



Research Institute for
Farm Animal Biology



Time-dependent molecular adaptation of immune and platelet function to heat stress in PBMC of Holstein dairy cows

Franziska Koch, Björn Kuhla, Christa Kühn

EAAP Florence – 01.09.2024

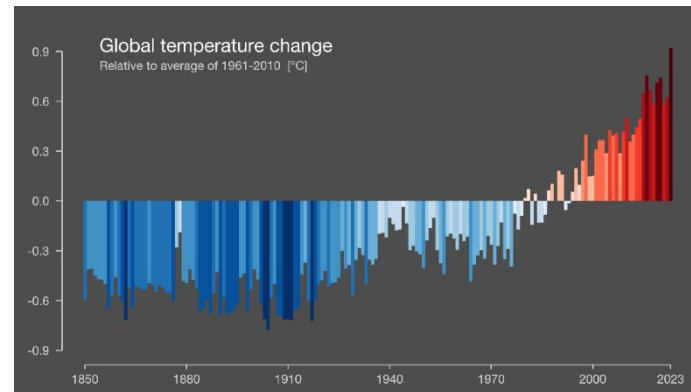
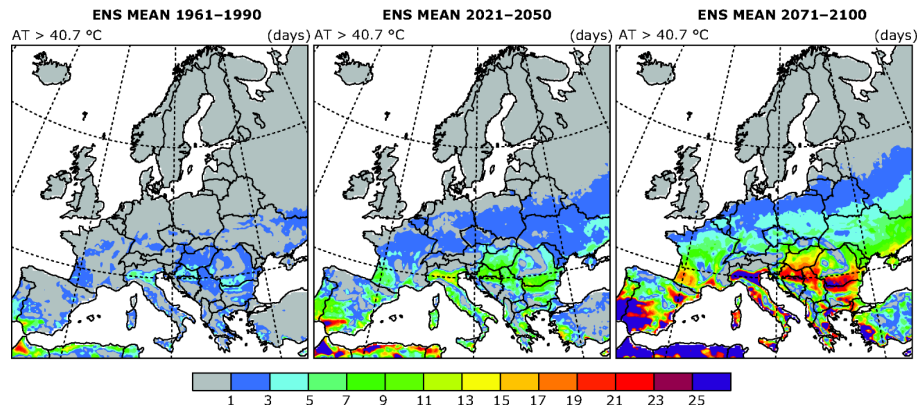
Funding:



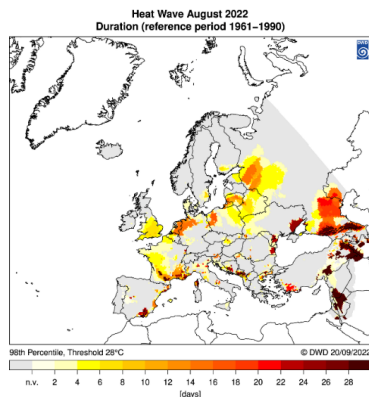
FLI

Consequences of global warming

Prediction



Reality



- ✓ Aim: limit global warming to 1.5°C until 2100
- ✓ Risk increases to exceed 1.5°C without changes
→ otherwise increase of the ambient temperature to 2.1 – 3.4°C expected
- ✓ Increase of extreme weather (heat, rain, flood)



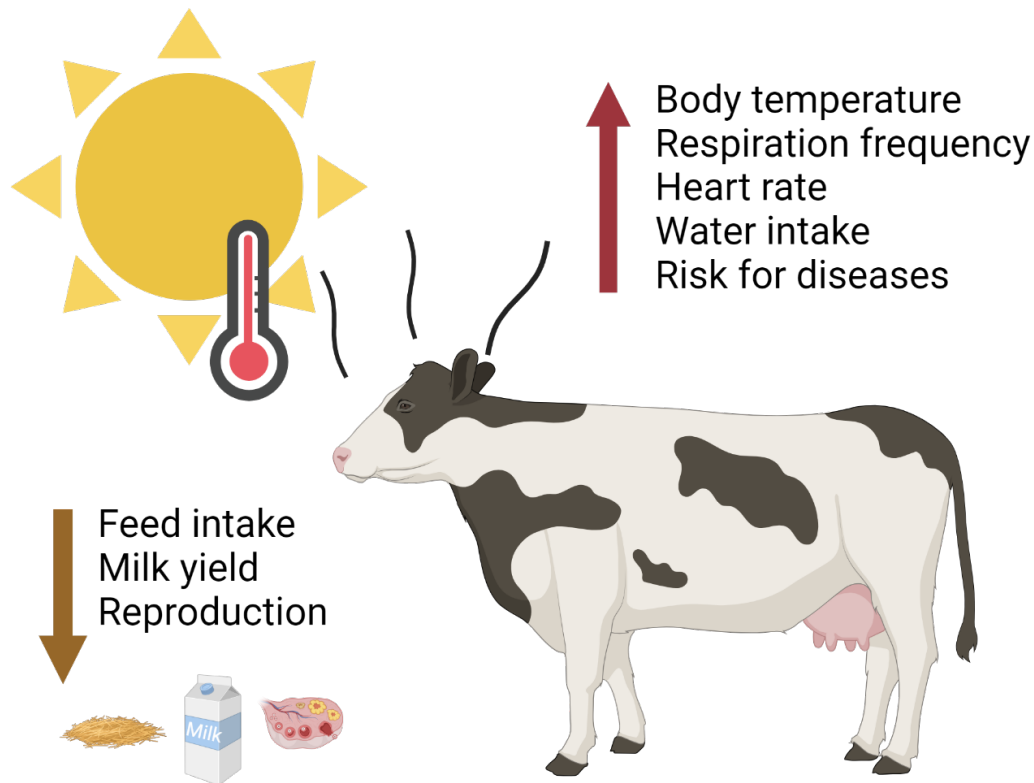
Consequences of global warming – heat stress

Temperature Humidity Index (THI)										
	Relative Humidity %									
C	20	30	40	50	60	70	80	90	100	
22	66	66	67	68	69	69	70	71	72	
24	68	69	70	70	71	72	73	74	75	
26	70	71	72	73	74	75	77	78	79	
28	72	73	74	76	77	78	80	81	82	
30	74	75	77	78	80	81	83	84	86	
32	76	77	79	81	83	84	86	88	90	
34	78	80	82	84	85	87	89	91	93	
36	80	82	84	86	88	90	93	95	97	
38	82	84	86	89	91	93	96	98	100	
40	84	86	89	91	94	96	99	101	104	

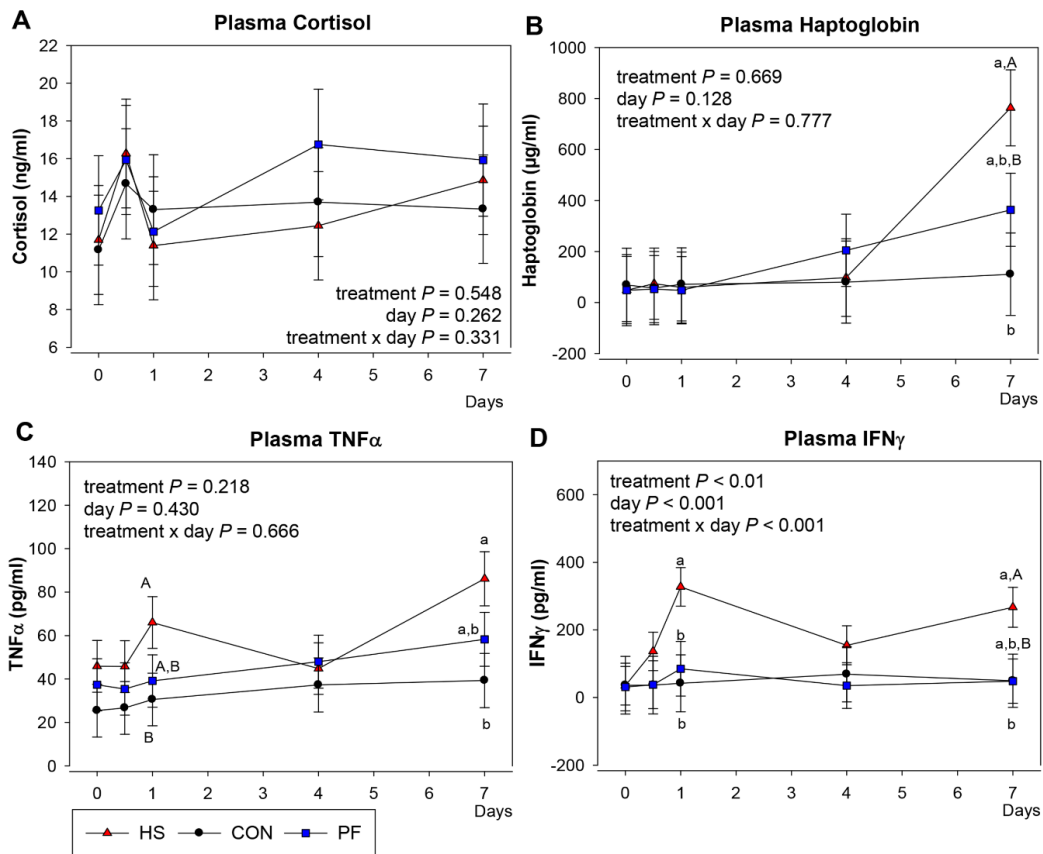
No heat stress
Moderate heat stress
Severe heat stress
Dead cows

