

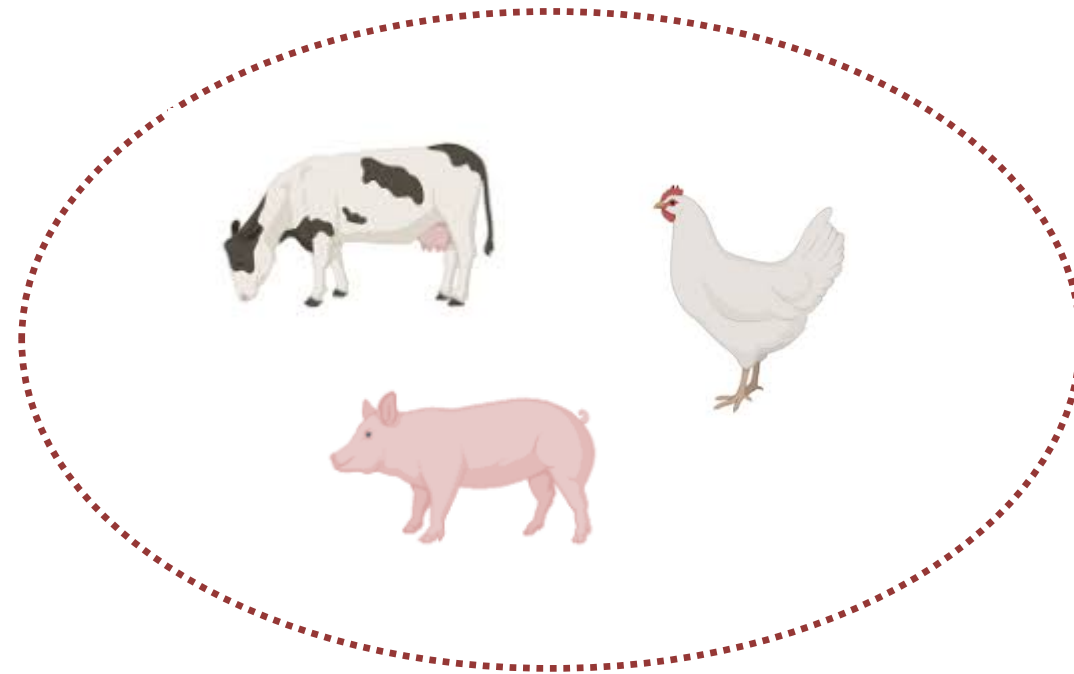
Genetik und Krankheitsresistenz

Claudia Klein
Institutsleitung
Institut für Nutztiergenetik (ING)



Relevanz „Genetik und Krankheitsresistenz“

Tierwohl



**Gesellschaftspolitische
Relevanz**

**Ökonomische
Aspekte**

**Reduktion
Antibiotikaeinsatz**

Mechanismen der Krankheitsresistenz

Polygene
Resistenz



Elimination
(Immunsystem)



Spezifische
Rezeptoren



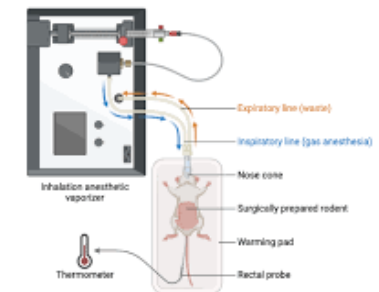
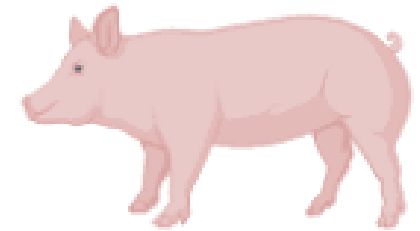
Enzyme des Wirts
welche zur Vermehrung
benötigt werden



