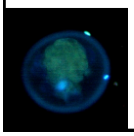
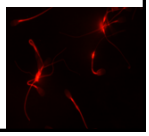



Reproductive Vaccine Effects on Reproductive Performance in Beef Cattle.

George A. Perry
Texas A&M AgriLife Research and Extension Center Overton, Tx

Russell F. Daly and Christopher C. Chase
Veterinary and Biomedical Sciences Department, South Dakota State University

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BVD = Bovine Viral Diarrhea

- a "family of viruses", many different strains
- Reproductive symptoms:
  - Dependent on dam's stage of gestation when infected:
    - Early embryonic death; low conception rates
    - Persistently infected calves
    - Birth defects, stunted calves
    - Congenitally infected calves
- Prevalence 15.74% worldwide
  - <1% in the United States
    - At least 1 PI in 5 of 30 herds tested

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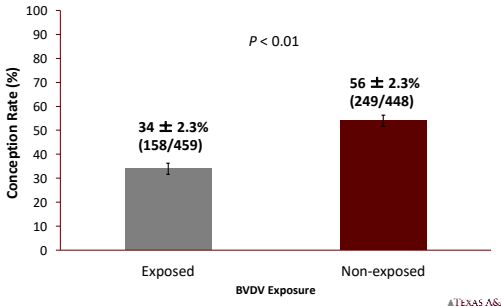
First Service AI Conception Rate



Epperson et al., The Bovine Practitioner 2021 54:120-125

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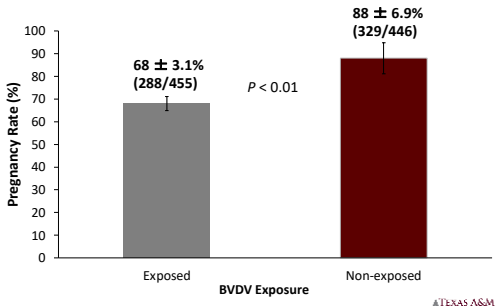
Breeding Season Pregnancy Rate



Epperson et al., The Bovine Practitioner 2021 54:120-125

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Infectious Bovine Rhinotracheitis: "Red Nose," IBR

- Agent = herpesvirus; may lay latent within the animal
- Symptoms
  - Late term (5th-9th month) abortion
  - Also causes respiratory symptoms, ocular symptoms, vaginitis

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Vaccination for IBR and BVD reproductive infections


- Combined with Vibrio + Lepto
- 30 days prior to breeding
- Modified Live Vaccines dogma
  - Better cell-mediated immunity (viral infections)
  - Booster requirements more flexible
  - **Live virus – handling and safety**
- Killed Vaccines dogma
  - Better antibody-mediated immunity (bacterial infections)
  - Need more frequent boosters
  - Safer

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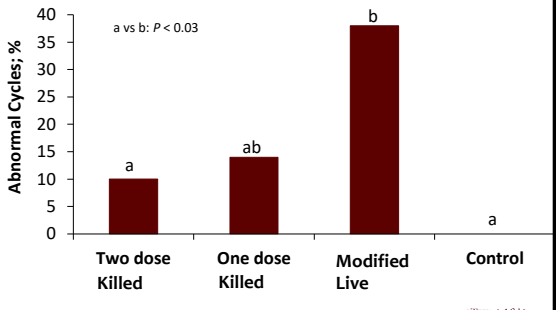
Percent abnormal cycles



Perry et al., 2013 Therio 79:2000-2005

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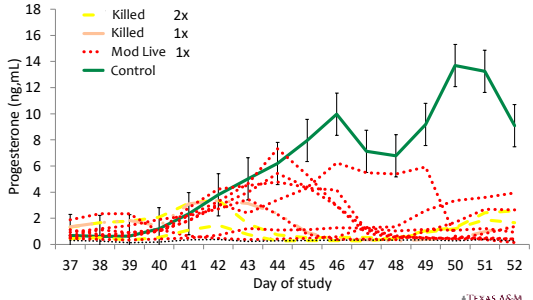
Abnormal Progesterone



