HONG KONG RNA CLUB
Seminar

19 Jun 2018 (Tue) / 5:00-6:00pm
Room 2-130, To Yuen Building (撘源樓)
City University of Hong Kong

Guest Speaker:
Prof. Ai Kotani
School of Medicine
Tokai University

Role of secretary small RNAs as a pro-inflammatory mediator in the development of EBV-associated lymphoma

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Role of secretory small RNAs as a pro-inflammatory mediator in the development of EBV-associated lymphoma

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Abstract
Epstein-Barr virus (EBV) causes various diseases in the elderly including B-cell lymphoma such as Hodgkin’s lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL). Here, we show that EBV acts \textit{in trans} on non-infected macrophages in the tumor through exosome secretion and augments the development of lymphomas. In a humanized mouse model, the different formation of lymphoproliferative disease (LPD) between two EBV strains (Akata and B95-8) was evident. Furthermore, injection of Akata derived exosomes affected LPD severity possibly through the regulation of macrophage phenotype \textit{in vivo}. Exosomes collected from Akata lymphoblastoid cell lines (LCLs) reportedly contain EBV-derived non-coding RNAs such as BamHI fragment A rightward transcript (BART) miRNAs and EBV-encoded RNA (EBER). We focused on the exosome-mediated delivery of BART miRNAs. \textit{In vitro}, BART miRNAs could induce the immune regulatory phenotype in macrophages characterized by the gene expressions of \textit{interleukin-10}, \textit{tumor necrosis factor-alpha}, and \textit{arginase 1}, suggesting the immune regulatory role of BART miRNAs. The expression level of an EBV-encoded miRNA was strongly linked to the clinical outcomes in elderly diffuse large B-cell lymphoma patients. These results implicate BART miRNAs as one of the factors regulating the severity of lymphoproliferative disease and as a diagnostic marker for EBV+ B-cell lymphoma.