



## Detection of a quantitative trait locus associated with resistance to whipworm infections in pigs

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## Why this project?

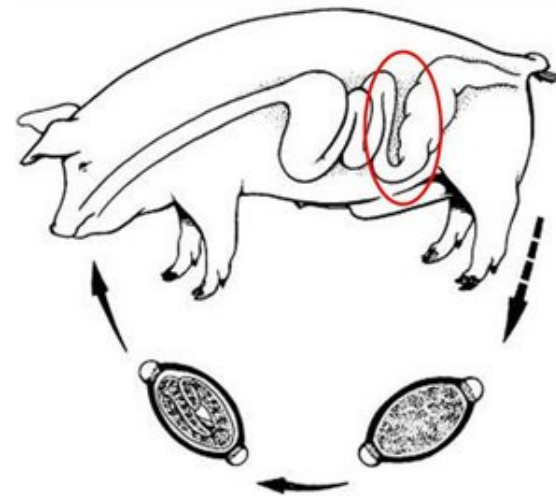
- Whipworms (*Trichuris* spp.) infect a variety of hosts, including production animals and humans.
- High infection levels may cause growth retardation, anaemia and haemorrhagic diarrhoea.
- Limited knowledge of how *Trichuris* spp. infections are regulated by the host's immune system.



Bethony et al. 2006

## *Trichuris suis*

- *Trichuris suis* has a global distribution with highest prevalence in outdoor production systems.
- The pig-*T. suis* system may serve as a unique model for *T. trichiura* in humans.



<http://para-tech.dk/the-product/>

# Elucidating the host genetic component in *Trichuris* infections

Breed and strain differences in resistance to gastrointestinal nematodes due to genetic variation

(Miller 1908; Ackert et al. 1935; Wakelin 1975)

Nematode infections have moderate to high heritabilities

(Stear et al. 1997; Davies et al. 2006; Kaufmann et al. 2011)

- *Trichuris suis* FEC in pigs:  $h^2=0.31-0.73$  (Nejsum et al. 2009)
- *T. trichiura* FEC in humans:  $h^2=0.28$  (Williams-Blangero et al. 2002)

A considerable part of the phenotypic variation can be explained by the host's genetic make-up



Find genetic marker/genes

## Objectives of the study

1. Conduct a genome-wide scan to detect quantitative trait loci (QTLs) associated with resistance to *Trichuris suis* (discovery study)
2. Validate the results in unrelated pigs (validation studies)



## Design of discovery study

19 sows (Landrace/Yorkshire) x 13 boars (Duroc)

195 DLY piglets (F1)

*T. suis* + *A. suum* trickle infection  
(10 wks-24 wks)

Phenotype:

