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Ancient positive selection on CD155 as a possible cause for susceptibility to poliovirus infection in simians

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Abstract

Poliovirus is the etiological agent of poliomyelitis. From the observations that only simians are susceptible to poliovirus infection and that 37 amino acid sites (the poliovirus-binding associated [PBA] sites) in the domain D1 of CD155 are involved in the binding to poliovirus, it is considered that the susceptibility to poliovirus infection evolved through amino acid substitutions that occurred at the PBA sites on the ancestral branch of simians. Here it is shown that positive selection has operated on these substitutions by analyzing the nucleotide sequences encoding almost the entire region of D1 in humans, non-human hominoids (chimpanzees and gorillas), Old World monkeys (African green monkeys), New World monkeys (brown capuchins, squirrel monkeys, and marmosets), prosimians (ring-tailed lemurs), and non-primate mammals (rabbits). Positive selection is unlikely to have operated on the susceptibility to poliovirus infection, but possibly on the binding to another molecule. Elimination of susceptibility to poliovirus infection in simians may be difficult, because it also requires elimination of advantageous effects that have been exerted by CD155.

Keywords: Poliovirus; Simian; CD155; Positive selection; Antagonistic pleiotropy

1. Introduction

Poliovirus, a member of the genus *Enterovirus* in the family *Picornaviridae*, is the etiological agent of poliomyelitis, which is an acute disease causing flaccid paralysis through selective destruction of motor neurons in the central nervous system (Landsteiner and Popper, 1909). Only humans are natural hosts for poliovirus. However, non-human hominoids and Old World monkeys are considered to be susceptible to poliovirus infection, because individuals or cell lines from these organisms may be infected by poliovirus under experimental conditions (Hsiung et al., 1964). New World monkeys are also known to be, at least partially, susceptible to poliovirus infection (Ida-Hosonuma et al., 2003). In contrast, prosimians and non-primate mammals do not appear to be susceptible.

Susceptibility to poliovirus infection is determined mainly by the interaction between the surface capsid proteins (VP1, VP2, and VP3) of poliovirus and the poliovirus receptor protein (CD155) on the host cell surface (Mendelsohn et al., 1989). CD155 (totally 417 amino acid sites) is a member of the immunoglobulin (Ig) superfamily, consisting of a signal peptide (amino acid positions 1–27), three extracellular Ig-like domains (D1 [positions 28–142], D2 [positions 143–242], and D3 [positions 243–330]), a transmembrane domain (positions 331–355), and a cytoplasmic tail (positions 356–417). (Note that the numbers and positions of amino acid sites are those for human CD155.) D1 is known to bind to poliovirus (Koike et al., 1991; Selinka et al., 1991). From the analysis of the three-dimensional structure of CD155–poliovirus complex, 26 amino acid sites (positions 29, 30, 60, 61, 63, 75, 81–84, 86, 88–91, 93, 98, 102, 124, and 126–132) in D1 were found to be located at its interface (He et al., 2003). In addition, from mutagenesis analysis, 20 amino acid sites (positions 78, 80, 82–87, 92, 99–102, 117–119, 124, 126, 130, and 131) in D1 were identified as important for

Abbreviations: Ig, immunoglobulin; PBA, poliovirus-binding associated; INSD, International Nucleotide Sequence Database; $r_{S\ (N)}$, rate of synonymous (nonsynonymous) substitution; $C_{S\ (N)}$, number of synonymous (nonsynonymous) differences per sequence; S (N), number of synonymous (nonsynonymous) sites per sequence; p, probability; DNAM-1, DNAX accessory molecule-1; Tactile, T-cell activated increased late expression; Tage4, tumor-associated antigen E4; BRCA1, breast and ovarian cancer susceptibility gene 1; ANG, angiogenin; AP, antagonistic pleiotropy.

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poliovirus binding (Bernhardt et al., 1994; Colston and Racaniello, 1994; Morrison et al., 1994; Harber et al., 1995; Liao and Racaniello, 1997). Therefore, 37 amino acid sites of D1 are involved in the binding to poliovirus, and are called the poliovirus-binding associated (PBA) sites in this paper.

