学位論文抄録

Abstract of Thesis

Functional analysis of a monoclonal antibody reactive against the C1C2 of Env obtained from a patient infected with HIV-1 CRF02_AG
（HIV-1 CRF02_AG 感染症例由来の Env C1C2 に対するモノクローナル抗体の機能解析）

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Background: Recent data suggest the importance of non-neutralizing antibodies (nnAbs) in the development of vaccines against HIV-1 because two types of nnAbs that recognize the coreceptor binding site (CoRBS) and the C1C2 region mediate antibody-dependent cellular-cytotoxicity (ADCC) against HIV-1-infected cells. However, many studies have been conducted with nnAbs obtained from subtype B-infected individuals, with few studies in patients with non-subtype B infections.

Results: We isolated a monoclonal antibody 1E5 from a CRF02_AG-infected individual and constructed two forms of antibody with constant regions of IgG1 or IgG3. The epitope of 1E5 belongs to the C1C2 of gp120, and 1E5 binds to 27 out of 35 strains (77%) across the subtypes. The 1E5 showed strong ADCC activity, especially in the form of IgG3 in the presence of small CD4-mimetic compounds (CD4mc) and 4E9C (anti-CoRBS antibody), but did not show any neutralizing activity even against the isolates with strong binding activities. The enhancement in the binding of A32, anti-C1C2 antibody isolated from a patient with subtype B infection, was observed in the presence of 1E5 and the combination of 1E5, A32 and 4E9C mediated a strong ADCC activity.

Conclusions: These results suggest that anti-C1C2 antibodies that are induced in patients with different HIV-1 subtype infections have common functional modality and may have unexpected interactions. These data may have implications for vaccine development against HIV-1.