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Mapping of 195 genes in cattle and updated comparative map with man, mouse, rat and pig

H. Hayes, C. Elduque, M. Gautier, L. Schibler, E. Crihiu and A. Eggen

Laboratoire de Génétique biochimique et de Cytogénétique, INRA-CRJ, Jouy-en-Josas (France)

Abstract. Our on-going goal is to improve and update the comparative genome organization between cattle and man but also among the most detailed mammalian species genomes i.e. cattle, mouse, rat and pig. In this work, we localized 195 genes in cattle and checked all human/bovine non-concordant localizations found in the literature. Next, we compiled all the genes mapped in cattle, goat, sheep and pig (2,166) for which the human ortholog with its chromosomal position is known, added corresponding data in mouse and rat, and ordered the genes

relatively to the human genome sequence. We estimate that our compilation provides bovine mapping information for about 89% of the human autosomes. Thus, a near complete, overall and detailed picture of the number, distribution and extent of bovine conserved synteny (regardless of gene order) on human R-banded autosomes is proposed as well as a comparison with mouse, rat and pig genomes.

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A major goal of livestock genomics is to map and identify genes involved in economically important traits and disease susceptibility and resistance. It requires powerful genome resources i.e. BAC and YAC libraries, radiation hybrid cell panels, detailed genomic maps and comparative maps. In recent years, human (International Human Genome Sequencing Consortium, 2001; Venter et al., 2001), mouse (Mouse Genome Sequencing Consortium, 2002) and rat (Rat Genome Project, 2003) genomes have been sequenced to near completion. This has provided an essential source of data for understanding genome organization and evolution, comparing genomes, identifying unknown genes, and analyzing gene expression and regulation. The cow is one of the economically most important species and over the past years, considerable work has been done to create detailed bovine gene maps but its

genome has yet to be sequenced. In this work, our aims were (1) to increase the number of genes mapped in cattle (195 new localizations), (2) to solve human/bovine non-concordant localizations currently found in the literature and (3) to update the organization of the cattle genome in relation to human, mouse, rat and pig.

Materials and methods

Primer pairs and probes for FISH mapping

Bovine YAC (Libert et al., 1993) and BAC clones (Eggen et al., 2001) were used to FISH-map 37 genes (see Table 3). They were obtained by PCR screening with three-dimensional pooling schemes as described in the respective publications using primer pairs listed in Tables 1 and 2. In addition, 151 caprine BAC clones isolated by Schibler et al. (1998) and corresponding to 151 genes (Table 3) were FISH mapped.

Chromosomal assignments on the INRA bovine × hamster somatic cell hybrid panel (SCH)

Chromosomal assignments for seven of the genes (see Table 3) were obtained by PCR analysis of the INRA bovine × hamster hybrid panel as described by Laurent et al. (2000).

Fluorescent in situ hybridisation (FISH)

Chromosome preparations, DNA labelling, FISH, and R-banding are described in Hayes et al. (1992, 2000). Chromosome and band numbering followed ISCNDB (2000).

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Request reprints from Hélène Hayes

Laboratoire de Génétique biochimique et de Cytogénétique
INRA-CRJ, 78352 Jouy-en-Josas cedex (France)
telephone: +33 1 34 65 26 73; fax: +33 1 34 65 24 78
e-mail: hayes@diamant.jouy.inra.fr

C. Elduque was a postdoctoral student in our laboratory for part of the work.

Table 1. List of genes localized with bovine YAC clones and corresponding primers. Thirty-five YAC clones were selected for 22 genes from human chromosomes 21 and 3 using specific primer pairs defined in conserved exons of the orthologous genes in man, cattle, sheep, pig, mouse and/or rat. Gene identity controls for bovine PCR products obtained with human or ovine primers revealed 88–100% sequence similarity. Note: 35 independent YAC clones were isolated but since 5 clones, each contained two genes, the total number in Table 1 amounts to 40.

Gene ^a	Number of YAC clones ^b isolated and hybridized/gene	Origin	PCR product size (bp)	Forward primer	Reverse primer
APP	3	bovine	99	GCAGAAGACGTGGGTCC	CTTCAGCATCACAAAGTTGA
IFNAR1	1	bovine	290	AGAAGTTTTCTGCGTCTTTGCC	TGATGGTGGTATTTCAGGTTCTTC
TIAM1	1	human	147	GAGCCGAAAGGATTTCCCTAAAG	GGCCTGGCCCCCTTCAGTG
ATP5O	2	bovine		AACCTGATCAATTTGGCTTGCTGA	GTAACCTGTGCATGGTACTTCTCCA
GRIK1	3 (1× nc)	human	130	GTTTTTCACCCTAATCATCAT	TGCCCATATTCTATCTTG
KCNE1	3	human	79	TGGGATTCTTCGGCTTCTTCA	GGGTCTGTCGAGTGCTCCAG
SON	3	human	104	GCTGTAACCACTTATCTAA	GAAATATTCTATCAGACCCTA
SLC5A3	2 (1× nc)	bovine		AGGCTCTGCTCATGATCGTT	GGTCCGCAACATTTTCAGT
SOD1	2 (2× nc)	bovine	280	GTTTGGCCTGTGGTGTAAATGGAA	GGCCAAAATACAGAGATGAATGAA
PRSS7	2 (1× nc)	bovine	97	ATTCAGCAAATGATAGATGAT	CCACTGGTCAAAGAGAAG
POU1F1	1	bovine	150	GTAGTTTAAACCCTTGTCTTTAT	TTGGCTCTTCCACCAATTTACTT
GAP43	1 (nc)	human	203	GATCCCAAAGTCAAACAGTGTG	TCAGATGAACGGAACATTGC
HES1	2 (2× nc)	human	153	ATTGGCTGAAAGTTACTGTGG	GAGGTAGACGGGGGATTC
KNG	1	bovine	286	CCTACTTCAGTTTTCTGAT	GAGATTACTAGCCATTTTGGAA
SIAT1	1	bovine		GCGTATTTTCTGCTCAGAACAGC	CCGGGAGGACTTCAGAGATCTCTG
ERG	2	human	295	CACCAACGGGGAGTTCAA	CGCCACAAAGTTCATCTTCTG
MX2	2	ovine	94	GGCCCTGCATTGACCTCATC	GAGCTCTGGTCCCCGATAACG
MX1	2	ovine	94	GGCCCTGCATTGACCTCATC	GAGCTCTGGTCCCCGATAACG
RUNX1	2 (1× nc)	human	135	CCTGTGCGCTGTGGTAGGAG	GCTCATCTTGCCTGGGCTCAG
TFF3	1	human	72	GCGGCTACCCCATGTCA	ACACCAAGGCACTCCAGGGAT
CBR1	2	human	125	AGCAGAGAAAGGGGACAAGA	GGCCAAGTACACAGGGGTCTC
HMGNI	1 (nc)	human	160	TCTTGTACAATCCAGGGAAT	AATAAAACAACCAGCAATGAT

