

**Date / Time:**  
**Tuesday 6 March 2012**  
**12pm – 1pm**

**Venue:**  
**CeLS Auditorium**  
**Centre for Life Sciences,**  
**Level 1,**  
**28 Medical Drive**  
**Singapore 117456**

**Convener:**  
**Dr Zhang Yongliang**

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## **Regulations of Cellular Antiviral Response**

### **Abstract**

Viral infection results in transcriptional induction of type I IFNs, which induce a set of IFN-stimulated genes (ISGs) that have inhibitory effects on viral replication in infected cells. Transcriptional activation of the promoters of type I IFN genes requires the coordinate activation of multiple transcription factors including NF- $\kappa$ B and IRF-3 and their cooperative assembly into transcriptional enhancer complexes in vivo. Induction of type I IFNs are tightly regulated because excessive production of these cytokines causes autoimmune diseases. In the past years, we have identified important signaling components that are required for virus-triggered induction of type I IFNs, such as VISA, MITA, WDR5 and GSK3 $\beta$ . We also identified regulatory proteins that are important for limiting virus-triggered induction of type I IFNs, such as A20, SIKE, RNF5, Otubin1/2 and SENP2. These signaling and regulatory proteins coordinate to ensure proper induction of type I IFNs after viral infection.

### **Selected Publications**

1. Xu, L.G., Wang, Y.Y., Han, K.J., Li, L.Y., Zhai, Z., **Shu, H.B.\*** (2005) VISA is an adapter protein required for virus-triggered signaling. **Molecular Cell** 19:727-740
2. Zhong, B., Yang, Y., Li, S., Wang, Y.Y., Li, Y., Diao, F., Lei, C., He, X., Zhang, L., Tien, P., **Shu, H.B.\*** (2008). The Adaptor Protein MITA Links Virus-Sensing Receptors to IRF3 Transcription Factor Activation. **Immunity**. 29:538-550.
3. Zhong B., Zhang L., Lei Z., Li Y., Mao A.P., Yang Y., Wang Y.Y., Zhang X.L., Shu H.B.\* (2009). RNF5 negatively regulates virus-induced IRF3 activation via ubiquitination and degradation of MITA, **Immunity**, 30, 397-407
4. Wang, Y.Y., Liu, L.J., Zhong, B., Liu, T.T., Li, Y., Yang, Y., Ran, Yong, Li, S., Tien, P., **Shu, H.B.\*** (2010) WDR5 is essential for assembly of the VISA-associated signaling complex and virus-triggered IRF3 and NF- $\kappa$ B activation. **Proc. Natl. Acad. Sci. USA**. 107:815-820.
5. Lei CQ, Zhong B, Zhang Y, Zhang J, Shu HB\* (2010) GSK3 $\beta$  regulates virus-triggered IRF3 activation and cellular antiviral response by promoting TBK1 activation. **Immunity** 33:878-889.