The genetic resistance of sows to *Escherichia coli* F4 adhesion reduces their response to a vaccine containing F4 fimbriae but does not affect the preweaning performance of their susceptible piglets

D. Hu[1,4], C. Ollagnier[2], A. Hofer[3], M. Girard[2], A. Gutzwiller[2], G. Bee[2], S. Neuenschwander[1]

[1]Institute of Agricultural Sciences, ETH Zürich, Zürich, Switzerland; [2]Swine Research Group, Agroscope, Posieux, Switzerland; [3]SUISAG, Sempach, Switzerland; [4]Present address: MGI Tech Co., Ltd., Shenzhen, China

Die genetische Resistenz von Sauen gegen die intestinale Adhäsion von *Escherichia coli* F4 verringert ihre Reaktion auf einen Impfstoff mit F4-Fimbrien, hat jedoch keinen Einfluss auf die Leistung ihrer Ferkel vor dem Absetzen

Schweine ohne intestinale Rezeptoren für F4-Fimbrien sind angeboren resistent gegen F4-Fimbrien tragende enterotoxische *Escherichia coli* (ETEC F4). Im Allgemeinen sind 50 % bzw. 100 % der Ferkel von resistenten (RR) Sauen, die mit heterozygoten bzw. homozygoten (SR, SS) Ebern gekreuzt wurden, empfänglich und erhalten keine kolostralen Antikörper gegen F4-Fimbrien, es sei denn, die Muttersauen wurden geimpft. Es stellt sich die Frage, ob resistente Sauen nach der Impfung schützende Mengen an F4-Antifimbrien-Antikörpern produzieren.

Die Serum- und Kolostrumantikörpertiter von 12 resistenten und 12 empfänglichen geimpften Jungsauen wurden verglichen. Die Auswirkung des Rezeptorstatus von Mutter und Vater auf die Leistungen von 5027 Ferkeln vor dem Absetzen wurde mit den Aufzeichnungen von Agroscope ausgewertet. Die Sauen der Versuchsherde, in der ETEC F4 im Umlauf war, wurden während der ersten Trächtigkeit zweimal und während jeder weiteren Trächtigkeit einmal geimpft.

Die log2-transformierten F4-Antikörpertiter nach der zweiten Impfstoffinjektion im Serum sowie im Kolostrum der 12 resistenten Tiere waren niedriger als die Titer der anfälligen Tiere (Serum: F4ab 11,19 ± 1,44 vs. 12,18 ± 1,33, P = 0,096; F4ac 10,03 ± 1,58 vs. 11,59 ± 1,43, P = 0,019; Kolostrum: F4ab 12,20 ± 2,41 vs. 14,02 ± 1,31, P = 0,033; F4ac 10,93 ± 2,46 vs. 13,03 ± 5,21 = 0,006). Die Antikörpertiter

Summary

Pigs without intestinal receptors for F4 fimbriae are congenitally resistant to F4 fimbriae-bearing enterotoxigenic *Escherichia coli* (ETEC F4). In general, 50 % and 100 % of piglets born to resistant (RR) sows crossed with hetero- or homozygous susceptible (SR, SS) boars, respectively, are susceptible but do not receive colostral antibodies against F4 fimbriae unless the sows have been vaccinated. The question arises as to whether resistant sows produce protective amounts of F4 antifimbrial antibodies after vaccination.

The serum and colostrum antibody titres of 12 resistant and 12 susceptible vaccinated gilts were compared. The effect of the receptor status of the dam and sire on the preweaning performance of 5027 piglets was evaluated using Agroscope's recordings. The sows of the experimental herd, where ETEC F4 was circulating, were vaccinated against ETEC twice during the first pregnancy and once during each following pregnancy.

The $\log_2$ transformed F4 antibody titres in the serum obtained after the second vaccine injection as well as in the colostrum of the 12 resistant animals were lower than the titres of the susceptible animals (serum: F4ab 11,19 ± 1,44 vs. 12,18 ± 1,33, P = 0,096; F4ac 10,03 ± 1,58 vs. 11,59 ± 1,43, P = 0,019; colostrum: F4ab 12,20 ± 2,41 vs. 14,02 ± 1,31, P = 0,033; F4ac 10,93 ± 2,46 vs. 13,03 ± 5,21, P = 0,006). The heat labile enterotoxin (LT) antibody titres after vaccination did not differ between susceptible and resistant animals (p > 0,10). Preweaning mortality in the offspring of RR sows × SS boars was slightly lower than in the offspring of SS sows × RR boars (P = 0,04), suggesting that the disease risk of susceptible piglets born to vaccinated resistant sows was not increased, even though they received

https://doi.org/10.17236/sat00430

Eingereicht: 24.04.2024
Angenommen: 17.07.2024

The genetic resistance of sows to *Escherichia coli* F4 adhesion reduces their response to a vaccine containing F4 fimbriae but does not affect the preweaning performance of their susceptible piglets

