Epidemiology of adenovirus type 5 neutralizing antibodies in healthy people and AIDS patients in Guangzhou, southern China

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Recombinant adenovirus serotype 5 (Ad5) viruses have been extensively explored as vectors for vaccination or gene therapy. However, one major obstacle to their clinical application is the high prevalence of pre-existing anti-Ad5 immunity resulting from natural infection. It has been reported that there are geographic variations in the prevalence of natural adenovirus infection. In the present study, we investigated the seroprevalence of Ad5 in Guangzhou, southern China by measuring the Ad5 neutralizing antibodies in blood samples collected from several sites. The seroprevalence was 77.34% in the general healthy population.

The prevalence and antibody titer increased with age, with the older population (41-72 years old) having the highest seropositivity (84.8%) and percentage (54.4%) of high Ad5 neutralizing antibody titer (>1000). The dynamics of Ad5 neutralizing antibodies were stable and persistent over the course of eight months. Furthermore, the seroprevalence of Ad5 in the HIV-infected AIDS patients was investigated and there was no significant difference from the general healthy population.

Introduction:

1) Pre-existing anti-Ad5 immunity (PAAI) remains a major obstacle for its use as a vaccine or gene therapy vectors.

2) The sero-prevalence of pre-existing Ad5 neutralizing antibodies (NA) varies among populations from different geographic settings.

Results and Discussion:

1) The practical application of Ad5 has been potentially limited by the high prevalence of pre-existing Ad5 immunity. Both preclinical animal models and human clinical trials have demonstrated that pre-existing Ad5 immunity can significantly reduce the expression level of transgene harbored in Ad5-based vectors, thus impair its ability to generate immune responses against the target antigens. Therefore, it is necessary to determine the Ad5 prevalence in local areas and the dynamics of anti-Ad5 neutralizing antibodies (NA) prior to the administration of Ad5-based products.

2) The sero-prevalence of pre-existing Ad5 neutralizing antibody (NA) varies among populations from different geographic settings. Ad5 prevalence has been investigated to guide the administration of Ad5 vector-based products in some districts and countries. Approximately 40%-60% of adult populations in America, and more than 93% of pediatric populations in Sub-Saharan Africa are Ad5-positive. The variation of NA titers by geographic locations emphasizes the necessity of the sero-prevalence survey before clinical trials with Ad5 vector-based productions. However, these studies did not include the Chinese populations.

3) The relationship between pre-existing Ad5 immunity and the acquisition of HIV infection needs to be clarified. At present, the impact of pre-existing adenovirus immunity to an Ad5-based HIV vaccine is controversial. Some studies have demonstrated that the vaccination of Ad5-naive subjects can cause the activation and expansion of Ad5-specific memory CD4+ T cells, potentially creating more targets for HIV. However, the above findings were derived from an artificial in vitro experimental system and were not consistent with data obtained from two independent studies utilizing samples directly isolated from Ad5-vaccinated people. Therefore, it is necessary to determine the correlation between Ad5 immunity and HIV infection to further develop Ad5-based HIV vaccines.

4) The aim of this study

Consequently, this study focused on the survey of Ad5 sero-prevalence in healthy and HIV-infected individuals in Guangzhou District, Southern of China. We measured the Ad5 neutralizing antibodies in blood samples collected from several sites, and detected the dynamics of anti-Ad5 NA titers during an 8 months course. Furthermore, we evaluated the anti-Ad5 seropositive proportion in HIV-infected AIDS patients. Our results provide insights for the development of Ad5-based HIV vaccines.

Anti-Ad5 seroprevalence in the general populations of Guangzhou

Table 1. Anti-Ad5 seroprevalence in the general populations of Guangzhou. Serum samples from healthy participants were collected from the Guangzhou Center for Disease Control and Prevention (CDC), Guangzhou Children’s Hospital, and Guangzhou Institutes of Biomedicine and Health (GIBH), and the samples from AIDS patients were collected from Guangzhou No. 8 People’s Hospital. Ad5 NA titers were quantitatively detected using recombinant adenoviruses expressing the secreted alkaline phosphatase (SEAP) reporter gene as reported.

Conclusions:

1) There was intermediate prevalence (77.34%) of Ad5 infection in a general population from Guangzhou as compared to the lower prevalence in Europe and American and higher prevalence in Africa and Thailand.

2) The anti-Ad5 antibody titers in human subjects are stable and persistent over time for at least 8 months.

3) The seroprevalence of Ad5 in the HIV-infected AIDS patients was investigated and there was no significant difference from the general healthy population.

Future work:

1) The prevalence of adenoviruses other than Ad5, such as Ad2, Ad26 et al. needs to be determined in the future studies.

2) The correlation of Ad5 neutralizing antibodies and HIV infections are under investigation with an enlarged HIV infected cohorts.

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