

Nutrition and antimicrobial resistance issues with zinc oxide in pigs

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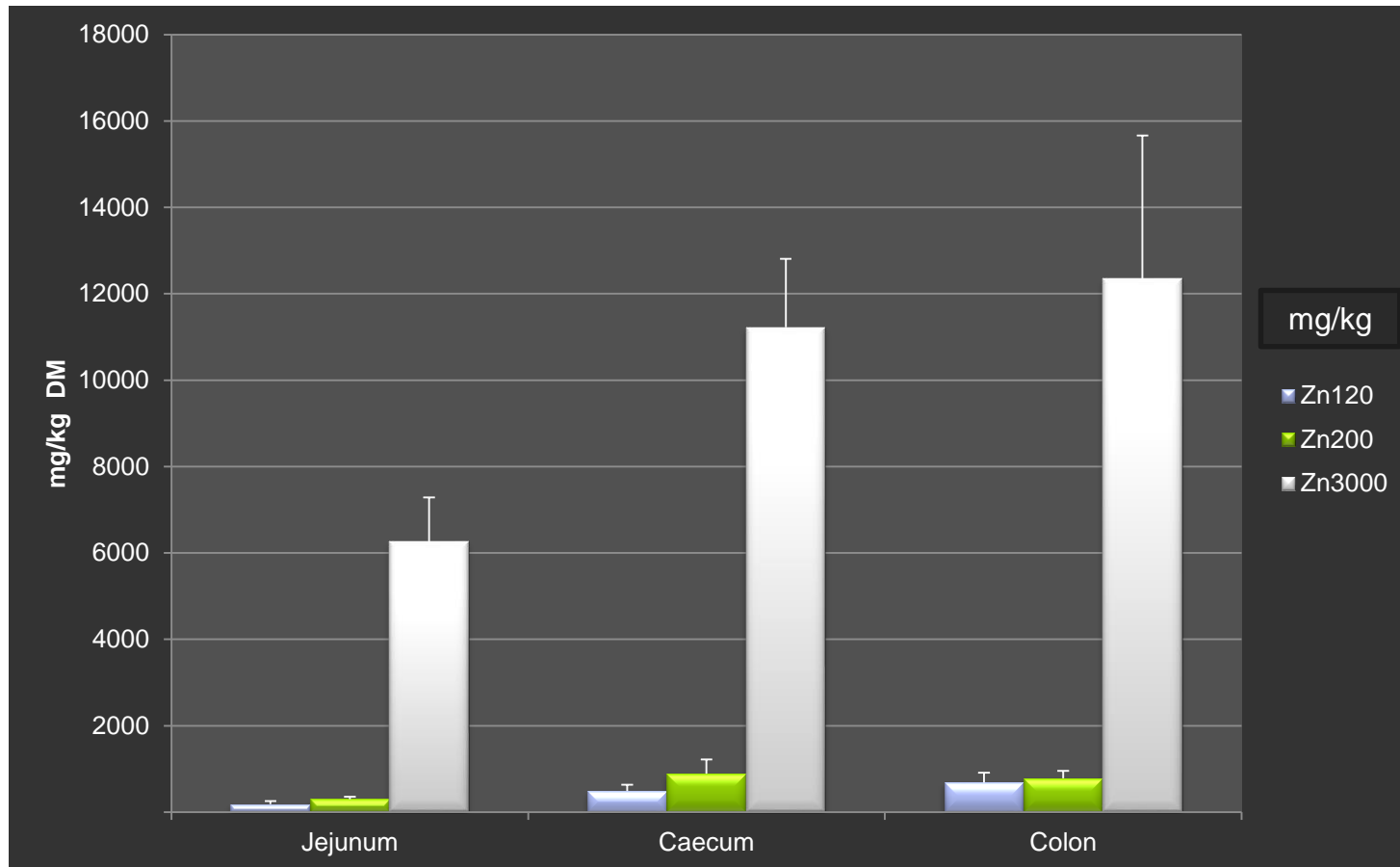
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Zinc

- Essential (Piglets: ~ 80 mg/kg feed)
 - Second most abundant trace element after iron
- > 300 physiological processes
 - Structural, catalytic, regulatory, activating function
 - e.g. Insulin, carbonic anhydrase, alkaline phosphatase
 - Zinc finger proteins (transcription factors)
- Homeostatic regulation of uptake and release

