Gene Ther Mol Biol Vol 9, 327-328, 2005

HIV-1 gp120 and human platelet glycoprotein GPIIIa: does structural homology exist?

Research Article

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Key words: HIV, thrombocytopenia, gp1202

Abbreviations: glycoprotein, (gp); immunodeficiency virus, (HIV); Immune thrombocytopenia (ITP)

Received: 23 August 2005; Revised: 28 September 2005
Accepted: 29 September 2005; electronically published: 1 November 2005

Summary

Chronic thrombocytopenia is a common hematologic disorder in patients infected with the human immunodeficiency virus (HIV). Although often asymptomatic, the thrombocytopenia may be associated with a variety of bleeding abnormalities. Antigenic homology between HIV-1 gp120 and human platelet glycoprotein GPIIIa was reported. Here, the author performed a study to assess the structural homology between HIV-1 gp120 and human platelet glycoprotein GPIIIa. To answer this question, a computer-based study for amino acid sequence comparison and protein structure modeling is performed. According to this study, gp-120 is totally difference from human platelet glycoprotein GPIIIa. It seems that the structural homology between HIV-1 gp120 and human platelet glycoprotein GPIIIa might not exist. This implies that gp-120 might not be an important underlying factor for ITP in HIV-infected patients.

I. Introduction

Chronic thrombocytopenia is a common hematologic disorder in patients infected with the human immunodeficiency virus (HIV) (Hoffman et al, 1989; Scaradavou, 2002). Although often asymptomatic, the thrombocytopenia may be associated with a variety of bleeding abnormalities (Hoffman et al, 1989; Scaradavou, 2002). Immune thrombocytopenia (ITP) is an important hematological disorder in HIV infected patients (Hoffman et al, 1989; Scaradavou, 2002). About 5-10% of HIV seropositive individuals, in all risk groups, develop a syndrome of immunological thrombocytopenic purpura (ITP) (Hoffman et al, 1989). Despite the clear association between HIV infection and thrombocytopenia, the exact immune mechanism leading to the peripheral platelet destruction remains unclear (Hoffman et al, 1989).

Karpatkin et al demonstrated that immune platelet destruction observed in HIV-infected patient was associated with the presence of a cross-reactive antibody recognizing both HIV-glycoprotein (gp)120 and platelet GPIIIa (Karpatkin and Nardi, 1992). The presence of a cross-reactive antibody between HIV-gp120 and platelet GPIIIa was demonstrated (Karpatkin and Nardi, 1992). They suggested that molecular mimicry between HIV-gp120 and platelet GPIIIa might be important in the pathogenesis of immune thrombocytopenia in HIV-infected patients (Karpatkin and Nardi, 1992). Although antigenic homology is confirmed (Karpatkin and Nardi, 1992) no report on the structural homology is documented. To answer this question, a computer-based study for amino acid sequence comparison and protein structure modeling is performed.

II. Materials and methods

A. Getting the sequence

The database ExPASY (Gasteiger et al, 2003) was used for data mining of the amino acid sequence for HIV-1 gp120 and human platelet glycoprotein GPIIIa.

B. Structure modeling

Concerning secondary structure modeling, the author performs protein secondary structure predictions of HIV-1 gp120 and human platelet glycoprotein GPIIIa from its primary sequence using NNPREDICT server (Kneller et al, 1990). The calculated secondary structures were presented and compared.

III. Results

A. Sequence of HIV-1 gp120 and human

platelet glycoprotein GPIIIa

From searching of the database ExPASY, sequence of HIV-1 gp120 and human platelet glycoprotein GPIIIa were derived as "NIGPGRAFYTTGEIIGDIRQAHC" and "DRKEFAKFEEERA"

B. Structure modeling

Using NNPREDICT server, the calculation for secondary structure of HIV-1 gp120 and human platelet glycoprotein GPIIIa was performed (**Figure 1**). The calculated structures written 23 and 13 orderly. According to this study, no part of HIV-1 gp120 is similar to GPIIIa.

A. HIV-1 gp-120

------EEE----EEE-HH----

B. human platelet glycoprotein GPIIIa

----H--HHH---

Figure 1. Calculated secondary structures of HIV-1 gp-120 and human platelet glycoprotein GPIIIa (Secondary structure prediction: *H = helix, E = strand, - = no prediction)*

IV. Discussion

Karpatkin et al reported that anti-CD4 antibody was found in 30% of HIV-1-seropositive thrombocytopenic patients compared with 5% of nonthrombocytopenic seropositive patients and was shown by the following observations to contain internal-image anti-idiotype antibody (Ab2) directed against the antibody (Ab1) to gp120, the HIV-1 envelope glycoprotein that binds to CD4 (Karpatkin et al, 1992). Indeed, gp-120's structure was first defined by Kwong et al (1998). According to their study, the structure reveals a cavity-laden CD4-gp120 interface, a conserved binding site for the chemokine receptor, evidence for a conformational change upon CD4 binding, the nature of a CD4-induced antibody epitope, and specific mechanisms for immune evasion.

The mimicry theory between platelet GPIIIa and HIV-1 gp120 is proposed as the underlying pathogenesis of thrombocytopenia in HIV-infected patients (Kneller et al, 1990; Karpatkin and Nardi, 1992; Karpatkin et al, 1992; Gasteiger et al, 2003). Chia et al (1998) noted that anti-HIV antibodies could be eluted from platelets. They found that platelet crossreactive antibodies in HIV infection were primarily alkaline-sensitive and were associated predominantly with HIV p24 and gp-120 antibody (Chia et al, 1998). Chia et al (1998) proposed that these antibodies might play a role in the immune thrombocytopenia of HIV-infected patients.

Here, the author used computational hematology technique to evaluate the molecular structural similarity between HIV-1 gp-120 and human platelet glycoprotein GPIIIa. The database ExPASY (Gasteiger et al, 2003) was used for data mining of the amino acid sequence for HIV-1 gp-120 and human platelet glycoprotein GPIIIa. Concerning secondary structure modeling, the author performs protein secondary structure predictions of HIV-1 gp-120 and human platelet glycoprotein GPIIIa from its primary sequence using NNPREDICT server (Kneller et al, 1990).

In conclusion, gp-120 is totally difference from human platelet glycoprotein GPIIIa. It seems that the structural homology between HIV-1 gp120 and human platelet glycoprotein GPIIIa might not exist. This implies that gp-120 might not be an important underlying factor for ITP in HIV-infected patients. However, it is important to note that both HIV-1 gp120 and GPIIIa are highly glycosylated proteins and any cross reactivity to antibodies that recognize complex sugars cannot be ruled out by either the sequence or secondary structure predictions. A more involved analysis with sugars might throw some light and recommended as a future study. Indeed, it was demonstrated that fibronectin (FN) could bind HIV-1 envelope proteins, in particular gp 120 and gp 120 was also bound to the FN present on the surface of platelets (Pugliese et al, 1996). The specificity of this binding was confirmed by the inhibition obtained by pretreating platelets with anti-FN antibodies (Pugliese et al, 1996). The consequence of the surface modifications of the platelets could explain the thrombocytopenia that frequently occurs in patients infected with HIV and suggests also the possibility that platelets could be a vehicle for the virus in the circulation (Pugliese et al, 1996).

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