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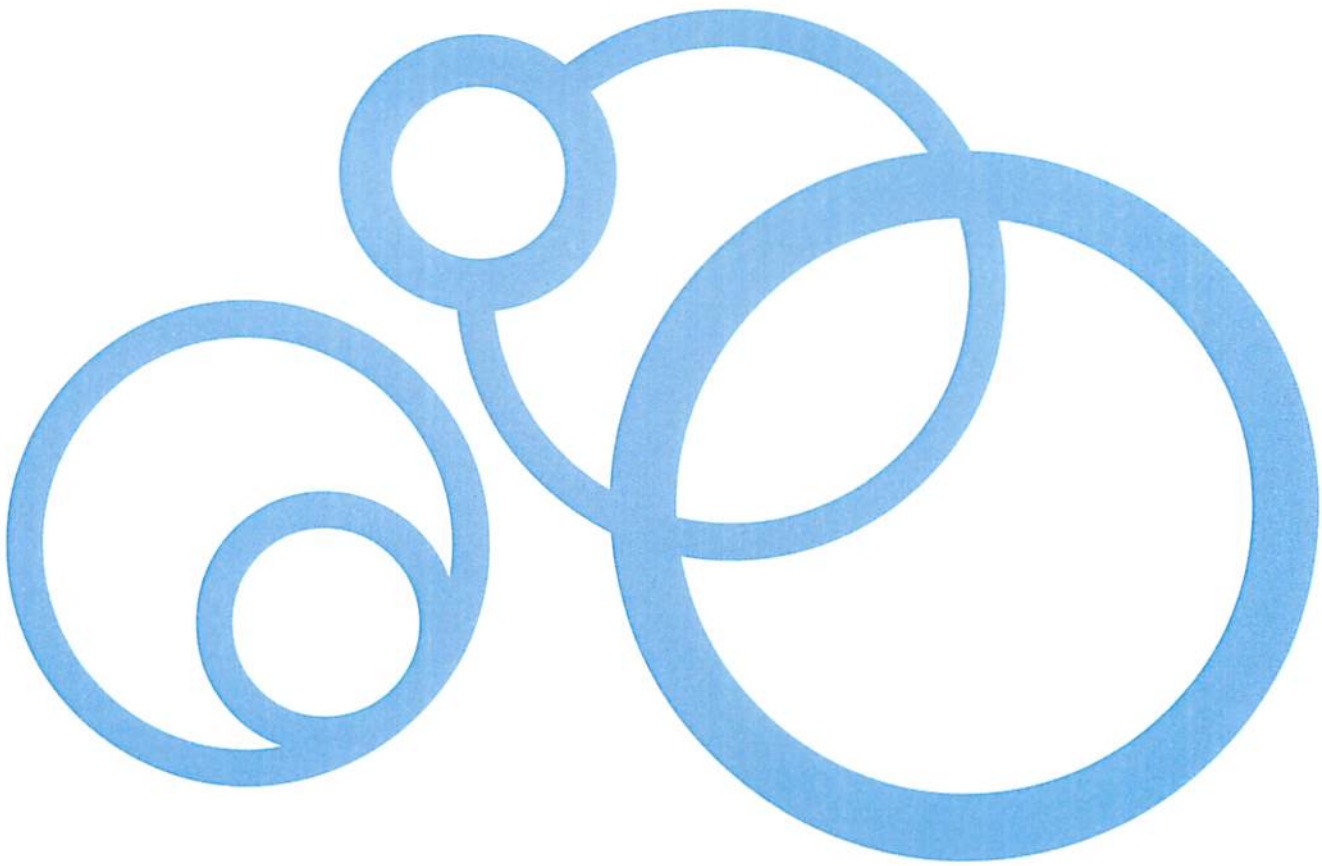

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【Short Communication】

Nutritional Food Active Hexose Correlated Compound (AHCC) Enhances Resistance against Bird Flu

健康補助食品 AHCC (Active Hexose Correlated Compound) が示す鳥インフルエンザに対する抵抗性

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[Abstract]

AHCC is a nutritional food that has been broadly adopted in Japan as well as other countries. Several laboratories have demonstrated that AHCC has immune modulating effect. Increasing immunity against bird flu virus, H5N1, may help to prevent the next pandemic. We hypothesize that uptaking AHCC improve immunity against infection with this virus. Administration of AHCC for 7 days effectively improved survival rate by 30%, and this effect can last for 3 to 4 weeks. Our results indicate a potential role of AHCC in helping to build up immunity for preventing the pandemic of bird flu.