<http://www.nadis.org.uk/disease-a-z/cattle/managing-heat-stress-in-dairy-cows/>

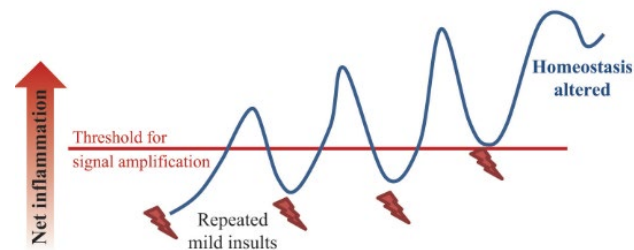
- ✓ Acclimation to heat is a trade-off between survival and metabolic maintenance including immune response



Immune response under heat stress



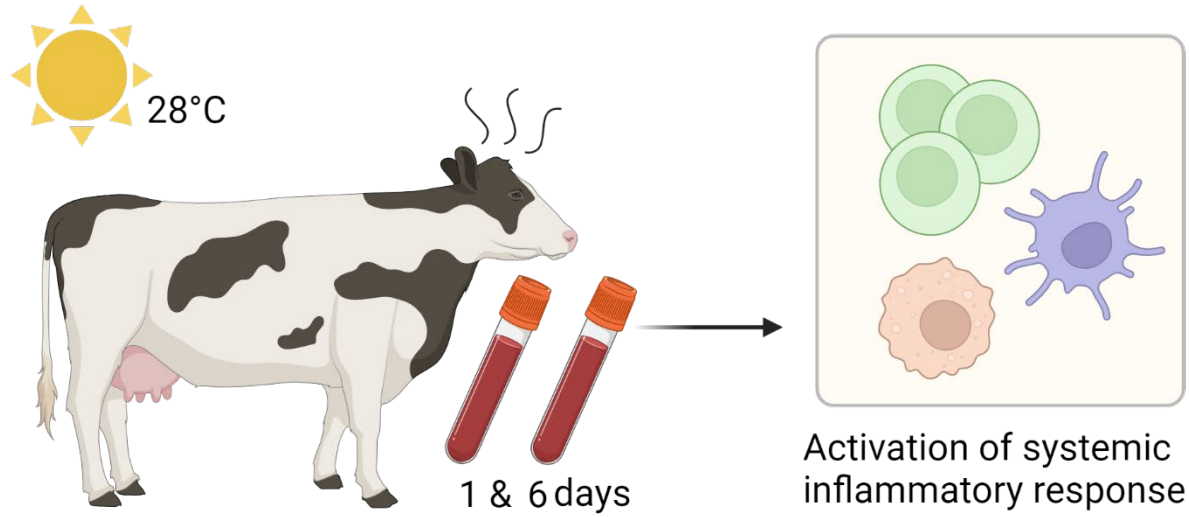
Small letters indicate $p < 0.05$. Capital letters indicate $0.05 < p < 0.1$



Bradford et al. 2015, J Dairy Sci,
10.3168/jds.2015-9683

Koch et al. 2023, J Dairy Sci
doi:10.3168/jds.2022-22520

Hypothesis



Our objective was to elucidate the time-dependent effects of moderate chronic heat stress in peripheral blood mononuclear cells of Holstein cows by altering the transcriptomic profile.

Experimental Design



Climate chamber 28°C



Climate chamber 16°C

Experimental Design



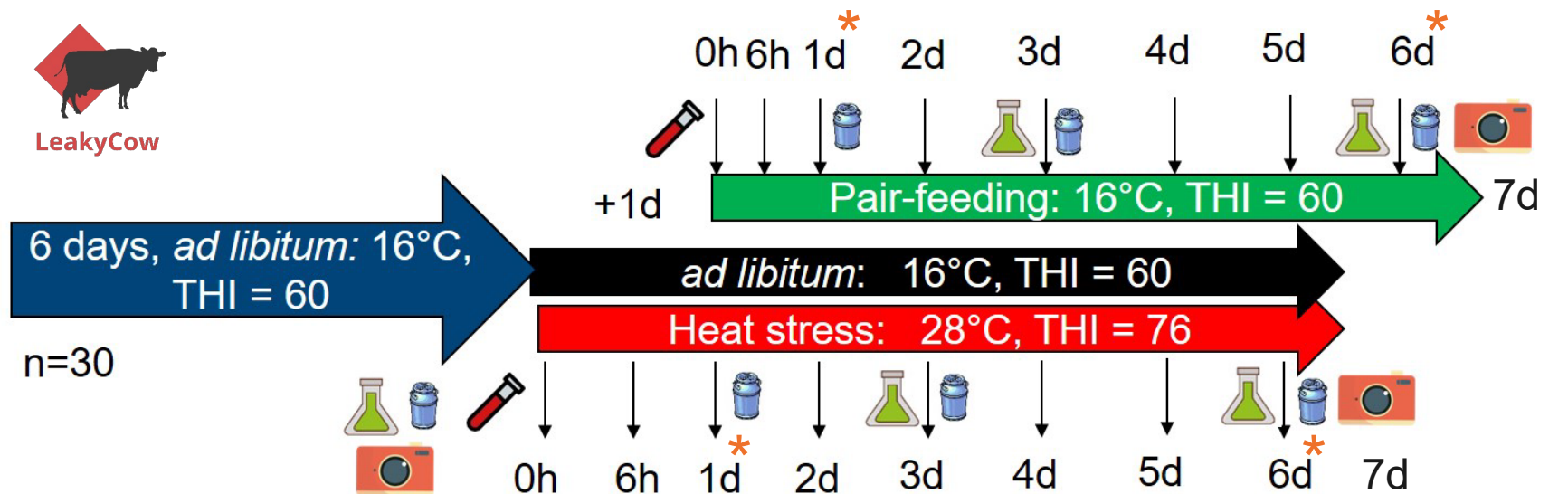
30 Holstein dairy cows in 1st lactation (mean $\pm$ SEM: 169 $\pm$ 9 days in milk)

- genotyped by HSP70.1 5' UTR 895

- in 2 climate rooms (permanent 16°C or 28°C)