Monogene Resistenzen

Maligne-Hyperthermie-Syndrom

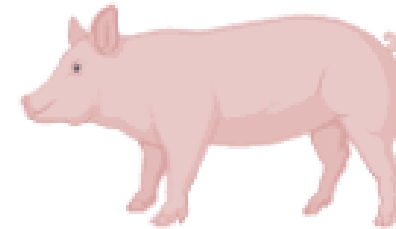
- Porcine Stresssyndrom (PSS)
- Selektion durch die Bestimmung der Halothanempfindlichkeit
- Punktmutation des Ryanodin-Rezeptor-Gen, RYR1
- C → T Substitution
- Arginin wird durch Cystein im Kalzium-Abgabe-Kanal ersetzt ist
- Cystein lässt einen größeren Fluss von Kalziumionen zu → PSS
- autosomal rezessiver Erbgang



Monogene Resistenzen

Ödemkrankheit/Diarröh

- E.Coli-Durchfall bei Absatzferkeln



E. coli ETEC F18

- FUT1 (Fucosyltransferase 1)
- FUT1 - 307^{A/A} → reduzierte Enzymaktivität (im Vergleich zu FUT1 – 307^{G/G})
- Reduzierte/keine Anheftung von ETEC F18

E. Coli ETEC F4

- TFRC (Transferrin Rezeptor)



Porzines reproduktives und respiratorisches Syndrom

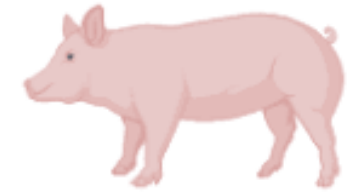
An investigation of susceptibility to porcine reproductive and respiratory syndrome virus between two genetically diverse commercial lines of pigs¹

A. L. Vincent,* B. J. Thacker,†² P. G. Halbur,† M. F. Rothschild,‡ and E. L. Thacker*³

*Department of Veterinary Microbiology and Preventive Medicine,

†Department of Veterinary Diagnostic and Production Animal Medicine, and

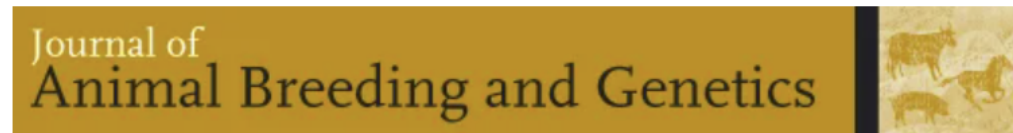
‡Department of Animal Science and the Center for Integrated Animal Genomics,
Iowa State University, Ames 50011



Original Article

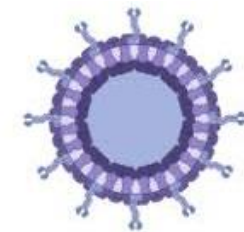
Validation and further characterization of a major quantitative trait locus associated with host response to experimental infection with porcine reproductive and respiratory syndrome virus

N. J. Boddicker, D. J. Garrick, R. R. Rowland, J. K. Lunney, J. M. Reecy, J. C. M. Dekkers ✉



Differences in susceptibility of Duroc, Hampshire, and Meishan pigs to infection with a high virulence strain (VR2385) of porcine reproductive and respiratory syndrome virus (PRRSV)

P. G. Halbur, M. F. Rothschild, B. J. Thacker, X.-J. Meng, P. S. Paul, J. D. Bruna



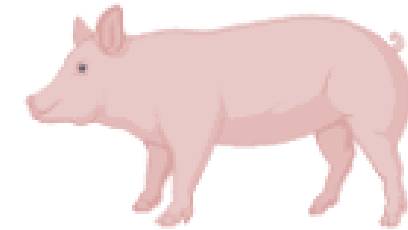
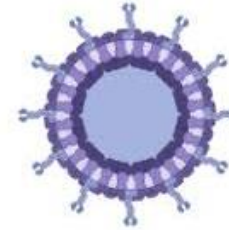
Afrikanische Schweinepest

Bisimwa et al. *Virology Journal* (2024) 21:93
<https://doi.org/10.1186/s12985-024-02351-9>

Virology Journal

RESEARCH

Open Access



Resistance to African swine fever virus among African domestic pigs appears to be associated with a distinct polymorphic signature in the *RelA* gene and upregulation of *RelA* transcription

Patrick N. Bisimwa^{1,2*}, Juliette R. Ongus^{3,4}, Ronald Ton

Grundlagenforschung zur Afrikanischen Schweinepest – warum erkranken Warzen- und Pinselohrschweine nicht?

