St. Croix sheep as a model for immune function and parasite resistance

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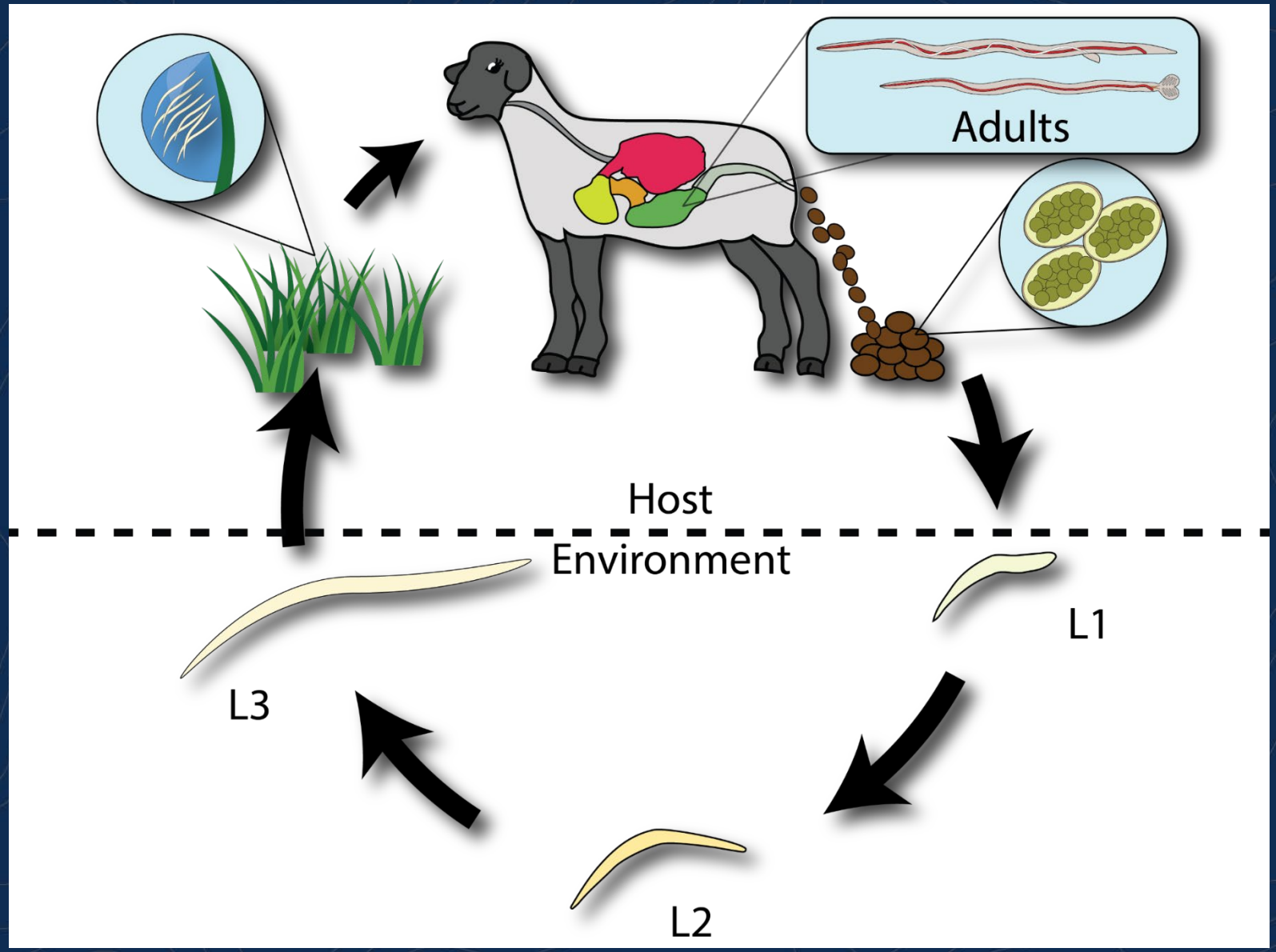
WV EXTENSION

Agriculture and Natural Resources

Lifecycle of GIN Parasites



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What Haemonchus contortus does to its host

- Raise pH
- Suppress immunity
- Mobile
- Feed on blood (0.05ml/worm/day)
  - 1000 worms = 50ml blood

Why parasitism in sheep matters

	H contortus			
Resistance status	**BZ**	**LEV**	**IVM**	**MOX[a]**
All farms				
Susceptible	1	7	7	32
Suspected resistant	0	14	4	3
Low resistant	2	21	11	4
Resistant	43	4	24	7
Sheep farms				
Susceptible	1	6	5	19
Suspected resistant	0	6	4	3
Low resistant	2	13	6	1
Resistant	23	1	11	3
Goat farms				
Susceptible	0	1	2	13
Suspected resistant	0	8	0	0
Low resistant	0	8	5	3
Resistant	20	3	13	4

How did we get here?

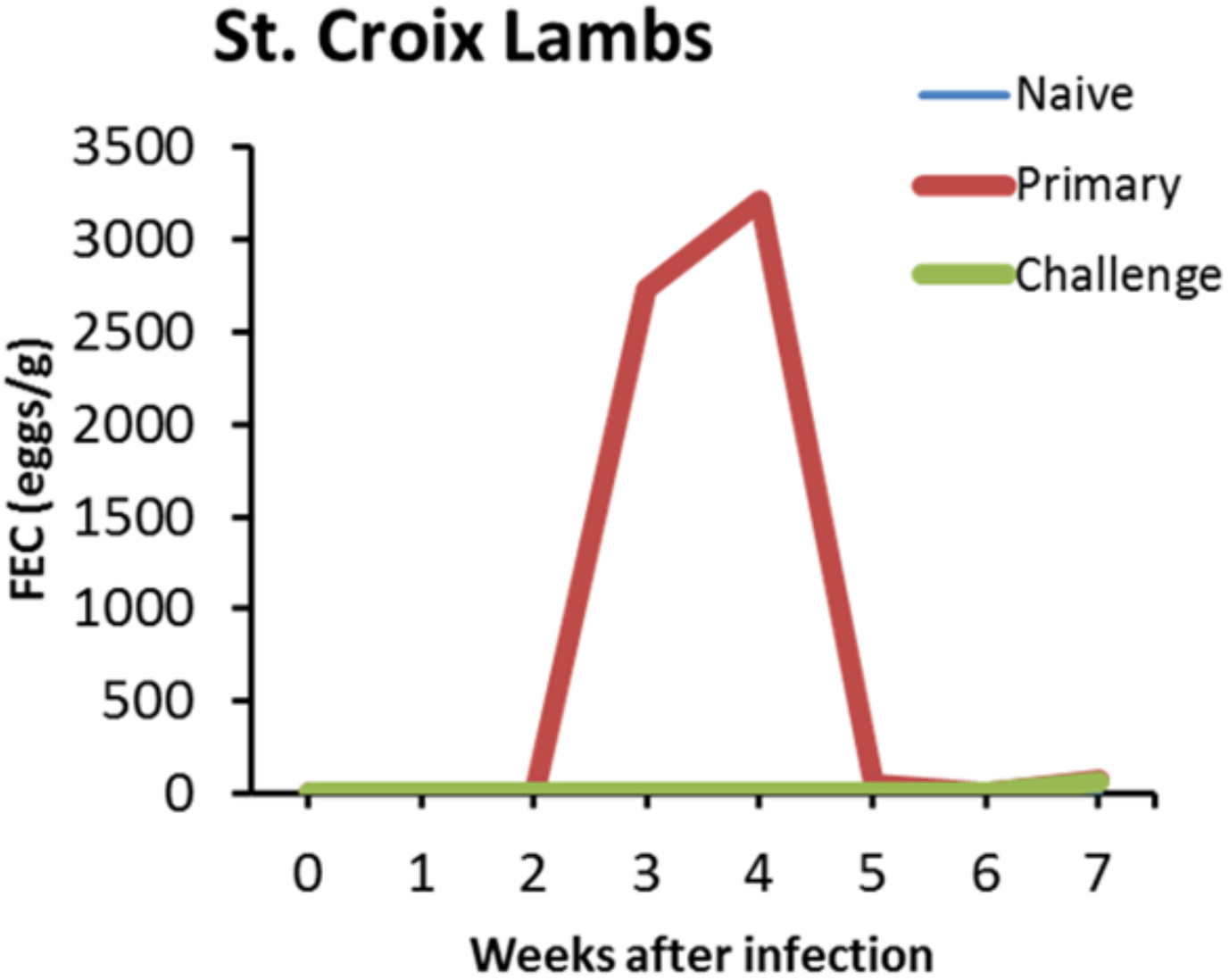
- Courtney et al., 1985 – St. Croix and BB show greater response to worm infection
- Gamble and Zajac, 1992 – Comparison of St. Croix sheep and Dorset
- Notter, 2000 – Reviewed genetic potential for island hair breeds in disease resistance in breeding systems
- Burke and Miller, 2002 – St. Croix sheep more resistant than other hair breeds