^a Gene symbols are from the HUGO Nomenclature database (<http://www.genec.ucl.ac.uk/nomenclature/>).

^b nc = non chimeric bovine YAC clones.

Table 2. List of genes localized by FISH with bovine BAC clones (F) or by somatic cell hybrid mapping (SCH) and corresponding primers. Bovine BAC clones for 15 genes were isolated with primers defined from bovine or human sequences. Regions sharing a high sequence similarity with the orthologous human gene were determined using the Iccare program (T. Faraut; <http://genopole.toulouse.inra.fr/Iccare>). Gene symbols are from the HUGO Nomenclature database except when no official nomenclature is available to date as indicated by an asterisk.

Gene	Origin	GenBank accession no.	PCR product size (bp)	Forward primer	Reverse primer	Mapping procedure
CCT8	bovine	AF136609	150	GTGCCCTGGACTTGAACAGTA	CCAACGTTTTTATTTCCTTCTTG	F
COL6A1	human	X99136	282	TCTCCTCCCCGGCTGACATCACC	TCGTTGACGTCGGTGGCGTCGTTG	F
SMP1*	human	NM_014313	102	TTACCTTTAGCAACATAACCTC	TTGAAGGTGCTCGCATTGGCT	F
COP9*	bovine	AW464695	165	AGCAGCAGTTAGCCAGACTCA	TCAGTAAAGTATGCCGAGGTGA	F
COL6A3	bovine	AW356722	200	TCAATACCTACCCAGCAAGA	GACCCATCTAGGGACTTACC	F
CDC20	bovine	BF193752	201	ACATCCACCACCATGACGTT	CTTGATGCTGGGTGAAGGCT	F
IVL	bovine	AV618666	106	CACACTCTGCCAGTGATTCAG	TGAAGTTGGCTTGTCTCACT	F
SSBP1	bovine	BE722675	100	AGTTGCTCGGTTCGAGTAGGTC	GATCGCCACATCTATTGTT	F
HADHSC	bovine	BM481145	141	ATGAGTTTGTGGCGAAGACC	ACTTGTCCAGCCTCTTGAACA	F
VAV1	bovine	BE485884	100	CTACCAACAGAACTCTCTGAAGGA	TGATGGTTTGTGATGGCTCT	F
HSPA4	bovine	BI537416	196	TGACGAGTATCTGCAGCCCTA	TCAATGTCCATTTTCAGGAAGC	F
RAB18	bovine	BM967938	168	ACAAGGCTGTGGTTTTGGCTCT	CATCCTAGGAAAGCTGTGGAA	F
PSMA7	bovine	BF045709	112	CCTCACTGCTGATGCAAGAAT	GGCGATATAACGGGTGATGTA	F
GNAO1	bovine	BM286134	182	CGACCAACAACATCCAGTT	TGCAAGGGCAGAGAGTGG	F
SERPINO1	bovine	AV606014	102	TCACCATGAGCAGCTGAG	AGGGGAGATGAAGATGTTTC	F
TRIM17	bovine	BE668983	176	TCTTCTGGATTTTGAAGCTG	CTATCCCTTACCACAGAGTCT	SCH
ELF2	bovine	AW463485	104	GCTGAGCCTAACTTCCGAGT	CTGGCCTTTTGTATAACACG	SCH
IL6R	bovine	BE685522	121	CAGGAGCCCTGCCAGTATT	ACTTGTCCCGGCACTGTT	SCH
RAB33B	bovine	AV594098	199	CAATGACATGCTGGTGCTAAA	GTGTCACAGCGACAACATTGA	SCH
OSBPL8	bovine	BE665912	174	CGGGTAACCTCGAGCCATAAAT	TGCAAACTTGTAATGCCATTCT	SCH
ARF1	bovine	AV601289	147	GACCTCCCTAATGCCATGAAC	GAGCTGATTGGACAGCCAGT	SCH
SAG	bovine	JO2955	189	GTACGTGTCTCTGACGTGTGC	AGCAGGAAGGGGTAGGTGTT	SCH
ACK1	bovine	BG690194	194	CTGTCTCCACAAGGCTCCAG	ACGATGGGCAAGATGCAG	F (unexpected)
NDUFC1	bovine	X63214	106	CCGTAAAGTGATTATAGCAGTTC	AAAACACAAATGCTGACTTGACA	F (unexpected)
NDUFV2	bovine	M22539	157	GCAGAAATTTACAAGTACCTCCA	TCTGAATGGTCCAGTATGC	F (unexpected)

Table 3. List of new gene localizations on bovine chromosomes obtained by FISH and somatic cell hybrid mapping in this study. Normal characters FISH with caprine BACs, bold italic with bovine YACs, bold normal with bovine BACs, in shaded background somatic cell hybrid mapping.

