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Vishweshwar Kumar Ganji
FMD Research Lab, Indian Veterinary Research Institute, Bengaluru, Karnataka, India

Mallesh Pottabathula
Department of Veterinary Parasitology, CVSc, PVNR Telangana Veterinary University, Hyderabad, Telangana, India

Sampath Kontham
Department of Agb, CVSc, PVNR Telangana Veterinary University, Hyderabad, Telangana, India

Pruthvi raj boga
Veterinary Assistant Surgeon, PVC, Peddakondur, Bhongir, Telangana, India

Correspondence
Vishweshwar Kumar Ganji
FMD research lab, Indian Veterinary Research Institute, Bengaluru, Karnataka, India

Foot-and-mouth disease and vaccination

Vishweshwar Kumar Ganji, Mallesh Pottabathula, Sampath Kontham and Pruthvi Raj Boga

Abstract
Foot and mouth disease is an infectious and highly contagious viral disease of domestic and wild cloven-hoofed animals. Vaccination is a major means to control FMD in most endemic areas. Current FMD vaccines are typically produced by inactivation of cell culture virus with binary ethylenimine and formulated with oil adjuvant. This vaccine has a subset of limitations such as requirement for frequent booster doses, poor cellular response, improper inactivation of virus. The focus has been shifted for production of an alternative, more desirable vaccine formulations like live attenuated vaccines, live vectored vaccines, DNA vaccines, subunit vaccines, virus like particles *etc.*, which are achieved through rDNA technology.

Keywords: FMD, vaccination, VLP, subunit, alternate vaccines

Introduction
Foot and mouth disease is an infectious and highly contagious viral disease of domestic and wild cloven-hoofed animals causing a huge economic loss in agriculture worldwide [1]. As per the latest ICTV virus taxonomy release the etiological agent, FMD virus was grouped under the genus *Apthovirus* of family *Picornaviridae* [2]. FMD was first recognised by a Francisian monk Hieronymus Fracastorius (1546) in cattle [3], and Loeffler and Frosch (1897) [4] demonstrated for the first time a filterable agent causing animal disease, FMD [4].

History of vaccination in FMD
Vaccination is a major means to control FMD in most endemic areas [5]. In 1927 Belin for the first time described his experiments with attenuation of the virus [6]. The first practical vaccine against FMD relied on Formalin inactivated virus obtained from tongue epithelium of infected cattle [7]. Frenkel (1947) used bovine tongue epithelial cells for growing virus [8]. The use of suspension cultures of BHK cells was found to support the growth of virus at Pirbright laboratory [9].

Current vaccines and the pitfalls:
Today, most FMD vaccines are typically produced by inactivation of virus generated in suspension cell cultures with binary ethylenimine and formulate with an oil based adjuvant [10]. There are several limitations of current vaccine, such as short duration of immunity typically only lasts for six months, requirement for frequent booster doses, poor cellular response, improper inactivation of virus [11]. Further inability to differentiate infected recovered animals from vaccinated animals lead to focus on designing improved vaccines.

Improved alternate vaccines:
The research went on for production of more desirable vaccine formulations like live attenuated vaccines, live vectored vaccines, DNA vaccines, subunit vaccines, virus like particles *etc.*, which are achieved through rDNA technology. Interestingly studies reported that 141 to 160 epitope peptide of VP1, so called 'FMDV loop' [12, 13] could induce not only neutralizing antibodies but also FMDV specific T cells [14] but the problem is it alone cannot induce sufficient neutralizing antibodies to ensure immunity against FMD [15]. Further the researchers developed several subunit vaccines using VP1, either isolated from purified virus or produced by recombinant DNA technology [16], the use of VP1-derived peptides [12] or chemically synthesized VP1 peptides [17], the use of live vectors expressing VP1 fusion proteins [18], inoculation with DNA expressing VP1 epitopes alone [14] or co-administered with DNA encoding IL-2 [19], and use of transgenic plants expressing the entire VP1-coding region

or plants infected with a recombinant tobacco mosaic virus expressing VP1 [20]. All of these strategies present a limited subset of viral immunogens to the vaccinated animal, and although they often induce high titers of neutralizing antibodies, protection against virus challenge in livestock was questionable. The guinea pigs challenged after vaccination with recombinant P1 polyprotein expressed in *Pichia pastoris* shown protective immune response [21]. Calcium phosphate nanoparticle prepared with FMDV P1-3CD gene construct protected mice and guinea pigs against virus challenge [22]. Long lasting protective immune response was seen in guinea pigs by cationic PLG micro particle based delivery of DNA vaccine construct pVAC-1D [23]. The vaccine comprising an adjuvanted formulation of replication deficient Ad5 engineered to encode the FMDV structural proteins VP0, VP1 and VP3, alongside the viral protease 3C required for their cleavage from the polyprotein was used as a novel viral vector vaccine [24]. Efficacy studies of different vaccines in cattle showed protection from as early as 7 days post vaccination following a single immunization [25]. The VLP based FMD vaccines produced in baculovirus expression system, and by a replication deficient human adenovirus vector based system are reported to be successful recombinant vaccine candidates in protecting the target species against FMDV challenge [26]. Many attempts were made to increase the stability of the empty capsids by genetically engineering the capsid [27-29].

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