LeakyCow



* Isolation of PBMC



Milk samples



Blood samples



Rumen samples



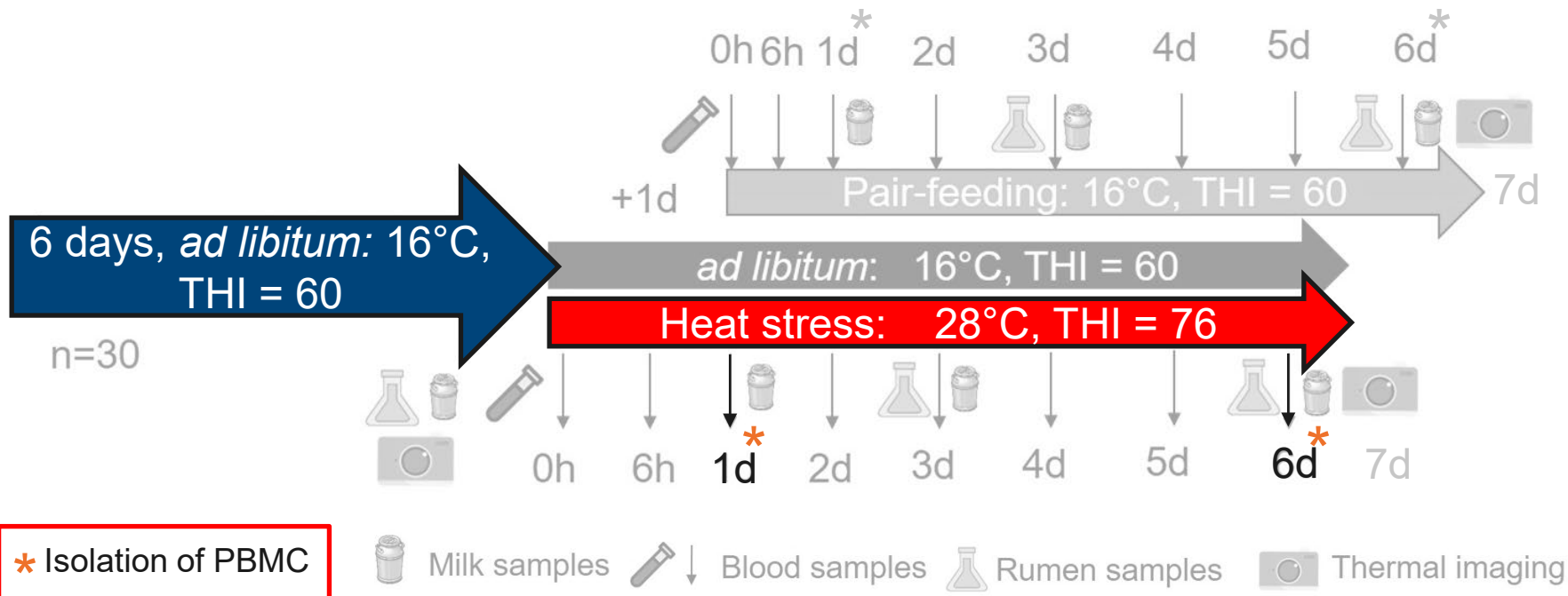
Thermal imaging

Experimental Design



30 Holstein dairy cows in 1st lactation (mean $\pm$ SEM: 169 $\pm$ 9 days in milk)

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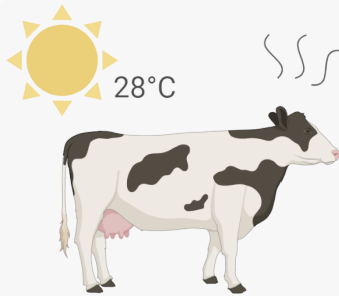


Experimental Design



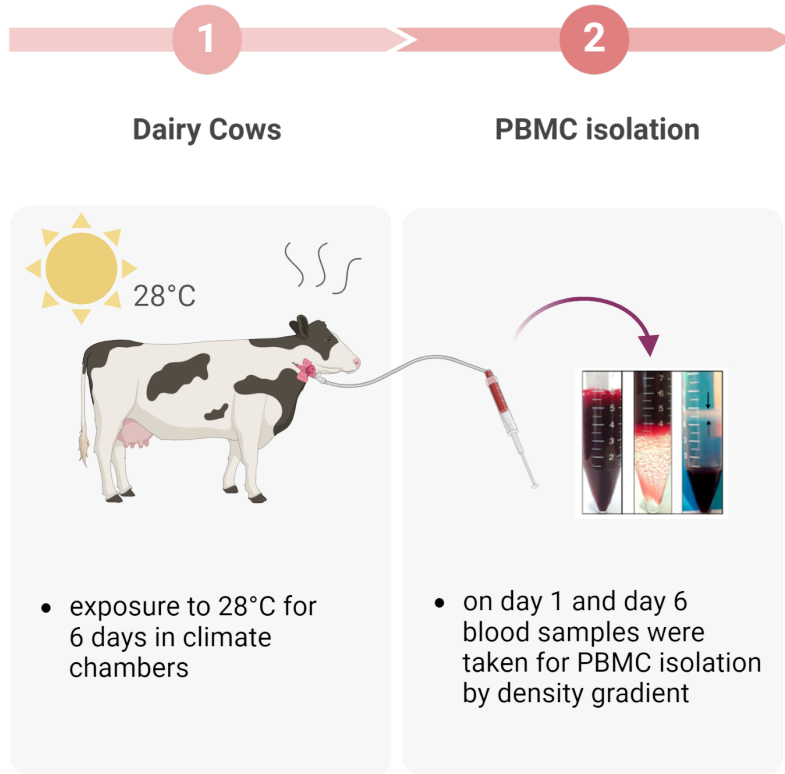
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Dairy Cows