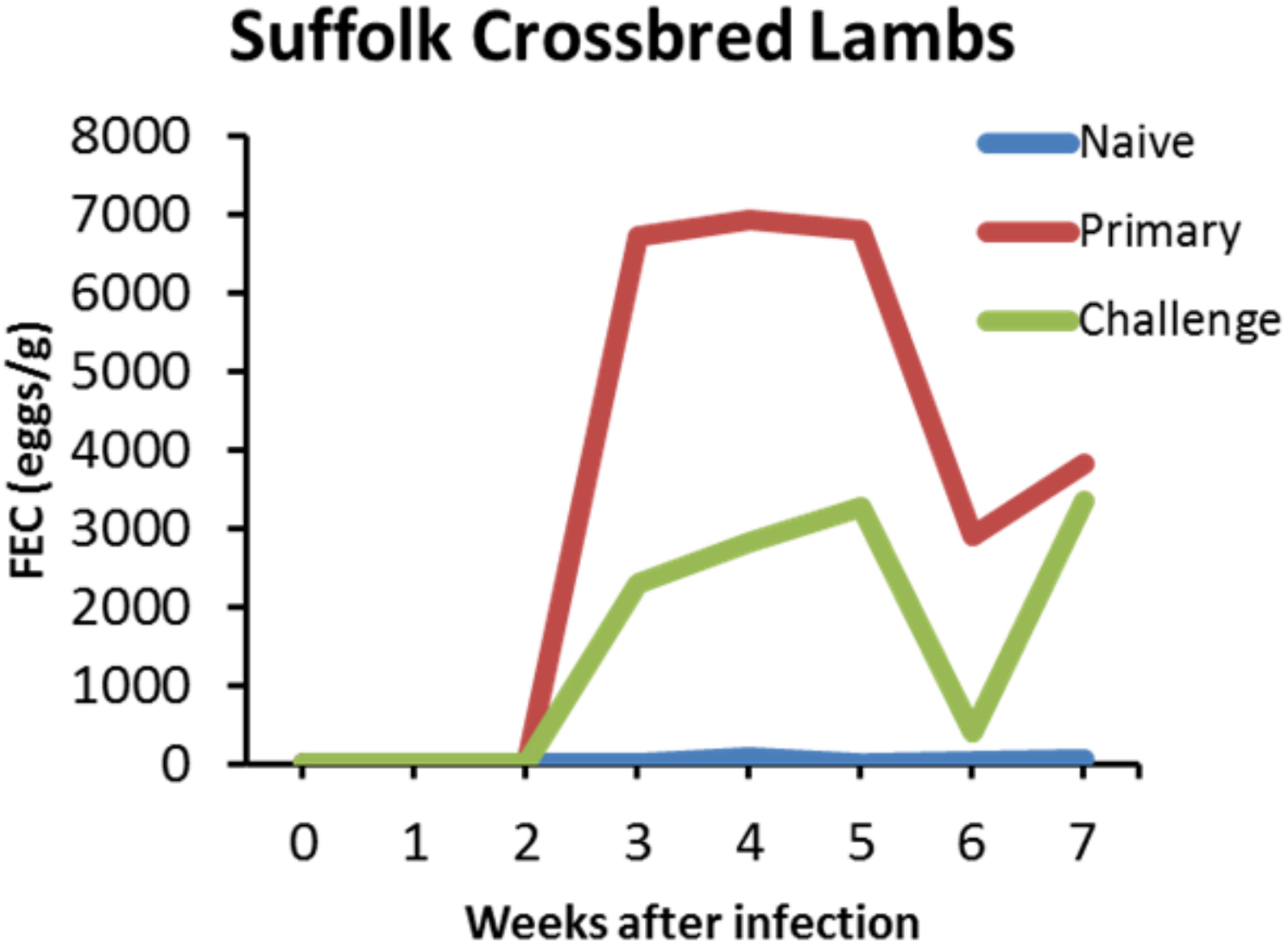
What did everyone find…

Once infected St. Croix sheep had lower egg shedding and fewer worms in their abomasum

No discernable differences in their immune response at the time of egg shedding

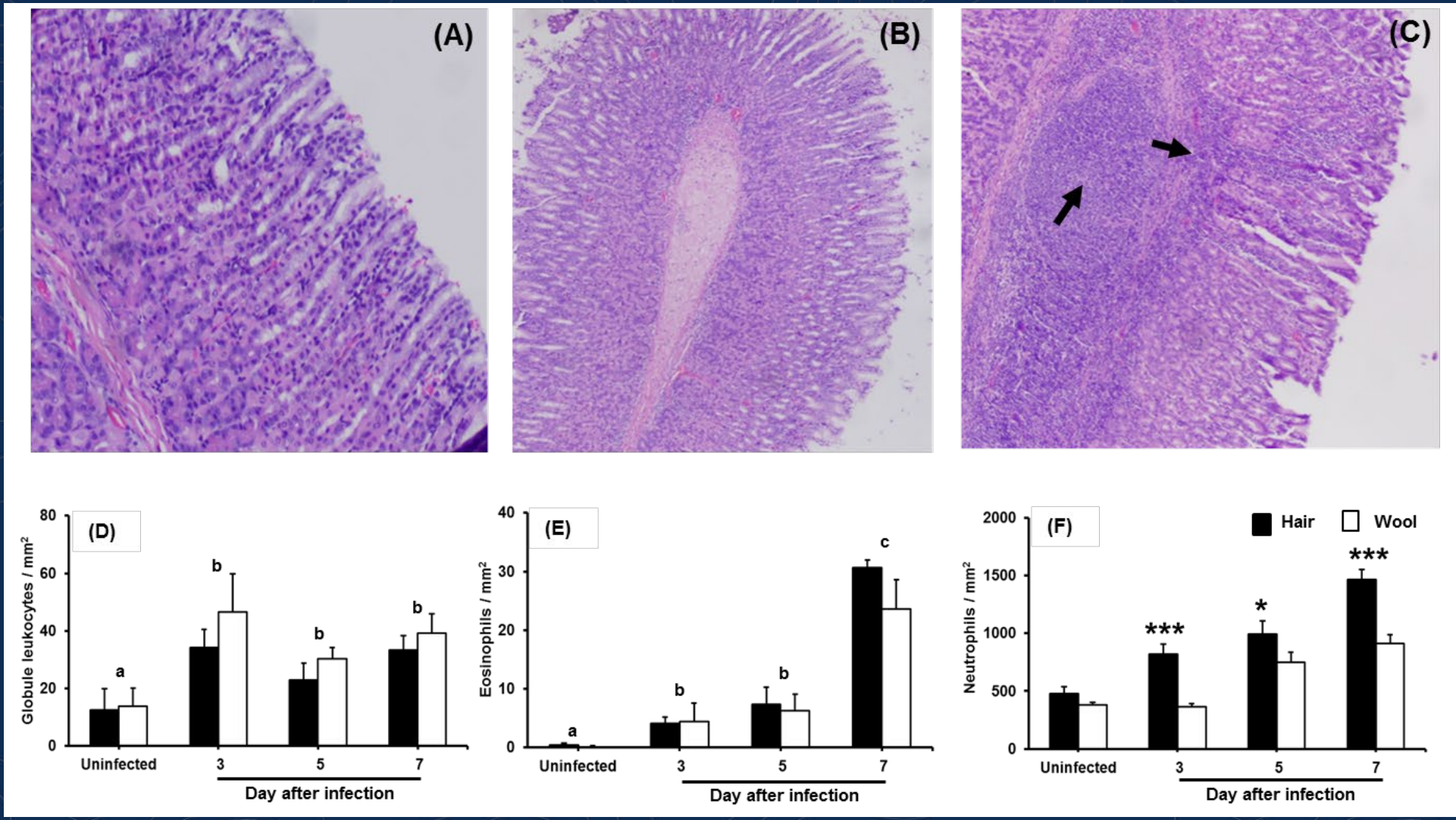
WHY!!!


St. Croix Lambs
Naive
Primary
Challenge
FEC (eggs/g)
3500
3000
2500
2000
1500
1000
500
0
0
1
2
3
4
5
6
7
Weeks after infection

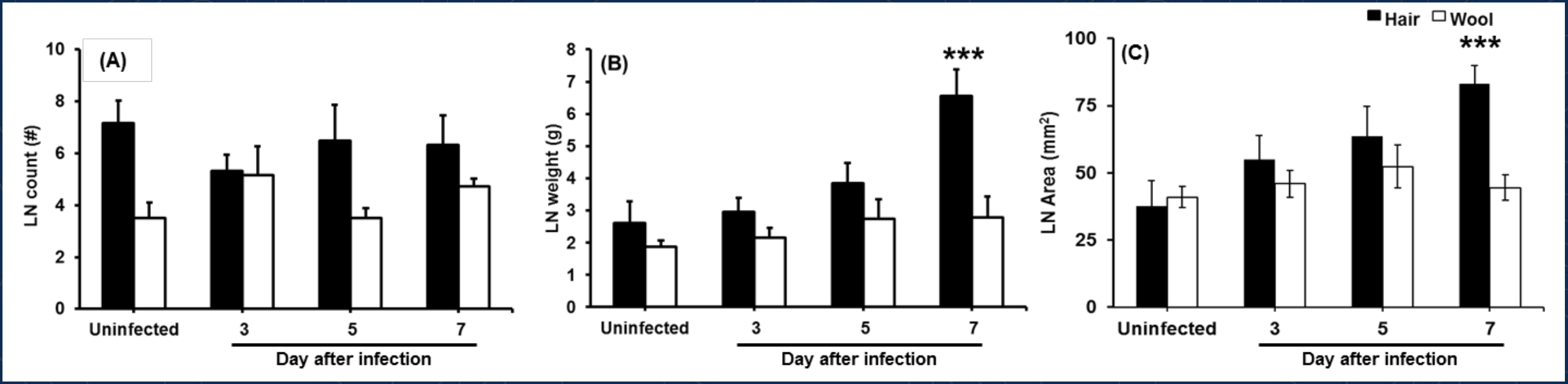

Suffolk Crossbred Lambs
8000
7000
6000
5000
4000
3000
2000
1000
0
FEC (eggs/g)
Naive
Primary
Challenge
0
1
2
3
4
5
6
7
Weeks after infection

What is happening in these sheep early that could be responsible for resistance?

