## The genomic region responsible for E. coli F4ab/ac susceptibility in pigs: Characterization and Application

SABRE CUTTING EDGE GENOMICS FOR SUSTAINABLE ANIMAL BREEDING

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## E. coli F4ac in the pig

- 10 % of all piglets suffer from *E. coli* diarrhoa.
- 20% of infected piglets die
- 37% caused by *E. coli* O149,F4ac
- 170.000 piglets/year in Denmark
- Resistance is autosomal recessive (SSC13)

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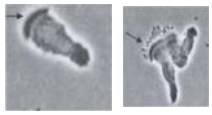
## Adhesion of E. coli F4ac

Adhesion
- Fimbriae type
- Susceptible cell

Colonisation
- Toxin production



*Python et al. 2002*

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## Characterization

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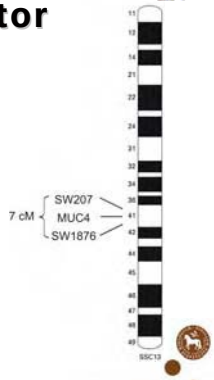
## Mapping of the F4ac-receptor

- **F4ac receptor locus has firmly been linkage mapped between the SW207 and SW1876 (7 cM). (Python *et al,* 2002; Jørgensen *et al*, 2003).**
- **This region contains approx. 150 genes (comparative mapping).**
- **SNP in *MUC4* shows complete LD with the phenotype (*Xba*I polymorphism) (PCT application, Jørgensen *et al*, 2004)**
- **Fine mapping of the *MUC4* flanking region**
- **Detect ancestral haplotype**

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## Fine mapping of the *MUC4* region

**The 3 generation material consists of:**

**10 founders**

**2 Boars** x **8 sows**



**26 F1 and 200 F2**

**18 informative founder chromosomes (12 susceptible and 6 resistant)**

**SNP discovery in EST-data and by genomic re-sequencing in founders**

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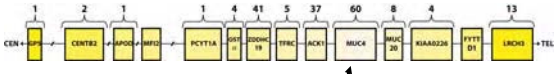
## Fine mapping of the *MUC4* region

- **Identified 177 polymorphic sites, mostly SNPs and a few small deletions/insertions**




***Xba*I-polymorphism used in F4-test**

*Mette Juul Jacobsen*

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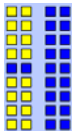
## *SNP-typing in founders*

- Large unique haplotype block on susceptible chromosomes.
- *MUC4* in the center
- Resistant haplotype pattern is complex
- Resistant is wildtype
- SNP-typing in additional Swiss founders
- Crucial to determine minimal shared haplotype in susceptible



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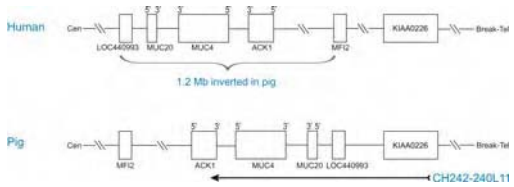
## Sequencing of *MUC4*-BAC Sanger Institute

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## Application

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dr. van haeringen laboratorium b.v
quality - service - know how

GENESEEK
Molecular Solutions for Life

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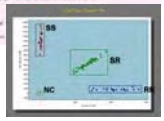
## *MUC4 marker in use by Danish Pig Production*

*Initially selection only on Yorkshire and Landrace boars*

*Selection of Yorkshire boars*
- *RR ~ 20%*

*Selection of Landrace boars*
- *SR ~ 10%*
- *RR ~ 2%*

**Resistens mod smågrisediarré inddrages i avlsmålet**

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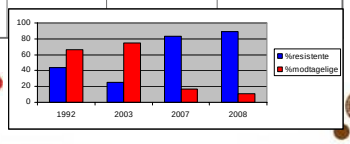
## F4 selection in Denmark

| Breed | 1992 | 2003 (prior to testing) | 2007 (4 years of testing) |
|---|---|---|---|
| Duroc | 100% | 88% | 90% |
| Landrace | 20% | 2% | 50% |
| Yorkshire | 20% | 19% | 85% |
| Production pigs DxLY | 44% | 25% | 83% |




Dansk Svineproduktion

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## Evaluation of the MUC4 selection programme

- Difficult to assess direct effects due to:
  - Uneven distribution of genotypes in the three breeds over time
  - Adjustment in breeding goal over time
  - Only top boars are *MUC4*-genotyped. Boars without known genotype = 00

Number of animals in Landrace

| Year | 00 | RR | SR | SS |
|---|---|---|---|---|
| 1995 | 26895 | 0 | 0 | 0 |
| 1996 | 32859 | 0 | 0 | 0 |
| 1997 | 35531 | 0 | 0 | 0 |
| 1998 | 38183 | 0 | 0 | 0 |
| 1999 | 31975 | 0 | 2 | 3 |
| 2000 | 37929 | 0 | 4 | 15 |
| 2001 | 40947 | 1 | 23 | 46 |
| 2002 | 39961 | 1 | 97 | 210 |
| 2003 | 41415 | 45 | 470 | 1795 |
| 2004 | 38168 | 259 | 2144 | 2392 |
| 2005 | 34277 | 679 | 3124 | 1328 |
| 2006 | 36052 | 1854 | 5429 | 3 |
| 2007 | 33989 | 5123 | 3010 | 0 |
| 2008 | 17779 | 3411 | 454 | 0 |

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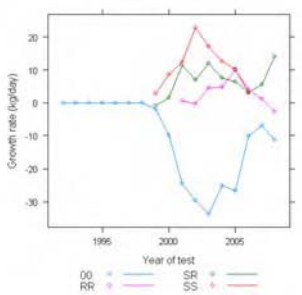
## Landrace: Growth rate 30-100 kg




*SS better 2000-2004*

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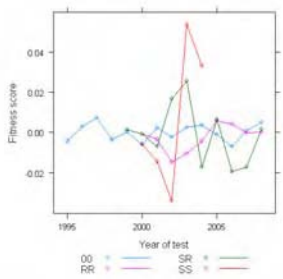
## Yorkshire/Large White: Fitness score




*No effect*

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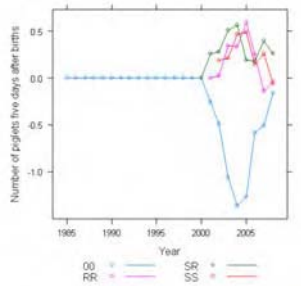
## Yorkshire (LW): Piglets at day 5 after birth




*Change in weight of trait in breeding index*

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## Summary and perspectives

- The MUC4-marker based test is currently the best available test for F4ac-susceptibility in pigs according to the Nordic and Swiss material.
- The ancestral haplotype for susceptibility has been established and is currently being minimized.
- Small effects of the selection scheme in Denmark were expected and are recognized. Presented data preliminary
- Full effect of selection scheme will be evident at the production level in a couple of years

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