Commentary

Antigenic Domains of Avian HEV: Bases for Serological Diagnosis of HEV in Avian, Swine and Human

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Abstract | Avian HEV capsid protein contains immunodominant epitopes and is responsible for the induction of the protective humoral immune response. Six antigenic domains in the capsid protein have been identified. The fragmented proteins in these domains are analyzed for their application in serological diagnosis of HEV.

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Big liver and spleen disease and hepatitis-splenomegaly syndrome mainly result in an increase in mortality (1-4%), a decrease in egg production (20-40%) and an enlarged liver and spleen in broiler breeder and laying hens from 30 to 72 weeks of age (Meng and Shivaprasad, 2013). In 1990s, the big liver and spleen disease caused substantial economic losses in the commercial broiler breeder flocks in Australia (Payne et al., 1999). In 2001, avian Hepatitis E virus (HEV) was determined as the principal causal agent of the two diseases in chickens (Haqshenas et al., 2001). In the past decade, serological and molecular investigations have shown that subclinical infection in chicken flocks with avian HEV is very popular in United States, Europe, China and Korea (Huang et al., 2002; Kwon et al., 2012; Peralta et al., 2009; Sun et al., 2004; Zhao et al., 2013).

Avian HEV, a non-enveloped, positive-sense, single-stranded RNA virus, belongs to the genus Hepevirus along with swine and human HEVs. To date, avian HEV possesses three major genotypes and one serotype (Bilic et al., 2009). The full-length avian HEV genome is approximately 6.6 kb, consisting of two non-coding regions and three partially overlapping open-reading frames (ORFs). The ORF2 encodes capsid protein which contains immunodominant epitopes and is responsible for the induction of the protective humoral immune response (Guo et al., 2007; Haqshenas et al., 2002; Zhou et al., 2008). Six antigenic domains (I to VI) were characterized in avian HEV capsid protein using synthetic peptides and truncated recombinant proteins. Antigenic domains I to VI are located in amino acid (aa) 389-410, aa 461-492, aa 556-566, aa 583-600, aa 339-389 and aa 23-85, respectively (Dong et al., 2011; Guo et al., 2006; Haqshenas et al., 2002; Wang et al., 2014).

Currently, enzyme-linked immunosorbent assay (ELISA) using the truncated capsid proteins as the coating antigens are used for serological diagnosis of avian HEV infection (Huang et al., 2002; Zhao et al.,

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2013). However, because of the different antigenicity of six antigenic domains, the sensitivity and specificity of these assays in clinical and epidemiological settings remain to be determined.

Antigens from domains I and V can induce strong immune responses to avian HEV in chickens. However, since these two antigens share the common epitopes with swine and human HEVs (Guo et al., 2006), they are not suitable for differential sero-diagnosis of avian from human and swine HEV infections.

The antigen of domain II is unique to avian HEV and can also induce immune response in chickens. Further investigation is needed to confirm the specificity of this antigen. The antigens in domains III and IV are not the immunodomaint antigenic domains in avian HEV and after the infection in chickens, they induce weak immune response. Therefore, the antigens in domains III and IV are not suitable for detecting antibodies against avian HEV.

Two indirect ELISAs using the truncated capsid proteins generated from the five antigenic domains as the coating antigens have been developed for the detection of chicken IgG antibodies against avian HEV. However, based on the antigenicity of the proteins generated from these antigenic domains, it indicates that the two indirect ELISAs may not differentiate avian from human and swine HEV infections. The specificities of these antigens need further investigation by testing large numbers of clinical serum samples.

Recently identified domain VI (aa 23-85) is unique to avian HEV and can induce strong immune response in chickens (Wang et al., 2014). By detecting the sequential sera from the avian HEV challenged chickens, we found that transient antibodies against domain VI were induced in some chickens from 21 to 49 day post challenge. This domain is the target antigen for detecting avian HEV emerging infection. In addition, the indirect ELISA using domain VI as coating antigen for detection of anti-avian HEV antibodies can support the detection of the two indirect ELISA using the C-terminal 268 amino acid residues of capsid protein.

In summary, in the past ten years, significant progress has been made for the characterization of the avian HEV capsid protein antigenic domains. The applications of six antigenic domains in avian HEV capsid protein for serological detection of avian HEV infection were documented. Further studies are needed for the development of sensitive and specific serological assays for the detection of avian HEV infection.

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