

A detailed gene map of pig chromosome 4, where the first quantitative trait locus in livestock was mapped

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Summary and Implications

The first quantitative trait locus (QTL) in pigs, *FATI*, was found on chromosome 4 using a wild-boar intercross. Further mapping has refined the *FATI* QTL to a region conserved on both human chromosome 1 and 8. We have now improved the comparative map of the entire SSC4 by mapping 105 loci to pig chromosome 4 (SSC4) and defined the specific human chromosome region with conservation to *FATI*, using a combination of physical and linkage mapping. These types of analysis have resulted in maps with very good agreement. Comparative analysis revealed that the gene order is very well conserved across SSC4 compared to both human chromosome 1 (HSA1) and to HSA8. This refined SSC4 map and the comparative analysis will be a great aid in the search for the candidate genes for the *FATI* locus.

Introduction

Comparative genome analysis is a very powerful tool in the days of the post-genomic era where a wealth of information has been generated for many eukaryotic genomes. Although significant effort and resources have been dedicated to farm animals their genome maps are far from reaching the high resolution available for the human and mouse genome maps. Analysis of the genomes of farm animals such as the search for genes underlying complex traits; quantitative trait loci (QTLs) or economical trait loci (ETLs) can therefore greatly benefit

from the possibility of extracting information from homologous regions of other genomes. The molecular identification of genes underlying QTLs is a challenging task and there have not been many success stories presented yet. A recent compilation of genes identified from QTL studies summarized 29 genes so far; 28 those were identified in human/mouse/rat and only one in a livestock animal.

Porcine chromosome 4 (SSC4) harbor QTLs affecting growth, carcass traits and fat deposition. The first QTL on SSC4, denoted *FATI*, was identified in a European wild boar – Large White intercross. SSC4 has previously been shown to share homology with human chromosomes 1 (HSA1) and 8 (HSA8). SSC4 is divided into two chromosomal blocks where the entire p arm and the q arm proximal to 4q15-16 are homologous to HSA8 and the remaining major part of 4q shares homology with HSA1. We wanted firstly to establish a dense comparative map covering the entire SSC4 but also to define the HSA1-HSA8 breakpoint accurately. This has been achieved with a combined approach of EST mapping on a radiation hybrid (RH) panel covering the entire chromosome, and by linkage and RH mapping of new markers developed around the breakpoint and across the *FATI* QTL region.

Materials and Methods

Primers for physical mapping were designed from pig gene sequence (EST) obtained from the Midwest Consortium for Pig Reproduction Genomics project headed by C. Tuggle. These primers amplify specific gene loci so that the presence of the gene of interest can be mapped relative to other gene locations using available data (see URL). Genetic linkage mapping was performed in Sweden using the wild-boar-Yorkshire cross available there. All data was analyzed and a comprehensive physical and linkage map was created.

Results and Discussion

Genetic Map development

The markers developed were screened for polymorphisms among our 10 founder animals (2 wild boars and 8 Large White) and polymorphism was detected. Altogether, 11 genes were added to our previously published linkage map of SSC4. The linkage map comprising altogether 34 markers spans 135.9 cM (Figure 1).

Physical mapping

As part of an EST-based comparative mapping project with the aim to add 700 genes to the RH map (<http://pigest.genome.iastate.edu/>), we selected HSA1 and HSA8 genes to improve gene marker density across the entire SSC4. For HSA1, emphasis was placed on HSA1q21-24, as we previously showed this was the region on HSA1 closest to the FAT1 QTL. Genes were selected for RH mapping based on strength of BLAST score; agreement of human cytogenetic mapping localizations; and equal distribution across human chromosomes. A total of 103 new genes were successfully mapped onto SSC4.

Comparative mapping

Comparative mapping of SSC4 confirms clearly that SSC4 corresponds to two large blocks on human chromosomes 1 and 8 (Figure 2). Information of the corresponding human gene homology is presented for 101 genes/markers from the RH and linkage maps, 34 that maps to HSA8 and 67 to HSA1. The markers cover the entire length of SSC4 but an emphasis has been made to put markers within the region harbouring the *FAT1* QTL, 23 markers has been added to this region (Figure 2).

