BREEDING PIGS RESISTANT TO *ESCHERICHIA COLI* F18 IN THE FIELD – A PROGRESS REPORT FROM SWITZERLAND

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Introduction

Postweaning *Escherichia (E.) coli* diarrhoea and enterotoxaemia (oedema disease) cause significant loss mainly in newly weaned pigs. Out of 125 pigs in this age group examined post mortem in 1999, 39% died from *E. coli* diarrhoea and 27% from enterotoxaemia (4). In both diseases, the pathogenesis is characterized by at least two essential steps, I. colonisation of the small intestine and II. production of one ore more toxin(s). Adhesion of the bacteria to the intestinal wall is an indispensable prerequisite of colonisation. Adhesion depends on the higly specific interaction between bacterial fimbriae and host receptors. The two types of fimbriae F4 and F18 dominate in postweaning disorders. The type F4 comprises three antigenic variants and the type F18 the two variants F18ab and F18ac (7). In a Swiss survey of post mortem diagnoses with 125 pigs over two weeks of age, F4 was detected in 49%, F18ab in 41% and F18ac in 10% of the cases (8).

Receptor activity can be demonstrated either *in vivo* after oral challenge based on clinical outcome and faecal shedding of the organism, or *in vitro* by microscopic observation of intestinal villi, enterocytes or enterocyte brush borders after incubation with the fimbriated bacteria. The *in vitro* technique requires the pig to be killed. Both variants of fimbriae F18, i.e. F18ab and F18ac, bind to the same receptor (3,7).

Receptors for each of the two fimbrial types are not present in every individual pig. Adhesion is inherited in one locus with adhesion dominating over non-adhesion (1). The gene specifying for the F18 receptor forms part of the malignant hyperthermia syndrome (MHS) linkage group located on chromosome 6 (9) and is closely linked to or even identical with the fucosyl transferase 1 (*FUT1*) gene (6). In this gene, a guanine (*G*) / adenine (*A*) polymorphism at position 309 is highly correlated with the receptor genotype. This polymorphism allowed to develop a diagnostic DNA test based on PCR-RFLP for use in live pigs. *FUT1* genotypes *G/G* and *G/A* are highly correlated with adhesion and genotype *A/A* with non-adhesion of *E. coli* with fimbriae F18 (6).

The excellent concordance between *FUT1* genotypes and results of microscopic adhesion tests has been confirmed in several laboratories and populations of pigs. Strikingly, the *A* allele coding for resistance has not been detected in 20 out of 21 Chinese native breeds (10). In a recent Danish study (5) the microscopic adhesion test showed complete concordance with *FUT1* genotypes, but some pigs with the *A/A* genotype were not perfectly protected against a heavy challenge with a diarrhoeagenic F18 positive *E. coli.*

In Switzerland, the diagnostic DNA test has been available to pig breeders in the field for about 8 years. We therefore decided to collect and present data on the changing frequencies of the *A* and *G* alleles as well as on the strategies applied by the breeders and the disease status in pure *A/A* herds.

Material and methods

Data on *FUT1* genotypes of all pigs examined were obtained from the blood typing laboratory of the Swiss Federal Institute of Technology. Genotypes of AI boars were provided by the Swiss AI stations, a branch of SUISAG at Sempach. Nucleus breeders and two breeding organisations provided the names of breeders who had bought breeding stock of *A/A* genotype. These breeders were sent a questionnaire asking about the breeding strategy, the present status of the herd regarding F18 resistance, occurrence of oedema disease and post-weaning *E. coli* diarrhoea, and eventual positive or negative side-effects of breeding for resistance.

Results

In the blood testing laboratory between 400 and 800 pigs are examined per year. In samples from Swiss Large White pigs the frequency of the $FUT1^A$ allele increased from 0.31 in 1996 to 0.52 in 2004, whereas in Swiss Landrace samples it started from 0.07 and reached 0.24.

The number of AI boars with the *A/A* genotype increased from 8 in 1999 to 25 in 2004; only one out of the latter belonging to Swiss Landrace. However, more Landrace boars will soon be at disposition, since the frequency of the *A/A* allele in Landrace boars has been raised from 0 in 1996 to 0.21 in 2004.

The questionnaire was answered by 58 breeders who had bought *A/A* breeding stock. In only 12 herds all boars and sows were of the *A/A* genotype. Three out of the 12 pure *A/A* herds were nucleus herds. Most other nucleus herds know the genetic status of their pigs, but do not see a need to replace genetically valuable stock precipitately. Out of the 12 pure *A/A* herds, eight had suffered before from either oedema disease or post-weaning diarrhoea; all of them reported to be free from clinical disease now. Three herds had never suffered from problems, and one owner did not respond to this question.