Zinc concentrations

- Zinc concentrations (total) in the GI tract of piglets

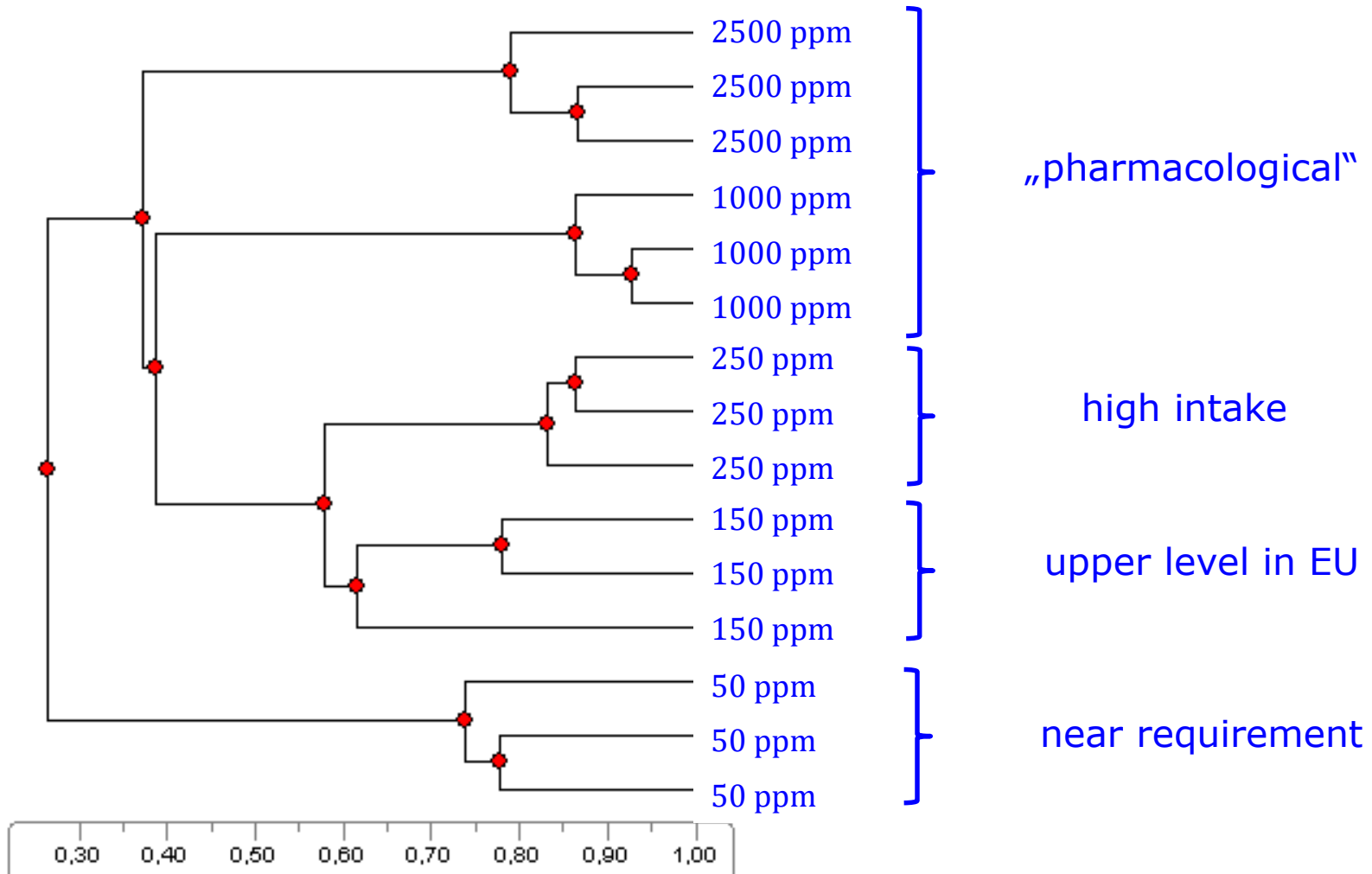


Zinc oxide and microbiota

- Microbiota – findings from different studies
 - Impact on Gram positive microbes
 - Lactobacilli, Lactic acid bacteria ↓
 - Yeasts ↓
 - Gram negative bacteria are less sensitive
 - Stability of the *E. coli*-populations ↑
 - Bacterial translocation in lymph nodes ↓