Gene	Localization	Gene	Localization	Gene	Localization	Gene	Localization	Gene	Localization
KRTAP8*	1q12.2	GDF8	2q12.2	CSN2	6q32	EDNRB	12q22	C9	20q17
<i>APP</i>	<i>1q12.2</i>	EN1	2q33	CSN1S1	6q32	IL2RA	13q13med	SLC6A3	20q24
<i>SOD1</i>	<i>1q12.2</i>	GLI2	2q33	CSN1S2	6q32	ITGB1	13q13dist	UBE3A	21q12
<i>IFNARI</i>	<i>1q12.2</i>	SLC11A1	2q43	PDE6B	6q36	VIM	13q14	MEF2A	21q13
<i>TIAM1</i>	<i>1q12.2</i>	PAX3	2q43	VAV1	7q15prox	RAB18	13q15prox	CHRNA7	21q17dist
<i>ATP5O</i>	<i>1q12.2</i>	AK2	2q45prox	GM2A	7q21	PSMA7	13q22prox	GRP58	21q23-q24
<i>GRIK1</i>	<i>1q12.2</i>	SMP1*	2q45prox	HSPA4	7q22.1	ASIP	13q22dist	SERPINA3	21q24prox
<i>KCNE1</i>	<i>1q12.2</i>	CRP	3q13	RASA1	7q25.2	ADA	13q24prox	CHGA	21q24prox
<i>SON</i>	<i>1q12.2</i>	S100A6	3q21	CAST	7q27	CYP11B1	14q13	SERPINA1	21q24prox
<i>SLC5A3</i>	<i>1q12.2</i>	THH	3q21	TRIM17	7	TG	14q15	MITF	22q22
CCT8	<i>1q12.2</i>	IVL	3q21	ARF1	7	MYC	14q15	PBXP1	22q22
<i>PRSS7</i>	<i>1q14</i>	NGFB	3q23	GALT	8q13	CRH	14q19	GPX1	22q24prox
<i>POU1F1</i>	<i>1q21dist</i>	NRAS	3q23	VLDLR	8q17	MMP1	15q12prox	HRH1	22q24dist
<i>GAP43</i>	<i>1q24</i>	TSHB	3q23	SFTPC	8q21dist	FDX1	15q21prox	GSTA1	23q22prox
NDUFB4	1q31prox	UOX	3q31-q32.1	CTSL	8q25	APOA1	15q21	BF	23q22
CASR	1q31	ACADM	3q32.2	GSN	8q28	HBB	15q25prox	OLADR	23q22
ZNF148	1q31	CDC20	3q35	COL9A1	9q12.2	FSHB	15q25dist-q26	EDN1	23q24prox
UMPS	1q31	COP9*	3q37	AMD1	9q16prox	PAX6	15q27	F13A1	23q24dist
<i>HES1</i>	<i>1q31dist</i>	COL6A3	3q37	CGA	9q22	WT1	15q27	SERPINO1	23q24dist
CRYGS	1q33	IL6R	3	HMGCR	10q12	PGD	16q21prox	CYB5	24q12
AHSG	1q33	SAG	3	MYH6	10q15-q21	NPPA	16q21	DSG2	24q21-q22
<i>KNG</i>	<i>1q33</i>	HGF	4q15dist-q21	MYH7	10q15-q21	LAMC2	16q23	ADCYAP1	24q23
<i>SIAT1</i>	<i>1q33</i>	LAMB1	4q22	HEXA	10q15dist	IL2	17q22dist	HBA1	25q12prox
CP	1q41dist	NPY	4q25-q26	NP	10q21	NOS1	17q25	EPO	25q22
AGTR1B	1q42	IGFBP3	4q26	THBS1	10q22	COMT	17q26	ACTA2	26q13
GYG	1q42	OPN1SW	4q32	MGAT2	10q24	ELF2	17	CYP17	26q21
RBP1	1q43	CLCN1	4q34	TPM1	10q26	RAB33B	17	DNTT	26q21
NCK1	1q43	SSBP1	4q34dist	CYP19	10q31	DPEP1	18q13	PAX2	26q21
TFDP2	1q43prox	KRTB@	5q21	SORD	10q32	MC1R	18q13	OAT	26q23prox
TF	1q43dist	AVPR1A	5q23	SPTB	10q34prox	MT2A	18q15	DEFB1	27q13
<i>MX1</i>	<i>1q45prox</i>	IFNG	5q23	TGFB3	10q34dist	GNAO1	18q15	F11	27q15
<i>MX2</i>	<i>1q45prox</i>	IGF1	5q31prox	TGM1	10q34	RYR1	18q24prox	ANK1	27q19
<i>TFF3</i>	<i>1q45prox</i>	FGF6	5q35prox	TGFA	11q14	PTGIR	18q24dist	PLAT	27q19
<i>HMGNI</i>	<i>1q45prox</i>	OSBPL8	5	IL1B	11q22	LHB	18q24dist	RBP3	28q18-q19
CRYAA	1q45med	UGT8	6q13	CAD	11q24dist	ACACA	19q13	AGT	28q19
<i>COL6A1</i>	<i>1q45med</i>	TXK	6q14	POMC	11q24dist	MYH2	19q15-q16	TYR	29q13
<i>CBR1</i>	<i>1q45med</i>	MTP	6q15	ASS	11q28prox	GAS	19q17	OPCML	29q22
<i>RUNX1</i>	<i>1q45med</i>	HADHSC	6q15prox	BRCA2	12q15	PNMT	19q17	COX8	29q24prox
<i>ERG</i>	<i>1q45dist</i>	GNRHR	6q32prox	SGCG	12q15dist	MAPT	19q22prox	LDHA	29q24prox

Results and discussion

Mapping of 195 genes on bovine chromosomes by FISH and SCH analysis

The gene mapping results (188 by FISH and seven by SCH analysis) are summarized in Table 3. New or refined gene localisations were obtained for all the bovine autosomes although gene density varies among chromosomes. Concerning the distribution of the genes in relation to chromosomal bands, most of those that we have mapped by FISH are located on R-positive bands confirming the general trend that R-positive bands are gene richer than R-negative bands.