Perry et al., 2013 Therio 79:200-2005

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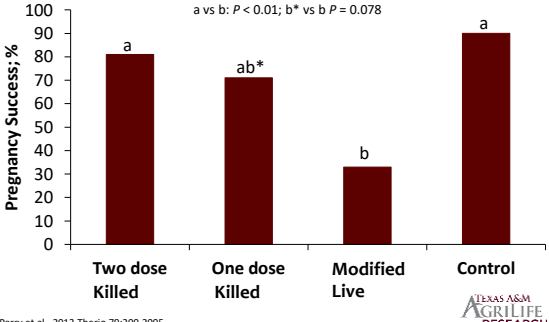
Naïve heifer - Pregnancy Rates (AI)



Perry et al., 2013 Therio 79:200-2005

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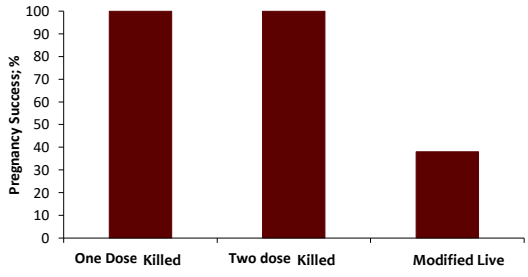
Second Service conception



Perry et al., 2013 Therio 79:200-2005

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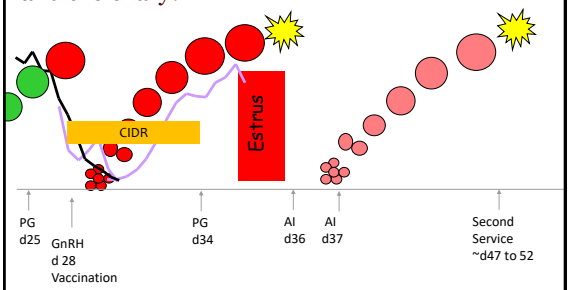
What does this tell us about the virus and the ovary?



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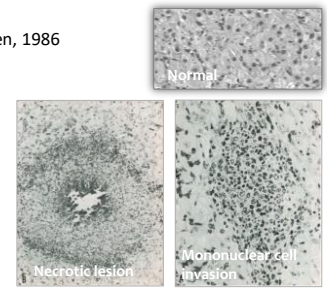
Virus induced damage to CL

- Miller and Van der Maaten, 1986
  - IBR given 7-28d post breeding
    - CL damage
      - Lesions
  - Immune cell invasion
    - Macrophages
    - Lymphocytes
    - Plasma cells
  - Virus not isolated but antigen detected



Miller and Van der Maaten, 1986; Am J Res (47) 223-8

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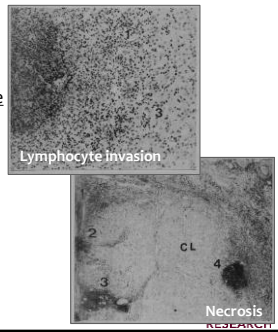
Ovarian damage by vaccinations

- Smith et al., 1990
  - Heifers vaccinated with a commercial IBR virus vaccine
  - Ovaries collected 9d later
- Necrotic oophoritis
  - Ovarian tissue necrosis
  - Hemorrhage
  - Mononuclear lymphocyte invasion



Smith et al., 1990; Am J Res (51) 969-72

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Adverse Effects of MLV IBR on Reproduction – Naïve Animals

1. Live IBR injected into 8 heifers d. 1 after estrus
   - Ovarian necrosis in 7 (VanderMaaten & Miller, 1985)
2. MLV IBR vaccine IV into 8 heifers d. 1 after estrus
   - CL and ovarian necrosis in 8 (VanderMaaten, et al, 1985)
3. MLV IBR vaccine IV into 18 heifers d. 4 after 2nd PGF
   - CL and ovarian necrosis, inflammation in 14 (Smith, et al, 1990)
4. MLV IBR vaccine IV – or control - into 19 heifers day of 2nd PGF (Chiang, et al, 1990)
   - Vaccinated heifers 3/10 calved, Control heifers 9/9 calved
5. MLV IBR vaccine in 8 heifers d. 14 after breeding
   - Infertility, embryonic death, return to estrus in 4 (Miller et al, 1989)

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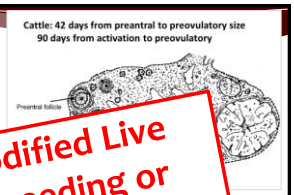
Effects on ovary extend past 1 estrus cycle



Don't use Modified Live vaccines at breeding or synchronization in never-vaccinated heifers!