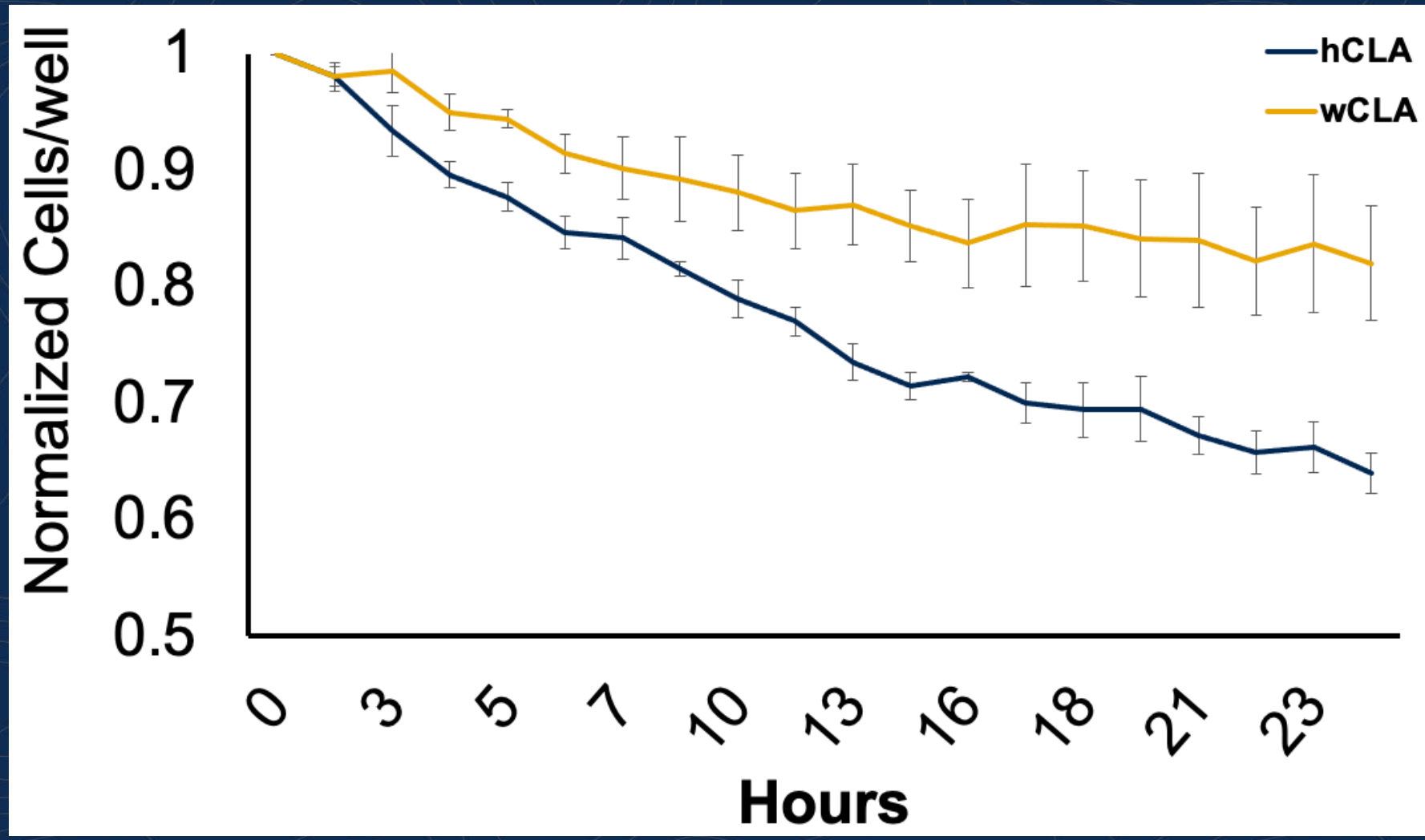
Immune cell infiltration to abomasum



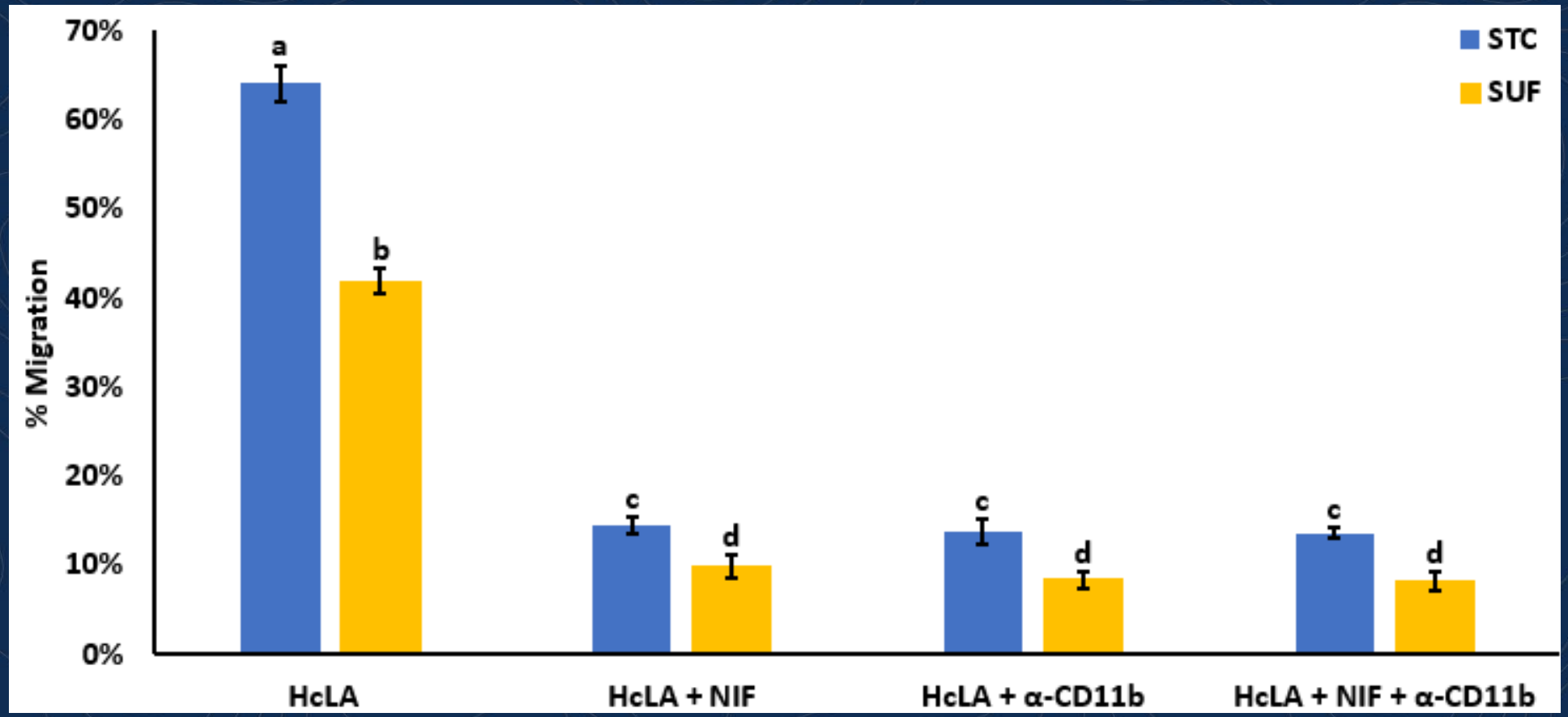
Draining LN development after infection



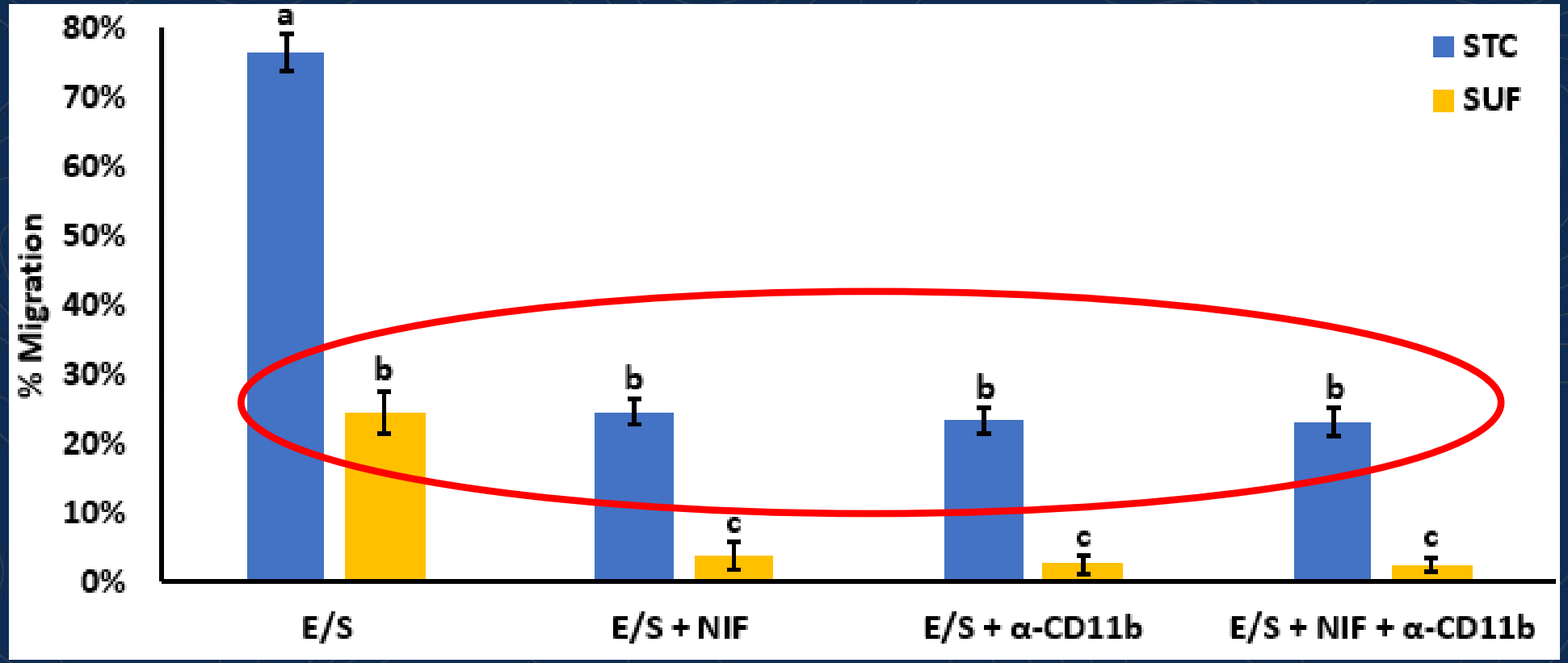
Neutrophil movement to antigen



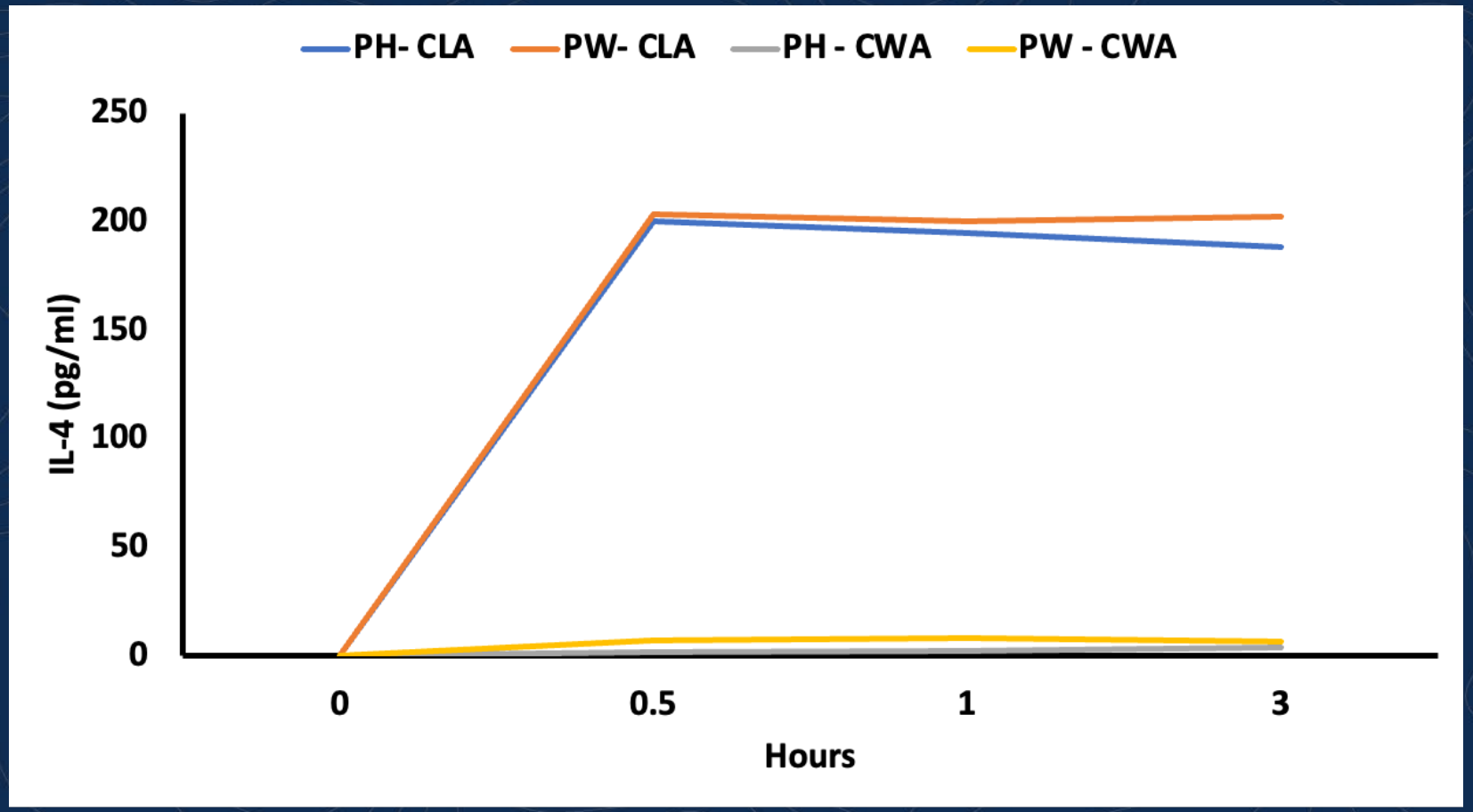
Neutrophil Chemotaxis: HcLA



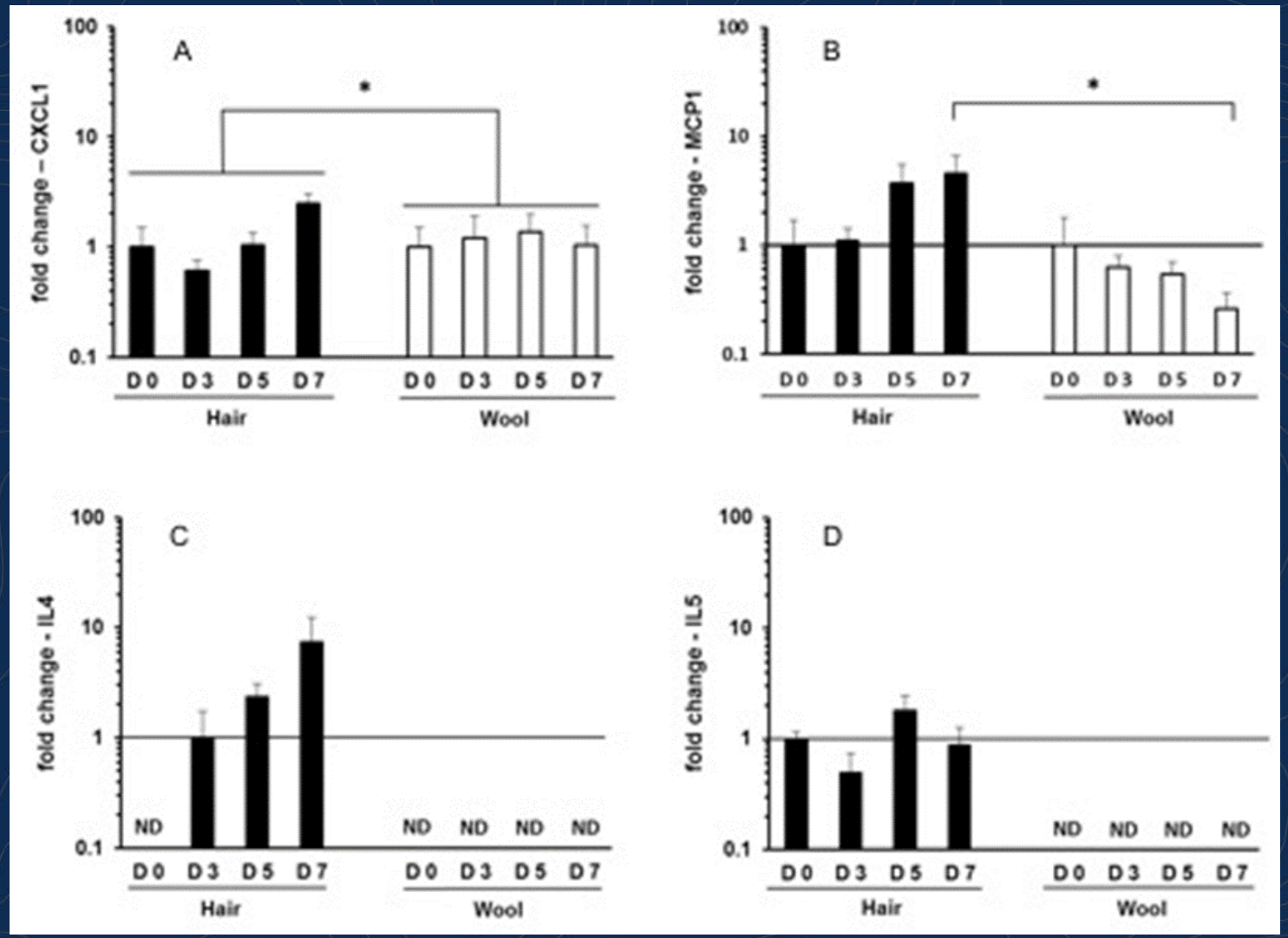