D. Hu et al.

gegen hitzelabiles Enterotoxin (LT) nach der Impfung unterschieden sich nicht zwischen anfälligen und resistenten Tieren (p > 0,10). Die Sterblichkeit vor dem Absetzen war bei den Nachkommen von RR-Sauen × SS-Ebern niedriger als bei den Nachkommen von SS-Sauen × RR-Ebern (P = 0,04), was darauf hindeutet, dass das Krankheitsrisiko anfälliger Ferkel, die von geimpften resistenten Sauen geboren wurden, nicht erhöht war, obwohl sie Kolostrum mit einem leicht reduzierten Gehalt an Antikörpern gegen F4-Fimbrien enthielten.

Schlüsselwörter: ETEC F4, Rezeptoren, Immunisierung, Kolostrum, Genotyp, Mortalität

colostrum with a slightly reduced content of antibody against F4 fimbriae.

Keywords: ETEC F4, receptors, immunisation, colostrum, genotype, mortality

Introduction

Enterotoxigenic *Escherichia coli* (ETEC) is a common cause of diarrhoea in suckling as well as in recently weaned piglets.[5] The widespread use of antimicrobials to treat the disease increases the risk for the development of antimicrobial resistance.[10] In the USA as well as in Switzerland, F4 fimbriae-carrying ETEC are frequently isolated from piglets suffering from diarrhoea.[22,27] Of the fimbrial variants F4ab and F4ac predominating in the Western hemisphere,[7] F4ac is the most frequently isolated variant in Switzerland with a proportion of around 50 % over the last two decades.[21,22] Variant F4ad occurs less frequently and has the lowest virulence of the three F4 variants known.[7] Since ETEC F4 need to attach with their fimbriae to specific receptors on the enterocytes to colonise the small intestine,[1] pigs without these receptors are resistant to ETEC F4 infection. A 1989 report showed that roughly 50 % of Swiss Large White and Swiss Landrace pigs are susceptible to ETEC F4ac infection[6] which was confirmed in a recent study in Large White pigs using genetic markers.[9]

Markers associated with the gene coding for F4ac receptor status have been identified[9,17] and shown to predict the disease susceptibility of piglets in an ETEC F4ab/ac challenge model,[20] confirming a previous finding, based on a microscopic adhesion test using enterocytes of the small intestine,[15] that ETEC F4ac resistance is associated with F4ab resistance. Marker-assisted selection of F4ac-resistant pigs thus provides the opportunity for creating pig populations that are resistant to the most common ETEC F4 variants.[26] Such a goal is achieved more quickly if resistant boars and sows are selected simultaneously. However, since the absence of this receptor is a recessive monogenetic trait, 50 % and 100 % of the piglets born to resistant sows (RR) crossed with hetero- or homozygous susceptible boars (SR, SS), respectively, will be susceptible but will not receive colostrum containing naturally acquired antibodies against F4 fimbriae, which have been shown to protect suckling piglets against ETEC F4 infection.[23,24,25] The increased preweaning mortality of the offspring of resistant sows × susceptible boars observed in Swiss herds[8] (Khayatzadeh and Hofer 2020, unpublished data) may thus be caused by the absence of colostral immunity against ETEC F4 infection.

To avoid an increase in preweaning mortality during the establishment of resistant pig populations, the selection should therefore start in the sire lines followed by the dam lines. As an alternative, sows could be parenterally vaccinated against ETEC F4. However, the antibody response of resistant pigs after a single injection of F4 fimbriae is reduced in comparison to susceptible pigs, presumably because their immune system has not been primed by a previous infection.[4] Since the immune response of resistant pigs to a vaccination protocol consisting of two injections of F4 fimbriae has, to our knowledge, not been studied, we compared the serum, colostrum, and milk antibody titres of resistant and susceptible sows immunised twice during their first pregnancy. To verify whether parental F4 receptor genotypes affect the performance of suckling piglets *per se* or via a lack of maternal antibodies against ETEC F4, the effects of the F4 receptor genotypes of boars and vaccinated sows on the preweaning performance of piglets were studied.