[Key words]
influenza, infection, AHCC

INTRODUCTION

Avian (bird) influenza (flu) is an infection caused by avian influenza viruses. Influenza A (H5N1) virus—also called "H5N1 virus"—is an influenza A virus subtype that occurs mainly in birds, is highly contagious among birds, and can be deadly to them. H5N1 virus does not usually infect people, but infections with these viruses have occurred in humans[1,2]. According to WHO report, there are a total of 244 reported cases of infection, and 144 deaths[3]. Although H5N1 is not yet capable of efficient human-to-human transmission, the protein nature of its genome could transform it into the source of the next human influenza pandemic[4,5].

AHCC is a mixture of polysaccharides, amino acids and minerals derived from fungi[6]. The chemical analysis has revealed that oligosaccharides are the major components, consisting about 74% of the mixture and nearly 20% of this fraction is composed of α-1,4-glucans. AHCC has been demonstrated to have immune modulating functions. AHCC enhances the activity of NK cells in cancer patients, enhances Th1-type cytokine production and increases immunity against pathogen infection and tumor immunity[7,8].

Based upon the immune-modulating potential of this nutritional food, we hypothesized that AHCC might reduce the mortality caused by infection with lethal doses of H5N1. We demonstrated in the present communication that AHCC uptaken increased resistance of lethal infection with H5N1 bird flu virus. Therefore, AHCC may potentially be useful to be used to prevent the pandemics of bird flu. This study has been

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conducted at the College of Veterinary Medicine, South China Agricultural University.

MATERIALS AND METHODS

Mice. BALB/c mice (female, 6 to 8 weeks old) were purchased from Experimental Animal Center, Sun Yat-sen University.

AHCC. AHCC powder was supplied by Amino Up Chemical Co., Ltd., Sapporo, Japan.

Virus. H5N1 subtype avian influenza virus was provided by Laboratory of Avian Medicine, South China Agriculture University.

AHCC treatment and infection with H5N1 virus. BALB/c mice (female mice at age of 6 weeks) were administered with AHCC (0.5 g/kg/day) or PBS through oral gavage (n=40 for each group) for 7 days. On day 21 post administration, 30 of these mice were then infected with 100 LD50 H5N1 intranasally (0.2 ml/mouse). And on the day 28 post administration, the remaining 10 mice were infected following the same procedure. In both groups, the death rate was recorded daily until 14 days post infection.

Statistics. The survival rate of infected mice was compared and analyzed using the log rank test, performed by GraphPad Prism version 3.0a for Macintosh (GraphPad). Throughout the text, figures, and legends, the following terminology was used to denote statistical significance: *, $p<0.001$; **, $p<0.01$.

RESULTS

To test the effect of AHCC on resistance against infection with bird flu virus, BALB/c mice (female mice at age of 6 weeks) were administered with AHCC (0.5 g/kg/day) or PBS through oral gavage (n=40 for each group) for 7 days. On day 21 post administration, these mice were then infected with 100 LD50 H5N1 intranasally (0.2 ml/mouse), and the survival rate was recorded daily until 14 days post infection. All mice in control group (with PBS) died on 11 days post infection, and about 50% mice died on day 8 following infection (Fig. 1). In contrast, administration of AHCC significantly increased the survival rate, and about 20% mice survived till 21 days post infection, and delayed the half survival rate by 3 days (from day 8 to day 11) (Fig. 1).

Even more impressively, the effect of AHCC is long lasting. On day 28 of AHCC post administration, mice were infected with H5N1 virus the same way as described above (n=10 per group), and AHCC uptaken significantly increased survival rate, and 30% mice survived till at least 28 days post infection (Fig. 2).