05.02.2024 Kurznachrichten

Die Afrikanische Schweinepest (ASP) ist eine der komplexesten Viruserkrankungen der Haus- und Wildschweine, mit enormen sozioökonomischen und ökologischen Auswirkungen. Hausschweine, europäische Wildschweine und vom Aussterben bedrohte Schweinearten erkranken schwer und sterben zumeist an der Erkrankung. Die aus Afrika stammenden Warzen- und Pinselohrschweine als ursprüngliche Wirte der ASP dagegen erkranken bei einer Infektion nicht. Welche Faktoren hierfür bei verschiedenen empfänglichen Schweinearten entscheidend sind, untersucht ein EU-finanziertes Forschungsprojekt (ASF-RASH: "African Swine Fever pathogenesis and immune responses in Resistant And Susceptible Hosts").



Warzenschwein (© pexels)

Genetische Diversität und Krankheitsresistenz



Genetische Diversität und Immunkompetenz

➤ Kinetic of the juvenile immune system after hatching

Unpublished results



Ramelsloher



Bielefelder
Kennhuhn



Altsteirer



Sources: Slow Food Deutschland,
huennerhaltung.org



Dr. Ulrike Blohm, FLI-IFI
Prof. Dr. Steffen Weigend, FLI-ING

Genetische Diversität und Krankheitsresistenz

- Immune Competence after infection with **influenza virus**

Unpublished results



Ramelsloher



Bielefelder
Kennhuhn



Altsteirer



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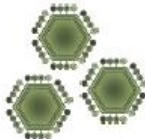
Genetik und Krankheitsresistenz

EuroFAANG Research Infrastructure

In 2023, EuroFAANG Research Infrastructure Project, was funded by the EU as a natural outgrowth of the EuroFAANG **collaborative effort** that had seen **6 European projects** come together since 2020 to **bridge the gap between genomics and phenomics at the European level**.



Genetische Diversität und Krankheitsresistenz

		
 <p>Highly virulent 'Armenia2008'</p>	<p>DP αβ T cells ↑ Perforin expression ↓↓ T-bet⁺ CD4⁺ Th cells ↑ Tregs ↑</p>	<p>Effector γδ T cells ↑ Perforin expression ↓ T-bet⁺ CD8α⁺ αβ T cells ↑ Tregs ↑</p>
 <p>Moderately virulent 'Estonia2014'</p>	<p>CD8α⁺ and DP αβ T cells ↑ Perforin expression ↓↓ T-bet⁺ CD4⁺ Th cells ↑ Tregs ↑</p>	<p>CD8α⁺ and DP αβ T cells ↑ Effector γδ T cells ↑ Perforin expression ↓ T-bet⁺ CD8α⁺ αβ and γδ T cells ↑ Tregs ↑↑</p>

ORIGINAL ARTICLE |  WILEY

T-cell responses in domestic pigs and wild boar upon infection with the moderately virulent African swine fever virus strain 'Estonia2014'

Alexander Schäfer¹ | Laura Zani¹ | Jutta Pikalo¹ | Jane Hühr¹ | Julia Sehl¹ | Thomas C. Mettenleiter¹ | Angele Breithaupt¹ | Sandra Blome¹ | Ulrike Blohm¹

ORIGINAL ARTICLE |  WILEY

Impaired T-cell responses in domestic pigs and wild boar upon infection with a highly virulent African swine fever virus strain

Jane Hühr¹ | Alexander Schäfer¹ | Theresa Schwalger² | Laura Zani¹ | Julia Sehl¹ | Thomas C. Mettenleiter¹ | Sandra Blome¹ | Ulrike Blohm¹