Materials and methods

Animals

Animals of Agroscope's Swiss Large White herd and its internal herd book data were used for the vaccination experiment and the preweaning piglet performance study. All animals were genetically resistant to ETEC F18 infection.[12,13] The genotype for ETEC F4 susceptibility of each breeding animal was known (SS or SR: susceptible phenotype; RR: resistant phenotype). Antimicrobial group treatment was never practised, and postweaning diarrhoea caused by ETEC F4 commonly occurred. To ensure that the colostrum and milk of all sows contained antibodies against ETEC, the vaccine Porcilis Porcoli DF® (MSD Animal Health GmbH, Werftstrasse 4, 6005 Luzern, Switzerland), containing the F4ab, F4ac, F5, and F6 fimbrial ad-

hesins as well as the toxoid of the heat labile enterotoxin (LT), was administered intramuscularly (i.m.) twice during the first pregnancy and once again during each subsequent pregnancy, as recommended by the manufacturer. The pregnant sows were group-housed in pens with straw bedding and individually fed. Shortly before farrowing, the sows were batchwise transferred into individual pens in a farrowing unit that had been thoroughly cleaned and left empty for at least one week before it was occupied. There was no surveillance of the farrowing during the night. All piglets born alive and dead were individually weighed and registered. At weaning at the average age of four weeks, the weight of each animal was registered.

Genotyping for ETEC F4 susceptibility

Ear biopsy samples of all pigs intended for breeding were genotyped either by sequencing PCR fragments[18] or using a KASP assay (LGC, Teddington, Middlesex, UK) with the markers *CHCF1* and *ALGA0106330*.[9]

Vaccination study

The 12 resistant (RR) and 12 susceptible (1 SS, 11SR) gilts used in the study (state veterinary approval 26734) received the first dose of the vaccine Porcilis Porcoli DF® seven weeks before the calculated farrowing date and the second dose four weeks later. Blood was collected from the jugular vein into tubes without anticoagulant immediately before the first and second vaccinations and one to two weeks after the second vaccination. Serum was obtained by spinning the clotted blood at 2000 g for 15 min. Within twelve hours and on day eight after farrowing, colostrum and milk samples were obtained by milking several teats after the i.m. injection of 40 IU oxytocin (Oxytocin-20, Dr. E. Graeub AG, Rehhagstrasse 83, 3018 Bern, Switzerland). The serum, colostrum, and milk samples were stored at -20° until they were analysed at the laboratory of Intervet (Boxmeer, the Netherlands) as previously described.[21]

Briefly, antibodies against LT and against the fimbriae F4ab and F4ac were assayed in serially diluted samples using enzyme-linked immunosorbent assays (ELISA). The reactions were read with an ELISA reader at 450 nm, and the titres were expressed as $\log_2$ values. Samples with a titre below the initial dilution of 1:48 ($\log_2$ value 5,6) were considered negative, titres between 5,6 and 8 doubtful, and titres >8 positive.[19] The titres were compared using the two-sided t-test. Given that the titres in many serum samples before vaccination and in many milk samples were negative, the proportion of resistant and susceptible animals having pre-vaccination serum and milk titres ≥ 5,6 were compared using Fisher's exact test.

Piglet performance survey

The records of 5027 piglets from 382 litters that were born between 2010 and 2017 were evaluated. All sows were of the Swiss Large White dam line breed. The sires of 4749 and 278 piglets were of the Swiss Large White dam line and the Swiss Large White sire line (PREMO), respectively. The data for five traits were analysed using statistical packages in R.[16] Birth weight (BW) of the piglets born alive and dead, average daily weight gain from birth to weaning (ADG), and weaning weight (WW) were analysed with a linear model using the lm package. The model included the fixed effects year of birth, parity of the dam, and sex of the piglet, as well as the combined effect of the F4 genotype (Gt) of the dam and sire (DamGt × SireGt). The survival rate at birth (SurB 0 = fully developed, found dead at first litter inspection after farrowing, 1 = alive) and the survival rate of live-born piglets at weaning (SurW: 0 = not weaned, 1 = weaned) were analysed using a logistic regression model with a logit link function using the glm package. The model fitted the same effects as the linear model. Preliminary analyses fitting SireGt and DamGt together with their interaction as separate effects resulted in a significant interaction effect for three out of the five traits, preventing a sound interpretation of the main effects of SireGt or DamGt independently.

An analysis of variance (ANOVA) was performed using the function ANOVA of the statistics package for both types of models. Estimates of the combined effect of SireGt and DamGt were computed as marginal means using the ls-means function of the emmeans package. For the logistic regression model, the marginal means were computed on the original scale of the survival traits (option: type = "response"). The performance of the offspring of RR dams × SS sires was compared with that of SS dams × RR sires, as in both cases, 100 % of piglets were susceptible, but in the first case, they were born from a resistant dam and in the second case, they were born from a susceptible dam. This comparison was computed as the linear contrast between the two groups of piglets and was tested using the t-test (lm) and z-test (glm). In both studies, P-values <0,05 were considered significant, and P-values between 0,05 and 0,10 were referred to as tendencies.

