セミナーのお知らせ

"Genetic variations of *APOBEC3C* and *APOBEC3H* influence HIV-1 restriction activity and genetic diversity"

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日時：平成 31 年 2 月 7 日(木)　16:00-

場所：微生物病研究所　本館 1 階　微研ホール

This seminar will be held in Japanese.
本セミナーは医学研究科の単位認定セミナーです。

連絡先:　ウイルス感染制御分野

櫻木　淳一（内線 8348）

Abstract:
The APOBEC3 (A3) family of proteins are single-strand DNA cytosine deaminases that provide an innate immune barrier against retroviruses including HIV-1. The HIV-1 accessory protein Vif counteracts up to five A3 enzymes (A3C, A3D, A3F, A3G and A3H) by proteasome-mediated degradation. It is known that the *A3* genes have significant variations within the human population. For example, the polymorphisms of A3C (Ser188 and Ile188) and A3H (7 haplotypes: I to VII and 4 splicing variants: SV154, SV182, SV183 and SV200) have been reported to exhibit differential restriction activity against Vif-deficient HIV-1. However, these A3C and A3H variants have yet to be fully characterized. Here, we show potential HIV-1 restriction activity of the A3C-I188 variant and accumulation of G-to-A mutations in proviral DNA using a T cell-based spreading infection system. We also elucidate the genetic and mechanistic basis for expression and function of the A3H splicing variants. For instance, A3H hapII splicing variant SV200 is at least 4-fold more restrictive against Vif-deficient HIV-1 than other A3H splicing variants. Interestingly, in addition to Vif-mediated degradation, we reveal that HIV-1 has evolved a Vif-independent mechanism to counteract elevated HIV-1 restriction activity by A3H hapII SV200. Taken together, our data support that genetic variations in *A3C* and *A3H* may influence HIV-1 adaptation and pathogenesis *in vivo*.

Reference:
Ikeda T., Symeonides M., Albin J.S., Li M., Thali M., & Harris R.S. (2018) HIV-1 adaptation studies reveal a novel Env-mediated homeostasis mechanism for evading lethal hypermutation by APOBEC3G. ***PLoS Pathog***., 14(4). Apr 20

Ebrahimi D., Richards C.M., Carpenter M.A., Wang J., Ikeda T., Becker J.T., Cheng A.Z., McCann J.L., Shaban N.M., Salamango D.J., Starrett G.J., Lingappa J.R., Yong J., Brown W.L., & Harris R.S. (2018) Genetic and mechanistic basis for APOBEC3H alternative splicing, retrovirus restriction, and counteraction by HIV-1 protease. **Nat Commun**., 9(1). Oct 8.

Anderson B.D., Ikeda T., Moghadasi S.A., Martin A.S., Brown W.L., & Harris R.S. (2018) Natural APOBEC3C variants can elicit differential HIV-1 restriction activity. **Retrovirology**, 15(1), Dec 17.