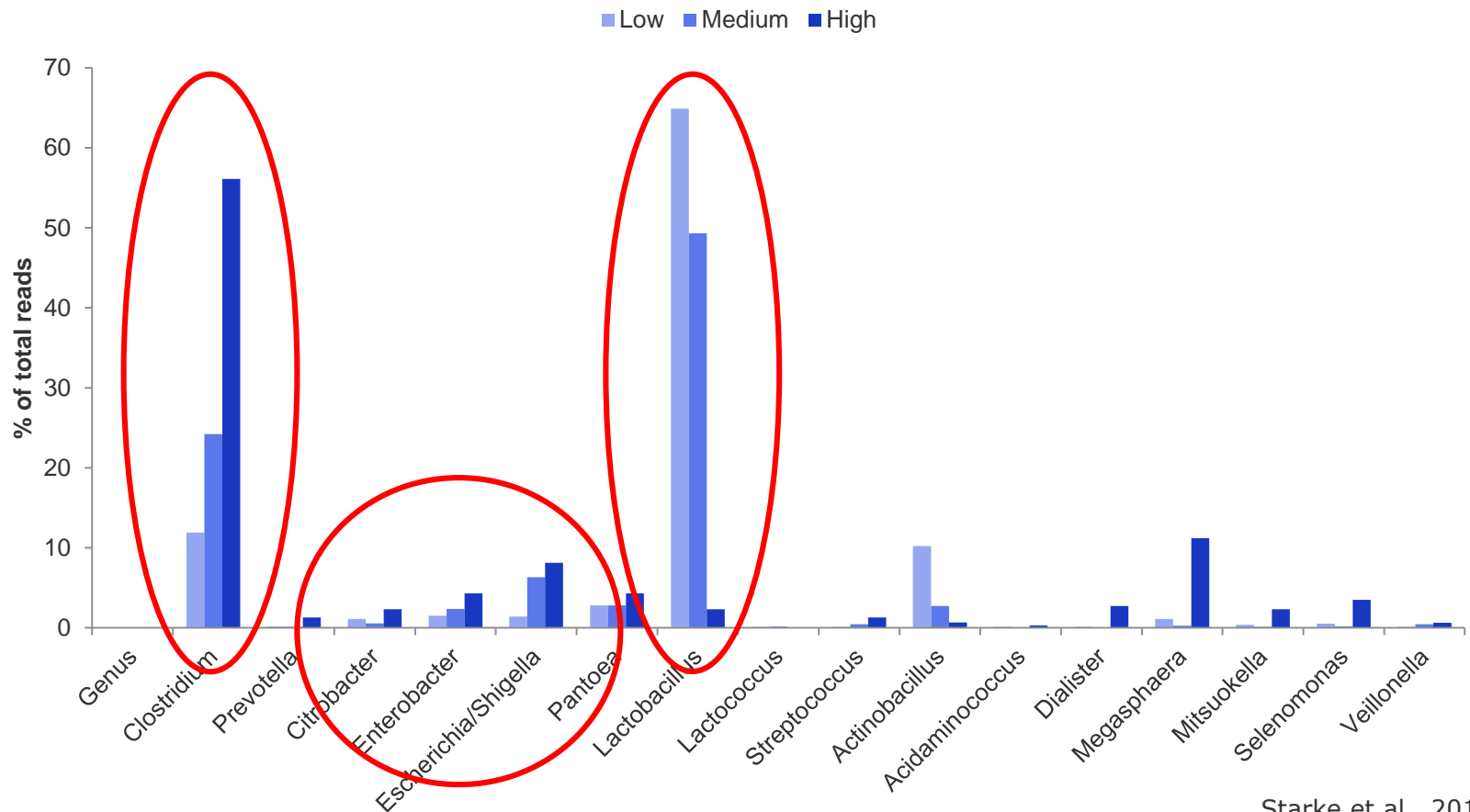
Zinc and intestinal microbiota

Cluster-Analysis from DGGE profiles in ileal digesta



Zinc and intestinal microbiota

- Core microbiota in the small intestine of piglets fed diets with different dietary ZnO concentrations