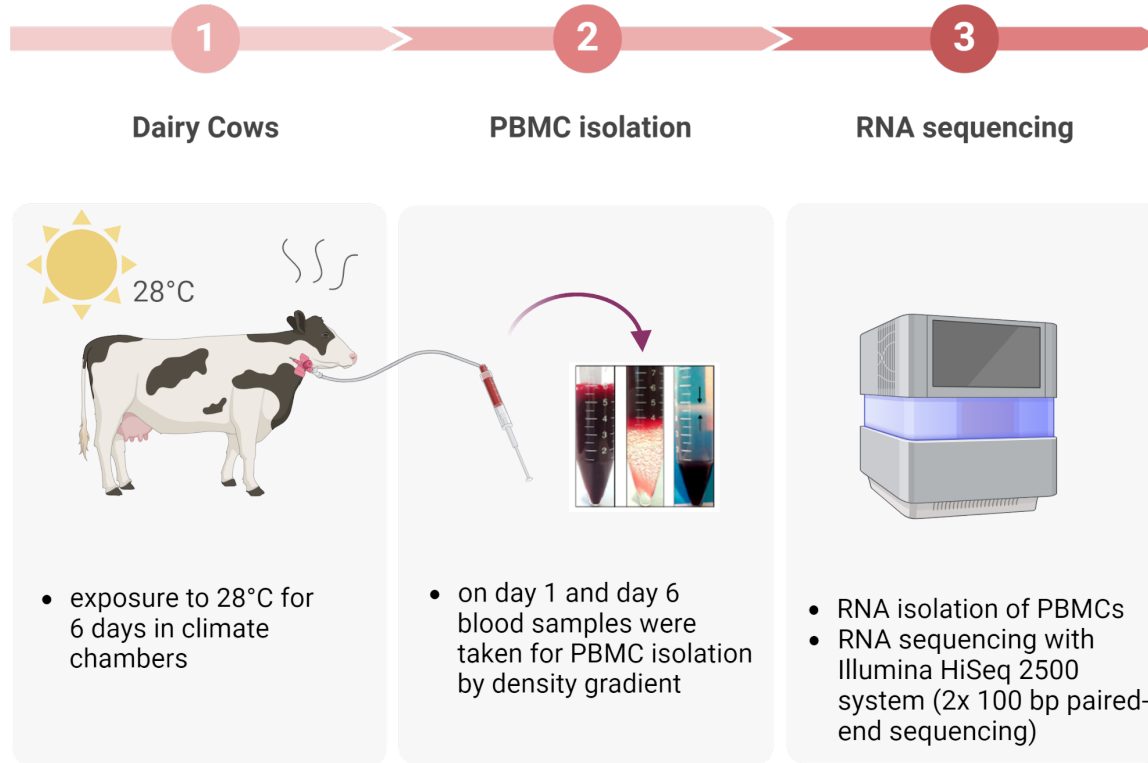


- exposure to 28°C for 6 days in climate chambers

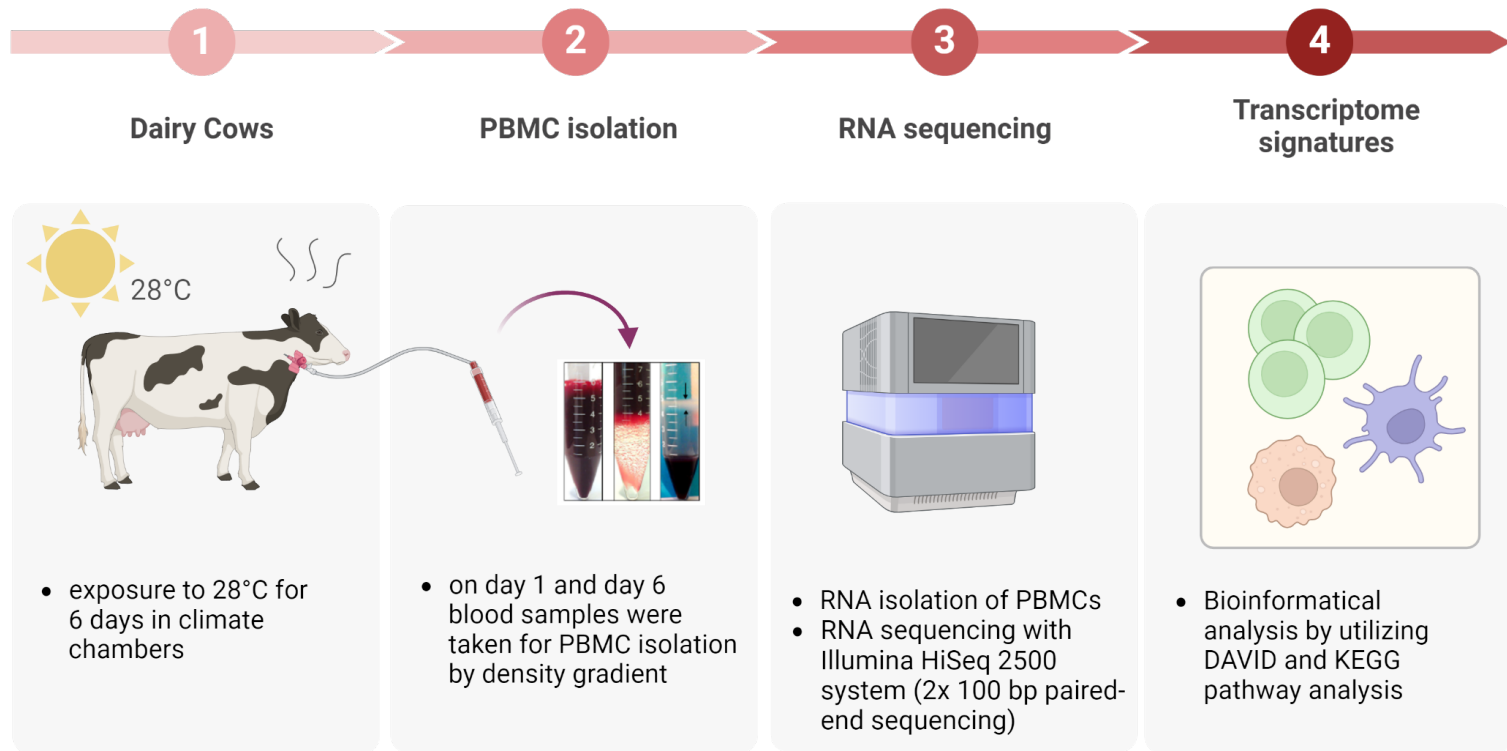
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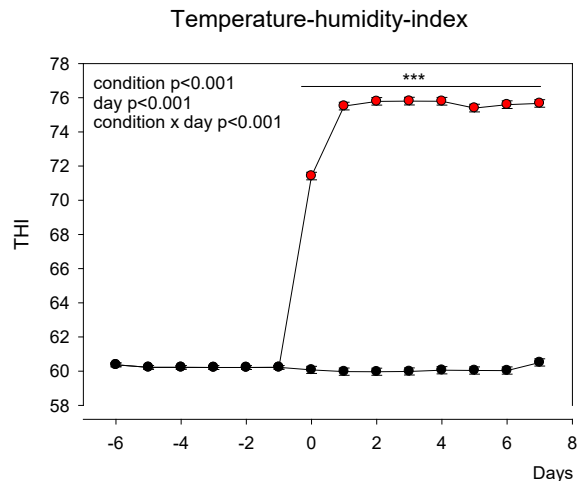
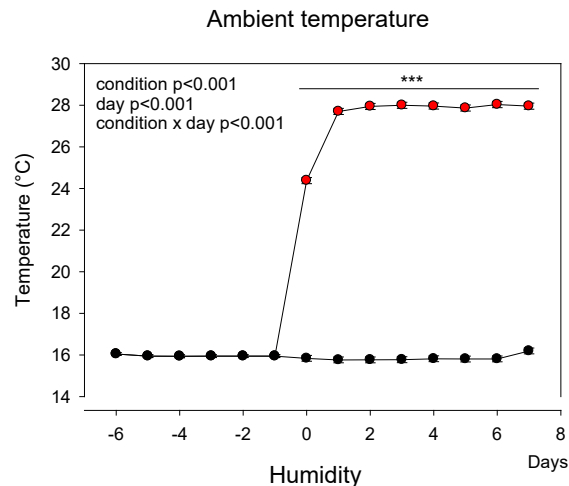
Experimental Design



Experimental Design

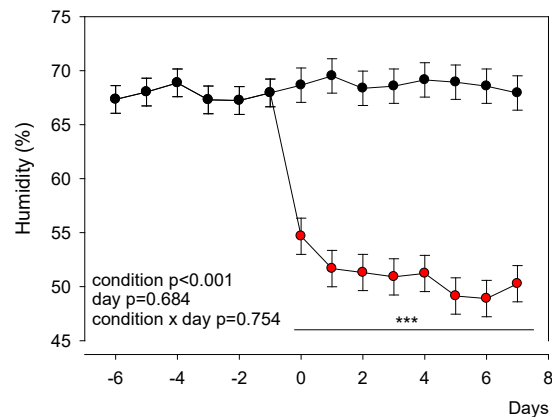


Climate chamber conditions



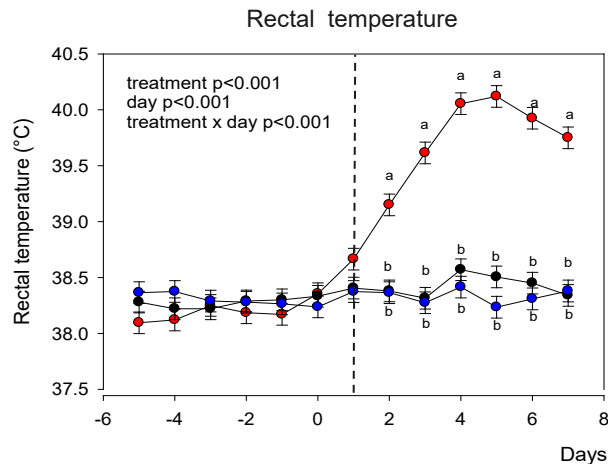
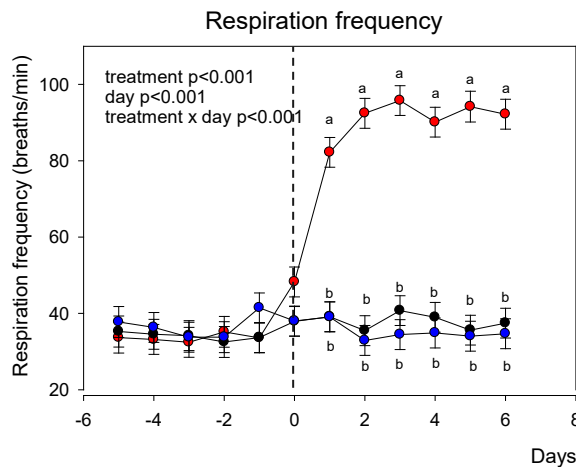
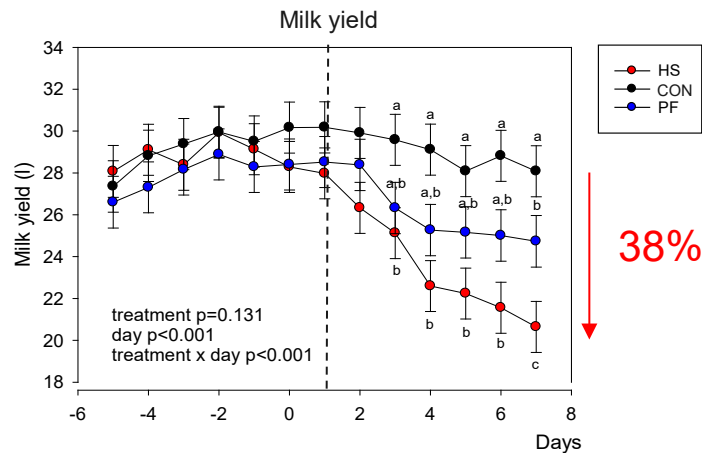
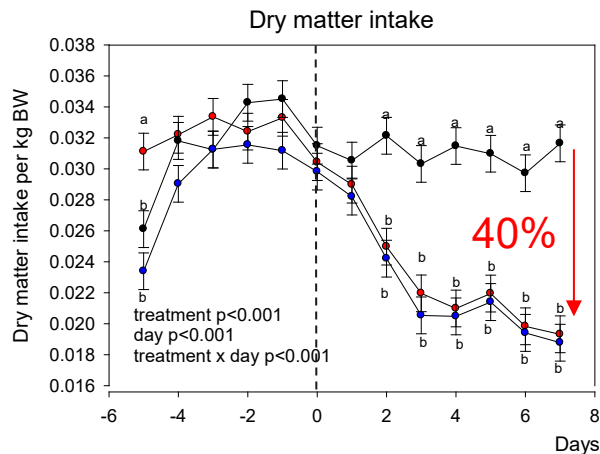
—●— heat stress
—●— thermoneutrality