Resolving non-concordant chromosome assignments between man and cattle

At the beginning of our work, we had listed 37 discrepancies (Table 4) between the bovine and human gene maps based on

existing comparative data. In order to establish the most accurate bovine/human genome comparison, these discrepancies were checked to determine whether they were due to true novel synteny groups, to mapping errors in the human or bovine maps or to false orthologous gene pairs. Based on our results (details in Table 4), these discrepancies were sorted into seven classes: (a) Two genes (GUK1 and SAG) belonging to two new synteny groups i.e. between HSA1/BTA7 and HSA2/BTA3; (b) two genes (SKI and PDE1A) originally mismapped on the human map and repositioned following the sequencing of the human genome; (c) five genes (CDC20, FABP3, IVL, COP9, CCT8) mismapped on the bovine map and remapped at expected localizations in this work; (d) eight genes (IL6R, HSPA4, SERPINB1, SSBP1, VAV1, HADHSC, RAB18, PSMA7) originally incorrectly identified and remapped either by FISH or SCH analysis at expected localizations in this work; (e) ten genes (SMP1, GAPDL, GLUL, ACTR2, PABPL1,

Table 4. BTA/HSA inconsistent localizations examined in this study. Note: localization of underlined genes (see multispecies comparative table) confirms or supports expected localization of neighbouring gene with grey background.

Gene ^a	HSA map	MMU map	RNO map	BTA map <i>published</i> expected	Reference and mapping mode ^b	BTA localization (this work) when available and comments
GUK1	1q42.13	11B2	(10q22)	7 28/16	Band et al. (2000) RH (new synteny group confirmed)	No BAC but GUK1 on BTA7 defines a new synteny group confirmed by the localization of <u>TRIM17</u> and <u>ARF1</u> on BTA7 (this work, Table 3)
SAG	2q37.1	1C5	9q34	3 2	Band et al. (2000) RH (new synteny group confirmed)	SAG assigned to BTA3 by SCH and defines a new synteny group confirmed by the localization of <u>COP9*</u> and <u>COL6A3</u> on BTA3 (this work, Table 3)
SKI	1p36.32	4E2	(5q36)	<u>16q21</u> 16/33	Sonstegard et al. (2000) F (previously SKI on HSA1q22-q24)	If SKI on HSA1p36.22 (cf UCSC database) OK with BTA16
PDE1A	2q32.1	2D	3q23	2 2/6	Barendse et al. (1997) L (previously PDE1A on HSA4)	If PDE1A on HSA2 (cf UCSC database) OK with BTA2
CDC20	1p34.2	4D1		6 3	Band et al. (2000) RH (mapping error)	CDC20 FISH-mapped to BTA3q35 (this work, Table 3)
FABP3	1p35.2	4D2.3	5q36	6 2	Barendse et al. (1997) L (mapping error)	FABP3 FISH-mapped to BTA2q45 (pers communication)
IVL	1q21.3	3F2	2q34	<u>1q41-46</u> 3	Schmutz et al. (1998) radioactive ISH (mapping error)	IVL FISH-mapped to BTA3q21 (this work, Table 3)
COP9*	2q37.3	(1C5)	(9q34)	25 2/3	Band et al. (2000) RH (mapping error)	COP9 FISH-mapped to BTA3q37 (this work, Table 3)
CCT8	21q21.3	16C3.3	(11q22)	7 1	Band et al. (2000) RH (mapping error)	CCT8 FISH-mapped to BTA1q12.2 (this work, Table 3)
IL6R	1q22	3F2	2q34	19 3	Barendse et al. (1999) L (no bovine sequence so gene identification?)	IL6R assigned by SCH to BTA3 (this work, Table 3)
HSPA4	5q31.1	11B1.3	10q22	<u>3q13</u> 7	Gallagher et al. (1993) FISH (no bovine sequence but the gene mapped in this paper is probably HSPA6)	HSPA4 FISH-mapped to BTA7q22.1 (this work, Table 3)
SERPINO1	6p25.2	13A4	17p12	21 23	Georges et al. (1990) L (no bovine sequence so gene identification?)	SERPINO1 FISH-mapped to BTA23q24 (this work, Table 3)
SSBP1	7q34	6B2	4q23	2 4	Barendse et al. (1997) L (no bovine sequence so gene identification?)	SSBP1 FISH-mapped to BTA4q34 (this work, Table 3)
VAV1	19p13.3	17E1.1	9q11-q12	28 7	Barendse et al. (1999) L (no bovine sequence so gene identification?)	VAV1 FISH-mapped to BTA7q15 (this work, Table 3)
HADHSC	4q25	3H1	2q42	26 6	Band et al. (2000) RH (Acc no AW289352 gives 93% sequence similarity on 87 bp so gene identification?)	HADHSC FISH-mapped to BTA6q15 (this work, Table 3)
RAB18	10p12.1	18A1	(17q12.1)	9 13	Karall-Albrecht et al. (2000) SCH (Acc no AI461405 gives 83% sequence similarity on 184 bp so gene identification?)	RAB18 FISH-mapped to BTA13q15 (this work, Table 3)
PSMA7	20q13.3	2H4	3q43	4 13	Karall-Albrecht et al. (2000) SCH (Acc no AI461430 gives 93% sequence similarity on 99 bp so gene identification?)	PSMA7 FISH-mapped to BTA13q22 (this work, Table 3)
SMP1*	1p36.11	4D3	5q36	14 2	Band et al. (2000) RH (Acc no U89254 in fact = RGS20)	SMP1* FISH-mapped to BTA2q45 (this work, Table 3)
GAPDL	2q11.2			11	Barendse et al. (1999) L (gene identification?)	No GAPDL in human database, in fact probably GAPDL3 on HSA2q11.2 OK with BTA11
GLUL	1q25.3	1G3	(13q21)	10 16	Masabanda et al. (1997) GLUL and GLULP FISH-mapped with sequences Acc no Y10347 (BTA10) and Y10348 (BTA16), respectively	In fact, Y10348 = GLUL (not GLULP) on HSA1q25.3 OK with BTA16q21 .
ACTR2	2p14	(11A3.2)	(14q22)	3 2/11	Band et al. (2000) RH (Acc no U83023 # ACTR2)	In fact, U83023 = GTF2B on HSA1p22.2 OK with BTA3
PABPL1	3q25.2			14 16	Band et al. (2000) RH (Acc no U83076 # PABPL1)	In fact, U83076 = PABPC1 on HSA8q22.3 OK with BTA14
ADCY2	5p15.31	13C1	17p14	15 20	Amarante et al. (1999) FISH (in fact, mapped NCAM1, ref*)	NCAM1 on HSA11q23.1 OK with BTA15