Starke et al., 2013

Zinc: Reports from Denmark

Tarmfloraen, zinkoxid og colidiarré hos svin

Af mikrobiolog Bent Borg Jensen, Statens Husdyrbrugsforsøg, Forsøgsanlæg Foulum

Bakterietype	Antal kolonier/g tørstof	
	Kontroldiæt (130 ppm zink)	Zinkoxid beriget diæt (1500 ppm zink)
Anaerobe bakterier	12.600 mio.	3.600 mio.
Lactobaciller	8.300 mio.	4.300 mio.
Aerobe bakterier	224 mio.	891 mio.
Gær	22 mio.	56 mio.
Colibakterier	11 mio.	18 mio.
Fækale streptokokker	310.000	490.000

bakterier. Hvis der da er en sammenhæng mellem brugen af zinkoxid og zinkresistens hos bakterier? Hvis dette er tilfældet, er der så en sammenhæng mellem zinkresistens og antibiotikaresistens? Endelig ville det også være rart at få afklaret, hvorledes tilsætning

Zinc oxide and microbiota

- Microbial diversity – antibiotic resistance

- *E. coli* genetic diversity ↑

- Multi-resistant *E. coli* ↑

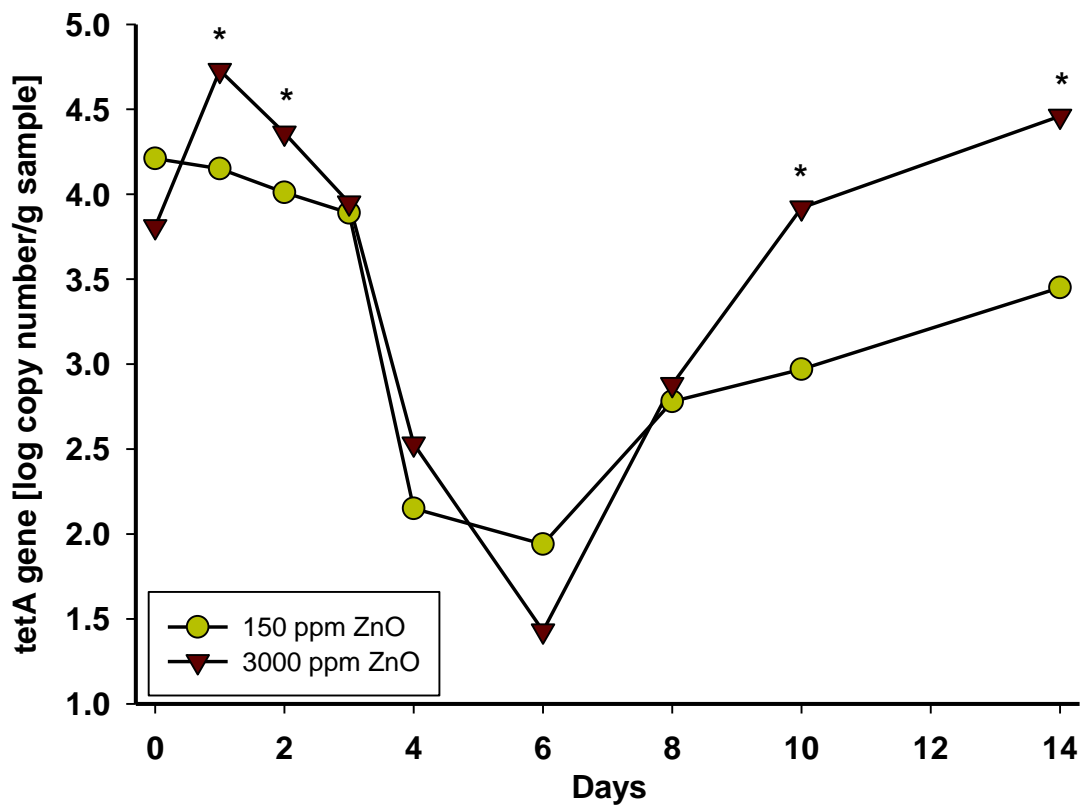
- compared to the control group: 18.6% vs. 0%

