INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE
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Seminar Notice

Speaker: Dr. Nishi Raj Sharma, UDSC, New Delhi-21
Date: June 30, 2017
Time :3:30 PM
Venue: S. N. Bose Hall

Title: Tumor virus Kaposi's Sarcoma Herpesvirus vs Host cell RNA Granules: Who regulates whom?

Abstract: Mammalian RNA granules, including processing bodies (PB) and stress granules (SG), regulate cellular homeostasis and RNA metabolism [1]and are important components of the host cell antiviral responses. GW182 and de-capping/de-adenylating enzymes are specific components of PB, where siRNA- or miRNA-guided mRNAs are processed and degraded. TIA-1 positive stress granules (SG) represent the storage sites of stalled mRNAs and are often associated with the cellular antiviral response. In this study, we provide evidence that Kaposi's sarcoma-associated herpesvirus (KSHV) overcomes the host antiviral response by inhibition of SG formation. By immunofluorescence analysis, we find that B lymphocytes with KSHV lytic infection are refractory to SG induction due to expression of a viral lytic protein ORF57, an essential post-transcriptional regulator of viral gene expression and the production of new viral progeny. We find that KSHV ORF57 inhibits SG formation induced experimentally by arsenite and poly I:C, but not by heat stress. KSHV RTA, vIRF-2, ORF45, ORF59 and LANA exert no such function. ORF57 binds both PKR-activating protein (PACT) and protein kinase R (PKR) through their RNA-binding motifs and prevents PACT-PKR interaction in the PKR pathway. ORF57 interacts with PKR to inhibit PKR binding dsRNA and its autophosphorylation, leading to inhibition of eIF2a phosphorylation and SG formation. Homologous protein HSV-1 ICP27, but not EBV EB2, resembles KSHV ORF57 in the ability to block the PKR/eIF2a/SG pathway. Altogether, our data provide the first evidence that KSHV ORF57 plays a critical role in modulating host antiviral defenses during virus lytic infection.

All are cordially invited.