Results

Vaccination study

All pre-vaccination titres were either negative (<5,6) or doubtful (5,6–8, data not shown). Pre-vaccination antibody titres ≥5,6 against LT were detected in a higher proportion of resistant gilts (9 of 12) compared to susceptible gilts (2 of 12; P = 0,0123). After vaccination, neither the serum nor the colostrum LT titres differed between the resistant and susceptible pigs (P > 0,10; Table 1).

Pre-vaccination titres ≥ 5,6 against F4ab were detected in 4 of the 12 susceptible, but in none of the resistant gilts (P = 0,0932). Two of the 12 resistant and 3 of the 12 susceptible gilts had F4ac antibody titres before vaccination (P = 1). Four weeks after the injection of the first dose of vaccine,

the resistant gilts had lower serum titres against both F4ab (*P* = 0,001) and F4ac (P < 0,001; Table 1) than the susceptible gilts. After the second dose, the difference in serum F4ab and F4ac titres diminished but remained significant for the F4ac titres (P = 0,019, Table 1). The F4ab and the F4ac serum titres of all fully vaccinated gilts were >8, except for the F4ac titre of one resistant gilt. Compared to the susceptible gilts, the resistant gilts produced colostrum with lower titres against both F4ab and F4ac (P = 0,033 and P = 0,006). The F4ab and F4ac titres in all colostrum samples were >8, except for the F4ac titre of one resistant animal. Whereas antibodies against LT were detected in only one milk sample of a susceptible sow and in none of the resistant sows (*P* > 0,10), a higher proportion of susceptible sows than resistant sows had milk antibody titres >5,6 against the fimbriae F4 (F4ab: 8 of 12 vs. 3 of 12, P = 0,0995; F4ac: 5 of 12 vs. 0 of 12, P = 0,037, data not shown).

Piglet performance survey

The numbers of records, means, and standard deviations (SD) of the five piglet performance traits are shown in Table 2. The year, parity, and the combined effect of dam and sire genotype (DamGt × SireGt) were significant for all traits (Table 2). The sex effect was significant only for birth weight and tended to affect survival at birth.

Although the combined effect of dam and sire genotypes was significant for all traits, the inspection of the marginal means of the 5 traits analysed shows no clear relationship with dam genotype (resistant RR vs susceptible, RS and SS) or the percentage of susceptible piglets in the litter (Table 3).

The statistical test of the contrast between RR dam × SS sire (column RR×SS) and SS dam × RR sire (column SS×RR) offspring was not significant for BW, WW, ADG, and SurB and only at the boundary of significance for SurW (P=0,04). The survival rate from birth to weaning of piglets born to RR dams × SS sires was higher than that of the offspring of SS dams × RR sires (P = 0,04).

Table 1: Serum and colostrum antibody titres (log2; mean ± standard deviation SD) against LT, F4ab, and F4ac after i.m. immunisation of 12 resistant and 12 susceptible gilts with LT toxoid and *E. coli* F4ab and F4ac adhesins.

Serum titres	Resistant	Susceptible	P
LT after 1st injection	8,00 ± 1,75	8,73 ± 0,95	0,216
LT after 2nd injection	9,43 ± 1,45	10,18 ± 1,33	0,195
F4ab after 1st injection	8,64 ± 0,88	9,99 ± 0,93	0,001
F4ab after 2nd injection	11,19 ± 1,44	12,18 ± 1,33	0,096
F4ac after 1st injection	8,01 ± 1,16	10,19 ± 1,04	< 0,001
F4ac after 2nd injection	10,03 ± 1,58	11,59 ± 1,43	0,019
Colostrum titres	**Resistant**	**Susceptible**	**P**
LT	9,83 ± 2,85	11,24 ± 1,69	0,155
F4ab	12,20 ± 2,41	14,02 ± 1,31	0,033
F4ac	10,93 ± 2,46	13,03 ± 5,21	0,006

Table 2: Mean and standard deviation (SD) of birth weight (BW), weaning weight (WW), and average daily weight gain from birth to weaning (ADG), survival rate at birth (SurB), survival rate of the live-born piglets at weaning (SurW), and P-values of analysis of variance (ANOVA) of the effects sex, year, parity, and the combined effect of dam and sire genotype (DamGt×SireGt).

