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The Epitopes of Foot and Mouth Disease

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ABSTRACT

In recent years, as the genome sequencing technology and protein peptide chemical synthesis technology become mature, especially the proposal of epitopic biology, more and more Foot-and-mouth Disease Virus (FMDV) antigenic epitopes are revealed. Studies on epitopes have greatly promoted the development of new-type vaccines since the early 1980s. Thanks to the consecutive discovery of new epitopes, people can overcome the Major Histocompatibility Complex (MHC) restriction between species more easily. Researchers could also produce poly-vaccine containing epitopes of different serotypes. The selected epitope sequences are highly conserved in different serotypes and this is the key guarantee of cross immune response of vaccine. It is obvious that epitope will play a key role in elaborating new-type FMDV vaccines. This study summarized the epitopes of FMDV.

Key words: Foot-and-mouth disease, epitope, new-type vaccines, synthetic peptide, B-cell site, T cell site

INTRODUCTION

Foot-and-mouth disease (FMD) is an acute, highly contagious disease of cloven-hoofed animals and is endemic in many regions in Africa, Asia and South America (Cottam *et al.*, 2008; Schumann *et al.*, 2008; Shawky and Daound, 2005; Ahad *et al.*, 2002). It is caused by the foot-and-mouth disease virus (FMDV), a member of the genus *Aphthovirus* of the family Picornaviridae, is highly transmissible and can causes high morbidity outbreaks with moderate to low mortality in most cases. Some clinical illness caused by FMDV infection such as mastitis are curable (Sharma, 2008). Vaccination is an effective way to limiting the spread of FMDV (Rizk *et al.*, 2011). Some FMDV vaccines were developed, such as, DNA vaccine (Rawat *et al.*, 2007; Liu, 2006; Wang *et al.*, 2011); transgenic plant vaccines (Aliahmadi *et al.*, 2006; Pan *et al.*, 2006, 2008) and so on. Disease outbreaks frequently during the winter months (Verma *et al.*, 2008). In the mountainous are of Turkey, the FMD incidence in goat is 23% (Darcan *et al.*, 2005). There are seven serotypes of FMDV (A, O, C, Asia1, SAT1, SAT2 and SAT3) with multiple subtypes (Paprocka, 2006). The virus genome consists of a positive stranded RNA molecule of about 8500

nucleotides which encodes four structural proteins (VP4, VP2, VP3 and VP1) and nine non-structural proteins (L/L', 2A, 2B, 2C, 3A, 3B, 3C and 3D) (Sobrino *et al.*, 2001). Non-structural proteins are very useful to distinguish animals between native infection and vaccination (Raof *et al.*, 2011; Hassanein *et al.*, 2011).

As the synthetic peptide vaccines, live vector vaccines, epitope peptide vaccines contain the antigenic epitopes, so the study on epitopes is crucial for the development of these novel vaccines. Epitope peptide vaccine is made from antigens amino acid sequence through artificial chemical synthesis or genetic engineering expression (Dakappagari *et al.*, 2005). Peptide vaccine is chemically synthetic peptides contain a number of B cell and T cell antigenic epitopes (Tam, 1988). In recent years, with the rapid development of genome sequencing technology and protein peptide chemical synthesis technology, more and more FMDV antigenic epitopes are revealed and this speeds up the pace of the new-style vaccine research. In this manuscript, based on the researches in our lab, the international research progress on FMDV antigenic epitopes was reviewed, hoping it is helpful to the FMD vaccines researchers.

FOOT-AND-MOUTH DISEASE EPITOPES

Epitopes in VP1: Amino acid residues between 144 and 159, LRGDLQVLAQKVARTL, of VP1 on FMDV serotype O1 K has been identified as a major antibody combining B/Th cell site (Pfaff *et al.*, 1982). At the same time, VP1 [25-41aa], [200-213aa] on FMDV serotype O, strain Kaufbeuren were also identified as a major B cell site (Bittle *et al.*, 1982). A novel specific T-cell epitope, LRTATYYFADLEVAV, between 66 and 80 of VP1 on FMDV strain O/UKG/35/2001 was identified by Gerner *et al.* (2007). Zhang *et al.* (2010) reported three linear epitopes on VP1 in their study, the peptides were 1-12aa, 17-29aa, 194-211aa. One year later, VP1 [106-115aa] and [4-13aa] were identified as two murine H-2d restricted cytotoxic T-cell epitopes (Liu *et al.*, 2011).