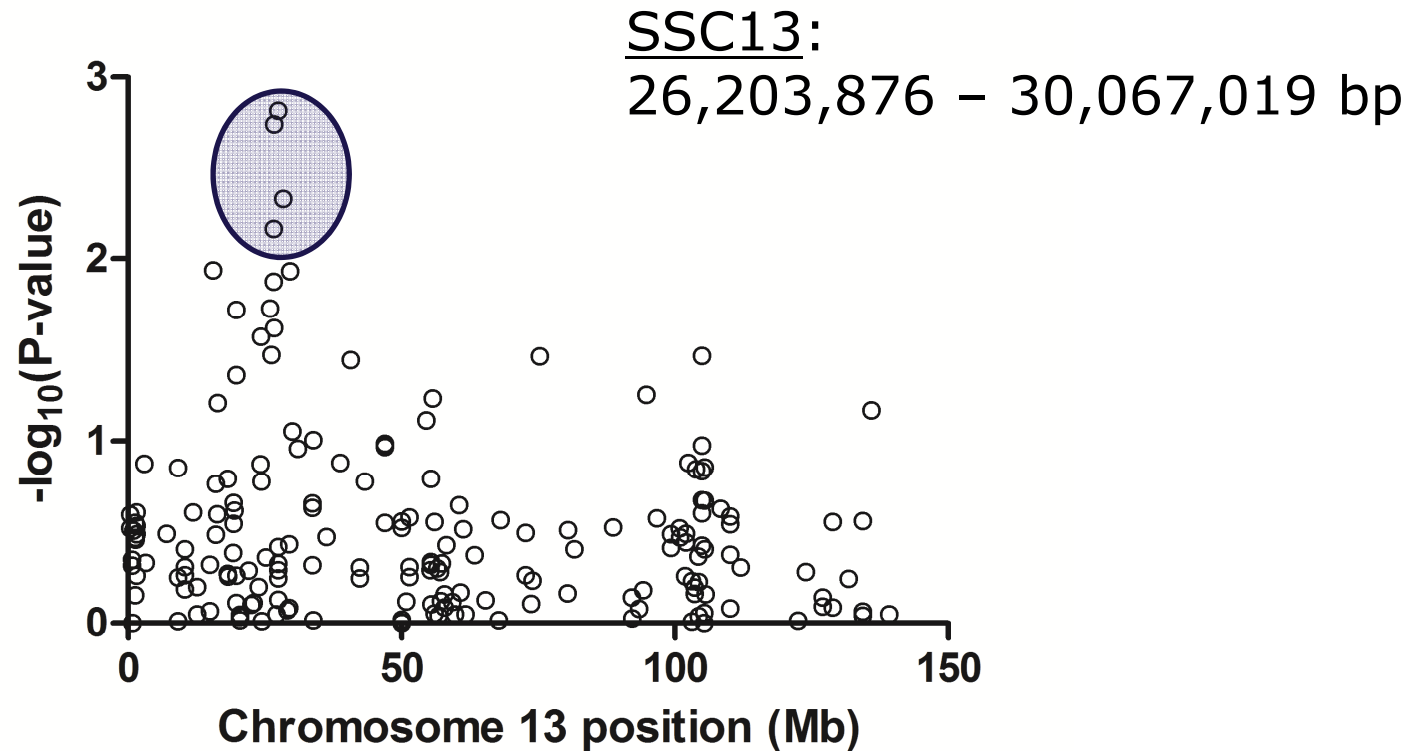
✓ FEC (week 8 p.i.)

SNP genotyping  
(Illumina 7K SNP chip)

Data cleaning  
Statistical analysis



## A putative quantitative trait locus (QTL) on porcine chromosome 13



Plot of P-values for the association between *T. suis* FEC (week 8 p.i.) and SNPs located on chromosome 13; n=195

## Validation studies

Three of the lead SNPs were selected for replication:

- stSG1354613\_233 ('ST')
- IL00001116 ('IL')
- 0\_DOCK3\_DS076720.1\_45 ('DOC')

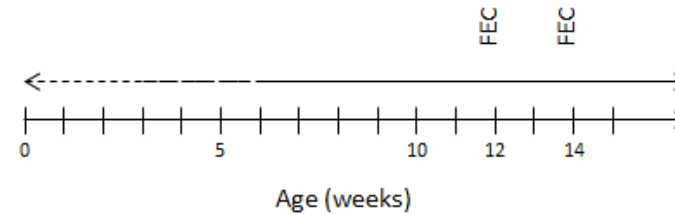




## Design of validation studies

### Validation Study 1

82 piglets  
 Natural infection (*T. suis* + *A. suum*)  
 Trait: FEC (mean week 12 and 14)



### Validation Study 2

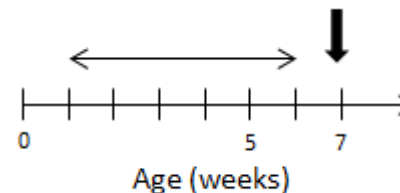
31 piglets, 8 weeks old  
 Single infection (5,000 *T. suis* eggs)  
 Trait: FEC (mean day 47 and 51)

Pigs were genotyped  
 (TaqMan assay)

Quantitative genetic analyses

### Validation Study 3

178 piglets  
 Trickle infection (weekly)  
 Duration: 6 wks  
 Trait: Worm counts