Gene ^a	HSA map	MMU map	RNO map	BTA map published	Reference and mapping mode ^b	BTA localization (this work) when available and comments
CACNO3	12q13	15F2	7q35	14	Band et al. (2000) RH (Acc no AW266991 # CACNO3)	In fact, AW266991 = MAF1 on HSA8q24.3 OK with BTA14
PLCG2	16q23.3	8E1	19q12	13	Schläpfer et al. (1997) SCH (Acc no Y00301 # PLCG2)	In fact, Y00301 = PLCG1 on HSA20q12 OK with BTA13
CSH1	17q23.3	11E1	10q32.1	23	Dietz et al. (1992) L (Acc no J02840 # CSH1)	In fact, J02840 = PRL on HSA6p22.3 OK with BTA23
MSF	17q23.2	11E2	(10q26)	16	Band et al. (2000) RH (Acc no AF056218 # MSF)	In fact, AF056218 = PRG4 on HSA1q31.1 OK with BTA16
NDUFC1	4q31.1	3D	(2)	12	Band et al. (2000) RH (member identification? of gene family)	NDUFC1 FISH-mapped again to BTA12q15 but expected localization on BTA17 supported by SCH mapping of <u>ELF2</u> and <u>RAB33A</u> flanking NDUFC1 (this work, Table 3)
NDUFV2	18p11.2	17E1.2	(9q38)	5	Barcndsc et al. (1997) L (member identification? of gene family)	NDUFV2 FISH-mapped again to BTA5q35 but expected localization on BTA24 supported by RH mapping of <u>TWSG1</u> (AW267141 on BTA24, Band et al, 2000) just below NDUFC1
NAP1L1	12q21.2	10D1	7q21	13	Ma et al. (1998) SCH (member identification? of gene family or mapping error?)	No BAC but expected localization on BTA5 supported by SCH mapping of <u>QSBPL8</u> (BTA5, this work Table 3) just below NAP1L1
UBE2I	16p13.3	17A3.3	10q12	6q34	Antoniou & Gallagher (2002) FISH (member identification? of gene family)	No BAC but expected localization on BTA25 supported by RH mapping of <u>TPSB1</u> (BTA25, Band et al, 2000) just above UBE2I
GNAZ	22q11.2	10B5.3	20p12	22	Aleyasin and Barcndsc (1997) L (gene identification?)	(FISH of "GNAZ" on BTA18q15? in fact = GNAO1) see text
ACK1	3q29	16B2	(11q11)	6	Band et al. (2000) RH (Acc no U96722 = ACK1)	ACK1 FISH-mapped to BTA15q23? open question
GDH	1p36.22	(4E1)	(5q36)	5	Monteagudo et al. (1992) Womack et al. (1986) SCH	No bovine sequence, no primers, no BAC, open question
NRGN	11q24.2	9B	8q21	10	Band et al. (2000) RH (Acc no S78295 = NRGN)	Primers but no BAC, open question
FKSG17*	8q22.3	(4)	(11)	8	Goldammer et al. (2002) SCH + RH (gene identification?)	No BAC, open question
PTGDS	9q34.3	2A.3	3P13	1	Roncoleta et al. (2002) SCH & RH (Acc no AB004647 = PTGDS)	No BAC, open question

^a Gene symbols are from the HUGO Nomenclature database except when no official nomenclature is available to date as indicated by an asterisk.
^b SCH = somatic cell hybrid mapping, RH = radiation hybrid, ISH = in situ hybridisation, FISH = fluorescent ISH, L = linkage mapping, reference: Gautier et al. (2002).

ADCY2, CACNB3, PLCG2, CSH1, MSF) originally misidentified but for which bovine sequences were available allowing us to recover concordant orthologous human/bovine gene pairs and localizations by BLAST analysis of corresponding accession numbers; (f) four genes (NDUFC1, NDUFV2, NAP1L1, UBE2I) for which close neighbouring genes support their expected localization and not that reported in the literature. These genes are members of large gene families sharing sequence similarities, which may impede identification of true orthologous gene pairs; (g) six genes (GNAZ, ACK1, GDH, NRGN, FKSG17, PTGDS) for which informative data could not be obtained. For the GNAZ gene, we isolated two bovine clones both found located on BTA18q15 but verification of the primers used (Table 2) revealed that in fact we had selected

clones for GNAO1 on HSA16q13 in agreement with the localization on BTA18. Furthermore, Pinton et al. (2000) have shown that the caprine "GNAZ" BAC clone (BTA/CHI22) maps to HSA3p21.3 in agreement with comparative mapping data between BTA22 and HSA3, which suggests that this clone may not contain the GNAZ gene. Finally, the ten genes of classes (f) and (g) were not included in our analysis because comparative mapping data were concordant among man, mouse and rat but not with cattle and we consider that a single gene is not sufficient to support the existence of a novel syntenic group. In addition, the existence of paralogs and pseudogenes sharing sequence similarities with a given gene can make it difficult to establish the complete and true comparative chromosome organization among species. Furthermore, as dis-

cussed by Ozawa et al. (2000) for recently duplicated genes a true orthologous gene may not exist in one of the compared species.

Comparative mapping analysis

All genes and ESTs mapped to date in cattle, sheep, goat and pig (2,166) were compiled with corresponding data in man, mouse and rat (see Multispecies Comparative Table accessible online at <http://locus.jouy.inra.fr/>) and a detailed human/cattle/mouse/rat comparative map (Fig. 1) was drawn to propose a direct visualisation of the distribution of conserved chromosomal segments among these four species. Several observations can be derived from our data:

1. The 151 FISH localisations in cattle obtained with caprine BAC clones were all (except one) concordant with those reported in goat by Schibler et al. (1998). This further confirms the high level of genome conservation between the two species and more generally among the three main domestic bovidae, cattle, goat and sheep. It also supports our decision of inferring bovine gene localisations from those mapped only in sheep or goat. Only the COL9A1 gene was found on non-homoeologous bovine and caprine chromosomes i.e. BTA9q12.2 and CHI14q11 → q12. The findings confirm a translocation involving a segment equivalent to the centromeric region of CHI14 or OAR9 (the ovine counterpart) to the centromeric region of BTA9 during evolution from ancestral chromosomes (Vaiman et al., 1996).