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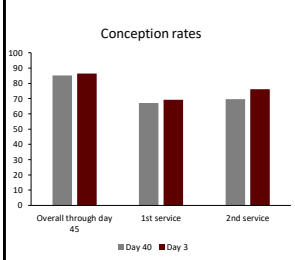
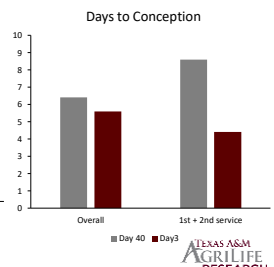
MLV in previously vaccinated cows

Animals (n = 799) vaccinated three times prior to breeding (Vista 5)
Second dose 90 d prior to peak breeding day
Third dose either 40 d or 3 d prior to peak breeding





Bolton et al., 2007 Vet Therap 8:177-182

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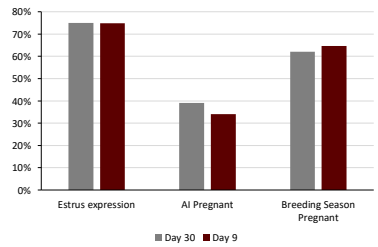
MLV in well vaccinated cows

Heifers (n = 295) were vaccinated with a MLV (CEVAX-8) vaccine either 30 d or 9 d prior to the start of the AI breeding program.



Stormshak et al., 1997 Therio 47:997-1001

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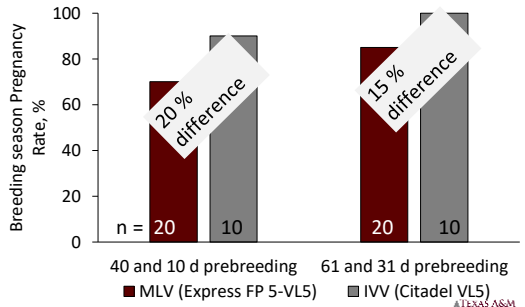
MLV vs. Inactivated



Walz et al., 1995 Therio 83:822-831

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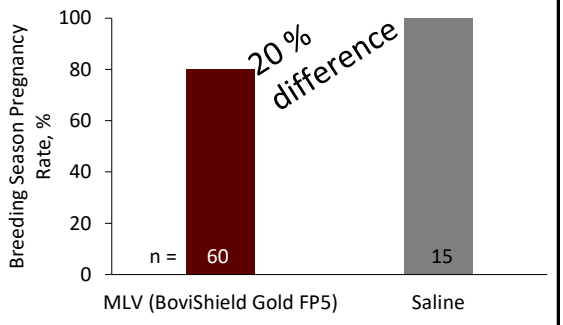
MLV (2x) vs. Control



Walz et al., 2017 Vaccine 35:1046-1054

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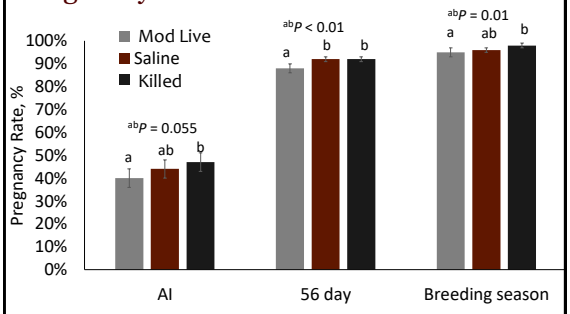
Pregnancy Success-SDSU field trial