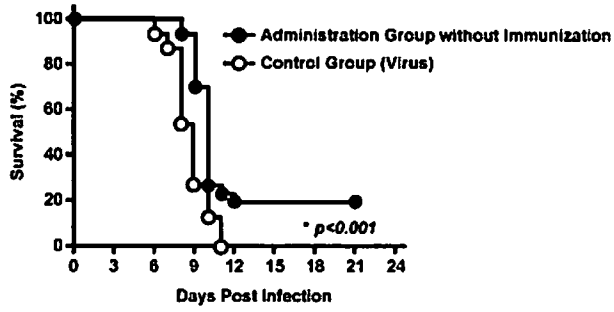

Fig. 1. AHCC treatment significantly increases survival of H5N1 infected mice. BALB/c mice (female, 6 weeks old, n=40) were treated with AHCC or water through oral gavage for 7 days. On day 21 post treatment, mice were infected with lethal dose of H5N1 virus and the death rate was recorded. One of three representative experiment is shown. ** $p<0.01$

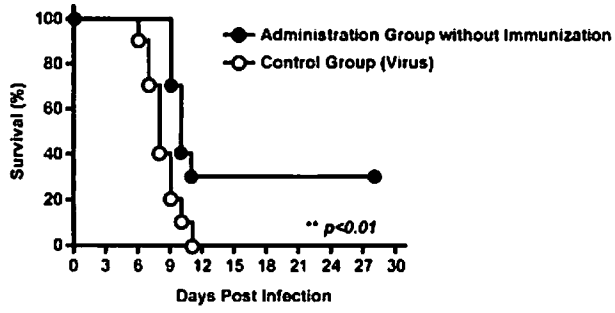

Fig. 2. AHCC has a long lasting effect on resistance to H5N1 infection. BALB/c mice (female, 6 weeks old, n=10) were treated with AHCC or water through oral gavage. On day 28 post treatment mice were infectred with H5N1 virus and the death rate was recorded. One of three repetitive experiments is shown. * $p<0.001$.

To explore whether AHCC enhanced the effect of immunization with inactivated avian influenza virus, BALB/c mice were immunized with inactivated H5N1 mixed with oil through intraperitonial injection at day 1 of AHCC treatment. Immunization with inactivated H5N1 offered 90 to 100% protection, and no significant difference was observed among immunization groups with or without AHCC treatment (data not shown).

DISCUSSION

Influenza pandemics are global outbreaks that emerge infrequently and unpredictably and involve strains of virus to which humans have little or no immunity. H5N1 is one such flu virus

strain. Recently, studying 18 human samples infected with H5N1 virus revealed a high level of viral load and increased inflammatory cytokines in the plasma[9]. AHCC has been demonstrated to modulate immune function, including enhancement of NK and CD8+ T cell function and Th1-type cytokine production [7,8]. Like any other pathogens, a favorable Th1-type immune response will help to clean the pathogen.

A greater cytokine response with predominant Th2 response (IL-4, IL-6, IL-10) has been observed in cultured spleen cells stimulated with LPS in the AHCC-treated mice[10]. It has been reported that the secretory IgA and serum IgG are mainly involved in protection against influenza in the upper respiratory tract and pneumonia in the lower respiratory tract, respectively[11]. It is also possible that administration of AHCC may increase the level of secretory IgA to promote the local protective immune response. The administration of AHCC may enhance Th2-mediated immune responses, which are particularly beneficial in the case of extracellular virus infections. Our results principally approved our hypothesis that AHCC can help to increase the immune-mediated resistance against bird flu. Our results about the effect of AHCC on reducing the death rate of H5N1 infection are very encouraging and may indicate a beneficial effect of this nutrition food in preventing the pandemic of human influnza with bird flu virus. It may provide a new kind of nutrition food for preventing the future influenza outbreaks. We are fully aware that our study is very preliminary, and we will further explore the molecular mechanisms by which AHCC has the effect, especially their immune modulating effect.

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