Neutrophil Chemotaxis: E/S



Neutrophil response to antigen



Expression of immune genes in abomasum

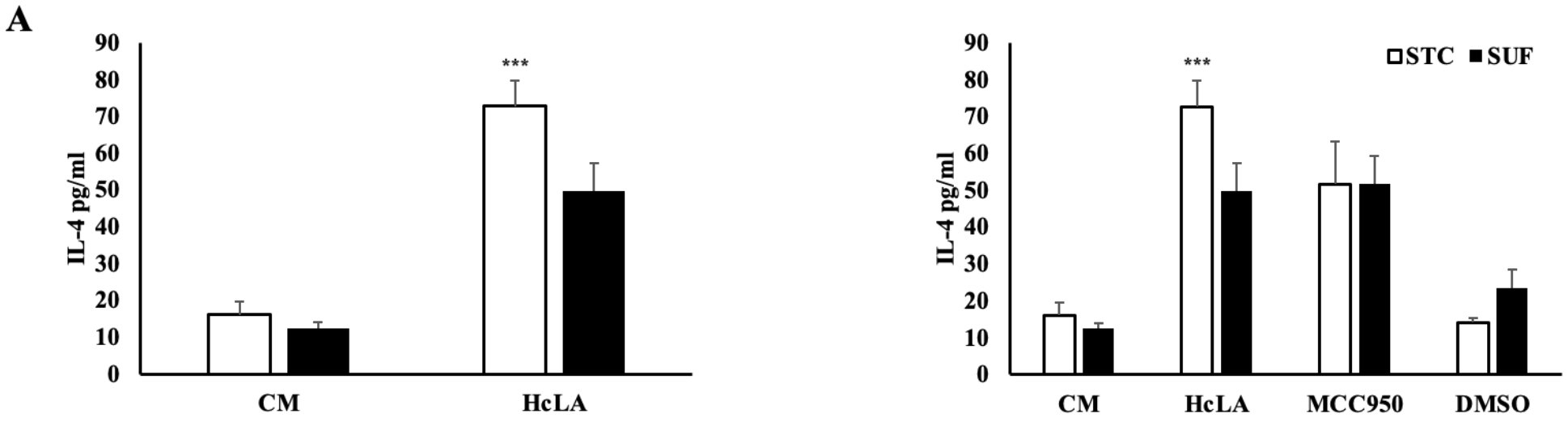


NLRP3 Predicted Protein Structure

St. Croix

Suffolk

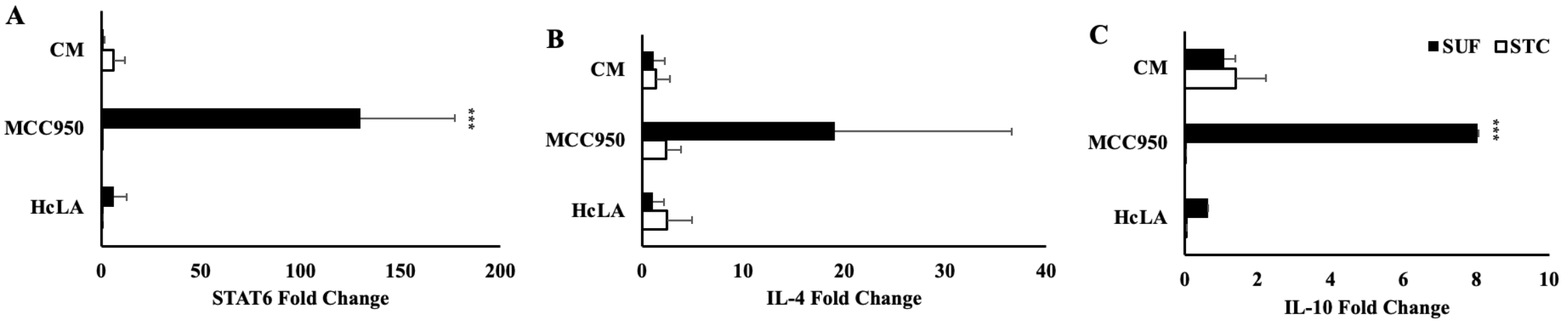
IL-4 PROTEIN PRODUCTION



- STC significantly produced greater amounts of IL-4 in response to HcLA