2. Correspondences between human and bovine autosomes proposed on the basis of mapped genes agree nearly completely with previous results obtained by heterologous chromosome painting of bovine chromosomes with human individual paints (Hayes, 1995; Solinas-Toldo et al., 1995; Chowdhary et al., 1996). We show the existence of two new synteny groups i.e. (1) between HSA1q42.13 and BTA7q12 and (2) between HSA2q37.1 → q37.3 and BTA3q37. Interestingly, group (1) is supported by comparative mapping data i.e. HSA1/BTA7/MMU11/RNO10, a combination also found on HSA19p and leads us to question the possibility that the telomeric tip of HSA1q44/MMU11/RNO10 may also be conserved with BTA7. At present, we have not succeeded in isolating BAC clones for this chromosomal segment. Group (2) is located at the telomeric end of both HSA2 and BTA3. These two new synteny groups are particularly interesting since they cover chromosome segments BTA7q12 and BTA3q37 not painted by any human chromosome paint (Hayes, 1995) and situated precisely in pericentromeric and telomeric regions with few known mapped genes. It also suggests that when the correspondence of other such small segments (BTA3q12, 4q12 → q13, 4q36, 8q12, 25q24, 28q12 → q13) with human chromosomes are determined, it may reveal conserved syntenies unknown up till now.

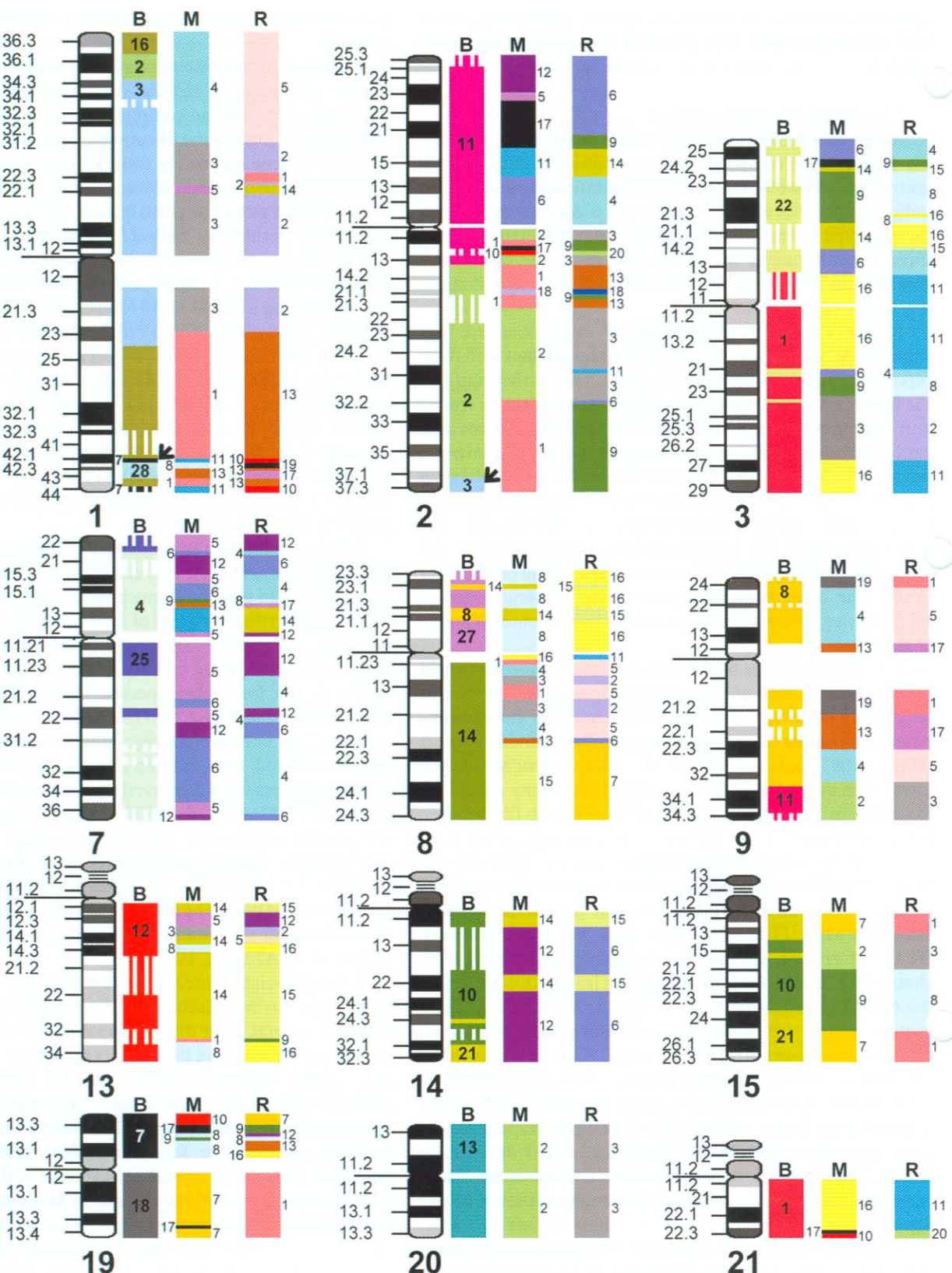
3. Based on Fig. 1, the coverage of bovine autosomes is estimated at ~ 76% if putative segments and centromere interruptions within the same segment are not considered and ~ 89% if they are included. Most of the putatively identified conserved regions are associated with R-negative bands known to be gene poor and the empty regions with pericentromeric, telomeric and satellite regions known to be difficult to map

and characterize because they contain specific repetitive sequences.

4. Figure 1 shows 84 bovine synteny segments conserved on human autosomes, regardless of gene order and excluding interruptions by human centromeres within the same bovine chromosome. Eight of the 84 conserved segments are supported by only one gene mapped in cattle (Multispecies Comparative Table) but were retained because identical synteny correspondences existed along the given human chromosome suggesting that minor reshuffling between these genome regions had occurred during evolution. These 84 bovine/human conserved segments represent a higher number than those in previous reports ranging from 44 to 58 (Hayes, 1995; Solinas-Toldo et al., 1995; Chowdhary et al., 1996; Iannuzzi et al., 1999; Schibler et al., 1998; Band et al., 2000). This increase in number is partly due to the mosaic organization of human/bovine chromosome synteny as for example between HSA11 and BTA15 and 29. Indeed, painting of bovine chromosomes with HSA11 revealed only two synteny groups (the entire BTA15 and BTA29) while comparison of HSA11 with the bovine genome displays a succession of ten segments conserved with BTA15 and 29 in our work (Fig. 1).