Trait	Unit	N	Mean	SD	P (ANOVA)			
					Sex	Year	Parity	DamGt×SireGt
BW	kg	5027	1,469	0,388	<0,001	0,030	<0,001	0,013
WW	kg	3652	7,337	1,873	0,290	<0,001	<0,001	<0,001
ADG	kg/day	3649	0,230	0,066	0,716	<0,001	<0,001	<0,001
SurB	%	5027	0,871	0,335	0,054	<0,001	0,010	0,009
SurW	%	4380	0,834	0,372	0,303	0,012	0,001	0,050

Discussion

The first vaccine injection induced a much weaker antibody response to the F4 fimbriae in the resistant gilts, whose immune system had not been primed by a previous ETEC F4 infection, as previously shown.[4] This difference diminished after the second administration of the vaccine but remained significant for the serum F4ac titres and for both the colostrum F4ab and F4ac titres. This result shows that the hybrid immunity against ETEC F4 induced by an infection followed by vaccination is superior to the immunity elicited by vaccination only; similarly, hybrid immunity caused by both a previous Covid 19 infection and vaccination protect humans better against Covid than either infection or vaccination alone[2]. Although the antibody response of the resistant animals was slightly reduced, their serum and colostrum F4ab and F4ac titres were > 8, with the exception of one serum and one colostrum titre. Serum and colostrum titres >8 were considered positive and potentially protective in an infection model with piglets whose dams had been immunised with the vaccine also used in our study.[19] The fact that the immunoglobulin concentration in sow's milk is roughly four to tenfold lower than in serum and colostrum, respectively,[3,11] may explain the absence of detectable antibody titres in most milk samples, which were assayed at the same dilution as the serum and colostrum samples. Nevertheless, more susceptible sows than resistant sows produced milk with detectable milk F4ab and F4ac antibody titres, which confirms the differences detected in the serum and colostrum titres.

Antibodies to LT were detected in the serum of the ETEC F4-resistant gilts before vaccination. This is not surprising because the heat labile ETEC toxin LT is secreted not only by ETEC F4 but also by ETEC F6, ETEC F18, and ETECs with unknown fimbrial types,[14] that is, by pathogens that can infect ETEC F4 resistant pigs. The question of why fewer susceptible pigs had LT antibodies before the vaccination is open to speculation, but the marked rise of their LT titres after vaccination, resulting in numerically higher values than those of the resistant animals, suggests that they too had previously been exposed to this toxin. The pre-vaccination antibody titres against F4ac detected in two resistant animals was unexpected. Their post-vaccination F4ac serum titres did not differ from those of the other resistant gilts, suggesting that their pre-vaccination titres, which were in the order of magnitude considered doubtful, did not result from an ETEC F4 infection.

The comparison of litters of susceptible piglets suckling either resistant or susceptible sows revealed that susceptible piglets born to resistant vaccinated sows were not at increased disease risk. The significantly lower mortality from birth to weaning of susceptible piglets of resistant sows was probably a false-positive result, attributable to the multiple testing of the performance traits. These results contrast with data obtained from the Swiss Large White herd book showing a reduced survival rate from birth to weaning of the offspring of resistant dams × susceptible sires[8] (Khayatzadeh and Hofer 2020, unpublished data). Only about 40 % of Swiss pig breeders vaccinate their sows against ETEC using one of the four vaccines registered for that purpose (Lüchinger, Swiss pig health service, pers. comm.). The omission of vaccination in many herds, differences in the vaccination protocol, and differences in infection pressure may thus explain the observed difference between the suckling piglet mortality rates in the Swiss pig population and in Agroscope's research herd. Based on the above-mentioned epidemiological data obtained from the Swiss herd book, the Swiss Breeding Organisation (SUISAG) recommends that F4-resistant dams should not be crossed with susceptible sires. The results of the present study show that these

Table 3: Marginal means of F4 genotype of the dam and genotype of the sire for birth weight (BW), weaning weight (WW), average daily weight gain from birth to weaning (ADG), survival rate at birth (SurB), and survival rate of the live-born piglets at weaning (SurW). Number of records per genotype (Npigs) at birth and at weaning, percentage of susceptible offspring expected (% susceptible).

	F4 genotype of the dam × genotype of the sire								
	RR×RR	RR×RS	RR×SS	RS×RR	RS×RS	RS×SS	SS×RR	SS×RS	SS×SS
Npigs birth	850	1181	200	793	1084	308	257	228	126
Npigs weaning	618	820	168	600	784	225	170	168	96
% susceptible	0	50	100	50	75	100	100	100	100
BW	1,464	1,463	1,482	1,498	1,479	1,523	1,517	1,558	1,481
WW	6,925	6,743	6,558	6,906	7,301	7,154	6,797	6,918	7,323
ADG	0,221	0,206	0,204	0,215	0,222	0,219	0,207	0,206	0,224
SurB	0,90	0,86	0,92	0,89	0,86	0,84	0,88	0,90	0,89
SurW	0,81	0,79	0,87	0,84	0,84	0,84	0,79	0,82	0,83

crossings do not necessarily affect the performance of suckling piglets born to resistant sows that have been immunised with the vaccine used in the study.