- NLRP3 inhibition results in a reduction in STC IL-4 responses, similar to SUF

*** P < 0.001

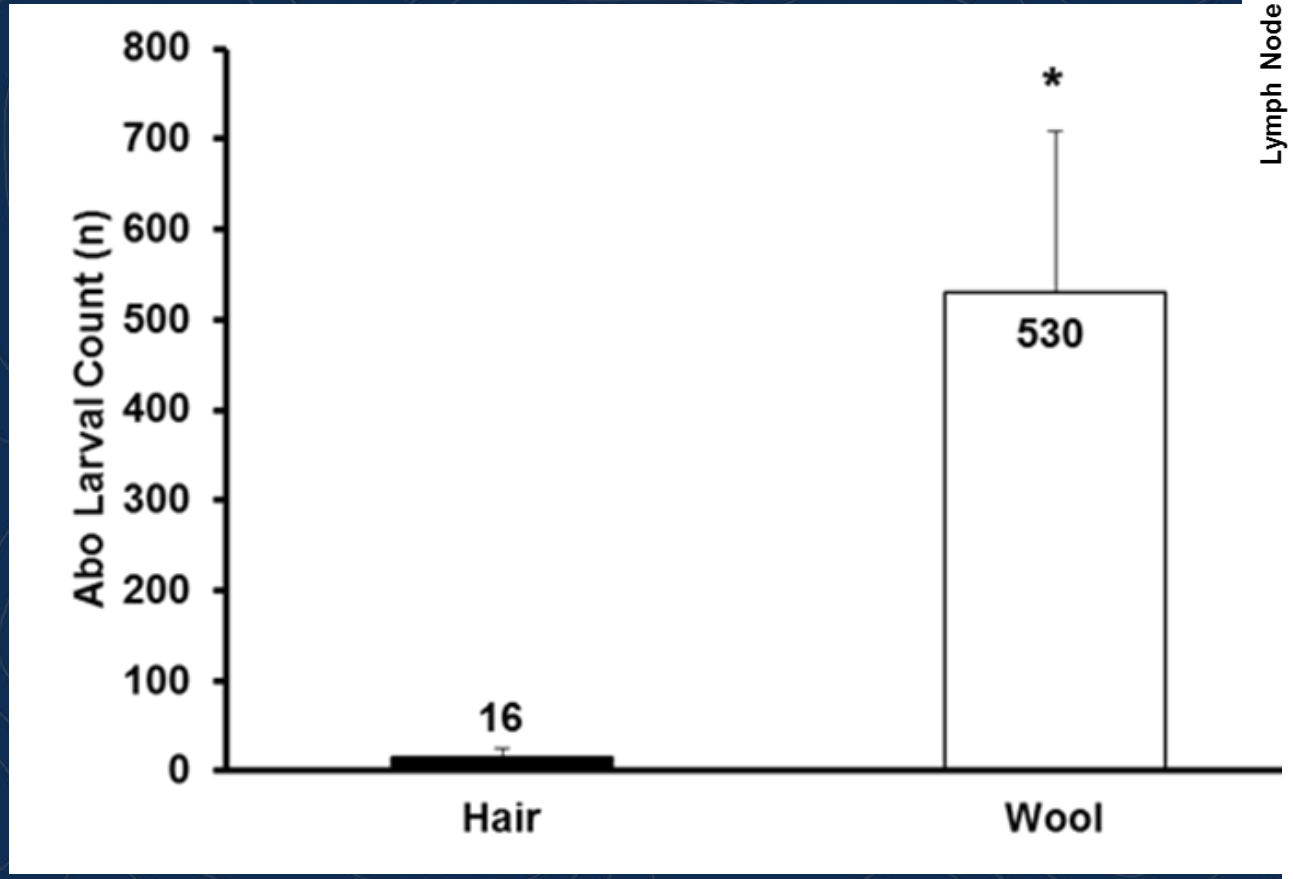
Further effects of NLRP3 inhibition

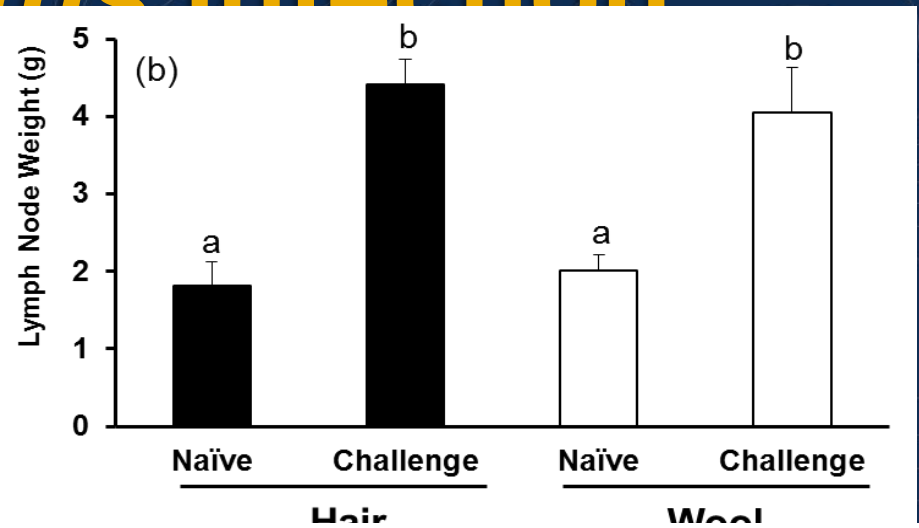


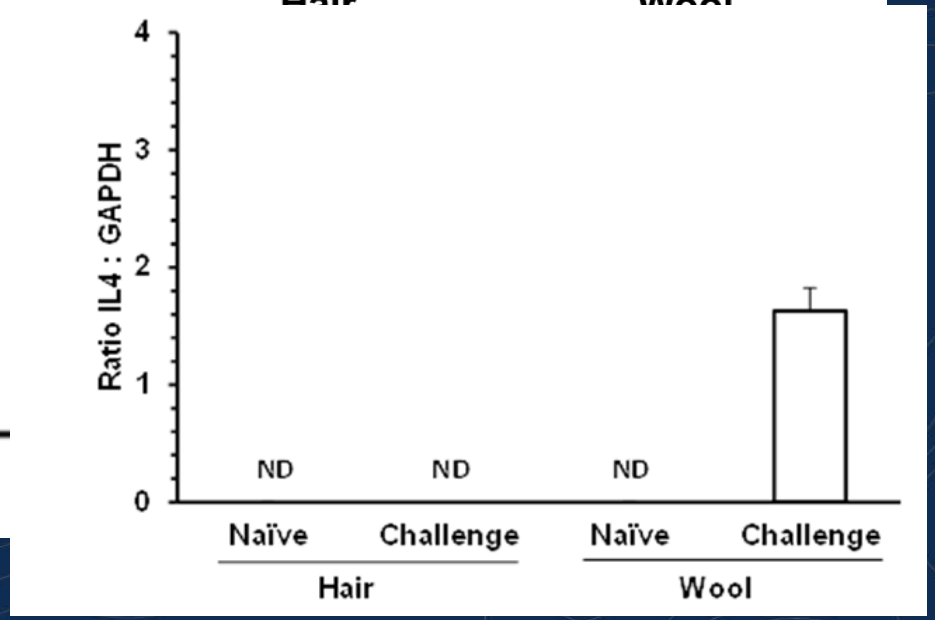
- Inhibition of NLRP3 in SUF PBMC has a restorative effect
- Are delays in SUF responses a result in a NLRP3 defect?