*** $p < 0.001$



THI: 76 → moderate heat stress

Physiological conditions

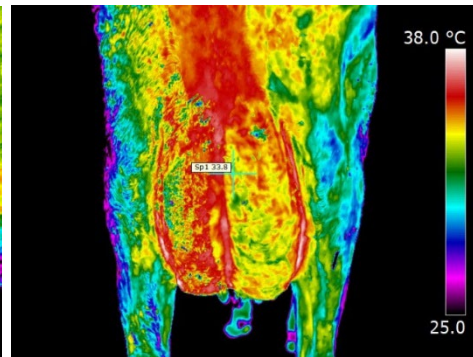
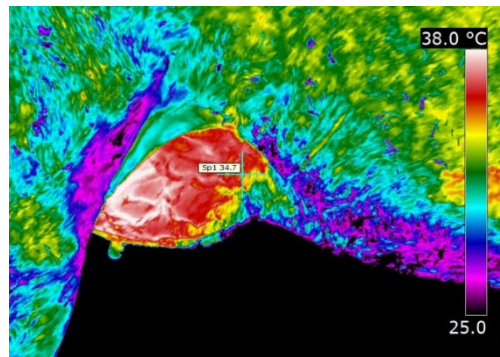
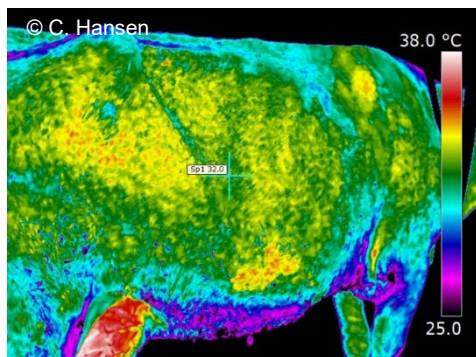


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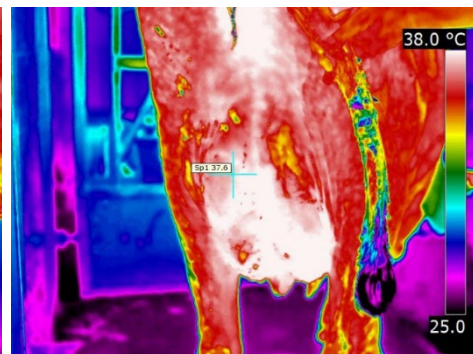
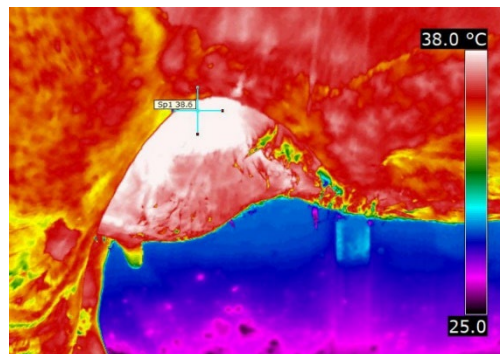
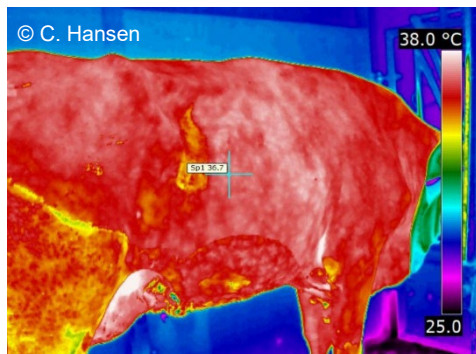
Physiological conditions



16°C



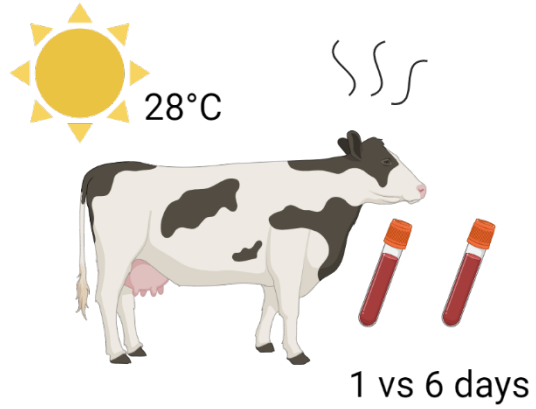
28°C



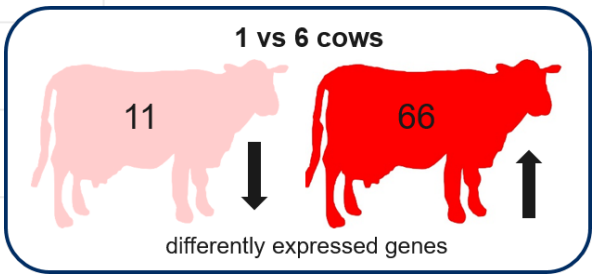
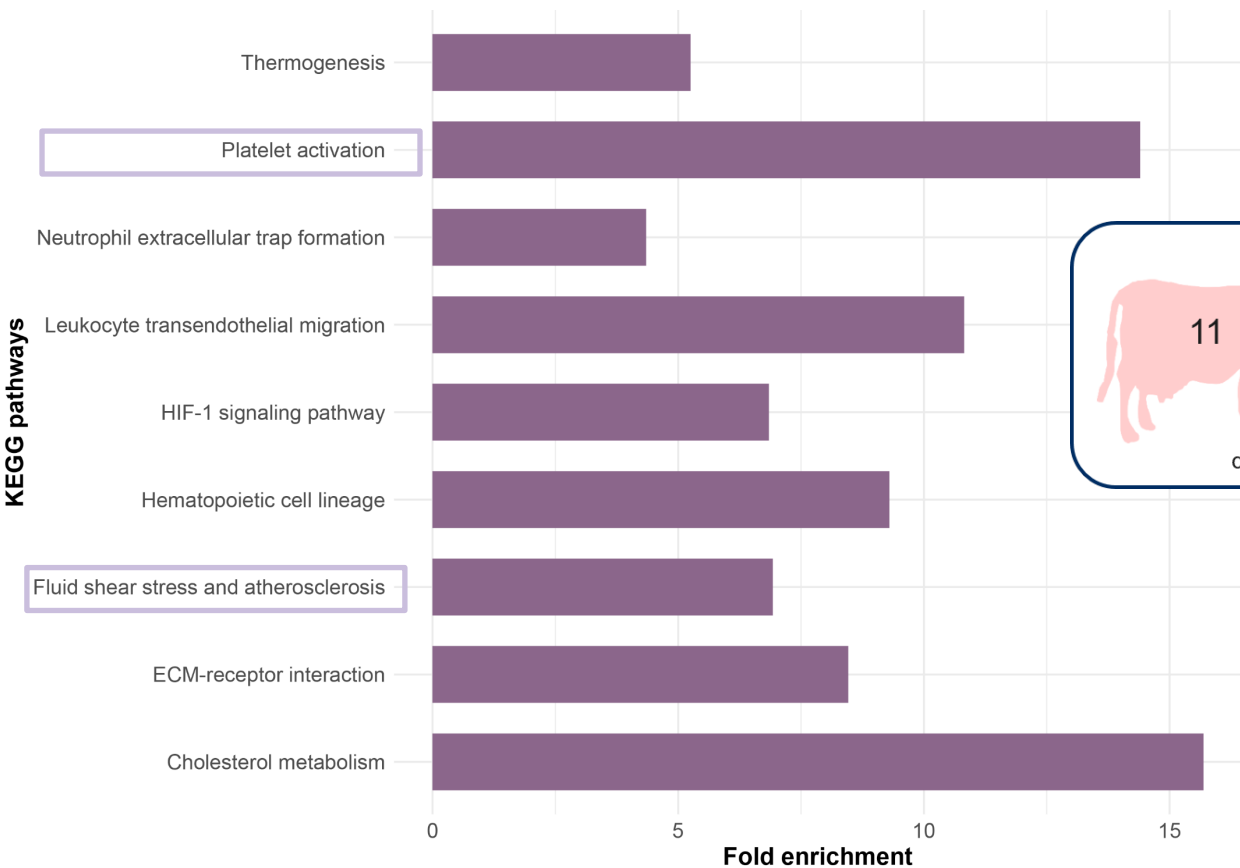
+4.3°C

