Assignment of the TYK2 gene to equine chromosome 7q12-q13
(Brief report)
(Kartierung des TYK2 Gens auf dem Pferdechromosom 7q12-q13)

Background: Tyrosine kinase 2 (TYK2) is a member of the janus kinase gene family and encodes an 1187 amino acid protein. All four members of the janus kinase family JAK1, JAK2, JAK3, and TYK2 associate with various cytokine receptors and mediate the signal transduction by tyrosine phosphorylation of downstream targets (YAMOAKA et al., 2004). Studies with tyk2 deficient mice demonstrated impairment of interferon α/β signaling (KARAGHIOSOFF et al., 2003). Mutations in the murine tyk2 gene are associated with increased susceptibility to infectious and autoimmune diseases (SHAW et al., 2003). The human TYK2 gene consists of 25 exons spanning 30,003 bp on human chromosome 19p13.2 starting at 10,322,209 bp. The objective of this study was to determine the chromosomal location of TYK2 in the horse by FISH and RH mapping.

Procedures: BAC library screening/sequence analysis/chromosomal location: The equine BAC library CHORI-241 was screened as per standard protocols (http://bacpac.chori.org) with a heterologous 32P-labelled insert of a human TYK2 cDNA clone (IRALp962L0830) provided by the RZPD (http://www.rzpd.de/). An equine genomic BAC clone (CH241-352C1) with an insert of approximately 200 kb containing the TYK2 gene was identified. BAC DNA was prepared from the BAC clone using the Qiagen plasmid midi kit (Qiagen, Hilden, Germany) and both BAC ends were sequenced. A BLASTN sequence comparison of the equine SP6 BAC end sequence (AccNo. AM113773) with the build 36.2 of the human genome sequence revealed a significant match (BLAST E-value 9.0e-51) over 196 bp (identity = 87%) starting at 10,606,427 bp of HSA19p13.1, approximately 254 kb downstream of human TYK2, and matching with exon 11 and parts of the flanking introns of SLC44A2 (solute carrier family 44, member 2). An internal BAC sequence for exon 18 of the human TYK2 gene with a product size of 552 bp was amplified and verified the human TYK2 gene.

Primer sequences/radiation hybrid (RH) mapping: Primers for PCR amplification of a 249 bp fragment were designed from the CH241-352C1 SP6 BAC end sequence using Primer3 software: F 5’-ATCACTGTAGGGGAGAGA-3’ and R 5’-CTGGTGTCCTGTGACGAGA-3’. To confirm the cytogenetic assignment, the 5,000 rad TAMU equine radiation hybrid panel (CHOWDHARY et al., 2003) was used to map the equine TYK2.

Results: The equine genomic BAC clone CH241-352C1 containing the TYK2 gene was located to ECA7q12-q13 by examination of 40 metaphase spreads (Fig.). The
sequence tagged site (STS) markers showed a retention frequency of 10.9% and the RH mapping revealed close linkage to \textit{HTG33} (6.19 cR; LOD >3.0) which had been previously mapped on ECA7 (CHOWDHARY et al., 2003). The physical assignment of the equine \textit{TYK2} and \textit{SLC44A2} genes on ECA7q12-q13 is in latest agreement with equine-human comparative maps for ECA7 and HSA19 (PENEDO et al., 2005; PERROCHEAU et al., 2006) but does not agree with the previously published equine-human comparative map of the centromeric region of ECA7p, which showed conserved synten to HSA11 (CHOWDHARY et al., 2003).

\textbf{Fig.}: Chromosomal assignment of the equine BAC containing \textit{TYK2} by FISH analysis. G-banded metaphase spread before (left) and after (right) hybridization. Double signals indicated by arrows are visible on both equine chromosomes. (Chromosomale Zuordnung des Pferde BAC mit dem \textit{TYK2} Gen mittels FISH. G-gebänderte Metaphase-Chromosomen vor (links) und nach (rechts) der Hybridisierung. Doppelsignale sind mit Pfeilen gezeichnet und auf beiden Chromosomen sichtbar).

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