

DBT-NII scientists get a deeper understanding of Dengue fever

New Delhi, Sep 17: Dengue fever is a mosquito borne disease identified over 100 years ago. It has reemerged in the past decade with an increasing geographic distribution of both the virus that causes it and its vector mosquitoes. Among other factors, global climatic changes are the biggest contributors for such rapid spread of this disease. Due to increasing global temperature, about half of the world's population is now at risk of contracting the disease (WHO-2019).



Dengue virus, the causative agent, is transmitted mainly by female *Aedes aegypti* and to a lesser extent by *A. albopictus*. Primary Dengue infection and disease is manifested as mild and self-limiting illness in the majority of individuals. Dengue Hemorrhagic Fever (DHF) is popularly known as 'severe dengue'. Molecular mechanisms of Dengue fever-associated 'Cytokine storm' are still enigmatic. Several neurological abnormalities such as metabolic encephalopathy, meningitis, myelitis, myositis, encephalitis, neuromyelitis optica and Guillain-Barré syndrome are often reported in case of severe dengue patients.

Recent research findings of scientists at the Department of Biotechnology's National Institute of Immunology (DBT-NII), New Delhi are throwing some light on how after the recovery phase, when the patients' plasma is still enriched with circulating viral proteins such as NS1 (non-structural protein) and various other host factors such as microRNA (miR-148a, in their study), transcription factors etc. can trigger the cascade of hyperinflammation.

Their study has also revealed that extracellular vesicles which are released upon dengue infection carry crucial cargo like miR-148a. These extracellular vesicles carrying miR-148a are internalized by microglia which are human brain cells. After internalization, miR-148a can degrade the molecular signaling pathway of USP33-ATF3 which is needed to suppress inflammation. By this route, the characteristic hyperinflammation also known as 'Cytokine Storm' during Dengue hemorrhagic fever can affect the human brain function, a situation collectively known as Neuroinflammation.

These results are very significant for understanding those pathogenic outcomes of Dengue fever which arise after the viral load from patients has gone down. Recently in the case of recovered COVID19 patients also, many patients have been reported to experience many complications related to heart, kidney and neurological anomalies after they recovered from disease and tested negative for viral replication. The results are providing a novel insight about how circulating plasma might contain many triggering factors for hyperinflammation which does contribute towards multi-organ complications. They are also relevant in the context of 'Plasma Therapy' which is recommended for treating critical patients.

Reference:

Mishra R, Lahon A, Banerjea AC. Dengue Virus Degrades USP33-ATF3 Axis via Extracellular Vesicles to Activate Human Microglial Cells. *J Immunol.* ji2000411. doi: 10.4049/jimmunol.2000411. Online ahead of print.

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