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

「単純ヘルペスウイルスの宿主への侵入とインテグリンによって誘導される自然免疫」

◆ 日　時： 平成 24 年 11 月 5 日 (月) 18 時～19 時 30 分まで (開場 / 17 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.　Gabriella Campadelli-Fiume　(University of Bologna, Department of Experimental Pathology)

◆ 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－

Pathogens are sensed by Toll-like (TLRs) and a growing number of non-TLR receptors. Herpes simplex virus 1 (HSV-1) infection is widespread among humans. Hitherto, the known innate defenses against HSV consist of TLR2, located at or around cholesterol–rich membrane microdomains, the endosomal TLR3 and TLR9, and the cytosolic RNA and DNA sensors. Opposing the host defenses are an array of viral proteins exemplified by the virion–host–shutoff Rnase, and the immediate-early infected cell protein 0 (ICP0) and ICP27. Integrins constitute a family of signalling receptors exploited by viruses and bacteria to access cells. In the case of HSV, my laboratory has shown that αVβ3-integrin serves as a routing factor at the time of virus entry into the cells, and redirects the HSV receptor nectin1, hence the virus, to cholesterol-rich membrane microdomains, from where the virus endocytosed in a dynamin-2-dependent acidic pathway.

By gain and loss-of-function approaches we found that αvβ3-integrin is a sensor of and plays a crucial role in the innate defense against HSV. αvβ3-integrin signalled through two pathways. One concurred with TLR2, affected activation/induction of IFNs-1 , NF-κB, and a polarized set of cytokines and receptors. The virion glycoproteins gH/gL induced IFN1 and NF-κB *via* this pathway. The other pathway was TLR2-independent, involved SRC-SYK-CARD9-TRIFF and affected IRF3-IRF7. The importance of αvβ3-integrin-mediated defense is reflected in the observation HSV evolved the immediate early ICP0 protein to counteract it. We propose that αvβ3-integrin is considered a novel class of non-TLR pattern recognition receptors, a role likely exerted towards viruses and bacteria which interact with integrins and mount an innate response.

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