Bednorz et al. 2013

- Zinc resistance of *Staphylococcus aureus* strongly associated with methicillin resistance

Cavaco et al. 2011

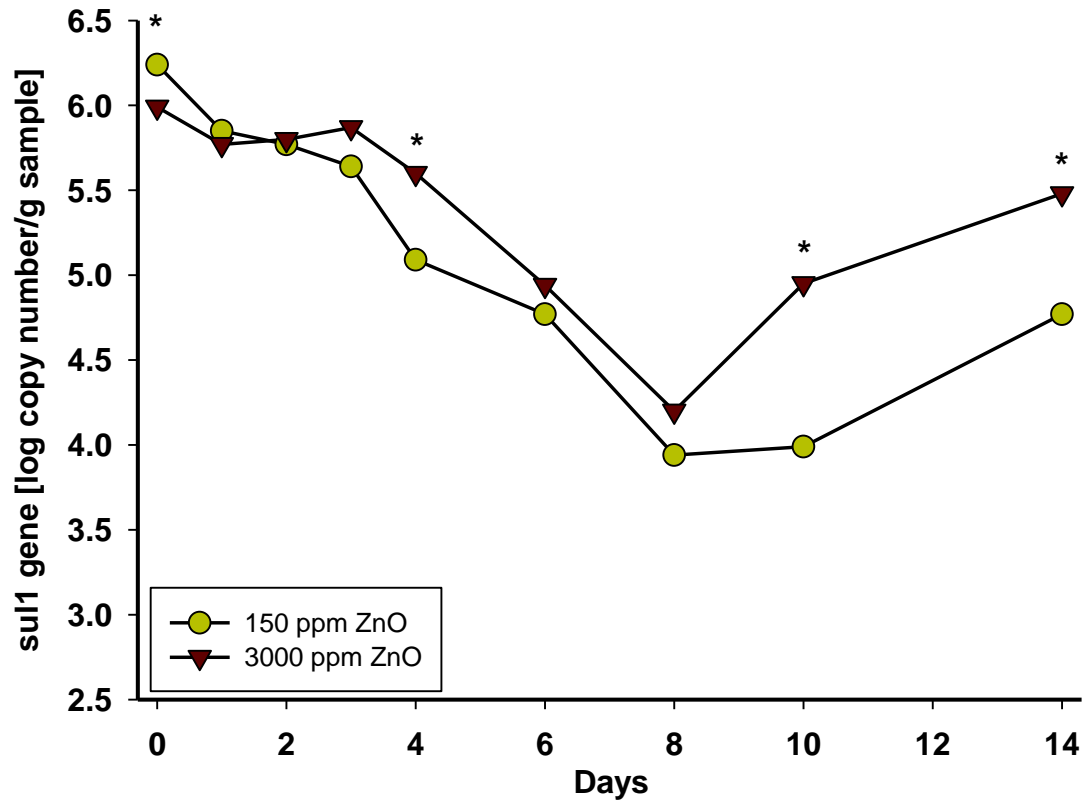
Development of the tetracycline resistance gene tetA in weaned piglets fed feed grade ZnO



* significantly different (Mann-Whitney test, $p < 0.05$)

