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Addition of Thirteen Genes to the Porcine Comparative Gene Map Reveals New Regions of Conserved Synteny

Abstract
Thirteen genes were mapped to the porcine genome by using either linkage mapping of the PiGMaP families (eight genes) or typing of a porcine somatic cell hybrid panel (12 genes). The genes were chosen from interesting locations in the human genome. The physical gene assignments to pig chromosomes (SSC) with corresponding human chromosome (HSA) locations include the following: FGF7 (HSA15), MADH4 (HSA18), and MC4R (HSA18) to SSC1, RXRB (HSA6), and SSTR1 (HSA14) to SSC7, UCP1 (HSA4) to SSC8, PGR (HSA11) to SSC9, TTN (HSA2) and ANT1 (HSA4) to SSC15, GRIA1 (HSA5) to SSC16, AR (HSA-X), and GRIA3 (HSA-X) to SSC-X. Additionally, CD59 (HSA11) was linkage mapped to SSC2. The majority of the assignments confirm results from bidirectional chromosome painting (4). A rearrangement in gene order was detected within the region of correspondence between SSC1 and HSA15. Two assignments were made that were not expected from the painting results (MC4R and GRIA1) and one assignment of a gene from a region where the painting study was not informative (ANT1).

Keywords
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Authors

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Addition of Thirteen Genes to the Porcine Comparative Gene Map Reveals New Regions of Conserved Synteny

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ASL-R1573

Summary and Implications

Thirteen genes were mapped to the porcine genome by using either linkage mapping of the PiGMaP families (eight genes) or typing of a porcine somatic cell hybrid panel (12 genes). The genes were chosen from interesting locations in the human genome. The physical gene assignments to pig chromosomes (SSC) with corresponding human chromosome (HSA) locations include the following: FGF7 (HSA15), MATH4 (HSA18), and MC4R (HSA18) to SSC1, RXRB (HSA6), and SSTR1 (HSA14) to SSC7, UCP1 (HSA4) to SSC8, PGR (HSA11) to SSC9, TTN (HSA2) and ANTI (HSA4) to SSC15, GRIAI (HSA5) to SSC16, AR (HSA-X), and GRIAI3 (HSA-X) to SSC-X. Additionally, CD59 (HSA11) was linkage mapped to SSC2. The majority of the assignments confirm results from bidirectional chromosome painting (4). A rearrangement in gene order was detected within the region of correspondence between SSC1 and HSA15. Two assignments were made that were not expected from the painting results (MC4R and GRIAI) and one assignment of a gene from a region where the painting study was not informative (ANTI).

Introduction

The porcine linkage maps now include approximately 1,550 anonymous markers and 250 genes. This density of genes is usually too low to enable the positional candidate gene approach for identification of quantitative trait loci (QTL [2]). Instead, the choice of candidate genes currently relies on information from the human and mouse genome projects, which requires well-developed comparative maps.

Between the pig and human genomes, bidirectional painting (Zoo-FISH) has produced valuable information including 37 chromosomal regions of homology (3, 4). Mapping of single genes, selected for their human genome location, is necessary to define the correspondence of unpainted regions and reveal possibly rearranged gene orders within regions of conserved synteny. In this study we have improved the resolution of the pig–human comparative map by adding 13 genes to the porcine map.

Materials and Methods

The genes investigated are in Table 1. Physical gene mapping was carried out using amplification by the polymerase chain reaction (PCR) on a pig–rodent somatic cell hybrid panel (12). In a few cases restriction fragment analysis was necessary to distinguish between pig and mouse–hamster panel products of equal or similar lengths.

Porcine polymorphisms were revealed using direct sequencing and/or restriction fragment length analysis of PCR products, or both, from individuals representing different breeds. Single nucleotide polymorphisms were genotyped as PCR-restriction fragment length polymorphisms (RFLPs) on agarose gels whereas microsatellites were analyzed using native acrylamide gels. The PiGMaP reference families (1), the USDA–MARC reference families (10) and CRI–MAP (v. 2.4 [5]) were used for linkage analyses.

Results and Discussion

Twelve genes were assigned to pig chromosome regions by using the SCHP. Seven of these assignments were confirmed by linkage analysis by using polymorphisms identified in this study. Additionally, CD59 was mapped by linkage to the middle region of pig chromosome 2 (SSC2). The types of polymorphisms found are given in Table 1, whereas mapping results are shown in Table 2. The distribution of the mapped genes over eight pig chromosomes also are illustrated in Figure 1a-g. Most results were expected from chromosome painting data (3, 4), but the locations of MC4R and GRIAI were unexpected.