Good hygiene, biosecurity measures and feeding strategies that prevent bacterial proliferation in the small intestine are key to successful piglet rearing. Animal welfare increases and reduces the use of antibiotics, which also reduces the spread of antibiotic-resistant bacteria. In addition, the breeding of disease resistant animals using reliable genetic markers has been successful for the prevention of diarrhoea and oedema disease caused by ETEC F18 and is a promising strategy to prevent piglet losses caused by ETEC F4 infection.

Acknowledgement

The authors would like to thank Guy Maïkoff and his colleagues at the Agroscope pig farm for their careful work with the pigs.

This article is dedicated to Prof. emer. Dr Hans Ulrich Bertschinger, who died in June 2024 at the age of 92. He and his group were at the forefront of *E. coli* research in pigs. His work on the *in vitro* adhesion of *Escherichia coli* to porcine enterocytes was instrumental in identifying the causal mechanism of F18 resistance. He also continued to work with us on the development of genetic markers for F4 resistance long after his retirement.

We will always remember him as an outstanding scientist, mentor, colleague and friend.

La résistance génétique des truies à l'adhésion de *Escherichia coli* F4 réduit leur réponse à un vaccin contenant des fimbriae F4 mais n'affecte pas la performance avant sevrage de leurs porcelets sensibles

Les porcs dépourvus de récepteurs intestinaux pour les fimbriae F4 sont congénitalement résistants aux *Escherichia coli* entérotoxinogènes porteurs de fimbriae F4 (ETEC F4). En général, 50 % et 100 % des porcelets nés de truies résistantes (RR) croisées avec des verrats hétéro- ou homozygotes sensibles (SR, SS), respectivement, sont sensibles mais ne reçoivent pas d'anticorps colostraux contre les fimbriae F4, à moins que les truies n'aient été vaccinées. La question se pose de savoir si les truies résistantes produisent des quantités protectrices d'anticorps antifimbriae F4 après la vaccination.

Les titres d'anticorps dans le sérum et le colostrum de 12 truies reproductrices vaccinées résistantes et de 12 truies reproductrices vaccinées sensibles ont été comparés et l'effet du statut récepteur de la mère et du père sur les performances avant sevrage de 5027 porcelets a été évalué. Les truies du troupeau expérimental, où circulait ETEC F4, ont été vaccinées deux fois au cours de la première gestation et une fois au cours de chaque gestation suivante contre ETEC.

Les titres d'anticorps F4 transformés en $\log_2$ dans le sérum obtenu après la deuxième injection de vaccin ainsi que dans le colostrum des 12 animaux résistants étaient inférieurs aux titres des animaux sensibles (sérum : F4ab 11,19 ± 1,44 vs. 12,18 ± 1,33, P = 0,096 ; F4ac 10,03 ± 1,58 vs. 11,59 ± 1,43, P = 0,019 ; colostrum : F4ab 12,20 ± 2,41 vs. 14,02 ± 1,31, P = 0,033 ; F4ac 10,93 ± 2,46 vs. 13,03 ± 5,21, P = 0,006). Les titres d'anticorps contre l'entérotoxine thermolabile (LT) après la vaccination ne différaient pas entre les animaux sensibles et résistants (p > 0,10). La mortalité avant sevrage dans la progéniture des truies RR × verrats SS était légèrement inférieure à celle de la progéniture des truies SS × verrats RR (P = 0,04), ce qui suggère que le risque de maladie des porcelets sensibles nés de truies résistantes vaccinées n'a pas été augmenté, même s'ils ont reçu du colostrum avec une teneur légèrement réduite en anticorps contre les fimbriae F4.

Mots clés: ETEC F4, récepteurs, immunisation, colostrum, génotype, mortalité

La resistenza genetica delle scrofe all'adesione dell'*Escherichia coli* F4 riduce la loro risposta a un vaccino contenente fimbrie F4 ma non influisce sulle prestazioni prima dello svezzamento dei loro suinetti suscettibili