+3.9°

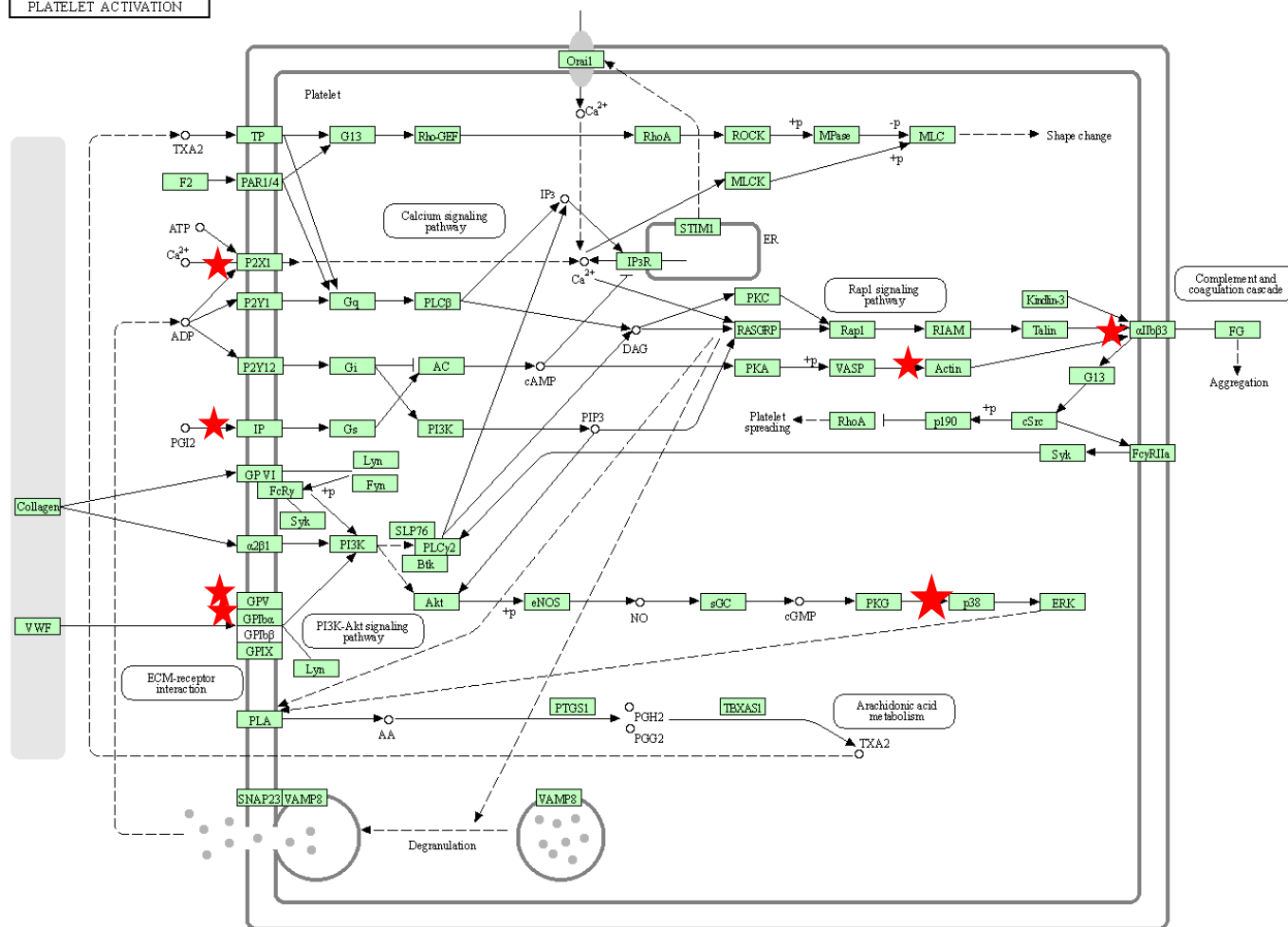
+3.0°C



Enrichment Analysis - DAVID



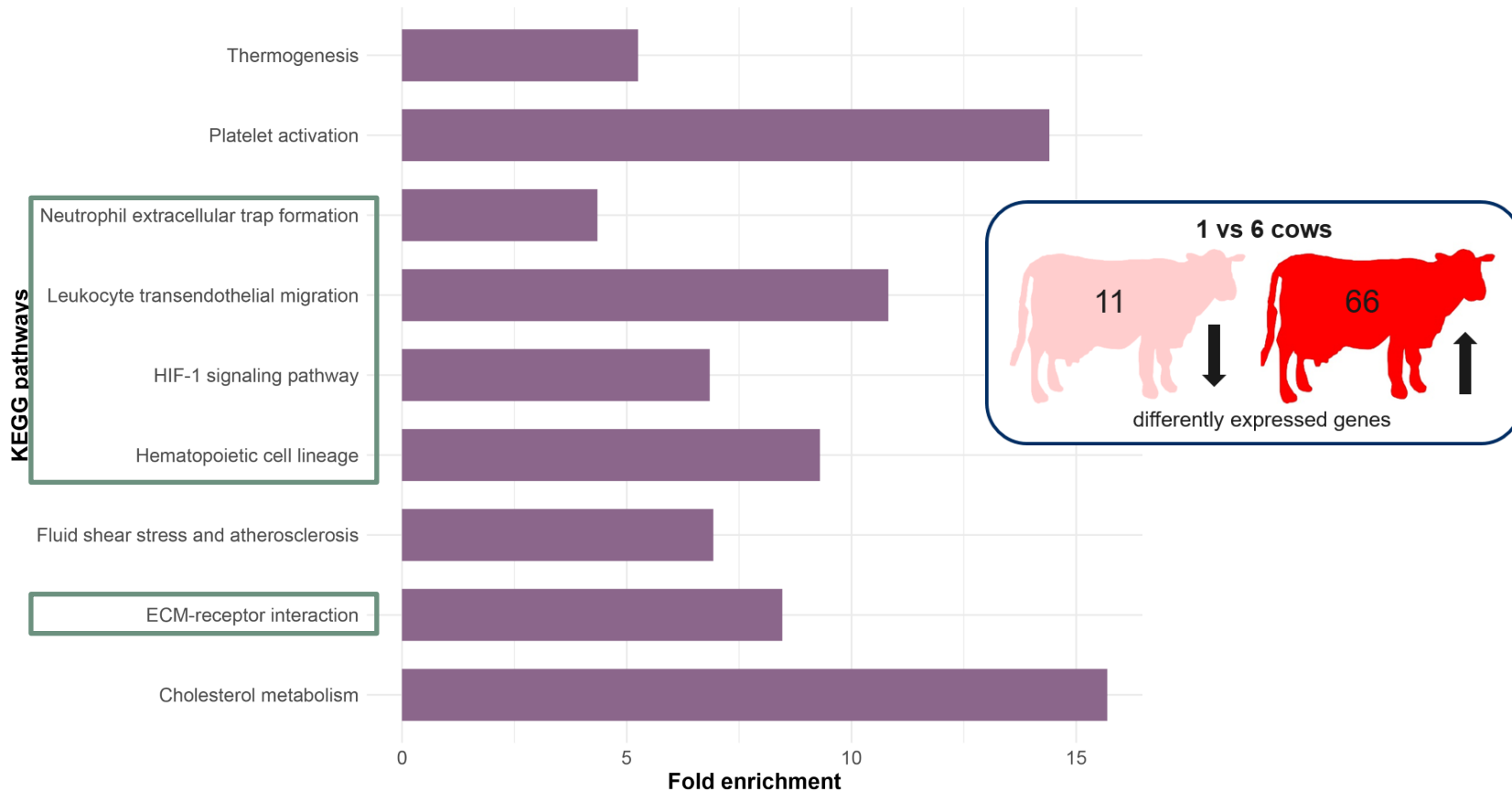
PLATELET ACTIVATION



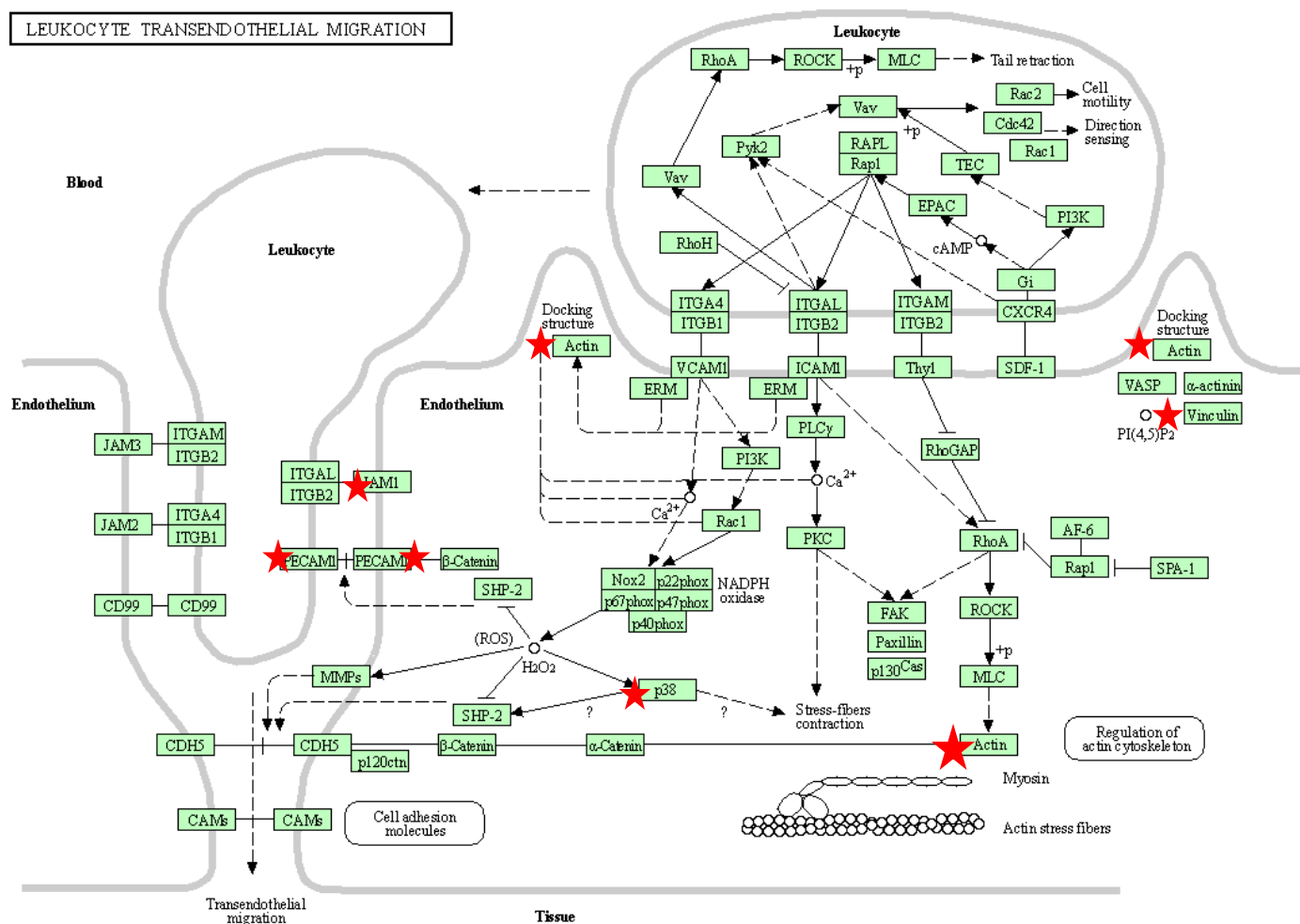
★ up-regulated in 6 days
HS cows

P2RX1 – purinergic receptor P2X 1
PTGIR – prostaglandin I2 receptor
ITGA2B – integrin subunit alpha 2b
GP1BA – glycoprotein Ib platelet
subunit alpha
GP5 – glycoprotein V platelet

Enrichment Analysis - DAVID



LEUKOCYTE TRANSENDOTHELIAL MIGRATION

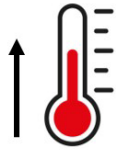


★ up-regulated in 6 days HS cows

F11R – F11 receptor