5. Based on the data compiled in the Multispecies Comparative Table and on Fig. 1, it is clear that at this level of resolution, the human genome is much more conserved with that of cattle (and pig) than with that of mouse and rat. However, some variation is observed among chromosomes. For example, HSA17 and HSA20 are entirely conserved on single chromosomes in the four other species: HSA17/BTA19/MMU11/RNO10/SSC12 and HSA20/BTA13/MMU2/RNO3/SSC17. In rare cases, the same synteny organisation relative to the human genome is found, as on HSA8p (see Fig. 1) with apparently an identical succession of conserved segments in cattle, mouse, rat i.e. BTA8/27, MMU8/14, RNO16/15, which suggests an ancestral genome organisation maintained in these species. At the other extreme, less than half of one of the smallest human chromosomes i.e. HSA22q11.21 → q12.3 shares conserved segments with two bovine or pig chromosomes and with seven different mouse or rat chromosomes revealing a complex pattern relative to HSA22 (Fig. 1).

6. Seventy-eight synteny interruptions were found between human and bovine autosomes (including centromere interruptions). In general, their distribution does not coincide with R-positive and R-negative band limits except for some instances e.g., along HSA1p, where regions 1p36.33 → p36.31, 1p36.13 → p35.1 and 1p34.3 → p11.2 correspond respectively to parts of BTA16, BTA2 and BTA3. Of the 78 synteny interruptions, 21 are also found in mouse and rat (e.g. see HSA12q23/q24.1, BTA5/17, MMU10C1/5F, RNO7q11/12q16) suggesting that they probably occurred before ruminants and rodents diverged.



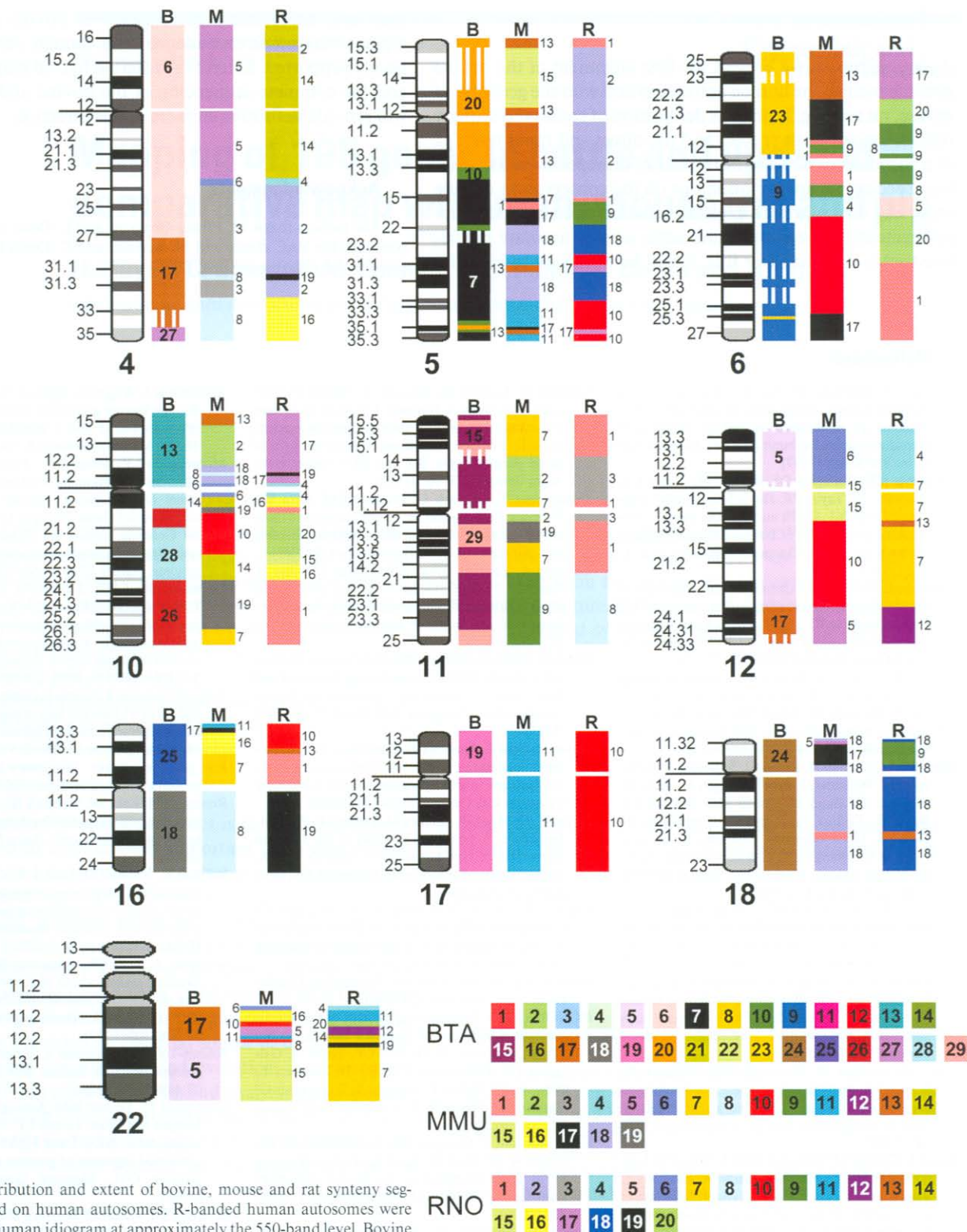


Fig. 1. Distribution and extent of bovine, mouse and rat synteny segments conserved on human autosomes. R-banded human autosomes were taken from the human idiogram at approximately the 550-band level. Bovine (B), mouse (M) and rat (R) conserved segments are aligned along each human autosome and represented by color-coded bars with corresponding chromosome numbers on the bars or next to the bars. The color-codes for each of the three species included in the figure i.e. bovine (BTA), mouse (MMU) and rat (RNO) are given at the bottom of the figure. Solid bars correspond to segments confirmed by at least three loci mapped in two or more species (except in a few cases, see text). Unfilled bars correspond to conserved segments between human and bovine genomes deduced from extended comparisons with mouse, rat and pig mapping data. In a few cases, no bar is drawn

because of lack of mapping information and comparative data among the species. Arrows indicate the two new HSA/BTA synteny groups revealed in this study. Pig was not included in Fig. 1 because the number of mapped loci shared by pig and cattle is relatively small (~ half of the total number of porcine mapped loci) and because bi-directional human/porcine chromosome painting has been reported by Goureau et al. (1996).

