Analysis and research of HIV outer membrane protein

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Abstract

By analyzing the HIV outer membrane protein, a research method was proposed to change the crack between the internal and external structural domains of gp120 protein molecules, so that the epitope was fully exposed and the human immune response was effectively induced.

Keywords

HIV, Outer membrane protein, Immune response.

1. Introduction

The medical name for the human immune system defects of HIV virus (HIV), is a kind of RNA virus, HIV is to rely on single structure of RNA carries genetic information, single structure of RNA can be folded into an intricate three-dimensional structure, its harder to crack than DNA encoding information, determine the role of each gene in the virus is more difficult Previous researchers have succeeded in the part of HIV RNA genome, simulated and analyzed for the AIDS virus RNA genome containing tens of thousands of nucleotides is far from enough.

HIV infection to target cells starts from gp120-mediated interaction between virus particles and cell surface, and gp120 can interact with CD4 and dc-sign on the cell surface, and then gp41 mediates the binding of virus envelope and cell membrane to transport virus contents to the infected cell cytoplasm.

Vaccines are currently considered the most effective way to control the spread of HIV. Gag protein is one of the main structural proteins of HIV. Since the amino acid sequence of gag protein is relatively conserved and the antigen variation is less, the use of gag protein as AIDS vaccine is likely to overcome the deficiency that env protein cannot effectively resist the attack of allogeneic mutant virus strains. At the same time, studies have shown that the gag protein contains many epitope antigens, which can cause the body to produce specific humoral immunity (including the production of neutralizing antibodies) and specific CTL response. In addition, gag protein also has an important feature of self-assembly, which can self-assemble into virus-like particles. This is very necessary for building macromolecule granulated antigen. Therefore, gag protein has become a new hot spot in the research of HIV vaccine, especially in the study of granular vaccine. Pasteurelpichia pastoris is a widely used gene expression system in recent years. It has many advantages, such as high expression rate, genetic stability, product secretion and mature fermentation process.

2. Some of successful cases

Protein conserved membrane vesicles during transport to inhibit virus transcription and replication

The process of membrane formation, membrane dissolution, and bud emergence requires specific proteins, and these proteins are called part of the membrane bubble.

In the fusion reaction, fusion is a feature of the membrane surface. In order to fuse with the target membrane, the membrane vesicle must remove the outer layer of the protein. The fusion target was identified by the interaction between the protein on the membrane and the protein on the membrane.

The vesicle runs in a circular motion, and thus acquires the outer capsule, which is released from the donor membrane and moved to the target membrane. The outer capsule is removed and then fused with the target membrane.

Proteins enter cells by packaging into phagocytes, which are released from the plasma membrane and transport their contents into the cell. The cargo is released when the phagocytes fuse with the

compartment membrane, including the endosome. Reversible reaction of teething and fusion is necessary. When a membrane is assembled with the outer protein, buds occur and eventually release in the form of a separate membrane bubble. When the coat protein is removed, fusion occurs, exposing the bare membrane surface and fusing with the target membrane. The coat is assembled by the protein or depolymerized by the disarmed gtp-binding protein state control.

After HIV enters the human body, immune cells with CD4 receptors are first searched for to fuse with the developing membrane, and then the genetic material of the virus is released into the target cells.

Classical anti-hiv drugs inhibit the transcription and replication of HIV after it enters human target cells, while invasion inhibitors inhibit HIV entering human target cells by interfering with the binding or fusion between HIV and target cells, that is, such drugs play a role before HIV enters human target cells.

There are two types of inhibition: inhibition of HIV and target cell surface receptor binding; Inhibition of membrane fusion between HIV and target cells.

HIV causes AIDS by binding, entering, and ultimately causing t-helper cell death. T-helper cells are immune cells necessary to fight infection by common bacteria and other pathogens. Because HIV reduces the number of t-helper cells, common pathogens can kill people.

An effective HIV vaccine causes the body to produce antibodies (immunoglobulin) that circulate in the blood, track and kill the virus before it is attacked by the virus.

However, most of the anti-hiv antibodies produced by the body are ineffective. Because the surface of HIV is coated with sugar molecules, antibodies can't penetrate, then block the proteins the virus USES, binds to, and eventually infects the cells. The situation is more complex, because HIV mutates all the time, so any vaccine-induced antibody must be able to detect and destroy the many strains of HIV that actually exist. This project intends to analyze gp120 glycoprotein to find an effective method to inhibit further HIV infection. Specific objectives are as follows:

HIV outer membrane protein is a kind of glycoprotein with high mutation rate. Through the comparison of env gene and protein level structure of different strains, it is found that the outer membrane protein of HIV has 5 variable domains (variable domains) V1 ~ V5 and 5 constant domains (conserved domains)C1 ~ C5. In hiv-1,V1 and V2 are connected, and other variable regions are separated by constant regions, while in hiv-2,V1 and V2 are close, and other variable regions are separated by constant regions.

