

Reduction of HIV-1 Replication by a Mutant Apolipoprotein B mRNA Editing Enzyme-Catalytic Polypeptide-like 3G (APOBEC3G)

Published date: Feb. 1, 2012

Technology description

Summary

The invention describes a single amino acid substitution, D128K, that renders the human apolipoprotein B mRNA-editing enzyme-catalytic-like 3G (APOBEC3G) (CEM15) capable of inhibiting HIV-1 replication in the presence of HIV viral infectivity factor (Vif). HIV-1 and other retroviruses occasionally undergo hypermutation, characterized by high rate of G-to-A substitution. Studies have shown that human APOBEC3G is packaged into the retrovirus and deaminates deoxycytidine to deoxyuridine in newly synthesized viral minus-strand DNA, thereby inducing G-to-A hypermutation and viral inactivation. This innate mechanism of resistance to retroviral infection is counteracted by the HIV-1 Vif, which protects the virus by preventing the incorporation of APOBEC3G into virions by rapidly inducing its ubiquitination and proteosomal degradation. The inventors substituted several amino acids in human APOBEC3G with equivalent residues in simian APOBEC3G, which are resistant to HIV-1 VIF and determined the effects of the mutations on HIV-1 replication in the presence and absence of Vif. The Vif-resistant mutant could interact with HIV-1, but unlike the wild type of APOBEC3G, its intracellular steady-state levels were not reduced in the presence of HIV-1 Vif.

This technology provides a potential breakthrough for the treatment of HIV through gene therapy. By introducing the mutant version of APOBEC3G into hematopoietic stem cells and transfusing into HIV/AIDS patients, a level of resistance can be acquired. Further, using this mutation in a more classical vaccine approach to gene therapy is also envisioned.

Institution

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