



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

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Why this project?

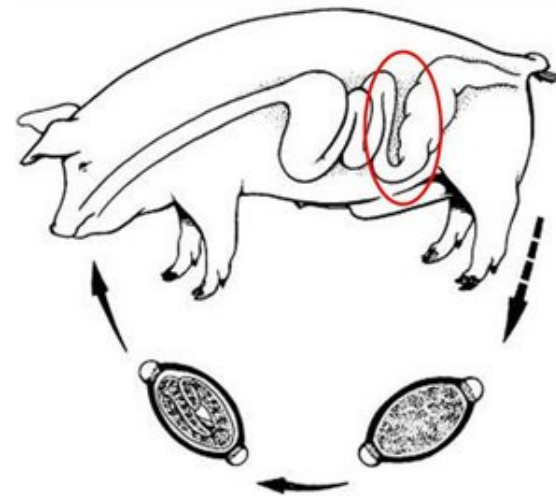
- Whipworms (*Trichuris* spp.) infect a variety of hosts, including production animals and humans.
- High infection levels may cause growth retardation, anaemia and haemorrhagic diarrhoea.
- Limited knowledge of how *Trichuris* spp. infections are regulated by the host's immune system.



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:

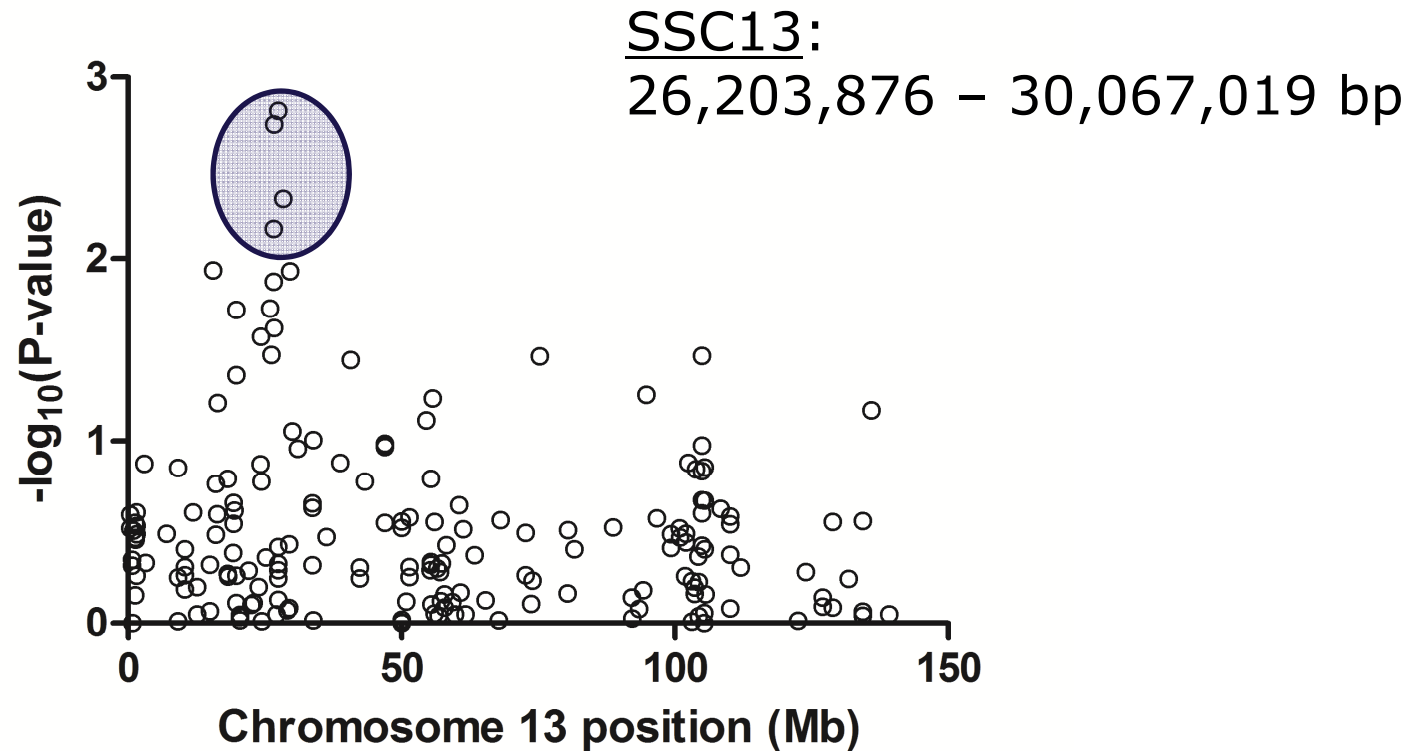
✓ FEC (week 8 p.i.)

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:

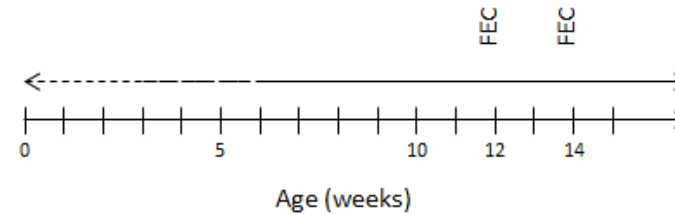
- stSG1354613_233 ('ST')
- IL00001116 ('IL')
- 0_DOCK3_DS076720.1_45 ('DOC')



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

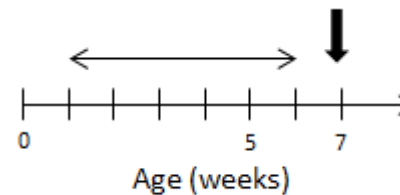
31 piglets, 8 weeks old
 Single infection (5,000 *T. suis* eggs)
 Trait: FEC (mean day 47 and 51)

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

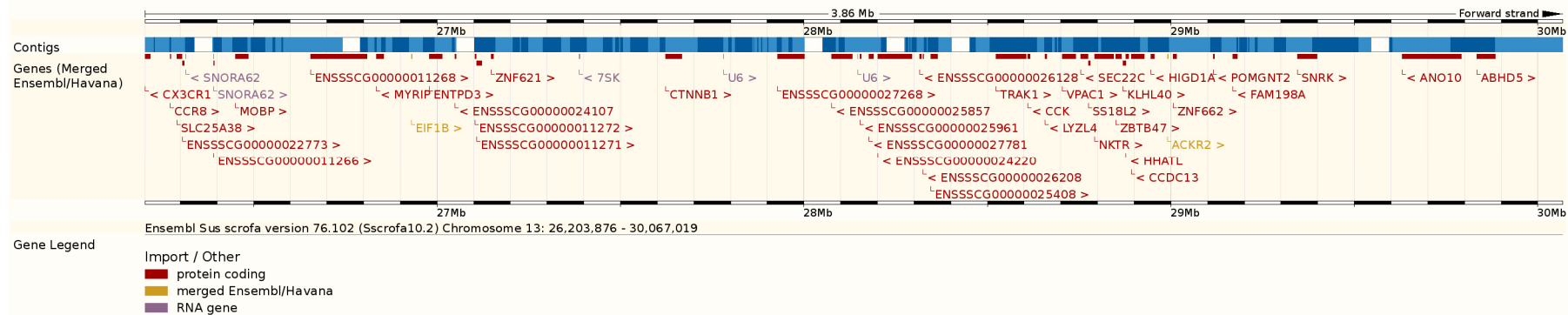


No association with worm counts

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.



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