At both ends of regions V1, V2, V3, and V4, there is a Cys residue, and the base disulfide bond is formed to form a circular structure (v1-v4) in regions V1, V2, V3, and V4, and is exposed to the virus surface. By changing the V4 area amino acid to inhibit HIV infections.

3. Research technique

First, the cracks between the internal and external structural domains of gp120 protein molecules were enlarged, which enabled the full exposure of antigen epitopes and effectively induced the human immune response.

Expand the cracks between the internal and external structural domains by changing the overall polarity of the regions on both sides of the cracks.

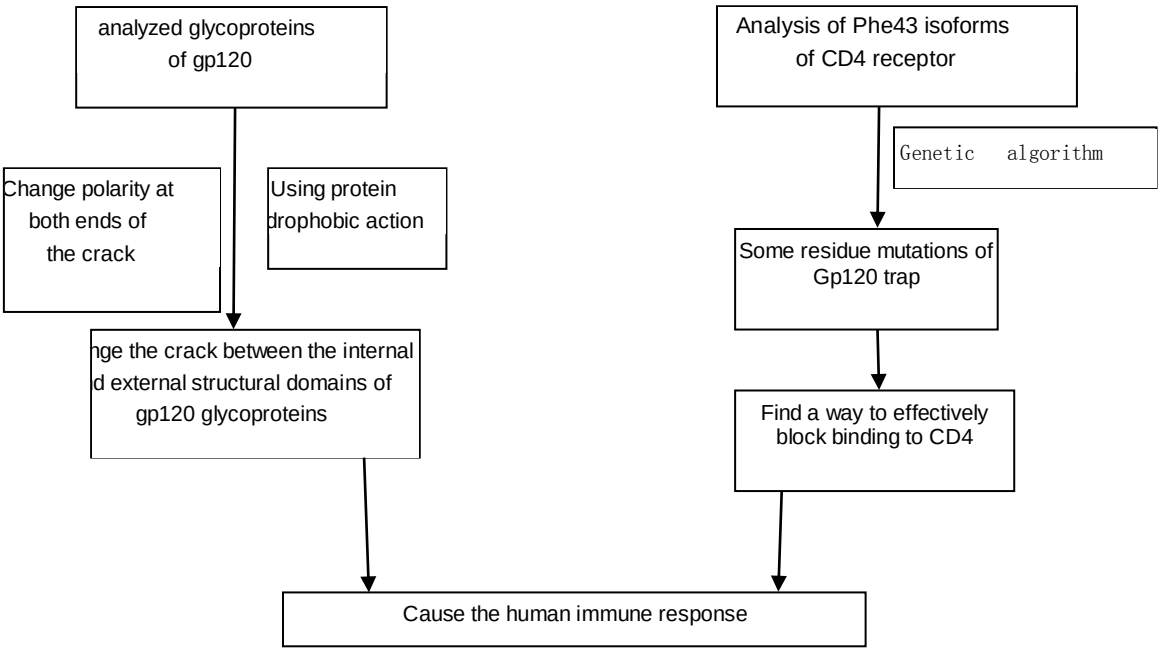
The polar nature of amino acid side chains is determined in most cases by the second nucleoside of the genetic code. When the second nucleoside is pyrimidine, the side chain is non-polar; when the second nucleoside is purine, the side chain is polar; but when the first nucleoside is U or A, if the second nucleoside is C, the side chain is no longer non-polar and has polarity; when the second nucleoside is U, it has absolute specificity. Only the Try group code (UGG) does not conform to this principle.

The genetic code with the following characteristics determines that the amino acid side chain is polar uncharged. The first nucleoside must be U or A (note that U and A have complementary structural conditions). Under this premise, the second nucleoside is C and the third nucleoside has no specificity.

The second nucleoside is purine and the third nucleoside is pyrimidine. Only Gin's two sets of codes, CAA and CAG, did not meet this principle.

Charged side chains of amino acids encoding is very concentrated, its characteristic is the second nucleotide is purine and the first nucleoside is not U. Under this premise, if the first nucleoside is C (except Gin's two groups of code: CAA and CAG) or the first nucleoside is A and the third nucleoside is purine, then the positive side chain amino acid coding is. The first and second nucleosides are GA codes that determine the amino acid side chain to be negatively charged.

4. Technical route



5. Conclusion

in this paper, a method is proposed to make the epitope fully exposed and effectively cause the human immune response by changing the cracks between the internal and external structural domains of gp120 protein molecules, which is theoretically feasible, but the actual effect has to be further studied and verified.

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