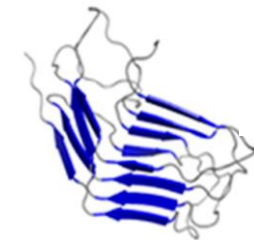
 pathogens | 

Article
 Comparative Pathology of Domestic Pigs and Wild Boar Infected with the Moderately Virulent African Swine Fever Virus Strain "Estonia 2014"

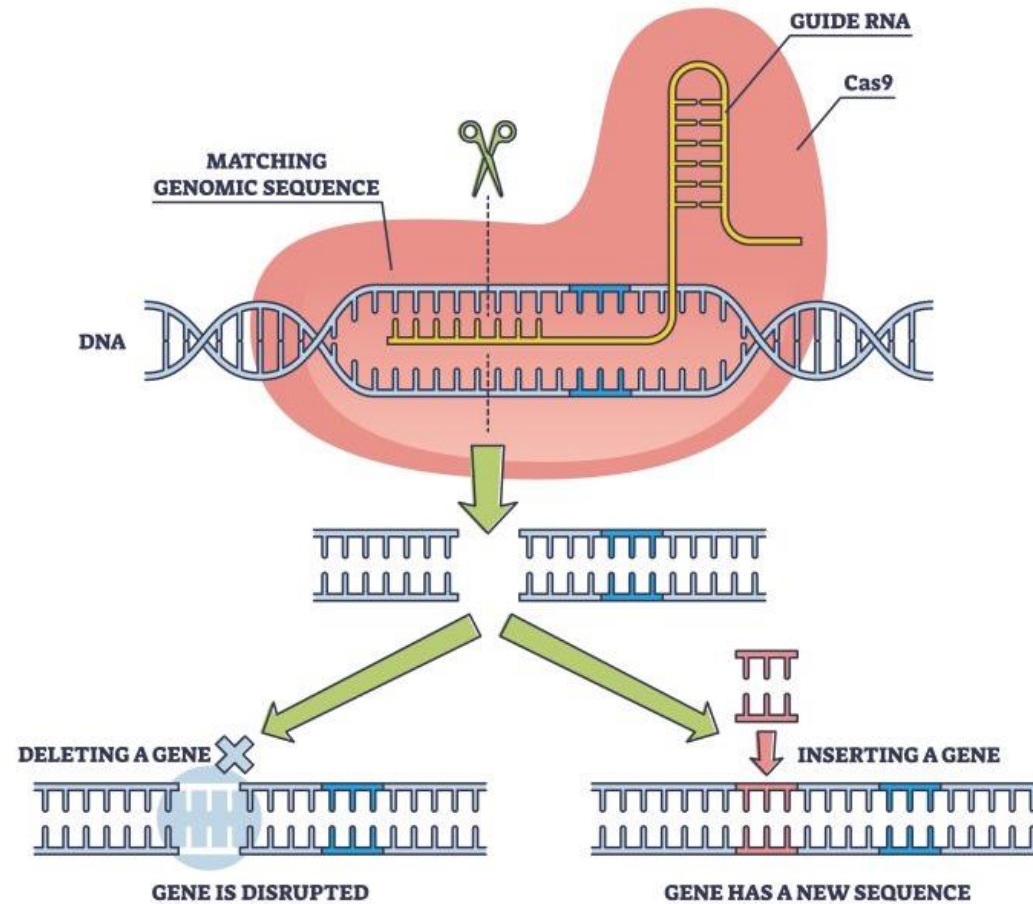
Julia Sehl¹, Jutta Pikalo¹, Alexander Schäfer¹, Kati Franzke, Katrin Panahorst, Ahmed Elnagar, Ulrike Blohm¹, Sandra Blome¹ and Angele Breithaupt

Scrapie Empfänglichkeit Schaf

Genotypklasse	Eiweißform	Erkrankungsrisiko
G1	ARR/ARR	extrem niedrig („resistent“)
G2	ARR/AHQ	geringes Risiko, wenn Anpaarung mit G1 oder G2
	ARR/ARH	
	ARR/ARQ	
G3	AHQ/AHQ	erhöhtes Risiko, für das Einzeltier, häufigster betroffener Genotyp in Deutschland ist ARQ
	AHQ/ARH	
	AHQ/ARQ	
	ARH/ARH	
	ARH/ARQ	
	ARQ/ARQ	
G4	ARR/VRQ	Hohes Risiko für das Einzeltier und die Hälfte der Nachkommen
G5	AHQ/VRQ	sehr hohes Risiko
	ARH/VRQ	
	ARQ/VRQ	
	VRQ/VRQ	