*** P < 0.001

Day 10 after *H. contortus* infection







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WHAT HAVE WE OBSERVED?

1. Reduced abomasal worm burden by D7 in STC

   Bowdridge et al., 2015

2. Lymph node hypertrophy by D7 in STC

   Bowdridge et al., 2015

3. Abomasal IL-4 expression upregulated between D3-7 in STC

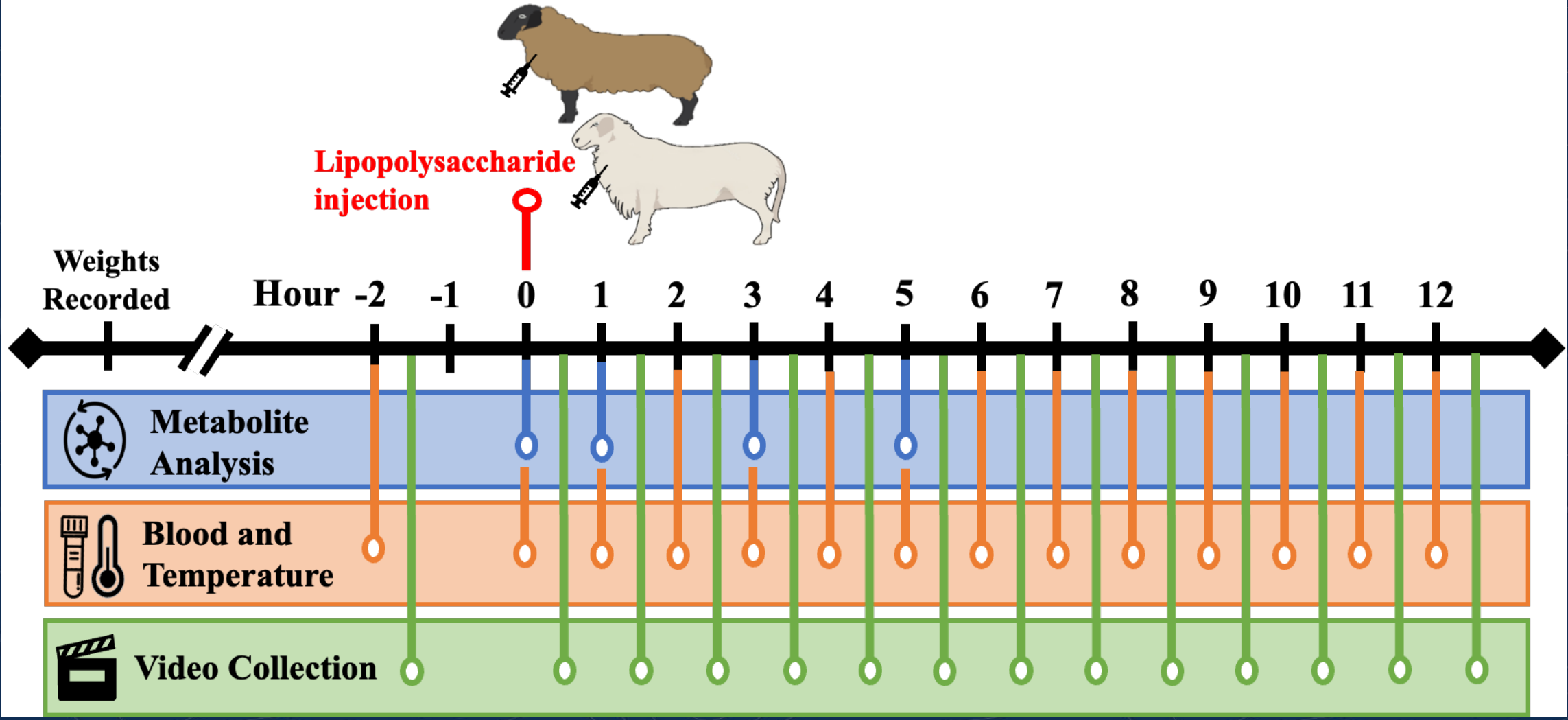
   Jacobs et al., 2015

4. Abomasal influx of Neutrophil between D3-7 in STC

   Bowdridge et al., 2015

Are St. Croix sheep just more immune competent?

Materials and Methods

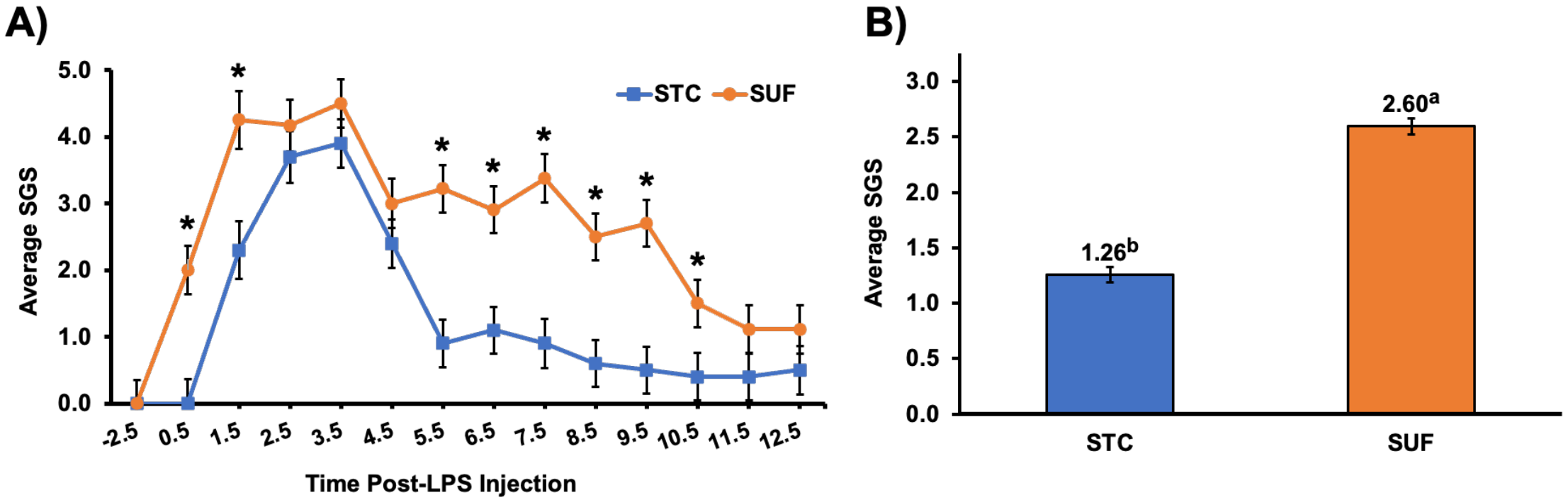


Materials and Methods

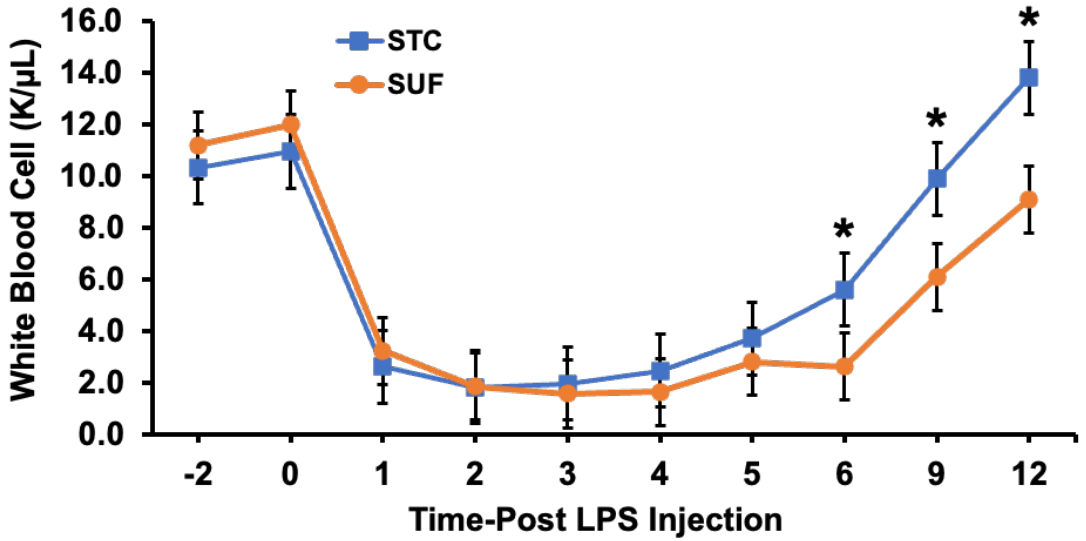
Sheep Grimace Score (SGS)