Perry et al., 2013 Jacobs J Vet Sci Res 2:35-41

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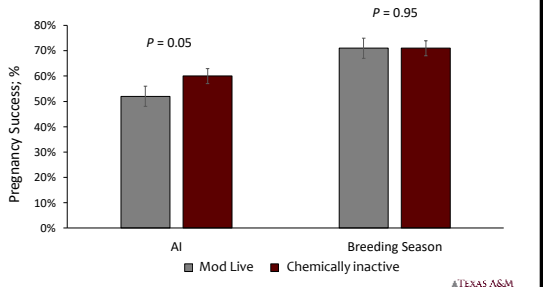
Influence of Treatment on Pregnancy Success-SDSU field trial



Perry et al., 2018 Bovine Practioners Accepted

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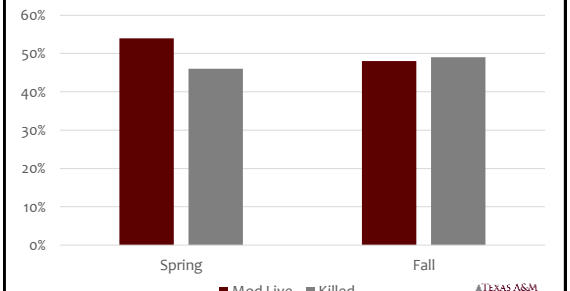
Virginia herds



Stewart et al., 2023

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Reasons

- A recent study - naïve heifers vaccinated at the start of a synchronization protocol with a MLV the Control animals housed in the same pen seroconverted before the end of the study (Chase unpublished data).
  - This indicates that when animals are vaccinated with a MLV, animals can shed the virus and impact animals that they are around.

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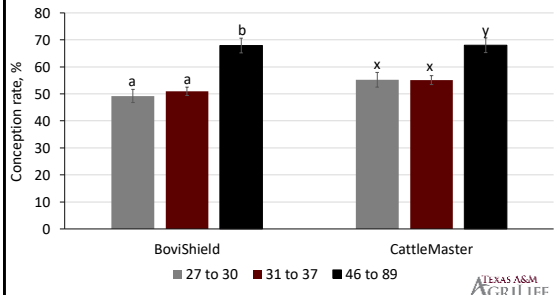
Influence of Vaccination Interval on Pregnancy Success-SDSU field trial



Perry et al., 2018 Bovine Practioners Accepted

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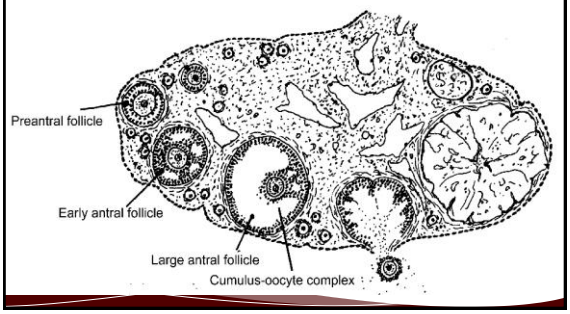
Cattle: 42 days from preantral to preovulatory size, 90 days from activation to preovulatory



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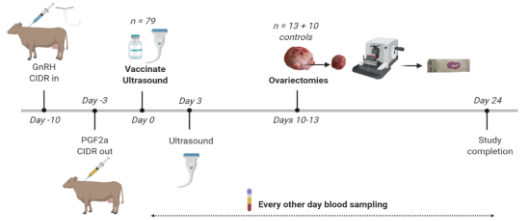
Timeline



Epperson et al., 2021

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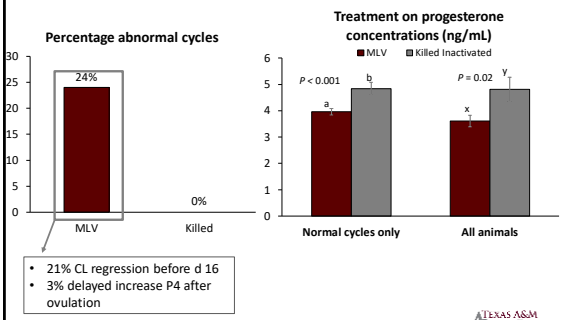
Progesterone



