Institute of Molecular and Cell Biology
A*STAR

SEMINAR ANNOUNCEMENT

DATE: 16 February 2012, Thursday
TIME / VENUE: 3:00PM @ Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis
SPEAKER: Dr. Dong-Yan Jin
TITLE OF SEMINAR: **PACT targeted by viruses is a cellular double stranded RNA-binding partner of RIG-I and MDA5 in innate antiviral response**



RIG-I and MDA5 are cytoplasmic sensors of viral RNA that initiate innate antiviral immune response. These DExD/H-box RNA helicases share structural similarity with Dicer nuclease which mediates RNA interference. It is noteworthy that optimal function of Dicer requires double-stranded RNA (dsRNA)-binding protein activators including PACT. In this study, we demonstrated PACT to be a novel cellular binding partner and activator of RIG-I and MDA5. PACT physically binds to the C-terminal regulatory domain of RIG-I and MDA5. Functionally, PACT acts as a potent activator of RIG-I- and MDA5-dependent production of type I interferons in normal human lung fibroblasts, mouse embryonic fibroblasts and other types of cultured mammalian cells. PACT augments the activation of RIG-I and MDA5 by poly (I:C) of both intermediate and long length. PACT also synergizes with RIG-I and MDA5 to amplify interferon-induced antiviral immune response in virus-infected and uninfected cells. Silencing of PACT by RNAi attenuated Sendai virus- and vesicular stomatitis virus-induced activation of type I interferon production. The activation of RIG-I and MDA5 by PACT requires neither dsRNA-dependent protein kinase PKR nor Dicer. Direct interaction of RIG-I and MDA5 with PACT results in the activation of their ATPase activity. Intriguingly, the RIG-I- and MDA5-activating activity of PACT is counteracted by well-known virus-encoded antagonists of interferon such as influenza A virus NS1 and herpes simplex type I Us11 proteins. Our work reveals a novel component and a new layer of regulation in RIG-I- and MDA5-dependent innate antiviral immune response. Our findings have implications in rationale design and development of new antiviral and immunomodulatory agents.

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Host: Prof. Haiwei Song