Leadership for Advanced Responses to Animal Diseases

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The Ideal Vaccine

• Efficacy – It must work
• Produce long-lived immunity
• Stable during storage
• Economical to produce
• Safe

The Problem: Conventional vaccines do not meet all these criteria and most are inadequate in multiple categories
Infectious Bursal Disease

- Acute, highly contagious disease of chickens.
- Usually seen in 4-6 week old birds.
  - Infections can occur from 1 week to 20 weeks of age.
- Bursa cells (B-Lymphocytes) are infected.
- Permanent immune suppression in young birds.
  - The immune suppression is transient (during the disease) in older birds.
Sub-Clinical IBDV

Variant scIBDV

Control
Classic Virulent IBDV
Very Virulent
IBDV
Infectious Bursal Disease Viruses Serotype 1

- Pathogenic Types
  - Sub-Clinical
  - Classic Virulent
  - Very Virulent

- Antigenic Types
  - Classic
  - Variant
  - New types (antigenic drift)

It is more complicated than this!
Infectious Bursal Disease Virus

- VP1: Polymerase
- VP2: Surface protein
- VP3: Internal Protein
- dsRNA Genome (2 segments)
VP2 Hypervariable Region

A          Mp1       Mp2       B

aa222

aa322

aa313

VP2 of Infectious Bursal Disease Virus

Coulibaly et al., Cell 120:761-772. 2005
Sequence analysis can identify amino acids responsible for antigenic drift.

Figure 1. Deduced amino acid sequences of VP-2 variable domain (numbers according to Bayliss et al., 1990). Major (Azad et al., 1987) and minor (Van den Berg et al., 1996) hydrophilic peaks are indicated.

<table>
<thead>
<tr>
<th>Major hydrophilic peak A</th>
<th>Minor hydrophilic peak 1</th>
<th>Minor hydrophilic peak 2</th>
<th>Major hydrophilic peak B*</th>
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<tr>
<td>Classic Consensus</td>
<td>AADYQFSSQQPQGTITLESANIDAITLSWGGELVQTSQGVLGATLIGFDGTPAVIRAVANGLTARTDINMPPNLVITPITQITSKLEIVTSKSGGQAGDRMSNSASGS</td>
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<td>STC</td>
<td>T</td>
<td>T</td>
<td>V</td>
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<tr>
<td>52/70</td>
<td>T</td>
<td>N</td>
<td>T</td>
</tr>
<tr>
<td>DV86</td>
<td>H</td>
<td>T</td>
<td>N</td>
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<tr>
<td>D78</td>
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<tr>
<td>Ref. Variant</td>
<td>K</td>
<td>N</td>
<td>I</td>
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<td>Delaware-E</td>
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<tr>
<td>05-059</td>
<td>S</td>
<td>T</td>
<td>T</td>
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</table>

* Major hydrophilic peak B is the single most critical region for the generation of escape mutants and affecting antigenic change.
New antigenic sites are created when the three molecules form a trimer.
Breeder Vaccination Program

• **Goal:** Provide a uniform high quality antibody to the chick by vaccinating the hens.
  – Maternal immunity should match the viruses found in the field.
  – This doesn’t always work because of mutations that occur in the field viruses.
• Autogenous breeder vaccines
The Problem

• Most breeder vaccines for IBDV are produced in chickens.
  – Birds are infected in isolation facilities and bursa tissues are harvested to prepare the vaccine.
    • High yields of virus but the process is slow, labor intensive and expensive.

• The vaccine virus must be inactivated to insure safety.

• One antigenic type of IBDV is produced with each batch of virus (Mono-valent).
The Answer
Virus-Like-Particles (VLPs)

• Vaccines
  – Safe, Economical, Effective

• Diagnostic Reagents
  – ELISA Antigens

Intellectual Property: Provisional patent 61/668,314 filed July 5, 2012 by The Ohio State University.
- License to LARAD, Inc.
What is a Virus-Like Particle?

IBDV

Structural Proteins

Self Assembly

VLP
Antigen Quality

Subunit IBDV Vaccine

VLP Vaccine

Protein Loops need to be exposed.
Antigen Quality

**IBDV Subunit Vaccine**

Tubular structures are poor vaccines

**IBDV Virus-like Particles**

VLPs are identical to the virus
Innovation
IBDV-VLP Product Advantage

Industry IBDV Vaccine Production
• Vaccine virus grown in live chicks
• Mono-valent vaccine
• Requires inactivation of virus
• Expensive and time consuming
• Animal use and containment issues

LARAD IBDV Vaccine Production
• VLPs produced in the Lab
• Multi-valent vaccine
• Safe (no live virus)
• Economical
• No animals needed
• Problems solved with VLP technology
  – VLP vaccines can be quickly engineered to protect against the mutating IBDV
    • Conventional vaccines do not account for antigenic drift
    • New VLP antigens for diagnostic assays (ELISA)
  – Eliminate the bottleneck that comes with using animals for vaccine production
    • Increased vaccine supply for unmet market demand
  – Product safety
  – Lower cost of production
Business Structure and Location

• Incorporated in Wooster, Ohio
  – Dr. Daral J. Jackwood – Founder and Science Advisor
    • Professor, The Ohio State University
    • Internationally recognized expert in virology and poultry health
  – Mr. H. Ken Rudd – CEO
    • BioBusiness Consultants
    • Marketing Manager/Marketing Director for several vaccine companies (Merial, Select Labs, Solvay)
  – The Ohio State University – Equity partner
  – Dr. Shauna R. Brummet – Business Advisor
    • President & CEO, BioHio Research Park
    • Entrepreneur with biotechnology business development experience
Vaccines Products for IBDV

• Off the Shelf – VLP Vaccine
  – Replaces current breeder flock vaccines

• Made-to-order VLP Vaccine
  – Addresses rapidly mutating virus

• Diagnostic Reagents for ELISA kits

VLP Products in the pipeline:  Swine – PRRS
                          Poultry - Reovirus
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