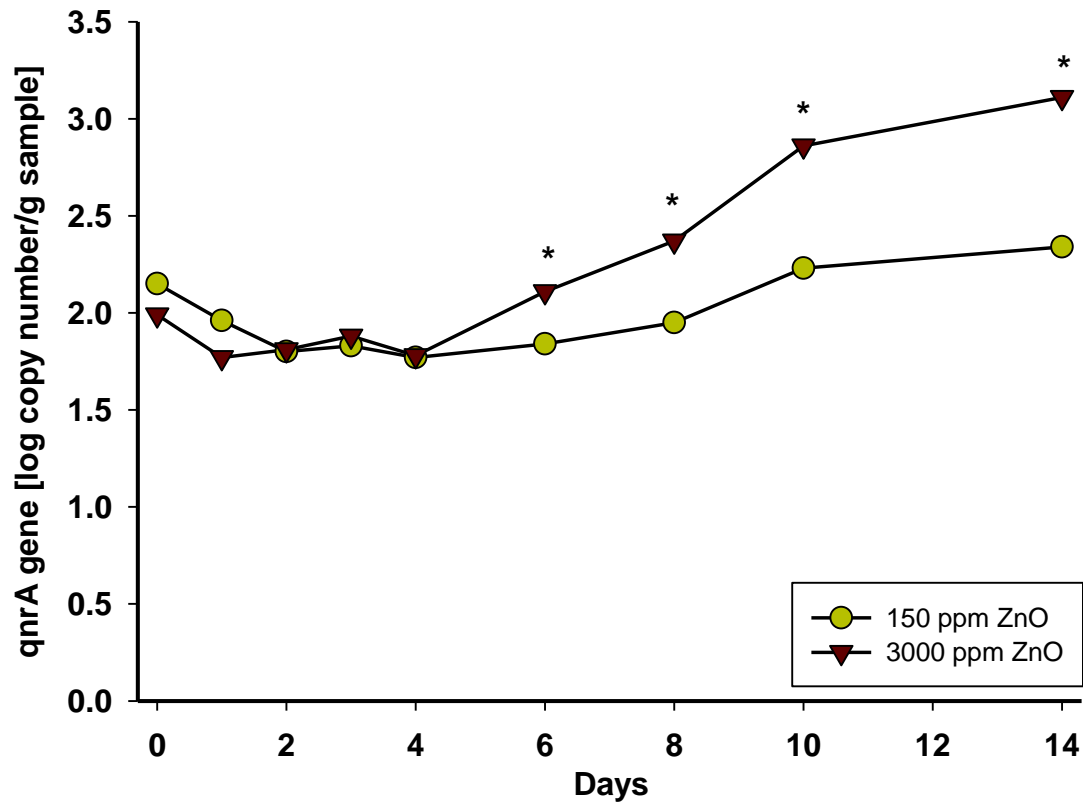
Vahjen et al. 2015

Development of the sulfonamide resistance gene *sul1* in weaned piglets fed feed grade ZnO



* significantly different (Mann-Whitney test, $p < 0.05$)

Development of the quinolone resistance gene qnrA in weaned piglets fed feed grade ZnO



* significantly different (Mann-Whitney test, $p < 0.05$)

Vahjen et al. 2015

Animal experiment

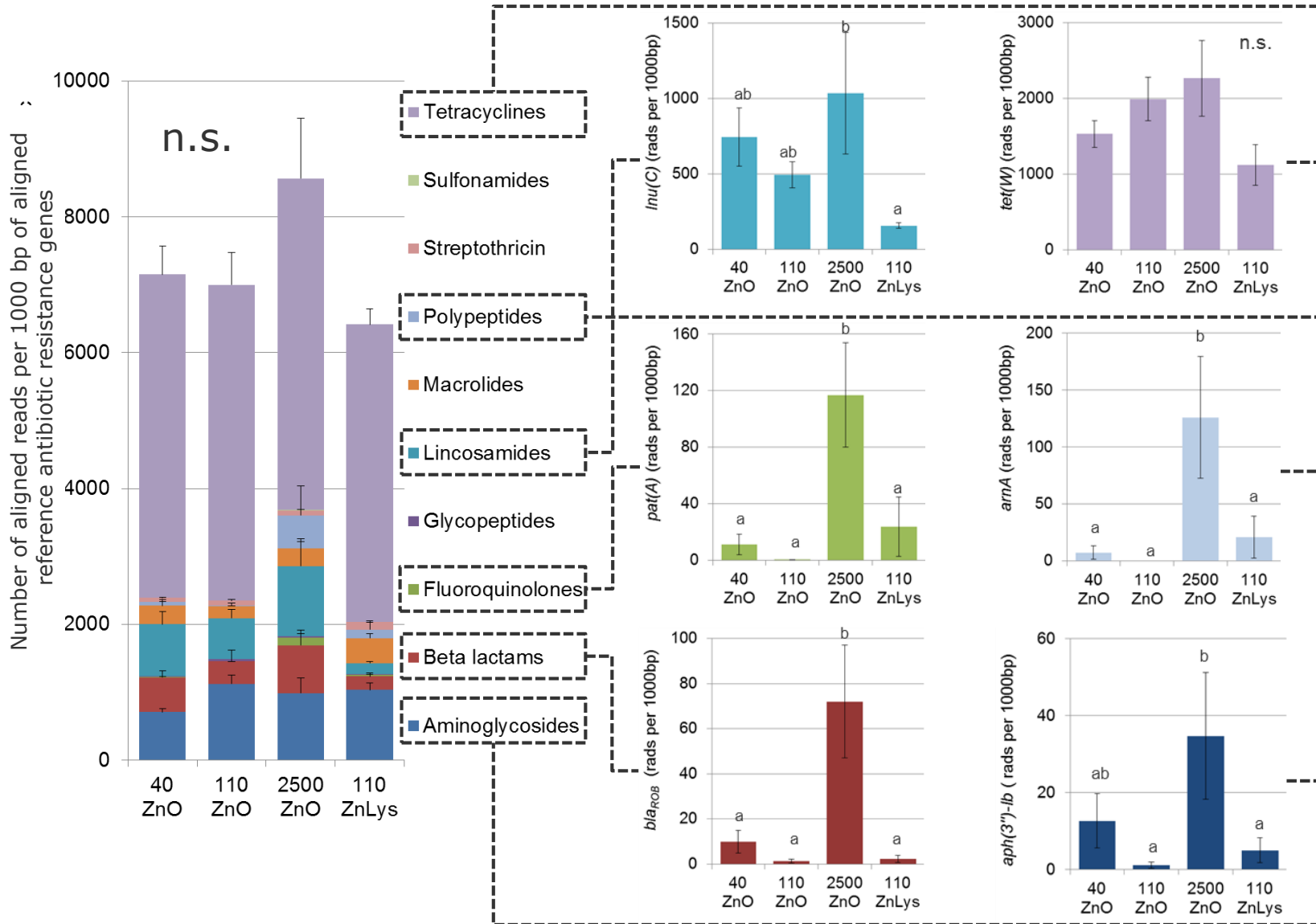
- 40 weaned piglets (m/f; 25 ± 1 days, 6.0 ± 0.1 kg BW))