I maiali senza recettori intestinali per le fimbrie F4 sono congenitamente resistenti all'*Escherichia coli* (ETEC F4) enterotossigenico portatore di fimbrie F4. In generale, il 50% risp. il 100% dei suinetti nati da scrofe resistenti (RR) incrociate con verri suscettibili eterozigoti o omozigoti (SR, SS), rispettivamente, sono suscettibili ma non ricevono anticorpi colostrali contro le fimbrie F4 a meno che le scrofe non siano state vaccinate. La domanda che sorge è se le scrofe resistenti producono quantità protettive di anticorpi antifimbriali F4 dopo la vaccinazione. I titoli di anticorpi nel siero e nel colostro di 12 scrofe resistenti e 12 suscettibili vaccinate sono stati confrontati, ed è stato valutato l'effetto dello stato del recettore della madre e del padre sulle prestazioni pre-svezzamento di 5027 suinetti. Le scrofe del branco sperimentale, dove circolava l'ETEC F4, sono state vaccinate contro l'ETEC due volte durante la prima gravidanza e una volta durante ciascuna gravidanza successiva. I titoli di anticorpi F4 trasformati log2 nel siero ottenuto dopo la seconda iniezione del vaccino così come nel colostro dei 12 animali resistenti erano inferiori ai titoli degli animali suscettibili (siero: F4ab 11,19 ± 1,44 vs. 12,18 ± 1,33, P = 0,096; F4ac 10,03 ± 1,58 vs. 11,59 ± 1,43, P = 0,019; colostro: F4ab 12,20 ± 2,41 vs. 14,02 ± 1,31, P = 0,033; F4ac 10,93 ± 2,46 vs. 13,03 ± 5,21, P = 0,006). I titoli di anticorpi contro l'enterotossina termolabile (LT) dopo la vaccinazione non differivano tra animali suscettibili e resistenti (p > 0,10). La mortalità pre-svezzamento nella prole di scrofe RR × verri SS era leggermente inferiore rispetto alla prole di scrofe SS × verri RR (P = 0,04), suggerendo che il rischio di malattia dei suinetti suscettibili nati da scrofe resistenti vaccinate non era aumentato, anche se hanno ricevuto colostro con un contenuto leggermente ridotto di anticorpi contro le fimbrie F4.

Parole chiave: ETEC F4, recettori, immunizzazione, colostro, genotipo, mortalità

The genetic resistance of sows to *Escherichia coli* F4 adhesion reduces their response to a vaccine containing F4 fimbriae but does not affect the preweaning performance of their susceptible piglets

D. Hu et al.

Literaturnachweis

[1] Bijlsma IG, de Nijs A, van der Meer C, Frik JF: Different pig phenotypes affect adherence of *Escherichia coli* to jejunal brush borders by K88ab, K88ac, or K88ad antigen. Infection Immun 1982; 37: 891–894.

[2] Bobrovitz N, Ware H, Ma X., Li Z, Hosseini R, Cao C, Selemon A, Whelan M, Premji Z, Issa H, Cheng B, Abu Raddad LJ, Buckeridge DL, Van Kerkhove MD, Piechotta V, Higdon MM, Wilder-Smith A, Bergeri I, Feikin DR, Arora R.K, Patel MK, Subissi L: Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. Lancet Infect Dis 2023; 23: 556–67.

[3] Butler J, Wertz N, Deschart N, Kacskovics I: Porcine IgG: Structure, genetics and evolution. Immunogenetics 2009; 61: 209–230.

[4] Edfors-Lilja I, Gustafsson N, Duval-Iflah Y, Ellergren H, Johansson M, Juneja RK, Marklund L, Andersson L: The porcine intestinal receptor for *Escherichia coli* K88ab, K88ac: regional localization on chromosome 13 and influence of IgG response to the K88 antigen. Anim Genet 1995; 26: 237–242.

[5] Fairbrother JM, Nadeau E, Gyles CL: *Escherichia coli* in postweaning diarrhea in pigs: An update on bacterial types, pathogenesis and prevention strategies. Anim Health Res Rev 2005; 6: 17–39.

[6] Gautschi C, Schwörer D: A study of the intestinal receptor for *E. coli* K88 in different Swiss pig breeds. Animal Genetics 1989; 20 (Suppl. 1): 38–39.

[7] Guinee PA, Jansen WH: Behavior of *Escherichia coli* K antigens K88ab, K88ac, and K88ad in immunoelectrophoresis, double diffusion, and hemagglutination. Infect Immun 1979; 23: 700–705.

[8] Häfliger I: Genomic predictions including known QTL for reproduction traits in swine. Master's thesis: Norwegian University of Life Science, Ås. (URL: http://hdl.handle.net/11250/2436690), 2016.

[9] Hu D, Rampoldi A, Bratus-Neuenschwander A, Hofer A, Bertschinger HU, Vögeli P, Neuenschwander S: Effective genetic markers for identifying the *Escherichia coli* F4ac receptor status of pigs. Anim Genet 2019; 50: 136–142.

[10] Jensen VF, Eborg HD, Aarestrup FM: Indications and patterns of therapeutic use of antimicrobial agents in the Danish pig production from 2002 to 2008. J Vet Pharmacol Ther 2012; 35: 33–46.

[11] Klobasa F, Werhahn E, Butler JE: Composition of sow milk during lactation. J Anim Sci 1987; 64: 1458–1466.

