Management tools for Brucellosis

Immuonocontraception
- GonaCon™

Vaccination
- Dry Dart
- Mucosal vaccination of killed, powdered vaccine
- Natural transmission model in elk

Detection
- Volatile Organic Compounds

Immuonocontraception

Background
- In female bison, brucellosis is transmitted if pregnancy occurs
  - In over 300 captures, B. abortus was isolated from vagina, milk, blood, feces, & products of parturition
- GonaCon™ (immunocontraceptive vaccine)
  - GnRH linked to sea mollusk protein and therefore looks large and foreign (not recognized as “self”)
  - Combined with adjuvant containing Mycobacterium avium
Immunocontraception

Current studies

- Study 1: Duration of infertility study in southern Colorado
- Study 2: Management of B. abortus in bison through immunocontraception (Corwins Springs, MT)

Study 1: Duration of infertility in southern Colorado

- Initiated Nov 2011
- Gonacon™ treatment group (N=10)
- Non-treatment controls (n=10)

Results

Number pregnant/number in group; total efficacy = 69%

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<tbody>
<tr>
<td>Treatment</td>
<td>4/10</td>
<td>3/9</td>
<td>1/10</td>
<td>3/9</td>
<td>3/10</td>
<td>10/38 (26%)</td>
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<tr>
<td>Control</td>
<td>4/10</td>
<td>9/9</td>
<td>6/9</td>
<td>9/9</td>
<td>6/9</td>
<td>30/36 (83%)</td>
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Study 2: Management of *B. abortus* in bison through immunocontraception

**First cohort (2011)**
- Treatment group (n=15; *B. abortus +)
  - Sentinels (n=5; *B. abortus −)
- Control group (n=14; *B. abortus +)
  - Sentinels (n=5; *B. abortus −)

**Second Cohort (2013)**
- Treatment group (n=20; *B. abortus +)
  - Sentinels (n=6; *B. abortus −)
- Control group (n=12; *B. abortus +)

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<tbody>
<tr>
<td>Controls</td>
<td>11/14 (79)</td>
<td>10/13 (77)</td>
<td>10/12 (83)</td>
<td>10/12 (83)</td>
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<tr>
<td>Efficacy</td>
<td>75%</td>
<td>88%</td>
<td>57%</td>
<td>66%</td>
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**Second Cohort:**

<table>
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<th>Group</th>
<th>2015</th>
<th>2016</th>
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<tr>
<td>Treatments</td>
<td>1/20 (5)</td>
<td>5/19 (26)</td>
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<tr>
<td>Controls</td>
<td>10/12 (83)</td>
<td>10/12 (83)</td>
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<tr>
<td>Efficacy</td>
<td>94%</td>
<td>69%</td>
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*Number pregnant/number in group (percent)
Study 2: Management of *B. abortus* in bison through immunocontraception

Results on the *Brucella* Side

• Control pasture:
  – 12 *Brucella* abortions + 1 positive weak calf + 5 positive live calves = 18 “shedding events” (SEs) from 11 cows
  – All 5 sentinels seroconverted 6 abortions
  – 12 calves (4 each year) have seroconverted at 1st calving season.
  – One cow had 1 culture positive calf, 2 culture negative calves, then a culture positive abortion
  – One cow (sentinel) had 1 negative calf then 3 culture positive abortions
  – One seroconversion of low-titered cow to seronegative

Control Pasture - continued

- Of the 14 original seropositive control cows, 2 died without positive cultures after the first calving season.
- 5 have never been culture positive (4 calving seasons so far)
- 7 have had 11 “shedding events” in 4 calving seasons
- Of the 5 seronegative sentinels, 4 seroconverted to positive during or immediately after 1st calving season and subsequently had 6 “SEs”.
- The 5th sentinel did not seroconvert until after her 3rd calving season, was pregnant Jan 2016 but did not calve
- Of total 11 shedding cows (controls plus sentinels), 6 have had single SE, 3 have had two SEs, and 2 have had three SEs.
Study 2: Management of B. abortus in bison through immunocontraception

Results on the Brucella Side (cont’d)
• Treatment (GonaCon™-vaccinated) groups:
  ─ Group 1: 0 seroconversions or SEs
  ─ 0 seroconversions of sentinels
  ─ 4 seroconversions to negative
  ─ Group 2: 1 Brucella-positive abortion after 1 year contraception
  ─ 0 seroconversions

Vaccination

Background
  ◦ Need effective/remote delivery of brucellosis vaccines in bison and elk
  ◦ Bison: RB51 given in two doses administered ~1 year apart induced increased protection against abortion vs. single dose
    (Olsen et al., 2015. Clinical Vaccine and Immunology 23)
  ◦ Elk: Continued research toward effective vaccine and challenge model
DryDart™
- Dart system to deliver lyophilized, powdered, pelleted, or encapsulated vaccines
- 2X the payload of biobullets
- Marks injection site.
- Fired from dart gun or shotgun
- Biodegradable

Pellet delivered by DryDart compared to larger Biobullet placed at site.
Dart marking injection site and bouncing out after depositing vaccine.

Mucosal vaccination with powdered, killed vaccine
Goal: Develop killed, *B. abortus* vaccine for use on feedlines.

Right parotid lymph node with colored clay after intranasal delivery into left nasal sinus
Mucosal vaccination with powdered, killed vaccine

Initial studies in mice: Powdered, killed *B. abortus* complexed with montmorillonite clay

- Group 1: Saline-vaccinated controls (n=15)
- Group 2: RB51 5X10^8 cfu IP (n=15)
- Group 3: Killed *B. abortus* 10^{11} cfu (n=15)
- Group 4: Killed *B. abortus* 10^{11} cfu with clay (n=14)
- Challenge elk strain 10^5 cfu IP

Developing a model for natural *B. abortus* infection in elk

- Natural exposure as challenge
- Potential model for vaccine studies
Developing a model for natural *B. abortus* infection in elk

- **Study 1: 2014**
  - 10 negative elk, 2 undiagnosed elk fetuses
  - In 24 hours, 227 contacts of elk with fetuses

- **Study 2: 2016**
  - 11 negative elk, 1 elk fetus, 9 positive pregnant elk

Results (so far)

- **Study 1**
  - No seroconversions

- **Study 2**
  - No abortions in the 9 pregnant cows
  - Status of calves pending
  - No seroconversions in naïve animals after 90 days
WiLDIT Future Works

• Continue GonaCon™ projects
• DryDart RB51 study in bison with B. abortus challenge
• Remote vaccination of bison calves and yearlings with DryDart RB51
• Second mouse study with powdered, killed B. abortus
• Powdered, killed B. abortus in elk

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