The comparative genome analysis also clearly reveals that there are no major rearrangements between the two synteny blocks. The gene order seems to be overall very well conserved as opposed to several other porcine chromosomes that display several large intrachromosomal rearrangements. However there is some evidence to suggest a small inversion of the gene order compared to HSA8 around the centromere on SSC4.

Improved Mapping of the *FAT1* QTL

There appears to be several QTLs affecting, growth, fat, and carcass traits on porcine chromosome 4. Our intention of creating a dense comparative gene map between SSC4 and HSA1/8 has clearly been fulfilled by adding another 101 genes/markers to the map and an additional 5 markers where comparative information has not yet been obtained. The *FAT1* QTL region which boundaries are defined by the *Sw1364* – *S0214* markers has had an increase of 23 genes/markers.

We used two different methods to develop SSC4 chromosome maps; radiation hybrid mapping and linkage mapping. The maps are in very good agreement, however on some parts of the linkage map, the gene order could not be resolved due to no recombination events between markers. To resolve the order of the markers on the most

dense area they could be mapped on the latest RH panel developed for pig by colleagues in France.

Acknowledgements

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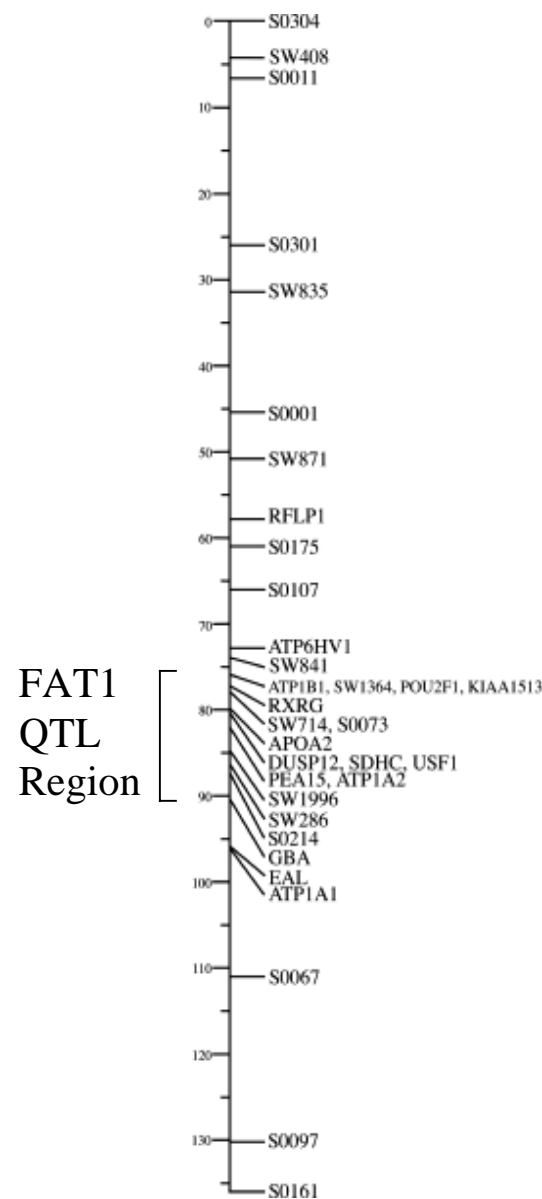


Figure 1. Genetic Linkage map of Pig Chromosome 4, emphasizing the *FAT1* region.

This map contains 33 markers, of which 11 are newly reported in this paper.

