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Letter

Therapeutic Antibody for Epidemic Keratoconjuctivitis in a Rabbit Model

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INTRODUCTION

Epidemic Keratoconjuctivitis (EKC) is a highly contagious infectious eye disease caused by Adenovirus (Ad) infection [1]. So far, neither vaccines nor effective therapy are available for this infection. In this study, we discovered an eye-drop antibody against Ad that inhibits Ad replication in an Ad5/NZ white rabbit ocular model [2]. Our results indicate that the Ad antibody may be used as therapy for EKC infection in the clinic.

An E1/E3-deleted Ad5 vector expressing green fluorescent protein (Ad5-GFP) reporter was prepared as previously described [3]. Eight-week-old female ICR mice were immunized intramuscularly with 10^{10} Viral Particles (vp) of Ad5-GFP on days 0 and 14. Ad5-specific serum antibody titer was detected by ELISA 8 weeks after the first immunization. The pooled serum titer of the antibody from 10 immune mice was 1:104,579 (1: 2^{20}). Mouse immune and normal sera were diluted with PBS for therapy.

Eight-week-old (1.3-1.6 kg) female New Zealand White rabbits were used for this study. A total of 11 rabbits were anesthetized with Somnopentyl (Kyoritsu Seiyaku, Tokyo, Japan), and inoculated in both eyes with 20 µL of 10^{11} vp/eye of Ad5 twice (with a 4-h interval between each dose) after 12 cross-hatched strokes of a no. 25 sterile needle on day 0. Further, six rabbits were topically administered with the diluted Ad5-specific mouse immune sera (titer: 1:1,000, 50 µL/eye, 3 times/day) from day 1 to day 7. Five rabbits were topically administered with 100-fold diluted normal mouse sera as control. Prior to sera treatment, ocular swabbing was performed on days 0, 1, 2, 3, 5, 7, 9, 12, 14, and 16. The swab from each eye was placed into 1.5 mL tubes containing 0.5 mL of DMEM supplemented with antibiotics. Ad5 titers were determined in A549 cells using a standard plaque assay of $TCID_{50}$ as described previously (http://www.virapur.com/protocols/TCID50%20Protocol.pdf).

As shown in the Figure 1, high viral titer was detected on day 2. Subsequently a gradual decrease in the titer was observed in the topical immune sera group, but not in the normal sera group. A significant difference was observed from day 5 to day 16 between the two groups. On days 14 and 16, the virus was undetectable in half of the samples in the topical immune sera group, but was still detected in the normal sera group.

Our data demonstrate that the anti-Ad antibody can be used for EKC therapy.

Grant

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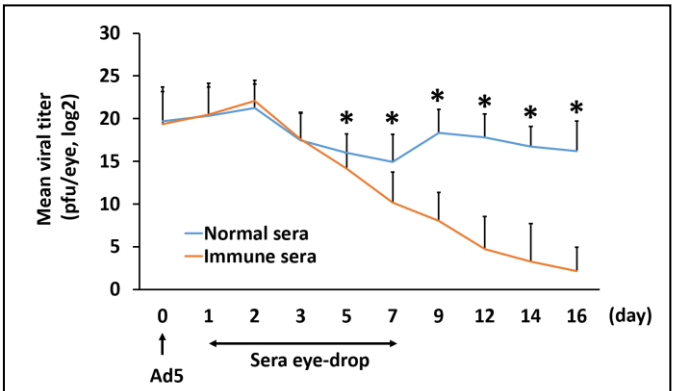

Figure 1: Therapeutic effect of anti–Ad antibody. Rabbits were injected with Ad5 in the eye on day 0, and topically administered with diluted anti-Ad5 immune sera (n=6) or normal sera (n=5) from day 1 to day 7. Viral titer was detected at indicated points. All values are expressed as mean ± SEM (standard error of the mean). Statistical analyses were performed by nonparametric Mann-Whitney U test for two groups using Microsoft Excel software Bell Curve.

*indicates significant difference between the groups at the time point ($p < 0.05$).

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