Epitopes in VP2, VP3 and VP4: Peptides PFGHLTKLELPTDHH on VP2 and DVSLAAKHMSNTYLS on VP3 of FMDV strain A10 Holland were two Th cell sites reported by Haghparast *et al.* (2000). Zhang *et al.* (2010) reported three linear epitopes: 40-50aa of VP2, 26-39aa of VP3 and 30-41aa of VP4. VP4 [20-35aa] was recognized as a immunodominant and heterotypic T cell site for pigs (Van Lierop *et al.*, 1995; Blanco *et al.*, 2000). Two other T-cell epitopes, VP4 [62-76aa], VP4 [67-81aa], were identified in *c/c* and *d/d* haplotype miniature swine (Gerner *et al.*, 2006).

Epitopes in 2B and 2C: The following peptides: PFFFSDVRSNFSKLV, FFRSTPEDLERAEEK of 2B and LKARDINDIFAILKN, SEEKFVTMTDLVPG, VTMTDLVPGILEKQR of 2C on FMDV serotype O1K were identified as specific linear B-cell epitopes in cattle (Hohlich *et al.*, 2003).

Epitopes in 3A, 3B and 3C: 3A[11-25aa], 3A[21-35aa], 3C[121-135aa] and 3C[166-180aa] on FMDV isolate O1Kb were identified as T-cell epitopes (Blanco *et al.*, 2001). The following amino acid residues of 3B on FMDV strain O1K were identified as B-cell epitopes in cattle: ERTLPGQKACDDVN, GPYAGPLETQKPLK, PLERQKPLKVRACL, GPYAGPMERQKPLK, PMERQKPLKVKAKA, QKPLKVKAKAPVVK and PVKKPVALKVKAKN (Hohlich *et al.*, 2003).

Epitopes in 3D: Isolates C-S8 of FMDV 3D [51-65aa], 3D [91-115aa], 3D [181-200aa], 3D [341-360aa] and 3D [381-400aa] were identified as T-cell epitopes (Garcia-Briones *et al.*, 2004). 3D [301-315aa], 3D [326-340aa], 3D [346-360aa], 3D [351-365aa], 3D [356-370aa] and 3D [406-

420aa], were also recognized as T-cell epitopes in swine by Gerner *et al.* (2006). One year later, Yang *et al.* (2007) reported a major antibody binding epitope on 3D of FMDV strain A24/Cruzeiro between the amino acid residues 16 and 33.

DISCUSSION

The foot-and-mouth disease which is the most devastating disease of livestock husbandry (James and Rushton, 2002), has caused huge loss economically and drastically hinders the development of stock raising. Economic loss in Bangladesh because of calf mortality, milk yield reduction resulted from FMDV infection would stand at US\$ 163329 per year (Howlader *et al.*, 2004).

At the moment, people have realized many disadvantages of inactivated vaccine. In order to resolve these problems, the scientists are conducting some new research about novel FMDV vaccine to seek for more secure and effective vaccines. In recent years, as the genome sequencing technology and protein peptide chemical synthesis technology become mature, especially the proposal of epitopic biology, more and more FMDV antigenic epitopes are revealed. Researchers take an interest in synthetic peptide vaccines in order to develop more effective and secure vaccines that may help control FMD in the future. As the production of multivalent vaccine is difficult due to the high diversity and variability of pathogenic microbes, people gradually pay more attention to polypeptide vaccine. The selected epitope sequences are highly conserved in different serotypes and this is the key guarantee of cross immune response of vaccine.

There is no doubt that the study on epitopes will greatly promote the development of novel vaccines. Thanks to the consecutive discovery of new epitopes, we could produce poly-vaccine containing epitopes of different serotypes (Hong *et al.*, 2007) to overcome the Major Histocompatibility Complex (MHC) restriction more easily. It is obvious that epitope plays a key role in elaborating new-type FMDV vaccines.

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