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Impact of V2 mutations for escape from a potent neutralizing anti-V3 monoclonal antibody during in vitro selection of a primary HIV-1 isolate ※Title in bold type

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KD-247, a humanized monoclonal antibody (MAb) to an epitope of gp120-V3-tip, has potent cross-neutralizing activity against subtype B primary HIV-1 isolates. To assess how KD-247 escape mutants can be generated, we induced esca 5 virus, MOKW in vitro. In the presence of relatively low c amino acid (aa) mutations (R166K/D167N) in V2 expande ip substitution (P313L) emerged in addition to the V2 mutations. On the other hand, a virus with a V2 175P mutation dominated during passaging in the absence of KD-247. By domain swapping analysis, we demonstrated that the V2 mutations and the P313L mutation in V3 contribute to partially and completely resistant phenotypes against KD-247, respectively. To identify the V2 mutation responsible for resistance to KD-247, we constructed pseudoviruses with single or double aa mutations in V2 and measured their sensitivity to neutralization. Interestingly, the neutralization phenotypes were switched, such that the 175th aa (Pro or Leu) located in the center of V2 was exchanged, indicating that the 175th aa has a key role in dramatically changing the Env oligomeric state on the membrane surface and affecting the neutralization phenotype against not only anti-V3 antibody but also rsCD4. These data suggest that HIV-1 can escape from anti-V3 antibody attack by changing the conformation of the functional envelope oligomer by acquiring mutations in the V2 region in environments with relatively low antibody concentrations.

※ Times New Roman font, size 12

※ Do not insert figure(s)