Group		40 ZnO	110 ZnO	2500 ZnO	110 Zn-Lys
Animals	n	10 (5 ♂; 5 ♀)	10 (5 ♂; 5 ♀)	10 (5 ♂; 5 ♀)	10 (5 ♂; 5 ♀)
Zinc oxide (p.a.)	mg/kg	40	110	2460	
Zinc-Lysinate	mg/kg				110

- 4 week feeding period
- Euthanasia and sampling of tissues and gut contents



Results - antibiotic resistance genes



Other ZnO sources

Product	Test dose, ppm Zn	Growth	Faecal Score	
Lipid coated ZnO	100 – 200 -400	+ (400 -)	ns	Song et al. 2018
ZnMet	500	+	+	Bouwhuis et al. 2017
Lipid microencapsulated ZnO	150/400	+	+	Grilli et al. 2015
Modified ZnO (small particles)	mixed	+	+	Cho et al. 2015
Coated ZnO	250 – 380 - 570 – 760 -1140	+	+	Shen et al. 2014
Zinc oxide-montmorillonite hybride	500 - 750	+	+	Hu et al. 2012

More studies...

Conclusion

- Zinc has a „janus head“



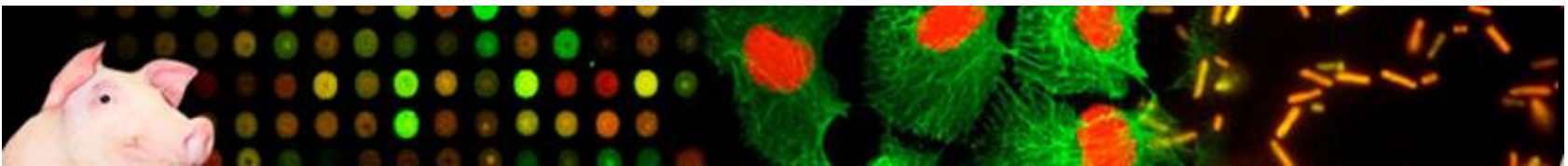
- Pharmacological ZnO → environment, AB resistance
- Requirements are covered by moderate dietary levels
- Alternative zinc sources may work – more studies needed



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...



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Nutrition and Intestinal Microbiota
Host Interaction in the Pig

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