令和 7 年度　第 52 回　大学院セミナー

令和 7 年 10 月 7 日

分 野 名 Area of Research (責任者名)(内線)	ウイルス生態学分野 責任者名（好井健太朗）　　内線（8595）
演　　題 Title	**What makes an effective live-attenuated vaccine? New insights into the innate cellular response to yellow fever virus 17D (YFV-17D)**
講 師 等 Presenter	Dr. Sonja Best Innate Immunity & Pathogenesis Section Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health
概要 Abstract	The live-attenuated yellow fever virus strain 17D (YFV-17D) is considered one of the safest and most effective vaccines ever developed, conferring lifelong immunity with a single dose. Although the vaccine has been used for over 80 years, the basis for its immunogenicity remains poorly understood. In vaccinated humans, transcriptional profiling of PBMCs suggests that innate immune gene signatures correlate with protection, while integrated stress response gene signatures predict the magnitude of CD8 T cell responses. To determine how YFV-17D infection induces these responses, we examined dynamics of IFN expression and virus replication compared to the parental strain, YFV-Asibi, and an additional hepatotropic flavivirus, dengue virus (DENV2). As expected, IFN expression required the signaling adaptor MAVS, indicating a central role for the mitochondria in driving these IFN dynamics. Biochemical analysis of mitochondrial function by Seahorse analysis and LC-MS for metabolites revealed that YFV-17D uniquely upregulated mitochondrial respiration, and induced mitochondrial uncoupling associated with depletion of intermediates from the glycolytic, pentose-5-phosphate and tricarboxylic acid cycle pathways. Importantly, pharmacological inhibition of specific mitochondrial stress pathways eliminated IFN expression without affecting virus replication in tissue culture, and greatly altered innate immune gene signatures of infected primary human dendritic cells. Thus, mitochondrial dysfunction in response to YFV-17D infection is a key driver of innate immunity, which has implications for further design of live-attenuated flavivirus vaccines.
開 催 日 時 Date and Time	令和 7 年 10 月 24 日（金） 16：00～17:00
開 催 方 法 Online/Face to face	高度感染症研究センター1F 大会議室
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