- 21% CL regression before d 16
- 3% delayed increase P4 after ovulation

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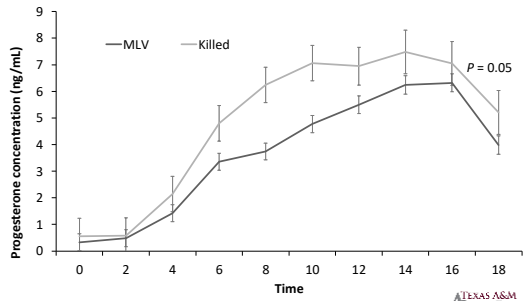
Progesterone



Epperson et al., 2021

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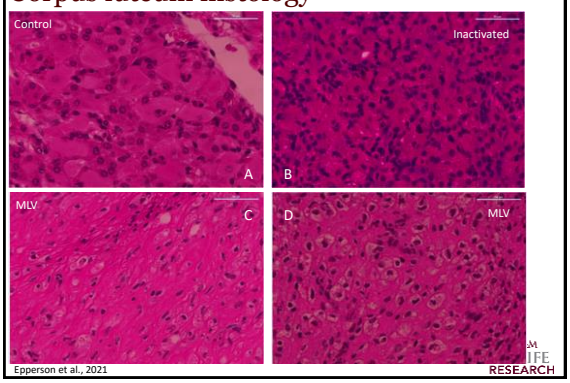
Corpus luteum histology



Epperson et al., 2021

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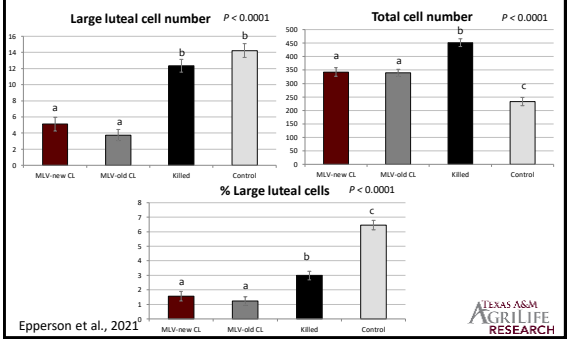
Histology Results



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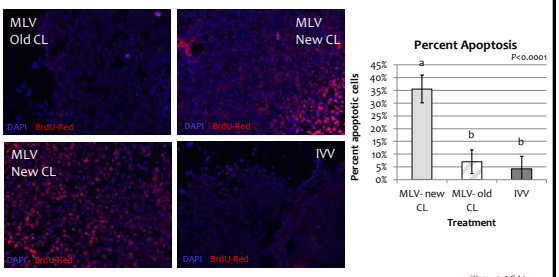
CORPUS LUTEUM APOPTOSIS



Epperson et al., 2021

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Cytokine Results

- Subset of animals (n=44) and number of collection days (d 2, 6, 12,18, 22)
- Analyzed for 15 cytokines

Epperson et al., 2023

	Cytokine Concentration (pg/mL) by treatment			
Cytokine	MLV-normal	MLV-abnormal	IVV-normal	P-value
IFN-γ	2.7624 ± 0.35	2.1165 ± 0.36	1.1258 ± 0.37	**0.0097**
MIP-1β	43.66 ± 8.00	66.42 ± 8.10	41.60 ± 8.38	0.0688
IL-4	14.40 ± 2.55	16.47 ± 2.63	8.91 ± 2.71	0.13
IL-10	86.79 ± 24.95	31.00 ± 25.15	35.67 ± 26.02	0.2
IL-1a	20.46 ± 6.36	6.84 ± 6.40	9.53 ± 6.62	0.29
TNFα	3059.93 ± 1014.37	939.61 ± 1020.35	1232.87 ± 1056.26	0.29
MIP-1α	329.02 ± 59.62	208.82 ± 59.81	249.84 ± 61.89	0.36
VEGFα	43.46 ± 12.57	32.17 ± 12.60	19.81 ± 13.04	0.43
IL-1β	9.46 ± 1.78	8.22 ± 1.92	6.10 ± 1.97	0.45
MCP-1	253.46 ± 42.42	181.40 ± 42.78	205.24 ± 44.25	0.4822
IP-10	329.42 ± 24.52	302.98 ± 25.24	287.28 ± 26.05	0.49
IL-6	15.27 ± 4.92	13.91 ± 4.93	20.50 ± 5.10	0.62
IL-36Ra	192.48 ± 20.39	171.65 ± 20.95	165.52 ± 21.62	0.63
IL-8	287.13 ± 36.65	236.36 ± 40.40	253.89 ± 41.39	0.64