PECAM1 – platelet and endothelial cell adhesion molecule
VCL - vinculin



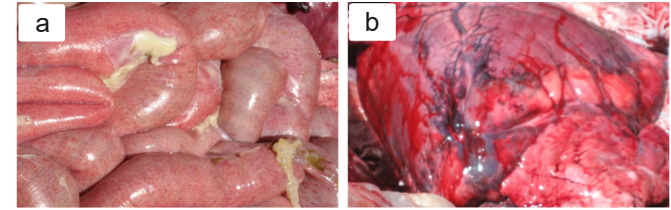
Progressing heat stress



Letal heat stress

Hyperthermia

- Hyperimmune response
- Inflammatory cytokine cascade
- Anti-inflammatory reciprocation
- Oxidative stress
- Anti-oxidative reciprocation



SIRS and DIC im (a) gut and (b) heart

- Coagulopathy
- Hypercoagulation
- Microthrombosis
- Vascular permeability

SIRS

(Systemic Inflammatory Response Syndrome)

DIC

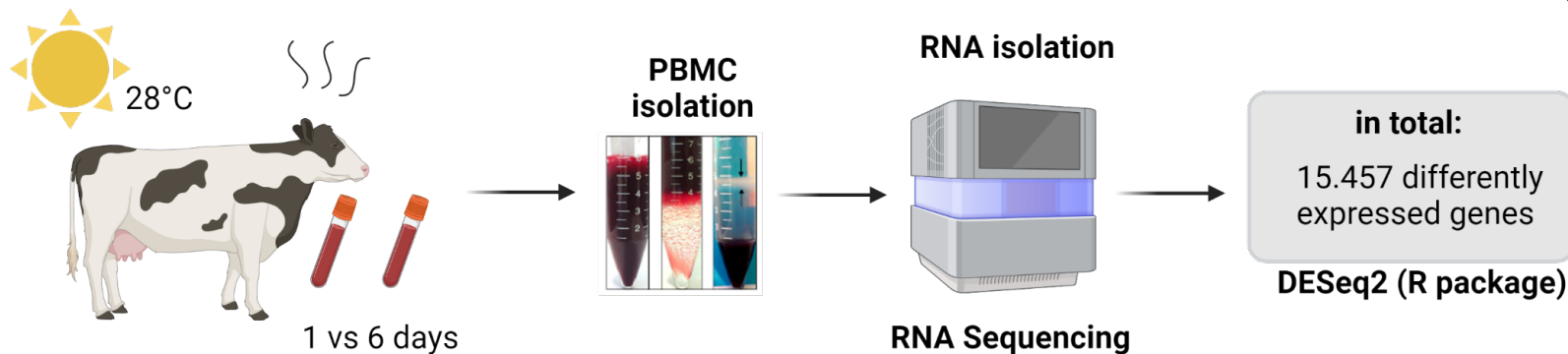
(Disseminated Intravascular Coagulation)