[12] Meijerink E, Fries R, Vögeli P, Masabanda J, Wigger G, Stricker C, Neuenschwander S, Bertschinger HU, Stranzinger G: Two alpha(1,2) fucosyltransferase genes on porcine chromosome 6q11 are closely linked to the blood group inhibitor (S) and *Escherichia coli* F18 receptor (ECF18R) loci. Mamm Genome 1997; 8: 736–741.

[13] Meijerink E, Neuenschwander S, Fries R, Dinter A, Bertschinger HU, Stranzinger G, Vögeli P: A DNA polymorphism influencing alpha(1,2)fucosyltransferase activity of the pig FUT1 enzyme determines susceptibility of small intestinal epithelium to *Escherichia coli* F18 adhesion. Immunogenetics 2000; 52: 129–136.

[14] Ojeniyi B, Ahrens P, Meyling A: Detection of fimbrial and toxin genes in *Escherichia coli* and their prevalence in piglets with diarrhoea. The application of colony hybridization assay, polymerase chain reaction and phenotypic assays. Zentralbl Veterinärmed B 1994; 41: 49–59.

[15] Python P, Jorg H, Neuenschwander S, Hagger C, Stricker C, Burgi E, et al.: Fine-mapping of the intestinal receptor locus for enterotoxigenic *Escherichia coli* F4ac on porcine chromosome 13. Anim Genet 2002; 33(6): 441–447.

[16] R Core Team R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/ 2020 (accessed 4.3.2024).

[17] Rampoldi A: Approach to the gene controlling the porcine receptor for Escherichia coli with fimbriae F4ab/F4ac and inheritance of the receptor for F4ad. Diss. ETH Zürich No. 2152. URL: https://doi.org/10.3929/ethz-a-009907149, 2013.

[18] Rampoldi A, Jacobsen MJ, Bertschinger HU, Joller D, Bürgi E, Vögeli P, Andersson L, Archibald AL, Fredholm M, Jorgensen CB, Neuenschwander S: The receptor locus for *Escherichia coli* F4ab/F4ac in the pig maps distal to the MUC4-LMLN region. Mamm Genome 22; 2011: 122–129.

[19] Riising HJ, Murmans M, Witvliet M: Protection against neonatal *Escherichia coli* diarrhoea in pigs by vaccination of sows with a new vaccine that contains purified enterotoxic *E. coli* virulence factors F4ac, F4ab, F5 and F6 fimbrial antigens and heat-labile *E. coli* enterotoxin (LT) toxoid. J Vet Med B Infect Dis Vet Public Health 2005; 52: 296–300.

[20] Rydal MP, Gambino M, Jorgensen CB, Poulsen LL, Brondsted L, Nielsen JP: Pilot study on CHCF1 genotype in a pig challenge model for enterotoxigenic *Escherichia coli* F4ab/ac associated post-weaning diarrhea. BMC Vet Res 2022; 18: 382.

[21] Sarrazin E, Fritzsche C, Bertschinger HU: [Main virulence factors in *Escherichia coli* isolates from swine over two weeks old with edema disease and/or *E. coli* diarrhea]. Schweiz Arch Tierheilkd 2000; 142: 625–630.

[22] Schneeberger M, Dietz O, Kirchgässner C, Schmitt S: Aetiologically relevant typing of *E. coli* isolates from diseased pigs in Switzerland during 2014 and 2015 ARC J Anim Vet Sci. 2017; 3: 1–7.

[23] Sellwood R: *Escherichia coli* diarrhoea in pigs with or without the K88 receptor. Vet Rec 1979; 105: 228–30.

[24] Sellwood R: *Escherichia coli*-associated porcine neonatal diarrhea: antibacterial activities of colostrum from genetically susceptible and resistant sows. Infect Immun 1982; 35: 396–401.

[25] Sellwood R: Inhibition of adhesion of *Escherichia coli* K88 antigen by mammary secretions of susceptible and resistant sows. Vet Microbiol 1984; 9, 477–486.

[26] Vögeli P, Bertschinger HU, Buergi E, Neuenschwander S: Vererbung und Krankheit beim Schwein: Möglichkeiten der züchterischen Nutzung [Inheritance and disease in the pig: possibilities of use for breeding]. Schweiz Arch Tierheilkd 2014; 156: 269–77.

[27] Zhang W, Zhao M, Ruesch L, Omot A, Francis D: Prevalence of virulence genes in *Escherichia coli* strains recently isolated from young pigs with diarrhea in the US. Vet Microbiol 2007; 123: 145–152.

Korrespondenzadresse

Stefan Neuenschwander
ETH Zürich, Institut für Agrarwissenschaften
Tannenstrasse 1 (TAN C1)
CH-8092 Zürich.
Telefon: 044 632 37 90
E-Mail: stefan.neuenschwander@usys.ethz.ch