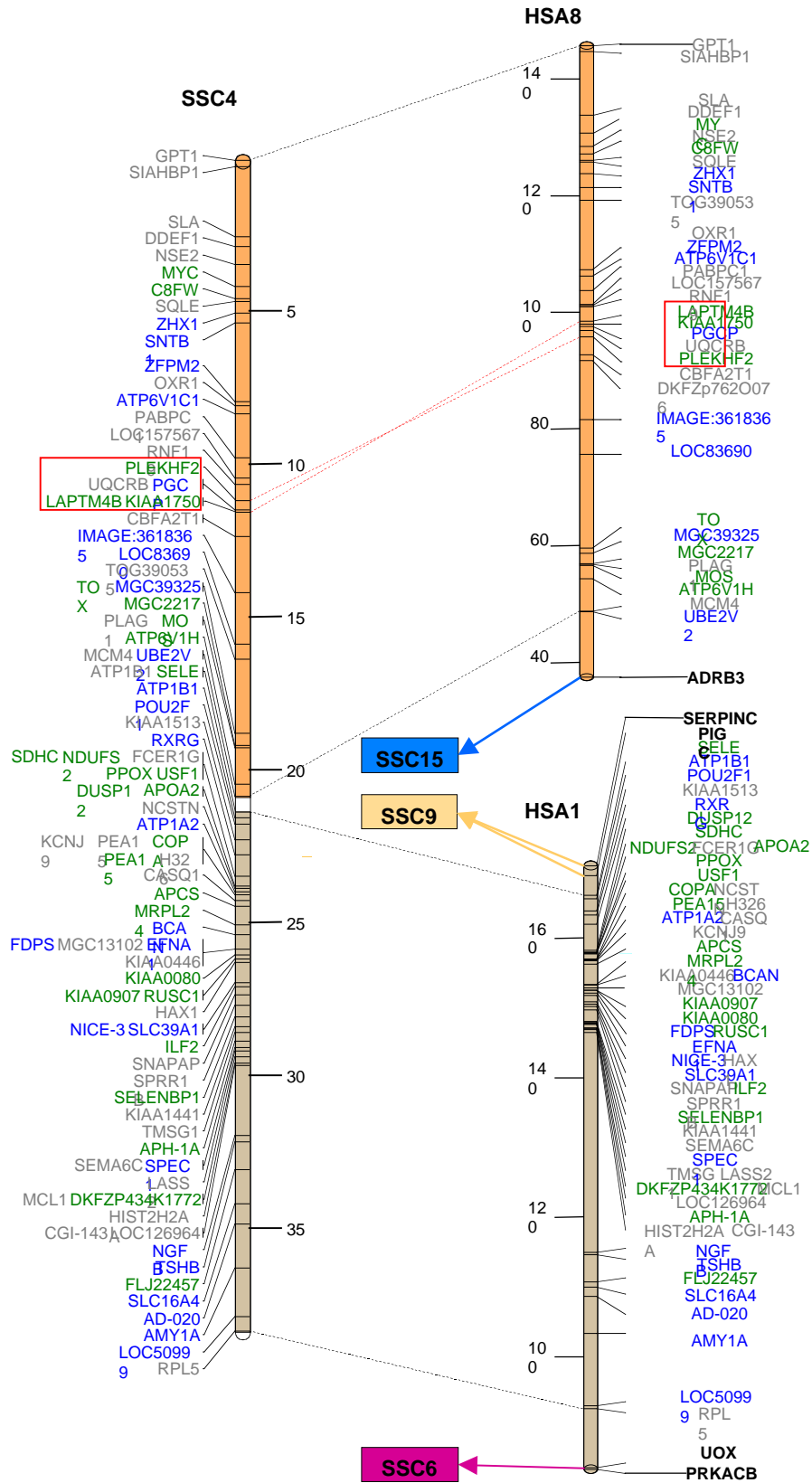


Figure 2. A comparative map of SSC4 and HSA1/HSA8 chromosomes. The porcine distances are given in Rays (measure of physical distance) and the human in Millions of base pairs from human genome sequence. Green signifies high level of confidence in the porcine position; while blue is most likely position for that gene. The red box indicates a region of possible gene order difference between pig and human.