## SNP ST: Association with faecal egg counts

SNP	Position on SSC13 (bp)	Study	Faecal egg counts (FEC)			
			Genotypic means $\pm$ SD (median)			P-value
			AA	AB	BB	
stSG1354613_233 (ST)	26,595,058	Discovery (n=195)	531 $\pm$ 516 (520)	225 $\pm$ 407 (20)	81 $\pm$ 207 (0)	0.007
		VS1+VS2 (n=113)	621 $\pm$ 1064 (75)	330 $\pm$ 1027 (50)	91 $\pm$ 279 (30)	0.007



## SNP IL: Association with faecal egg counts

SNP	Position on SSC13 (bp)	Study	Faecal egg counts (FEC)			
			Genotypic means $\pm$ SD (median)			<i>p</i> -value
			AA	AB	BB	
IL00001116 (IL)	26,667,538	Discovery (n=195)	533 $\pm$ 505 (530)	223 $\pm$ 399 (20)	51 $\pm$ 153 (0)	0.002
		VS1+VS2 (n=113)	704 $\pm$ 1117 (160)	314 $\pm$ 1002 (50)	93 $\pm$ 282 (30)	0.006

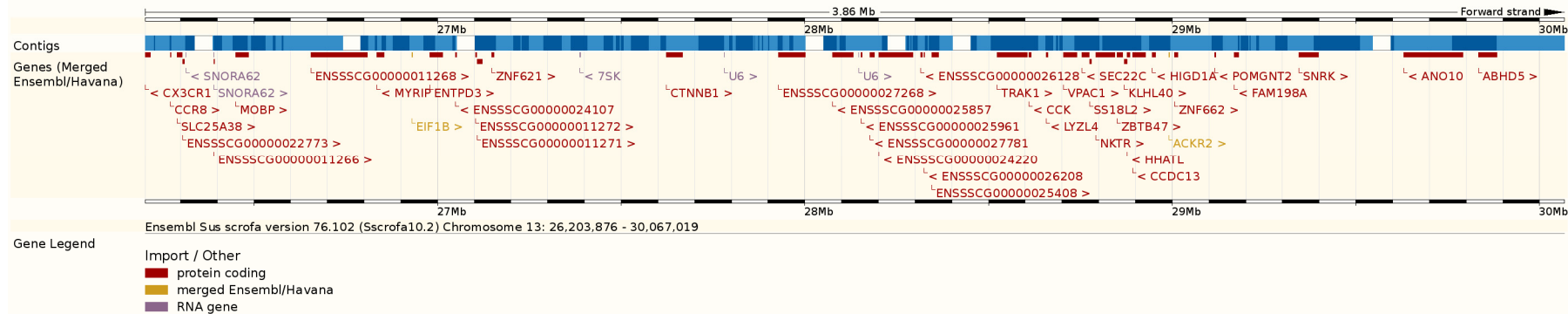


## No association with worm counts

SNP	Study	Worm burden			
		Genotypic means $\pm$ SD (median)			P-value
		AA	AB	BB	
ST	VS3 (n=178)	162 $\pm$ 119 (150)	139 $\pm$ 145 (90)	63 $\pm$ 71 (50)	0.076
IL		163 $\pm$ 120 (150)	144 $\pm$ 145 (90)	63 $\pm$ 71 (50)	0.136
DOC		137 $\pm$ 131 (95)	145 $\pm$ 135 (120)	170 $\pm$ 127 (150)	0.123



## Inspection of candidate region (SSC13)



Human homologue HSA 3p21.33-22.1:  
The QTL encompasses 31 genes

Four candidate genes were identified:

- ***CX3CR1*** - chemokine (C-X3-C motif) receptor 1
- ***CCR8*** - chemokine (C-C motif) receptor 8
- ***VIPR1*** - vasoactive intestinal peptide receptor 1
- ***ACKR2*** - atypical chemokine receptor 2

## What we have delivered in this project

- Whole-genome scan of a resource population revealed a putative QTL on SSC13.
- We validated the QTL in unrelated populations.
- We have identified four candidate genes (chemokine receptors).
- We encourage further studies of the ST and IL markers and the candidate genes.



# Acknowledgements

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