ИММУНОЛОГИЯ **IMMUNOLOGY**

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HIV/AIDS IMMUNOLOGY: CURRENT TRENDS

Review article discusses immunogenetic and pathogenetic features of HIV-infection/AIDS. Among immunogenetic factors in addition to traditional immune response genes – HLA-genes, highlighted the role of cytokine gene polymorphisms - regulators of the immune response. The role of chemokine receptors in the development and progression of HIV/AIDS was also shown.
Keywords: *HIV/AIDS, HLA-alleles, cytokines, polymorphisms of cytokines, chemokines receptors.*

Currently, most pressing issue for global health is HIV infection edging out to the second place cancer and cardiovascular disease [1]. By the growth rate of new HIV cases in the top three, except Africa, are countries of Southeast Asia and Russia [2, 3]. From Central Asia, Kazakhstan is holding first place for HIV infection, a retrospective analysis demonstrates further progression of the epidemic process in the country. First 4 cases of HIV infection in Kazakhstan were registered in 1987, and with the growing trend by 2008 there was in 2335 [4, 5].

Back in the early 80-ies of XX century, one of the most important provisions of the modern notion of immunity has become a point of view that the ability to respond or not respond to a particular antigen, as well as the strength of the immune response, genetically encoded. This concept has not lost its relevance, and today, after the decoding of the genome – the most important discovery of the XXI century, immunogenetic has received a new round of development [6].

So, according to researchers, HLA-alleles that determine susceptibility to HIV/ AIDS are DRB1*1301, 1302, 1303, DR2, DRB1*1501 [7, 8]. More protected against HIV-1 infection were people with most heterozygosity by class 1 HLA-locuses, that are not expressing HLA-B*35 and HLA-Cw*04 alleles. At the same time meeting with high frequency HLA-B35-allele is a major risk factor for contracting HIV among injecting drug users [8, 9, 10]. In addition, there was a high association of HLA-DR5-phenotype with an increased risk of Kaposi's sarcoma in AIDS [11].

At all stages of HIV-cell interaction, dissemination of retrovirus, immunodeficiency formation and development of opportunistic infections in macro organism cytokine network in functioning [12, 13]. At the same time noted that the expression level of the protein products of polymorphic cytokine genes determines the quality of the immune response and, accordingly, the course and outcome of the disease [14, 15].

Chronic immune dysregulation in HIV infection is characterized by marked overproduction of proinflammatory cytokines, implementing its action as cofactors of HIV activation [12, 13, 14, 16]. Cytokine imbalance controlled primarily by IL-10, which is a key cytokine, inhibition HIV replication. Polymorphism of the IL-10-5'A contributes to the defeat of $CD4^+$-cells by virus, resulting in the progression of immunosuppression and the further development of opportunistic infections, while hetero- and homozygous accelerate the progression of AIDS in this case, probably due to inhibition of synthesis of the cytokine IL-10 [14, 17, 18].

Also promotes HIV replication and horizontal dissemination of TNF-α) and cytokine regulatory gene IFN-γ, having a polymorphism T(-179)G in the promoter region, one allele of which is induced by tumor necrosis factor, and the second - none. Carriage of -179T allele of IFN-γ gene accelerates disease progression compared with homozygous -179G/G. [14, 18].

Thus, the presence of -308A variant in TNF-α gene promoter is associated with its increased production by immune system cells and for IL-4 gene was described -590T allele correlation with increased production of interleukin and rapid progression of HIV infection [8, 13, 14, 18]. The greatest risk of rapidly progressive course of HIV-infection is associated with a combination of genotypes AA (+874 A/T) gene IFN-γ and GG (G-308A) gene TNF-α (AA/GG). The degree of risk of progression, recurrent flow and adverse outcome of HIV is positively associated with G allele of the promoter region of the T-330G- IL-2 gene [19, 20].

The greatest protective effect against rapidly progressive flow of HIV infection has a combination of genotypes CC polymorphism C-590T of the IL-4 gene and promoter region C-592A of the IL-10 gene (CC/CC) [14, 16, 19].

In recent years, it became known that in addition to CD4 receptor for HIV entry into the cell co-receptors are required - in particular receptors for chemokines: for T- lymphocytotropic HIV – CXCR4 and for macrophage (monocytotropic and T- lymphocytotropic) – CCR5. After binding to chemokine receptors and CD4 receptors, the virus fuses with the cell membrane and penetrates into the cell, resulting in further progression of HIV infection into AIDS [7, 20, 21].

It appeared that cells with a deletion in the CCR5 gene do not express the protein encoded by it, and this subsequently prevents entry of HIV into the cell. Deletion in the CCR5 gene is a protective factor for HIV infection: homozygous genotype is associated with lower risk of HIV infection; heterozygous – with the positive dynamics of the disease flow [22, 23, 24]

Frequency distribution of the defective CCR5 allele showed the lowest frequency of the protective allele CCR5 in Tuva, Kazakhs, Kyrgyz, and Chechens populations, the highest rate occurred among the European population and almost absence of this allele - Africans [8, 23].

Researchers of Multi Center AIDS Cohort Study suggest that CCR5 and HLA-genotypes affect the resistance to HIV, independently of each other, but effect of HLA on this process is significantly more than the chemokine receptor mutations [21, 25].

Sensitivity to HIV in different human populations varies greatly. Most susceptible to the virus were Asian and Negroid ethnic groups, resistance to virus infection from other races, has a relative character. As a result of the formation HIV resistant populations, there is still a threat of AIDS epidemic spread and the inability of inhibition [26].

Nevertheless, complex population genetic studies on the establishment of distribution features of alleles that determine human resistance to HIV infection can help in assessing the dynamics of HIV progression to AIDS, the development of vaccines and strategies to control viral load in HIV infection.

Although these data gives us some optimism, unfortunately, the lack to date of fundamental data on the mechanisms of recognition of retroviral infection and induction of humoral and cellular responses of adaptive immunity along with antigenic variability and pronounced tropism of HIV to human cells complicate the search for the most promising approaches to the control strategy of HIV-infection/AIDS pandemic – the development of anti-HIV vaccines [27]. This problem is a broad and relevant at the moment, and requires a deep understanding.

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АИВ/ЖИТС иммунологиясы: қазіргі заманғы бағыттар

Түйін: Ғылыми шолуда АИВ-инфекциясының/ЖИТС-ның иммуногенетикалық және патогенетикалық ерекшеліктері көрсетілген. Иммуногенетикалық факторлардың арасында қалыптасқан ұғымды, HLA, – иммунды жауап гендерімен бірге цитокиндер гендерінің полиморфизмдерінің қызметі ұсынылған. Сонымен қатар, АИВ/ЖИТС-ның қалыптасуы мен өршуіндегі хемокиндер рецепторларының рөлі қарастырылған.
Түйінді сөздер: АИВ/ЖИТС, HLA-аллельдер, цитокиндер, цитокиндер полиморфизмдері, хемокиндердің рецепторлары

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Резюме: В обзорной статье рассмотрены иммуногенетические и патогенетические особенности ВИЧ-инфекции/СПИДа. В числе иммуногенетических факторов кроме традиционных генов иммунного ответа – HLA-генов, выделена роль и полиморфизмов генов цитокинов – регуляторов иммунного ответа. Также показана роль рецепторов хемокинов в развитии и прогрессировании ВИЧ/СПИДа.
Ключевые слова: ВИЧ/СПИД, HLA-аллели, цитокины, полиморфизм цитокинов, рецепторы хемокинов