第４０３回 難研セミナー

下記により難研セミナーを開催しますので、多数御来聴下さい。

記

日　時：2008 年 2 月 14 日（木）17:00～18:00

場　所：3 号館 6 階セミナールーム

演　者：Stuart F. J. Le Grice

（HIV Drug Resistance Program, National Cancer Institute）

演　題：Plus strand DNA synthesis in HIV as a Therapeutic Target

要　旨：

Second, or plus-strand, DNA synthesis in retroviruses and LTR-containing retrotransposons requires (i) recognition of the polypurine tract primer and cleavage at its 3' terminus by the C-terminal ribonuclease H (RNase H) domain of reverse transcriptase (RT), (ii) binding of the DNA polymerase domain to the newly-created PPT 3' terminus in order to initiate plus strand DNA synthesis and (iii), precise removal of the RNA primer from nascent DNA. Despite a wealth of biochemical data, the mechanism underlying PPT recognition be the N- and C-terminal domains of HIV-1 RT is still not fully understood. The significance of PPT utilization as a target of therapeutic intervention has also been implied from its sensitivity to inhibition by nonnucleoside RT inhibitors. In order to investigate PPT utilization more thoroughly, we have embarked on a micro-to-macro approach, studying RT/PPT complexes by both single molecule fluorescence and NMR spectroscopy. The former takes advantage of uniquely-positioned fluorophores on the retroviral polymerase, while the latter has exploited both nucleoside analogs and high affinity nucleic acid ligands. Together, these approaches suggest a unique architecture at the junction between the PPT and both 5' and 3' flanking sequences contributes to recognition by the retroviral polymerase. Duplication of our data for HIV-1 RT with its counterpart from the *Saccaromyces cerevisiae* LTR-retrotransposon Ty3, whose PPT sequence differs significantly, suggests a common mechanism for PPT recognition.

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