Nonsynonymous mutation in integrase catalytic core domain affects feline foamy viral DNA integration

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Integrase is the retroviral protein responsible for incorporating a double-stranded viral DNA copy into the host chromosome. Single amino acid substitution in integrase (IN) active site is replication-defective, and reduces viral infectivity. This study is to investigate whether mutation in DD(35)E motif and residues near the active site of catalytic core domain is critical for feline foamy viral integration. In vitro enzymatic activities of IN mutant proteins were analyzed by using p32-radiolabeled oligonucleotide substrates and 15% polyacrylamide gels. DDE mutation almost lost their IN activities. But Q165A, Y191A, and S195A showed reduced effects. Although DDE mutants produced replication-defective virions by one cycle transfection, Q165A, Y191A, and S19A mutants had infectivity on their natural host cells. Known as the immature virions containing integrated IN executed integration aberrantly and had trouble in producing viral DNAs for new virion particles, in the case of DDE mutants no integrated viral DNAs were detected at 24 h and 48 h post infected host chromosomal DNAs. However, integration of viral DNA whose virions have IN mutants in the amino acid residues present near the active site such as Q165A and Y191A were detected, and then quantitated by competitive PCR. Nonsynonymous substitutions in highly conserved region of feline foamy viral IN resulted in viruses with replication-defective. Defects in viral DNA synthesis, viral production, and integration processing were observed for all of the replication-defective mutants. Especially, feline foamy viral natural host cells are not infected with replication-defective DDE mutant viruses.

Biography
Cha Gyun Shin has completed his PhD from The Ohio State University and Postdoctoral studies from Dana Faber Cancer Institute. He is a Professor at Department of Systems Biotechnology, Chung-Ang University, Republic of Korea.

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