CD155 has been identified not only in simians, which are susceptible to poliovirus infection, but also in prosimians and non-primate mammals, which are not susceptible (Ida-Hosonuma et al., 2003). Therefore, the difference in the susceptibility to poliovirus infection between these organisms appears to result from the difference in the amino acid sequence of CD155. To understand the evolutionary mechanisms of the susceptibility to poliovirus infection, it is interesting to examine natural selection that has operated on CD155. In general, natural selection can be detected by comparing the rates of synonymous (r_S) and non-synonymous (r_N) substitutions for the protein-coding nucleotide sequences (Hughes and Nei, 1988). Positive and negative selection are inferred when $r_S < r_N$ and $r_S > r_N$, respectively. Ida-Hosonuma et al. (2003) analyzed the nucleotide sequences encoding almost the entire region (positions 36–132) of D1 obtained from humans, non-human hominoids (chimpanzees and gorillas), Old World monkeys (African green monkeys), New World monkeys (brown capuchins, squirrel monkeys, and marmosets), prosimians (ring-tailed lemurs), and non-primate mammals (rabbits). They observed that $r_S > r_N$ for all pairwise comparisons of these sequences, and concluded that positive selection had not operated on D1. However, the binding of CD155 to poliovirus is not mediated by the entire region of D1, but only by the PBA sites. In addition, according to the parsimony principle (Fitch, 1971), the ancestor of primates was not susceptible to poliovirus infection, but the susceptibility evolved on the ancestral branch of simians in the phylogenetic tree. Therefore, natural selection should be examined for the PBA sites on the ancestral branch of simians.

Here it is shown that ancient positive selection on CD155 is a possible cause for susceptibility to poliovirus infection in simians. The biological significance of the results is discussed.

2. Materials and methods

2.1. Sequence data

The nucleotide sequences encoding almost the entire region of D1, that were analyzed by Ida-Hosonuma et al. (2003), were used to examine natural selection that has operated at the PBA sites on the ancestral branch of simians. The accession numbers in the International Nucleotide Sequence Database (INSD) for the sequences of humans, chimpanzees, gorillas, African green monkeys (copies 1 and 2), brown capuchins, squirrel monkeys, marmosets, ring-tailed lemurs, and rabbits are M24407, AB086255, AB086253, D12611, D12613, AB086124–AB086131, AB086252, AB086254, AB086132–AB086137, and AB086138–AB086144, respectively. These sequences have been reported to be orthologous (Ida-Hosonuma et al., 2003). Note that African green monkeys possess two sequences because of the occurrence of gene duplication after speciation (Koike et al., 1992).

A multiple alignment of the nucleotide sequences was made using the computer program CLUSTAL W (version 1.81) (Thompson et al., 1994). The alignment contained a gap which was apparently accompanied by a frame shift. To eliminate the gap, a multiple alignment was also made for the amino acid sequences that were encoded by the nucleotide sequences (Fig. 1).

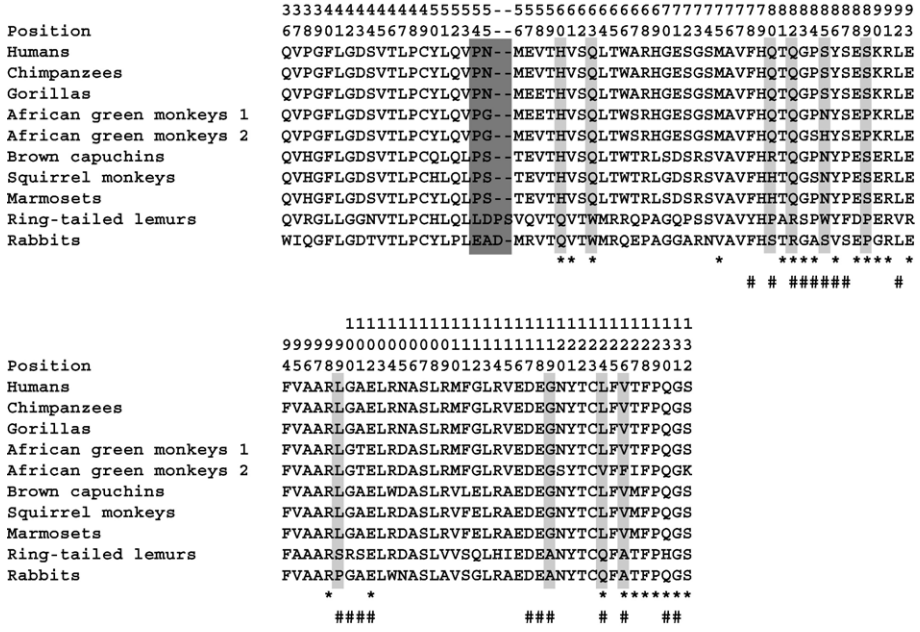

Fig. 1. Multiple alignment of the amino acid sequences for almost the entire region (amino acid positions 36–132) of D1 obtained from humans, chimpanzees, gorillas, African green monkeys, brown capuchins, squirrel monkeys, marmosets, ring-tailed lemurs, and rabbits. African green monkeys 1 and 2 indicate copies 1 and 2 of CD155 in this species, respectively. The amino acid sites that were located at the interface of CD155–poliovirus complex in the analysis of the three-dimensional structure and those that were important for poliovirus binding in the mutagenesis analysis are marked with * and #, respectively. The sites that were eliminated from the analysis of natural selection are dark-shaded. The PBA sites where amino acid substitutions occurred on the ancestral branch of simians are light-shaded.