MODS

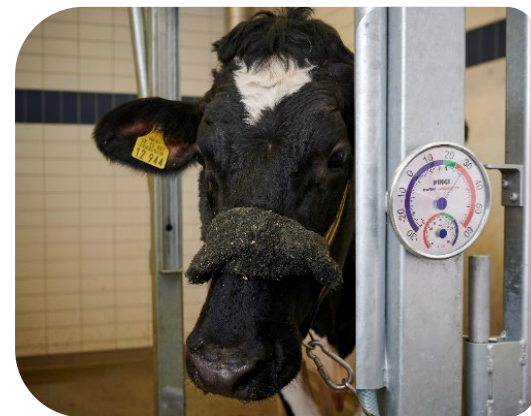
(Multiple Organ Dysfunction Syndrome)

Death

Summary



- ✓ 6 d of HS revealed an upregulation of pathways related to platelet activation, fluid shared stress and arteriosclerosis
→ HS-induced microvascular injuries or changes in hematocrit as a consequence of prolonged HS
- ✓ activation of leukocyte transendothelial migration, ECM-receptor interaction, neutrophil extracellular trap formation and HIF-signaling pathway
→ activation of the peripheral immune response and oxygen delivery to maintain homeostasis after heat



Acknowledgement



Technical support:

Dr. Andreas Vernunft
Hilke Brandt
Rico Fürstenberg
Sebastian Gaedecke
Simone Wöhl
Frieder Hadlich

Tiertechnikum:

Roland Gaeth
Tanja Lenke
Dirk Oswald
Kerstin Pilz
Astrid Schulz

Staff members of EAR:

Klaus-Dieter Witt
Hannes Rath

Experimental abattoir:

Dr. Ralf Pfuhl
Gido Nehring
Ilse Grünwald



DFG Deutsche
Forschungsgemeinschaft

DFG grant number: 441013809



8th EAAP International Symposium on Energy and Protein Metabolism and Nutrition (ISEP 2025)

15 – 18 September 2025

Rostock-Warnemünde, Germany



<https://isep2025-fbn.de/>

Abstract submission:

9 December 2024 – 1 March 2025



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Traditio et Innovatio

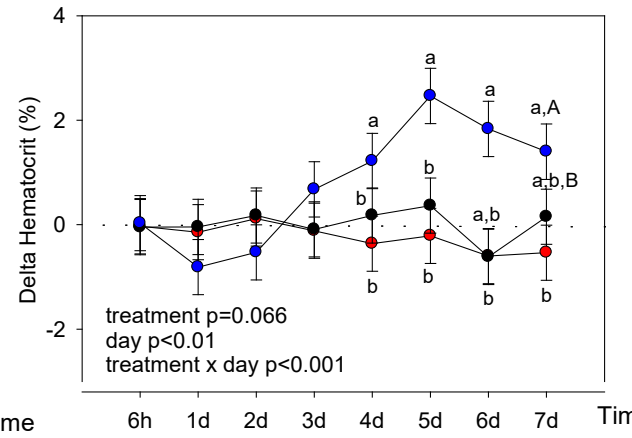
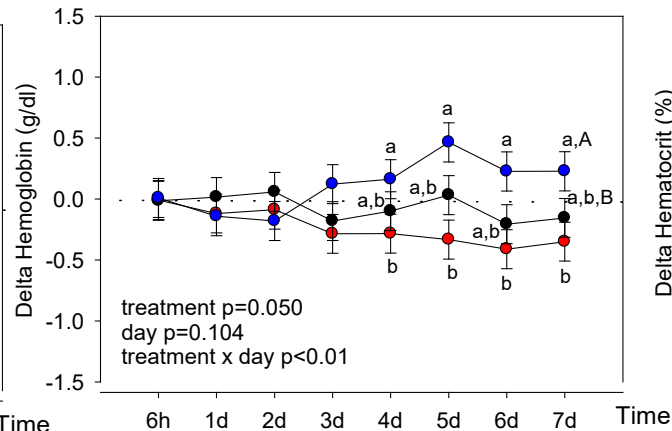
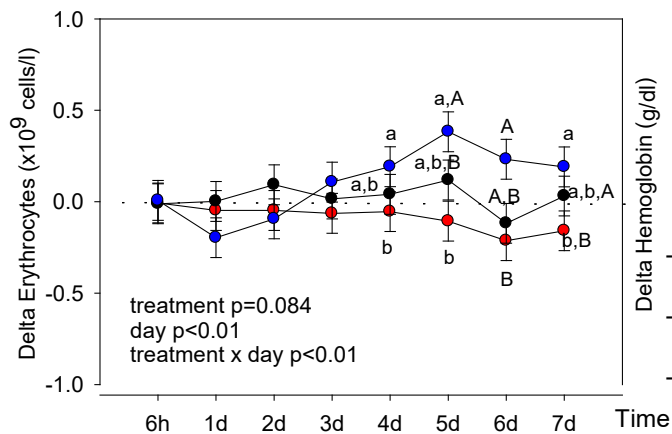
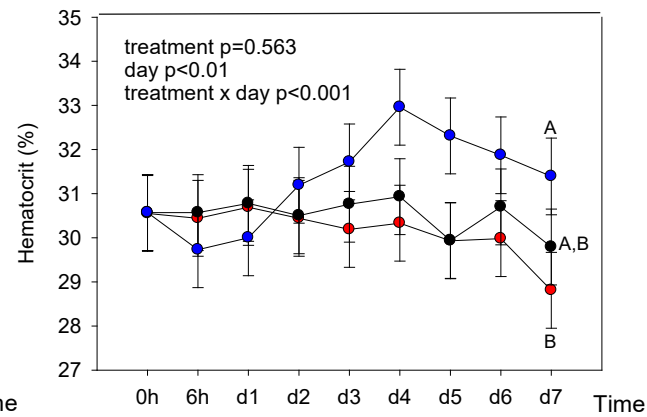
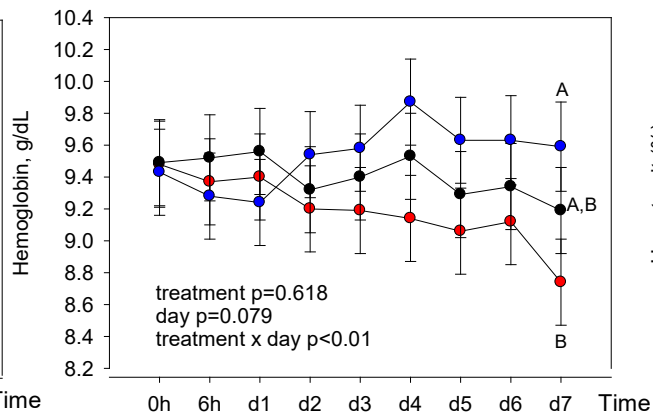
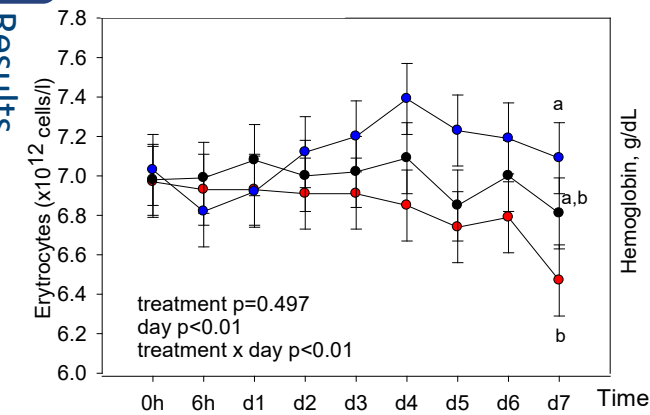


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Hematology



—●— HS —●— CON —●— PF

Enrichment Analysis - DAVID

NEUTROPHIL EXTRACELLULAR TRAP FORMATION