CRISPR-Cas 9 und Krankheitsempfänglichkeit



<https://labassociates.com/crispr-a-gene-editing-tool>

PRRSV resistente Schweine

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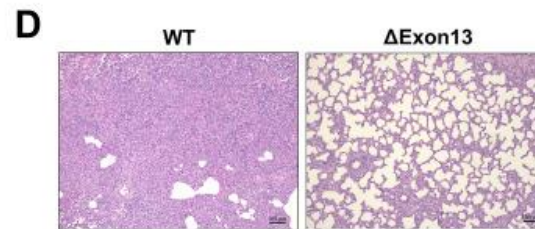
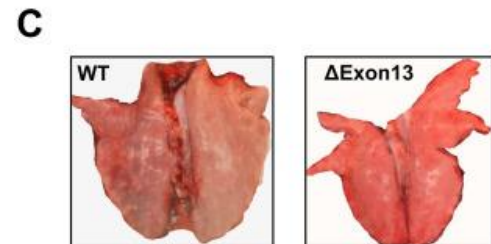
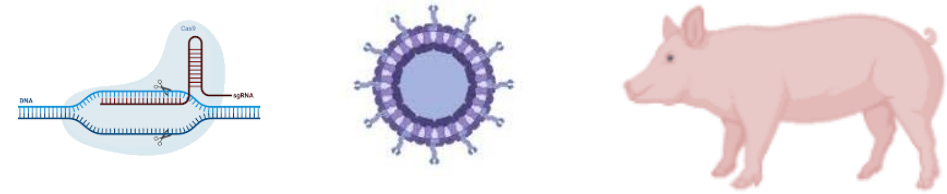
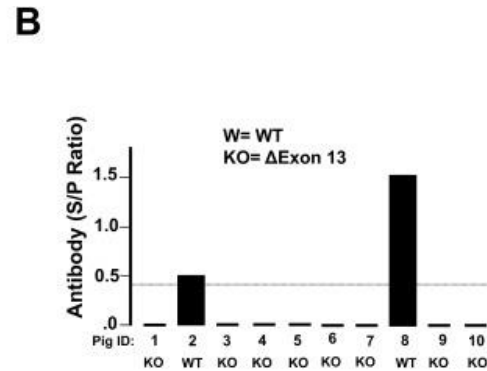
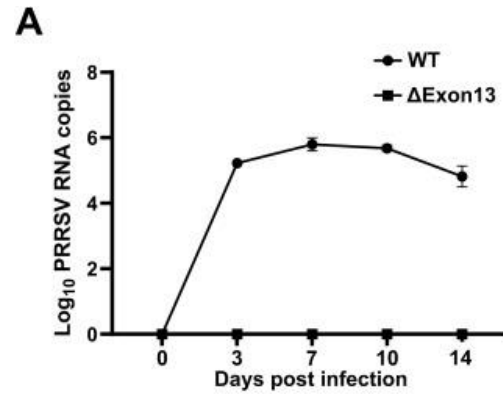
What is the PRRS-Resistant Pig?

Using gene editing technology, PIC developed pigs resistant to the PRRS virus by deleting a portion of a specific protein the virus needs to cause infection.

