Assignment\textsuperscript{1} of the methylmalonyl-CoA mutase gene (MUT) to porcine chromosome 7q13→q14 by in situ hybridization and analysis of radiation hybrid panels

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\textsuperscript{1} This is confirmation of mapping to swine chromosome 7 of a gene previously mapped to swine chromosomes 1 and 7 (Duscher et al., 2000, 2003).

Rationale and significance

Methylmalonyl-CoA mutase (MCM) is a nuclear encoded mitochondrial matrix enzyme which catalyses the isomerisation between methylmalonyl-CoA and succinyl-CoA. Inborn genetic defects in the MUT gene encoding human MCM give rise to a serious disorder of propionic acid and methylmalonic acid metabolism termed mut methylmalonic aciduria (Crane et al., 1994). The clinical manifestation of the disease varies from minor symptoms to severe neuro-muscular disorders (Ledley et al., 1997). The molecular cloning of the porcine MUT gene and its chromosomal localization will enable further investigations of the gene and its significance in neuromuscular disorders in pig and piglet survival. The human and mouse orthologous genes were assigned to HSA6p21→p12 and MMU17C–D, respectively (Ledley et al., 1988; Sertic et al., 1990; Threadgill et al., 1990).

Materials and methods

A porcine genomic PAC library (IVM PAC 714, Al-Bayati et al., 1999) was screened by PCR. PAC DNA was isolated with Qiagen Plasmid purification Kit according to the manufacturer’s instructions. Sequencing was carried out on a LI-COR DNA Sequencer Model 4000L (MWG) as described previously (Middendorf et al., 1992). Chromosomal localization of the PAC clone was ascertained by fluorescence in situ hybridization (FISH) as described elsewhere (Solinas-Toldo et al., 1995; Jang et al., 1997) and confirmed by PCR analysis of a porcine whole genome radiation hybrid panel (Yerle et al., 1998). PCR results were analyzed using the interpreting web pages at INRA (http://imprh.toulouse.inra.fr).

Hybrid panel analysis

\begin{tabular}{|l|c|c|c|c|c|c|c|c|}
\hline
Chr & Nearest marker & Ret. & Frac & -- & -- & -- & -- & P(Break) & Dist (Ray) & LOD \\
\hline
7 & SW859 & 25 & 86 & 1 & 1 & 29 & 0.04 & 0.04 & 24.65 \\
\hline
\end{tabular}

Table 1. Results of the PCR analysis of the INRA-Minnesota Porcine Radiation Hybrid (IMpRH)

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Fig. 1. Chromosomal assignment of the porcine MUT gene by FISH. Signals were detected on chromosome 7q13→q14 (Duscher et al., 2000, 2003).

Results

Mapping data
Most precise location: SSC7q13→q14
Range: 3.2–6.3 μm
Mean chromosome length: 4.5 μm
Standard deviation: 0.9
Number of chromosomes examined: 30

References