

Table 1 Studies Testing Infectious Disease Vaccines with CpG Oligodeoxynucleotide as Adjuvant in Animal Models and Demonstrating Enhanced Immunogenicity and/or Challenge Outcomes

Pathogen	Antigen	Immunogenicity	Challenge
Viral pathogens			
Foot and mouth disease virus (picornavirus)	Peptide	66	
Hepatitis B	Hepatitis B surface antigen (VLP)	67–69	
Hepatitis C	VLPs	25	
	Envelope, structural and nonstructural proteins	70–74	
Herpes simplex virus 2	gD	75	75
HPV	HPV 16 L1-E7 fusion proteins	76	
	HPV 16 major capsid protein		
Influenza	Killed split	31	31
Rotavirus	VP6	77	77
Japanese encephalitis virus	JE vaccine	78	
Orthopox	L1, A33, B5	79	
SARS	Receptor-binding domain of SARS-CoV spike protein	80	
	SARS-CoV inactivated vaccine	81	
West Nile virus	Envelope DIII glycoprotein	82	
HIV/SIV	Gag	21	
	opg140	(83)	
	gp160	(84)	
	gp120-depleted particles	20, 85–89)	
	Whole inactivated SIV	22	
Smallpox	Multiple recombinant subunit	(87)	(87)
	Modified vaccinia Ankara vaccine	90	90
Bacterial pathogens			
<i>Bacillus anthracis</i>	<i>B. anthracis</i> protective antigen	14, 16, 91	14
<i>Helicobacter pylori</i>	Whole-cell sonicate	92, 93	92
Meningococcus, group B	Recombinant proteins (5)	94	
<i>Mycobacterium tuberculosis</i>	Whole-killed mycobacterium	95	
Polymicrobial sepsis	<i>Escherichia coli</i> J5 LPS + OMP of group B <i>Neisseria meningitidis</i>	96	
Parasites			
<i>Eimeria coccidiosis</i>	Protein antigen 2/praline-rich antigen		97, 98
<i>Entamoeba histolytica</i>	Gal-inhibitable lectin	17	17
<i>Leishmania major</i>	Whole killed, recombinant	(99)	
<i>Leishmania infantum</i> (cutaneous)	<i>Infantum</i> acidic ribosomal P0 protein	(100)	
<i>Leishmania donovani</i>	Recombinant ORFF	(101)	
<i>L. donovani</i>	<i>Leishmania</i> soluble antigen	(102)	
<i>L. major</i>	Live attenuated	(103)	
Malaria: <i>Plasmodium falciparum</i>	AMA1	(104)	
	Pfs25	(105)	
Malaria: <i>Plasmodium vivax</i>	MSP1	(106)	
Malaria: <i>Plasmodium yoelii</i>	MSP1	(107)	(107)
<i>Trypanosoma cruzi</i>	ASP-2		(108)
<i>Toxoplasma gondii</i>	Toxoplasma lysate antigen		(109, 110)

Abbreviations: HPV, Human papillomavirus; CoV, coronavirus; gD, glycoprotein D; JE, Japanese encephalitis; SARS, severe acute respiratory syndrome; VLP, virus-like particle; LPS, lipopolysaccharide; OMP, outer membrane protein; ORFF, open reading frame; AMA1, anti-apical-membrane-antigen 1; MSP1, merozoite surface protein 1; ASP-2, actinobacteria specific protein.

asthmatic symptoms upon airway challenge (49). In theory, allergens in the vaccine could still induce anaphylactic reactions, especially during the early treatment period when strong T_H2 responses would still be present. However, it was shown that the allergenicity of the vaccine could be significantly reduced by chemically conjugating the allergen to the CpG ODN (123).

CpG-allergen conjugates were shown to be effective in treating mouse models of ragweed allergy, using the Amb a1 ragweed allergen (124), and dust mite allergic rhinitis, using a CpG-*Dermatophagoides farinae* conjugate (125). The ragweed vaccine did reach clinical testing, and this is discussed below under human experience.

VETERINARY APPLICATIONS OF CpG ODN VACCINE ADJUVANTS

In many countries, more doses of vaccines are sold for veterinary than for human use. The need for an effective adjuvant is important in these situations since profit margins are low, so antigen manufacturing costs need to be minimized, and for logistical reasons, it is necessary to protect animals with as few doses as possible. Strong CpG adjuvant activity has been demonstrated with a variety of vaccines in several companion and food source species of animals.

Chickens show enhanced protection against *Eimeria coccidiosis* (126) and Newcastle disease virus (127) with addition of