神戸大学大学院医学研究科附属感染症センター 主催講演会

「Nuclear DNA Sensing, Innate Immunity, and Epigenetic Regulation of Herpes Simplex Virus Lytic and Latent Infection」

◆ 日　時： 平成 25 年 9 月 9 日（月） 16 時～17 時 30 分まで（開場／15 時 30 分）

◆ 会　場： 神戸大学医学部 大講義室（外来診療棟６階）

◆ 演　者： Prof. David M. Knipe(Department of Microbiology and Immunobiology, Harvard Program in Virology, Harvard Medical School)

◆ 主　催： 神戸大学大学院医学研究科附属感染症センター

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－講演概要－

Detection of foreign DNA in the nuclei of mammalian cells leads to chromatinization and silencing of the DNA, DNA damage responses, and innate immune responses. We have found that herpes simplex virus 1 DNA, which is not associated with histones in the virion, rapidly associâtes with histones upon entry into the cell nucleus. In épithélial cells, viral proteins promote active chromatin and viral lytic transcription while in neurons the latency associated transcript promotes heterochromatin and lytic gene silencing. We have also found that the cellular IFI16 DNA sensor is nuclear in normal human fibroblasts and the viral DNA must be introduced into the nucleus for IRF-3 signaling. This pathway involves IFI16 binding to viral DNA in the nucleus and initiating a signaling pathway through STING in the cytoplasm that leads to activation of IRF-3 through IRF-3 phosphorylation dimerization, and transport into the nucleus where it activâtes transcription of interféron-β and interféron-stimulated genes. The viral IE protein ICP0 causes the dégradation of IFI16 and blocks this pathway. We have recently found that IFI16 sensing of HSV-1 DNA also leads to enhanced heterochromatinization of the viral DNA and reduced IE gene expression. A similar restriction was observed on transfected DNA but not SV40 and adénovirus virion DNAs. In this talk I will explore the mechanisms of foreign DNA sensing in the nucleus and the mechanisms of the host responses to foreign DNAs such as herpes simplex virus DNA.

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