of the UL54, preventing another significant accessory replication regulatory protein, UL44, from binding efficiently. This discovery could lead to innovative antiviral approaches targeting *Herpesviridae* and offer insights into regulating HCMV replication through host pathways manipulation.

Debsopan Roy.

Signature of the Candidate

Nilanjan Chakraborty

Signature of the Supervisor

(With Seal)

Dr. Nilanjan Chakraborty
Scientist-E
National Institute of Cholera & Enteric Diseases
P-33, CIT Road, Scheme-XM, Beliaghata
Kolkata-700 010