Several owners of herds of mixed resistance genotype reported severe post-weaning diarrhoea proven or suspected to be caused by *E. coli* with fimbriae of the type F4. There were no consistent answers to the question addressing side effects (e.g. health or reproduction) of breeding *A/A* pigs.

Discussion

The data presented show a steady increase of the $FUT1^A$ allele in the Swiss pig population. Most of this increase is due to the decision of the geneticists at the central genetics management and the AI adminstration to

systematically favour selection of carriers of the *FUT1*^{A} allele. In constrast, only a minority of the breeders are concerned about the frequency of the resistance allele in their herds.

The evaluation of the effectivity of breeding for resistance in the field is hampered by the fact, that the true incidence of post-weaning *E. coli* F18 diarrhoea cannot be determinded without laboratory investigations. More than half of this complex disease is caused by enterotoxigenic *E. coli* with fimbriae F4. A similar *in vivo* diagnostic test for genetic resistance against *E. coli* diarrhoea caused by F4 strains appears highly desirable. Anyway, none of the pure *A/A* herds previously affected by oedema disease had problems after replacement by *A/A* breeding stock. There was no indication that break-throughs of resistance occurred in the field. Hypothetically, toxigenic *E. coli* might be able to produce a mutant adhesin overcoming the lack of receptor in pure *A/A* herds.

Care must be taken that other important genetic traits are not negatively influenced in the process of breeding for disease resistance. Candidate litters in nucleus herds must be identified early to allow blood typing before castration of the male piglets is done. With this proceeding breeding for resistance does not slow down genetic progress for other traits.

The data available were not suitable to detect side-effects on production traits. An early analysis in the Swiss pig population had not revealed any impact of the *FUT1* genotypes on meat production traits (C. Stricker, personal communication). In Germany, Binder et al. (2) found no sigificant effect of the *FUT1* genotype on meat production and meat quality traits. Their investigation was based on 813 German Landrace, 576 Piétrain and 68 German Landrace pigs raised in a testing station. Care was taken by these authors to separately look at effects of the *FUT1* and the *MHS* loci. In a program for resistance breeding, the linkage of the *FUT1* gene with the *MHS* gene may lead to a concomitant change in the incidence of the MHS syndrome depending on the genetic situation in the pig population concerned.

Genetic disease resistance has the great advantage over other preventive measures that investment is mainly limited to nucleus herds, and that return in terms of reduced pig loss and lower cost for medical treatments will potentially flow for decades.

Conclusion

The still limited field experience indicates that breeding for resistance against *E. coli* with fimbriae F18 is feasible and has no unwanted side-effects, if it is practiced with due vigilance.

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References

1. Bertschinger H U, M Stamm, P. Vögeli (1993) Inheritance of resistance to oedema disease in the pig: Experiments with an *Escherichia coli* strain expressing fimbriae F107. Vet Microbiol *35*,79-89

2. Binder S, K-U Götz, G Thaller, R Fries (2002) Effects of variation in the *FUT1*-gene on various traits in swine. Proc Congr Internat Soc Anim Genetics, Göttingen, paper E006

3. Bosworth B T, T A Casey, E Nystrom, M F Rothschild (1994) Genetic resistance to porcine post-weaning diarrhea caused by enterotoxigenic *Escherichia coli* that express 2134P pili. Proc U.S. Animal Health Assoc *98*,73-78

4. Conzelmann C (2000) Schwein 99 – Ferkelverluste. Suisseporcs-Information, Heft 10, 22-23

5. Frydendahl K, T K Jensen, J S Andersen, M Fredholm, G Evans (2003) Association between the porcine *Escherichia coli* F18 receptor genotype and phenotype and susceptibility to colonisation and postweaning diarrhoea caused by *E. coli* O138:F18. Vet Microbiol *93*, 39-51

6. Meijerink E, R Fries, P Vögeli et al. (1997) 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 *8*,736-741

7. Rippinger P, H U Bertschinger, H Imberechts et al. (1995) Designations F18ab and F18ac for the related fimbrial types F107, 2134P and 8813 of *Escherichia coli* isolated from porcine postweaning diarrhoea and from oedema disease, Vet Microbiol *45*,281-295

8. Sarrazin E, C Fritzsche, H U Bertschinger (2000) Hauptvirulenzfaktoren bei *Escherichia coli*-Isolaten von über zwei Wochen alten Schweinen mit Ödemkrankheit und/oder Colidiarrhöe. Schweiz Arch Tierheilkd *142*,625-630

9. Vögeli P, H U Bertschinger, M Stamm (1996) Genes specifying receptors for F18 fimbriated *Escherichia coli*, causing oedema disease and postweaning diarrhoea in pigs, map to chromosome 6. Anim Genet *27*,321-328

10. Yan X M, Y M Guo, N S Ding et al. (2003) Research on the genetic variations of alpha-1-fucosyltransferase (*FUT1*) gene in 26 pig breeds. Acta Genetica Sinica *30*,830-843