

P37 Development of a Vaccine against *Coccidioidomycosis*
G.W. Rutherford¹, D. Blume², R. Geigle² ¹University of California, San Francisco, ²California State University, Bakersfield, CA.

We have undertaken the development of a vaccine against *Coccidioides immitis*, the fungus that causes coccidioidomycosis. Coccidioidomycosis is a serious airborne fungal infection endemic in the desert southwest of the United States, the desert northwest of Mexico and various parts of Latin America. It is estimated that there are 70,000 new infections and 8,500 clinical cases per year in the United States; most people living in endemic areas will eventually be infected. There have been recent surges in the number of cases of coccidioidomycosis in California and Arizona due to climatic changes and immigration of a non-immune population. Studies conducted during the late 1970s and early 1980s showed that mammals could be successfully immunized against coccidioidomycosis using a formalin-inactivated whole spherule vaccine. However, in clinical trials, the whole killed spherule vaccine was insufficiently protective at the extremely low doses needed to minimize side effects. Because of the successful experience with animal immunization using whole spherules, we have undertaken the identification of surface proteins that are immunogenic *in vitro* and *in vivo*. Our basic strategy is to (1) identify, clone and immunologically characterize a variety of candidate surface epitopes, (2) screen combinations of candidate epitopes and adjuvants using animal models and (3) sequence large parts of the genome of *Coccidioides immitis*. We are currently working with five separate proteins. Funding for this project has been provided by a unique combination of foundations, state government and grass-roots organizations.

P38 Protection against Bovine Viral Diarrhea Virus (BVDV) of Calves Vaccinated with a Bovine Herpesvirus-1 (BHV-1)-BVDV Recombinant

H.J. Swan¹, R.D. Neiger¹, L.J. Braun¹, L.J. Bello², W.C. Lawrence² and C.C.L. Chase^{1*}. ¹Dept. Vet. Sci., South Dakota State University, Brookings, SD; ²Dept. Pathobiol., School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA

Bovine viral diarrhea virus (BVDV) and bovine herpesvirus 1 (BHV-1) infections are a major source of respiratory and reproductive problems in cattle. A recombinant BHV-1 virus containing the envelope protein gp53 of BVDV type 1 was developed. Four calves were vaccinated intranasally with the recombinant BHV-BVDV vaccine and did not exhibit any clinical signs. The virus was recovered from all vaccinated calves on days eight through ten. Twenty eight days after vaccination, the four vaccinated and four control calves were challenged with the type 1 BVDV, NY-1. All calves had slight temperature elevations but the clinical signs were more severe in the control calves. The platelet counts were depressed in the control calves. Prior to challenge neither group had BVDV neutralizing antibody. Following challenge, the vaccinated calves developed higher serum antibody levels indicating a secondary immune response. Necropsy was performed 6 weeks following infection. No latent BHV-1 virus was detected from the trigeminal ganglion of any of the vaccinated calves. Work continues to evaluate the nasal antibody levels. The recombinant BHV-1 virus vaccine containing a single BVDV protein provided partial protection against BVDV infection. This recombinant virus replication appeared to be restricted to the nasal passages.

P39 Investigation of the protective capacity of commercial vaccines against challenge of foals with equine herpesvirus-1
CC Breathnach*, MR Yeagan & GP Allen

108 MH Gluck Equine Research Center, Department of Veterinary Science, University of Kentucky, Lexington, KY 40546

Equine herpesvirus-1 (EHV-1), primarily an upper respiratory tract pathogen, is also an important cause of viral abortion in horses. Commercial vaccines have contributed to the decline in the incidence of EHV-1 induced abortion cases. However, these vaccines offer only suboptimal protection. Therefore, upper respiratory tract disease and an unacceptable number of abortions still occur annually in vaccinated herds. This study examines the ability of these vaccines to protect foals from upper respiratory tract disease following experimental challenge.

In the first part of this study, 6 foals were infected intranasally with EHV-1. Later 12 foals were assigned to 3 groups of 4 animals, along with 2 untreated control foals. Each of the 12 foals received 2 doses of vaccines, 3 weeks apart. Each group received a distinct combination of the 2 commercially available vaccines.

All foals were challenged intranasally with EHV-1. No clinical signs were shown by the 6 animals which had been previously infected. However, all vaccinates, while exhibiting reduced clinical signs in comparison to the 2 untreated controls, were insufficiently protected. Virus was detectable in the nasopharynx of vaccinates for between 2 and 6 days post-infection, and febrile responses persisted for between 4 and 7 days despite treatment with antipyretics as necessary.

Therefore, the immune response elicited by the commercial vaccines offers only partial protection against virus replication in the nasal cavity and the subsequent febrile response.

P40 Live Attenuated Salmonellae As Carriers In The Construction Of Oral Multivalent Vaccines For Dogs

José A. Chabalgoity^{1*}, M. Moreno¹, H. Carol², G. Dougan³ and C.E. Hormaeche⁴. ¹Laboratory for Vaccine Research, Department of Biotechnology, Institute of Hygiene, Uruguay; ²Immunology Department, Institute of Hygiene, Uruguay; ³Department of Biochemistry, Imperial College, London, UK; ⁴School of Microbiol., Immunol. and Virological Sciences, Univ. of Newcastle, UK.

Live attenuated salmonellae expressing recombinant antigens from other pathogens have proven a good system for the construction of multivalent vaccines in experimental models. This system could have broad application as cost-effective multivalent vaccines in veterinary medicine. However, for their use in different species, strains that are adapted to infect and live within each particular specie should be considered. We describe here a system that allows the rapid preparation of attenuated strains of *Salmonella* with genetically defined mutations on genes of the aromatic pathway (aro strains). The system was used to construct an attenuated strain (LVR01) from a *S. typhimurium* that had been isolated from dogs, and the capacity of the attenuated strain to deliver heterologous antigens to the dog immune system was tested.

Strain LVR01 was transformed with a plasmid that express a fusion of the fragment C of tetanus toxin (TetC), with the fatty acid binding protein (FABP) from the intestinal dog parasite *E. granulosus* (EgDf1) driven by the *nirB* promoter. The recombinant strain was used to immunize dogs by the oral route. Two separate sets of experiments showed that LVR01 is well tolerated by 6 months old dogs, that there is no shedding of the bacteria in the faeces of the dogs two days after the immunization, and that the recombinant bacteria is capable of trigger humoral and cellular responses against its own antigens as well as to the recombinant antigens that it is carrying. We propose that LVR01 may represent a good carrier for recombinant antigens in the construction of oral multivalent vaccines for dogs.