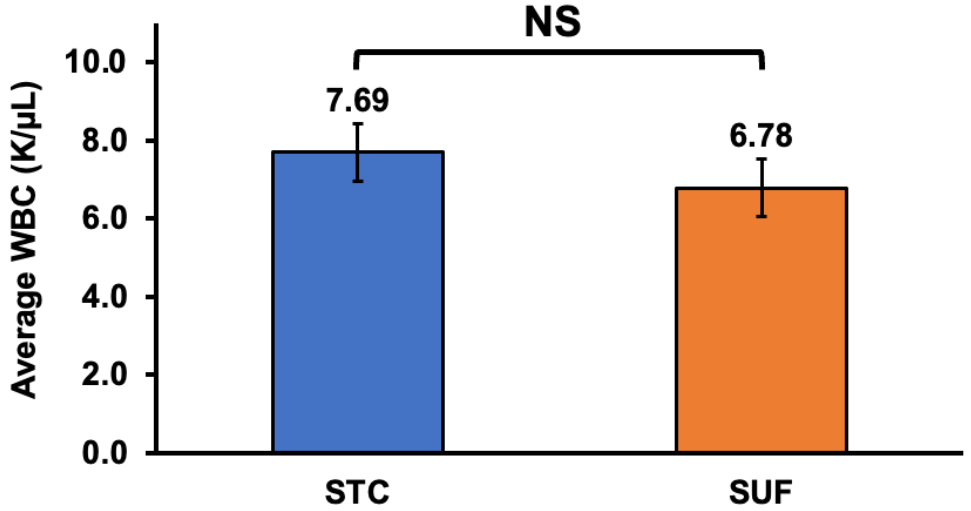
Orbital	2
Ear/Head	2
Flehming	1
Total	**5**

Results - SGS

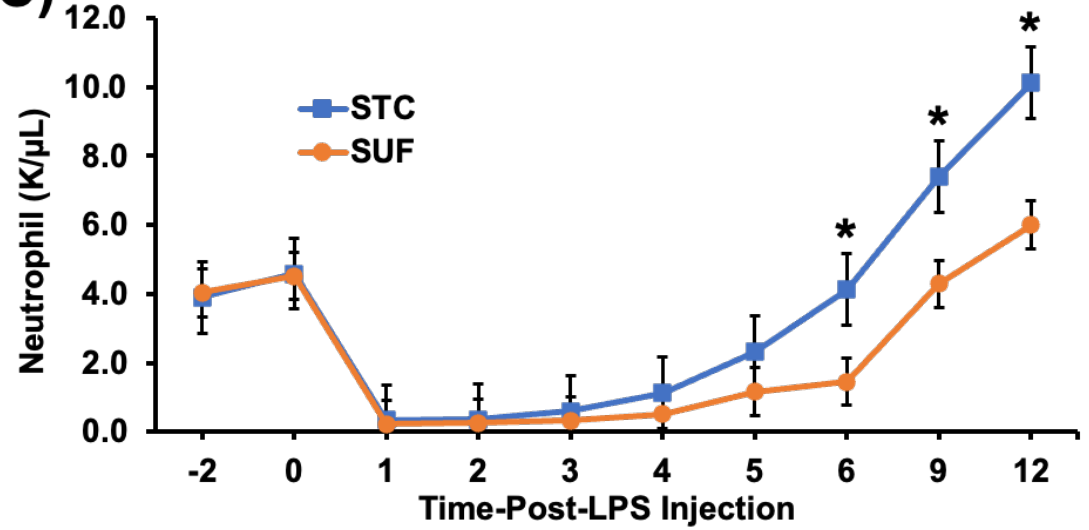


Group	$P < 0.0001$
Group*Time	$P < 0.0001$

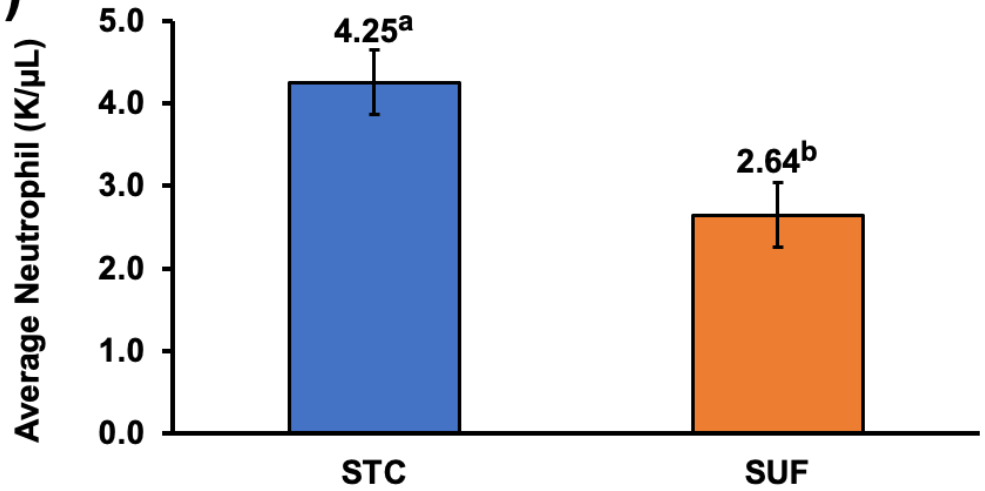

White Blood Cell (K/µL)
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
STC
SUF
*
*
*
-2
0
1
2
3
4
5
6
9
12
Time-Post LPS Injection


NS
Average WBC (K/µL)
10.0
8.0
6.0
4.0
2.0
0.0
7.69
6.78
STC
SUF

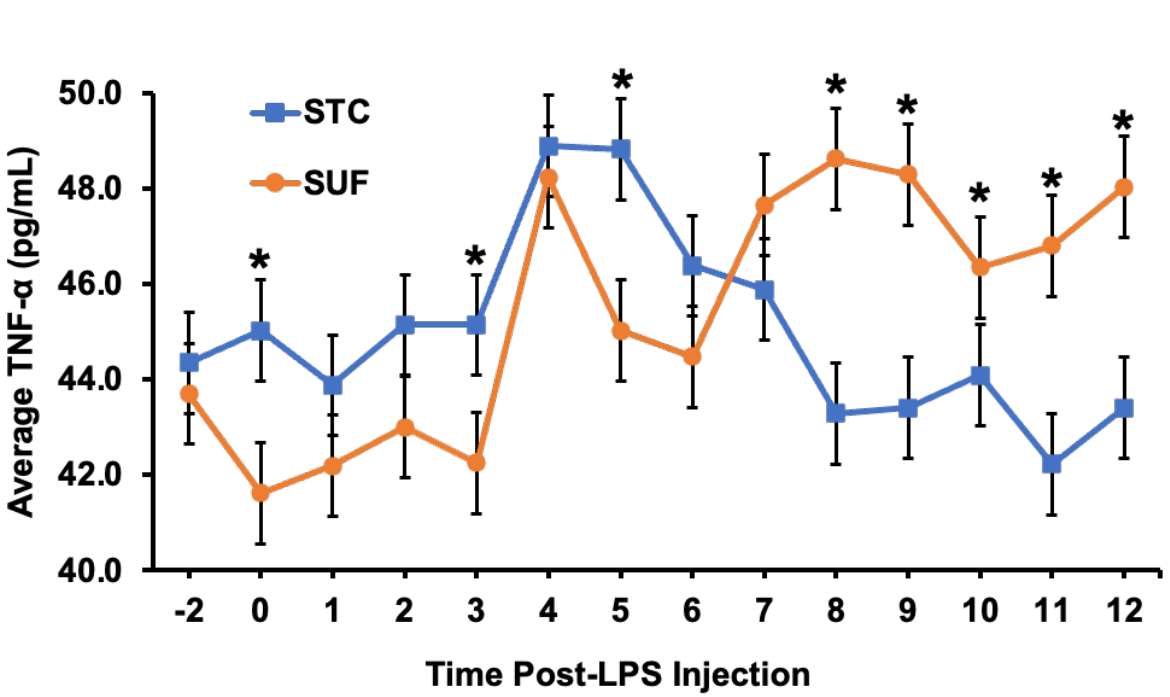
C)


Neutrophil (K/µL)
12.0
10.0
8.0
6.0
4.0
2.0
0.0
STC
SUF
*
*
*
-2
0
1
2
3
4
5
6
9
12
Time-Post-LPS Injection

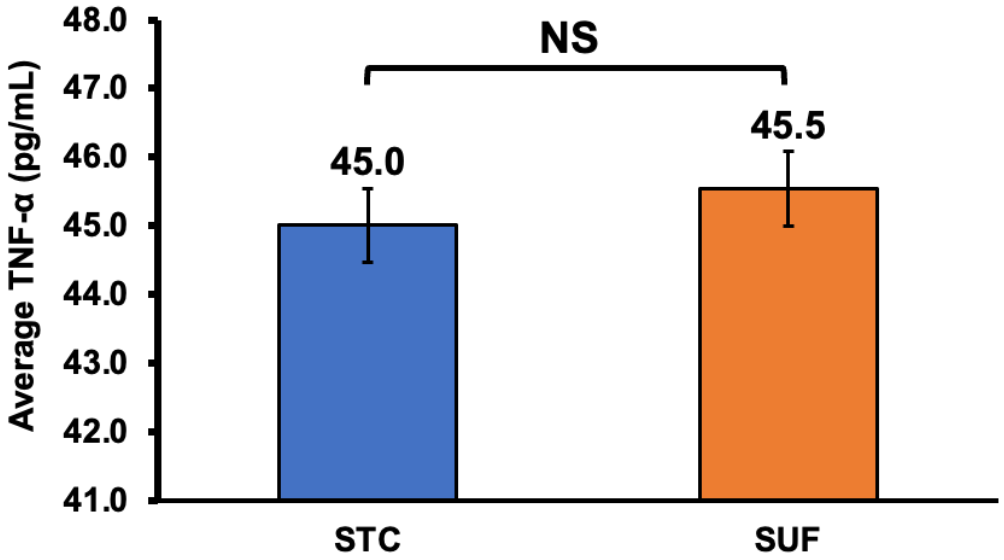
D)