This genetic innovation prevents pigs from PRRS infection, improves herd health, reduces worker demands, and enhances farm sustainability



PRRSV resistente Schweine



Antiviral Research 221 (2024) 105793

Contents lists available at ScienceDirect

Antiviral Research

journal homepage: www.elsevier.com/locate/antiviral



Genetically modified pigs lacking CD163 PSTII-domain-coding exon 13 are completely resistant to PRRSV infection

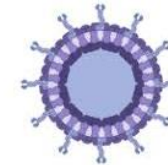
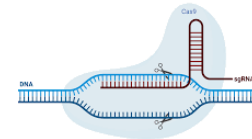
Brianna Salgado^{a,1}, Rafael Bautista Rivas^{a,1}, Derek Pinto^a, Tad S. Sonstegard^b, Daniel F. Carlson^b, Kyra Martins^b, Jonathan R. Bostrom^b, Yamlak Sinebo^b, Raymond R. Rowland^a, Alberto Brandariz-Nuñez^{a,*}

^a Department of Pathobiology, College of Veterinary Medicine, University of Illinois at Urbana-Champaign, Champaign, IL, USA

^b Acceligen, Eagan, Minnesota, USA

CRISPR-Cas9 aviäre Influenza

Chickens genetically resistant to avian influenza could prevent future outbreaks. In chickens, influenza A virus (IAV) relies on host protein ANP32A. Here we use CRISPR/Cas9 to generate homozygous gene edited (GE) chickens containing two ANP32A amino acid substitutions that prevent viral polymerase interaction. After IAV challenge, 9/10 edited chickens remain uninfected. Challenge with a higher dose, however, led to breakthrough infections. Breakthrough IAV virus contained IAV polymerase gene mutations that conferred adaptation to the edited chicken ANP32A. Unexpectedly, this virus also replicated in chicken embryos edited to remove the entire ANP32A gene and instead co-opted alternative ANP32 protein family members, chicken ANP32B and ANP32E. Additional genome editing for removal of ANP32B and ANP32E eliminated all viral growth in chicken cells. Our data illustrate a first proof of concept step to generate IAV-resistant chickens and show that multiple genetic modifications will be required to curtail viral escape.



nature communications



Article

<https://doi.org/10.1038/s41467-023-41476-3>

Creating resistance to avian influenza infection through genome editing of the ANP32 gene family

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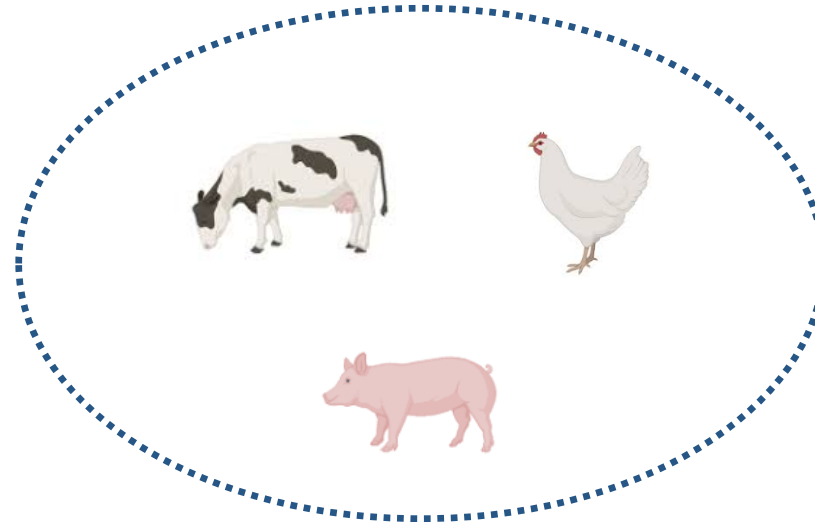
Published online: 10 October 2023

Check for updates

Alewo Idoko-Akoh¹ , Daniel H. Goldhill^{2,3}, Carol M. Sheppard², Dagmara Bialy⁴, Jessica L. Quantrill², Ksenia Sukhova², Jonathan C. Brown², Samuel Richardson⁴, Ciara Campbell², Lorna Taylor¹, Adrian Sherman¹, Salik Nazki⁴, Jason S. Long^{2,5}, Michael A. Skinner², Holly Shelton⁴, Helen M. Sang¹ , Wendy S. Barclay^{2,6} & Mike J. McGrew^{1,6}

Tierwohl

**Ökonomische
Aspekte**



**Gesellschaftspolitische
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