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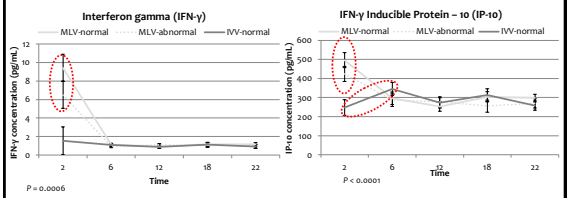
Cytokine Results



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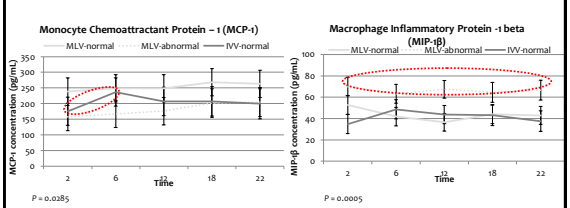
Cytokine Results



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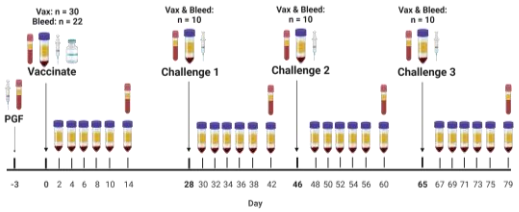
Timeline



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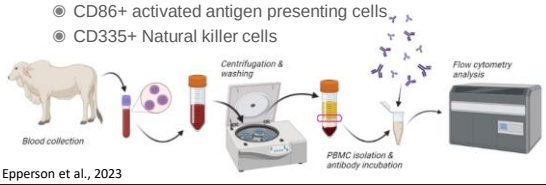
Materials & methods

- Buffy coat extraction for peripheral blood mononuclear cells (PBMC)
  - CD8+ cytotoxic T-cells
  - CD4+ T-helper cells
  - CD25+ activated T-cells
  - CD14+ Antigen presenting cells (monocytes, dendritic cells, macrophages)
  - CD86+ activated antigen presenting cells
  - CD335+ Natural killer cells



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Leukocyte Changes after vaccination: Days 0 - 14

	P-value		
Cell Type	Treatment	Day	Treatment*Day
Antigen Presenting Cells (APCs)	0.61	**<0.0001**	**0.02**
Natural killer cells	0.25	**0.03**	0.27
Activated APCs	0.35	**0.0006**	0.56
T-helper cells	0.27	**0.006**	0.14
Cytotoxic T-cells (CTLs)	0.80	**<0.0001**	0.16
Activated T-cells	0.84	**<0.0001**	**0.01**
Activated CTLs	0.89	0.41	0.14
Activated T-helper (T-regulatory)	0.96	**0.0005**	**0.05**

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Cytokine changes after vaccination: Days 0 - 14

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	P-value		
Cytokine	Treatment	Time	Treatment * Time
IFN-γ	**0.0274**	0.8314	**0.0032**
IL-1α	0.2639	**0.005**	0.5714
IL-1β	0.64	0.0856	0.2955
IL-4	0.8022	0.1645	0.2028
IL-6	0.7557	0.3119	**0.0459**
IL-8	0.0706	0.0758	0.1918
IL-10	0.2223	**0.0416**	0.9598
IL-17A	0.3164	**0.0034**	**0.0536**
MIP-1α	0.5178	**0.0543**	0.5525
IL-36RA	0.2466	**<.0001**	**0.0351**
IP-10	**0.0344**	**0.0161**	**0.0162**
MCP-1	0.8437	**<.0001**	0.6227
MIP-1β	0.3597	**0.0125**	0.1367
TNFα	0.205	0.1092	0.8819
VEGF-A	0.3837	**0.0004**	0.5294

