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Further evidence for the relationship of HIV-1 gp120 V3 loops with Ig superfamily members: similarity with the putative CDR3 region of T-cell receptor δ-chains

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1. Summary

Twenty-five V3 loops of envelope gp 120 extracted from 30 HIV-1 isolates were compared with T-cell receptor (TCR) subunits variable (V) portions using pairwise alignments of 11-residue peptides. The results indicate that, in comparison with random sequences, the analyzed V3 loops, unlike control (unrelated) sequences, display highly significant local similarity with TCR V_δ ($p \approx 10^{-20}$). However, pattern-matching searches were performed on a much larger number of V3 loops (484). In particular, selective pattern TR* * * NT * K * I is shared by V_δ from human T-cell line KT19E and 230 HIV-1 V3 loops (N-terminal portion). Pattern RA* YT * * * I * G is common for V_δ chain isolated from T-cell line DS6 of an immunodeficient patient and 69 V3 loops (C-terminal portion). The presented δ-chain portions of sequence similarity with the V3 loops overlap the putative complementarity-determining region (CDR3), thus possibly indicating functional similarity too.

2. Introduction

A number of autoimmune reactions observed in individuals infected with HIV could be the result of virus-induced lymphocyte activation and antibody production [1–4]. The unique biochemical and immunogenic properties of the HIV-1 envelope gp120, including regions of sequence similarity with HLA antigens [5], T-cell antigens [6] and, in particular, immunoglobulin heavy- and light-chain variable (V) regions [7–9], might enable gp120 direct interaction with antigen or with immune system constituents in an idiotype (Id)-anti-Id fashion [10,11]. However, for better understanding of the deceptive imprinting and the failure of the immune response against HIV-1 variants [12] it would be of particular importance not only to delineate an immune response to autoantigen(s) that might be affected by an anti-idiotypic or suppressor cell network, but also the types of T cells participating in direct intercellular contacts.

According to Jerne's network hypothesis, immune regulation results from lymphoid cell receptor recognition of determinants on other lymphoid cell receptors [13]. Antigen recognition by Id-specific T cells, besides being conventionally MHC restricted, may occur in the absence of antigen-presenting cell (APC). Thus, an antigen-specific T-cell receptor (TCR) recognition was observed both by auto anti-idiotypic clones [14,15] and by anti-idiotypes to T-cell idiotopes (clonotypic antibodies) [16,17]. It was also found that some TCRs of autoreactive cytotoxic T cell clones respond to unprocessed antigen such as myelin basic protein (MBP) [18]. Furthermore, it seems that T cells may respond directly to antigens on the surface of bacteria and viruses [19]. These results provide evidence for both direct interaction between TCRs and antigens and for the role played by the idiotype-like determinants on TCRs. Since we have shown the presence of Ig-like features in the gp120 immunodominant V3 loop and its flanking region [7–9], it would be of interest to analyze limited stretches of sequence homology between such an Ig-like

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