A rearrangement within the region of SSC1 - HSA15 correspondence was indicated by the close proximity of FGF7, IGF1R (6, 7) and MEF2A (8) in the middle of the SSC1 region painted by human chromosome (HSA)15 (Figure 1a). This may be a pig-specific organization as further indicated by the mouse map where FGF7 and IGF1R/MEF2A are located on MMU7 and 2, respectively.
The HSA18q11-q12 should correspond to SSC6q27-q31, and the remainder of HSA18q should correspond to SSC1q12-q14 although SSC1 did not produce a painting signal anywhere in the human genome (4). The MC4R mapping in this study, however, indicates that the distal half of HSA18 also shares homology with middle region of SSC1q (Figure 1a).

The mapping of GRIA1 to SSC16 was unexpected. The GRIA1 is a distal marker on HSA5q. Painting results show correspondence between HSA5q and SSC2 and also between the complete SSC16 and HSA5p plus proximal HSA5q. Thus, GRIA1 may be a part of a rearrangement in the HSA5 - SSC16 homology that has not been resolved by painting studies (Figure 1f).

Large parts of HSA4 correspond to SSC8; UCP1 was mapped to SSC8q21 as one additional gene assignment in this region of conserved synteny (Figure 1c). HSA4q32-q35, however, was not painted by any porcine chromosome (4). One gene from this region, MTNR1A from HSA4q35, was mapped to SSC17 (9), but in the current study ANTI, a second gene from HSA4q35, mapped to SSC15. This is consistent with a recent mapping of the IRF2 (interferon regulatory factor 2) gene to SSC15 (HSA4q35 [11]), which shows that sequences present on HSA4q35 are divided onto at least two different pig chromosomes. The split between ANTI and MTNR1A to different pig chromosomes contrasts to the situation in cattle and mouse where ANTI and MTNR1A are syntenic.

Conclusions

The porcine gene map was expanded with 13 genes; 12 genes were mapped physically using a somatic cell hybrid panel and eight genes were mapped by linkage.

Ten assignments corroborate chromosome painting studies between the human and porcine genome.

Three gene mapping results indicate new regions of conserved synteny or rearranged correspondence between human and pig chromosomes, which have not been predicted by published Zoo-FISH painting studies.

The unpainted telomeric region HSA4q35 contains segments of correspondence to at least two pig chromosomes (SSC15 and SSC17).

Acknowledgments

The authors are grateful to Geoff Lee (BBSRC, Roslin, UK) for performing two-point linkage analyses, to Jeannine Helm for technical support, and to Gary Rohrer (USDA, Meat Animal Research Center, NE), for providing DNA from USDA-MARC reference families and making it possible to map markers to the USDA map. DNA from PiGMaP families was kindly provided by Alan Archibald (BBSRC, Roslin, UK), as part of the EEC PigMaP program, and distributed by the US Pig Genome Coordinator. This work was supported in part by the Iowa Agriculture and Home Economics Experiment Station, Ames, Project Nos. 3148 and 3231, and by USDA NRI grant No. 95-37205-2189.

References


Table 1. Genes and mapping methods included in this study.

<table>
<thead>
<tr>
<th>Gene abbreviation</th>
<th>Gene name</th>
<th>Mapping methods⁴</th>
<th>Type of polymorphism³</th>
</tr>
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<tbody>
<tr>
<td>ANT1</td>
<td>Adenine Nucleotide Translocase 1</td>
<td>Linkage/SCHP</td>
<td>STR</td>
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<td>AR</td>
<td>Androgen Receptor</td>
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<td>CD59</td>
<td>Complement Regulatory Protein 59</td>
<td>Linkage</td>
<td>HincI⁶</td>
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<td>Fibroblast Growth Factor 7</td>
<td>Linkage/SCHP</td>
<td>AluI⁶</td>
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<td>GRIA3</td>
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<td>MADH4</td>
<td>Pancreatic Carcinoma Gene (DPC4)</td>
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⁴ SCHP - somatic cell hybrid panel;
⁵ STR - short tandem repeat;
⁶ Restriction endonuclease used for PCR-RFLP analysis;
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<th>Gene</th>
<th>Pig expected by painting</th>
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*The map positions of the loci are from Genbank database (pdb).*
Figure 1 (a-g) Schematic diagram showing gene assignments distributed over eight porcine chromosomes. Dotted shades represent pig-homologous regions, and gradient shades represent approximate correspondence between the porcine physical map and the porcine linkage map. Solid vertical bars indicate physical map locations. One line and similar lines have been used for the previously mapped gene KIRREL1 (67), RFLP (11), CAPN3, MEF2A, and TSHR (8) genes, which have been included for clarity.