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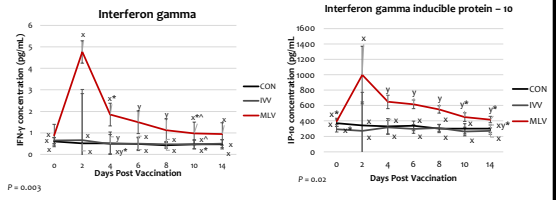
Cytokine Changes after Vaccination: Days 0 - 14



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Season

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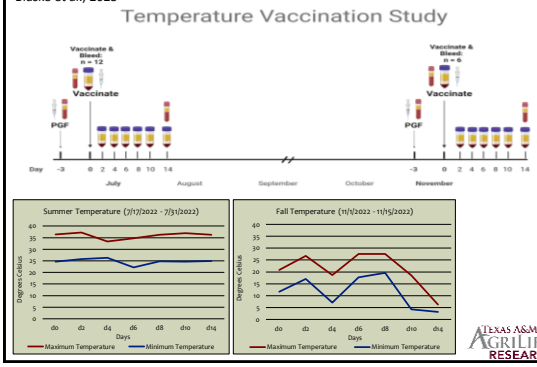

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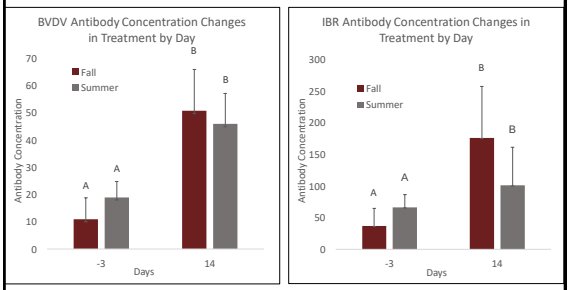
Antibody production



Blaske et al., 2023

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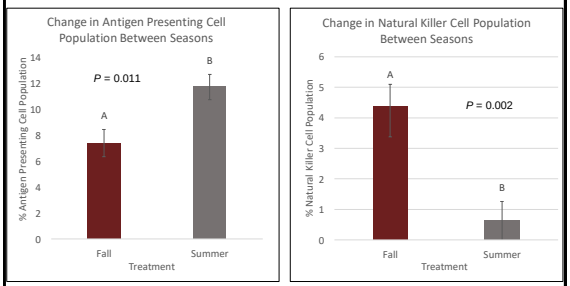
Leukocyte population



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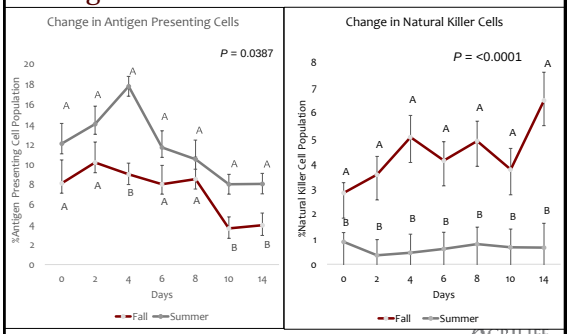
Changes over time



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AGRILIFE RESEARCH

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ccines have the potential to
oduction
e effects of MLV in well-vaccinated

luteal function
immune response

ons – interval to breeding
grams: get veterinary input
eeds differ among herds

TEXAS A&M AGRILIFE RESEARCH

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Texas A&M University
Chloey Guy
Dr. Rodolfo Cardoso
Dr. Tom Welsh

University of Missouri
Dr. Michael F. Smith
Dr. Thomas Spencer

USDA-ARS Ft. Keogh
Dr. Tom Geary

USDA-ARS US-MARC
Dr. Robert Cushman
Dr. Harvey Freetly

South Dakota State University
Dr. Russ Daly
Dr. Julie Walker
Dr. Chris Chase
Stephine Perkins

Iowa State
Dr. Karl Kerns

University of Wisconsin
Dr. Sofia Ortega

Grad Students
Chanda Engel
Josh Nelson
Sarah Fields
Jennifer Grant
Erin Larimore
Crystal Madsen
Olivia Amundson
Steve Crego
Brittany Richardson
Emmalee Northrop
Jerica Rich
Erin Beck
Kaitlin Epperson
Saulo Menegatti Zoca
Taylor Andrews
Adalaide Kline
Lacey Quail
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