Average Neutrophil (K/µL)
5.0
4.0
3.0
2.0
1.0
0.0
4.25a
2.64b
STC
SUF

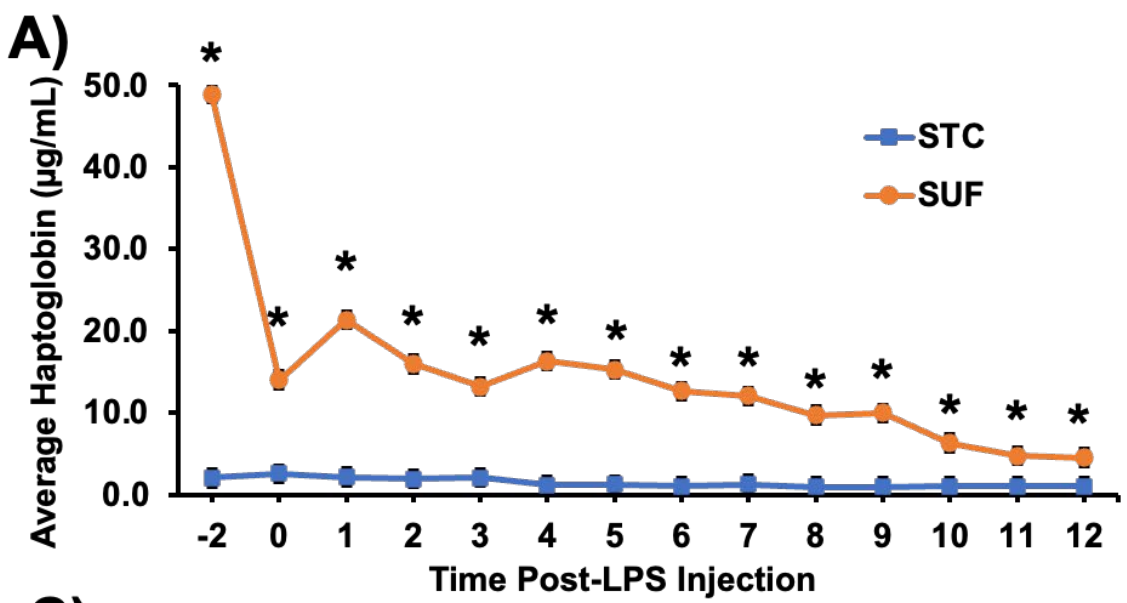
Results – TNF-α

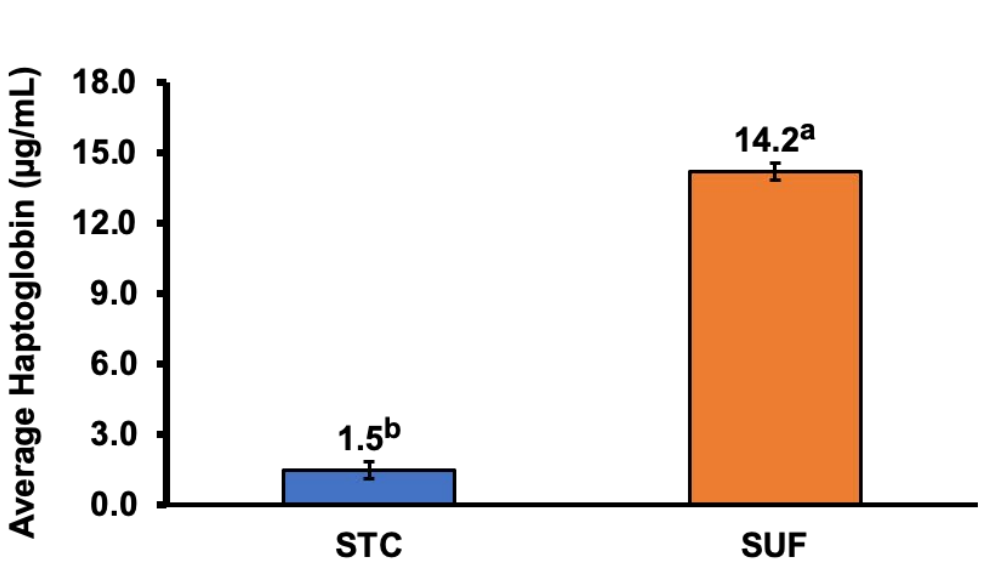


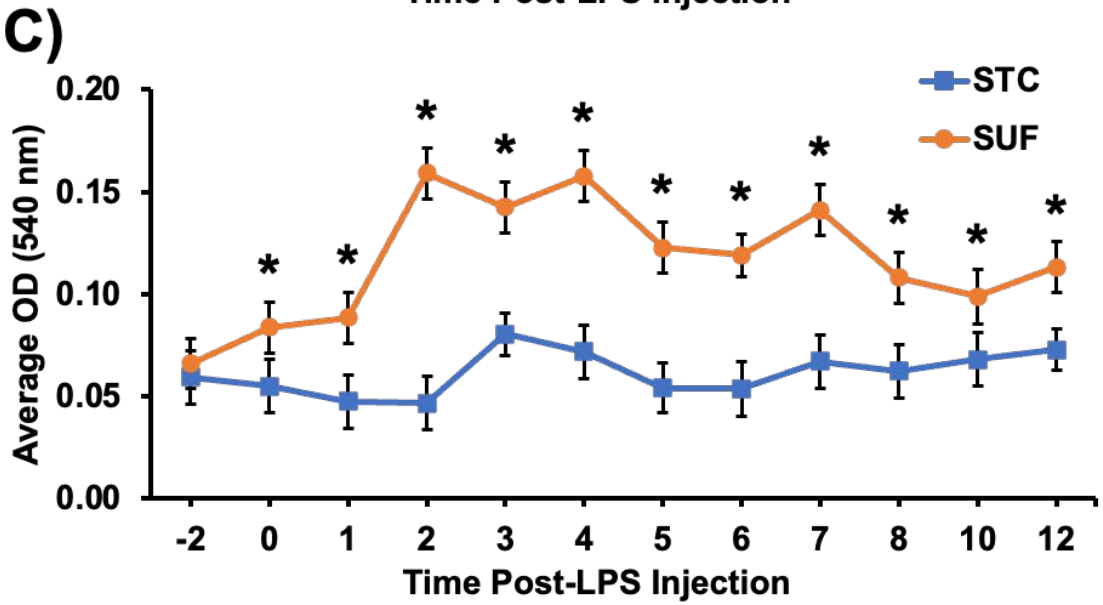
B)

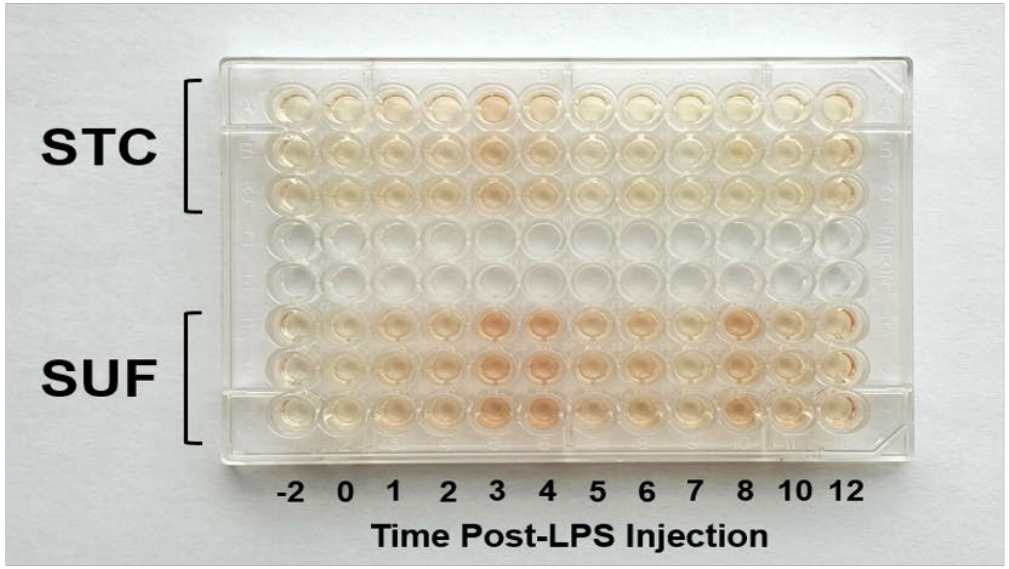


Group	$P = 0.5125$
Group*Time	$P < 0.0001$


A)
Average Haptoglobin (µg/mL)
50.0
40.0
30.0
20.0
10.0
0.0
STC
SUF
-2 0 1 2 3 4 5 6 7 8 9 10 11 12
Time Post-LPS Injection


B)
Average Haptoglobin (µg/mL)
18.0
15.0
12.0
9.0
6.0
3.0
0.0
1.5b
14.2a
STC
SUF


C)
Average OD (540 nm)
0.20
0.15
0.10
0.05
0.00
STC
SUF
-2 0 1 2 3 4 5 6 7 8 10 12
Time Post-LPS Injection


D)
STC
SUF
-2 0 1 2 3 4 5 6 7 8 10 12
Time Post-LPS Injection

The St. Croix Breed has Immunological Superiority

- This is a trait within this breed that MUST not be lost!
- Careful balance should be considered when selecting for other traits
  - – see Suffolk sheep!
- There is extraordinary opportunity for this breed in crossbreeding systems
  - Requires maintenance of seedstock producers!

Acknowledgements

VIRGINIA TECH™

WEST VIRGINIA UNIVERSITY FOUNDATION

ASI

NORTHEAST SARE
Sustainable Agriculture Research & Education

USDA

NCVP
National Center for Veterinary Parasitology

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