Conclusions

In this report, we present the first alignment of the bovine genome with all the human autosomes and with the genomes of mouse, rat and pig. It permits delineation of conserved syntenic regions among these species and the direct and rapid tracking of a chromosomal region of interest of one species in the other four species. To answer questions on the conservation of gene order and on a more complete distribution of conserved syntenic segments between man and cattle, a more accurate predictive tool is essential. For this, it will be necessary to identify,

map and order many more genes in bovine chromosomal regions where correspondence with human chromosomes is poorly supported. Extensive radiation hybrid mapping of genes and the complete sequencing of the bovine and pig genomes will provide definitive answers in this direction.

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References

- Aleyasin A, Barendse W: Novel conserved synteny between human chromosome 22 and cattle chromosome 22 established by linkage mapping of transducin alpha-1 subunit (GNAZ). *Mammal Genome* 8:458-459 (1997).
- Amarante MR, Gallagher DS, Burzlaff JD, Lopes CR, Womack JE, Taylor JF, Davis SK: Physical mapping of ADCY2, FSHB and HBB to bovine chromosome 15 by FISH of bovine bacterial artificial chromosome clones. *Cytogenet Cell Genet* 85:271-272 (1999).
- Antoniou E, Gallagher D: Chromosomal assignment of the bovine ubiquitin-conjugating enzyme E21 (UBE21) gene to BTA6q34 defines a new fragment of conserved synteny with human chromosome 16. *Anim Genet* 33:388-389 (2002).
- Band MR, Larson JH, Rebeiz M, Green CA, Heyen DW, Donovan J, Windish R, Steining C, Mahyuddin P, Womack JE, Lewin HA: An ordered comparative map of the cattle and human genomes. *Genome Res* 10:1359-1368 (2000).
- Barendse W, Vaiman D, Kemp SJ, Sugimoto Y, Armitage SM, Williams JL, Sun HS, Eggen A, Agaba M, Aleyasin SA, Band M, Bishop MD, Buitkamp J, Byrne K, Collins F, Cooper L, Coppettiers W, Denys B, Drinkwater RD, Easterday K, Elduque C, Ennis S, Erhardt G, Li L, et al: A medium-density genetic linkage map of the bovine genome. *Mammal Genome* 8:21-8 (1997).
- Barendse W, Fries R: Genetic linkage mapping, the gene maps of cattle and the lists of loci., in Fries R, Ruvinsky A (eds): *The Genetics of Cattle* (CAB International, Wallingford 1999).
- Chowdhary BP, Fronicke L, Gustavsson I, Scherthan H: Comparative analysis of the cattle and human genomes: detection of ZOO-FISH and gene mapping-based chromosomal homologies. *Mammal Genome* 7:297-302 (1996).
- Dietz AB, Georges M, Threadgill DW, Womack JE, Schuler LA: Somatic cell mapping, polymorphism, and linkage analysis of bovine prolactin-related proteins and placental lactogen. *Genomics* 14:137-143 (1992).
- Eggen A, Gautier M, Billaut A, Petit E, Hayes H, Laurent P, Urban C, Pfister-Genskow M, Eilertsen K, Bishop MD: Construction and characterization of a bovine BAC library with four-genome-equivalent coverage. *Genet Sel Evol* 33:543-548 (2001).
- Gallagher DS Jr, Grosz MD, Womack JE, Skow LC: Chromosomal localization of HSP70 genes in cattle. *Mammal Genome* 4:388-390 (1993).
- Gautier M, Hayes H, Eggen A: An extensive and comprehensive radiation hybrid map of bovine chromosome 15: comparison with human chromosome 11. *Mammal Genome* 13:316-319 (2002).
- Georges M, Lathrop M, Bouquet Y, Hilbert P, Marcotte A, Schwers A, Roupain J, Vassart G, Hanset R: Linkage relationships among 20 genetic markers in cattle. Evidence for linkage between two pairs of blood group systems: B-Z and S-F/V respectively. *Anim Genet* 21:95-105 (1990).
- Goldammer T, Dorroch U, Brunner RM, Kata SR, Womack JE, Schwerin M: Identification and chromosome assignment of 23 genes expressed in meat and dairy cattle. *Chrom Res* 10:411-418 (2002).
- Goureau A, Yerle M, Schmitz A, Riquet J, Milan D, Pinton P, Frelat G, Gellin J: Human and porcine correspondence of chromosome segments using bidirectional chromosome painting. *Genomics* 36:252-262 (1996).
- Hayes H: Chromosome painting with human chromosome-specific DNA libraries reveals the extent and distribution of conserved segments in bovine chromosomes. *Cytogenet Cell Genet* 71:168-174 (1995).
- Hayes H, Petit E, Lemieux N, Dutrillaux B: Chromosomal localization of the ovine beta-casein gene by non-isotopic in situ hybridisation and R-banding. *Cytogenet Cell Genet* 61:286-288 (1992).
- Hayes H, Di Meo GP, Gautier M, Laurent P, Eggen A, Iannuzzi L: Localization by FISH of the 31 Texas nomenclature type I markers to both Q- and R-banded bovine chromosomes. *Cytogenet Cell Genet* 90:315-320 (2000).
- Iannuzzi L, Di Meo GP, Perucatti A, Incarnato D: Comparison of the human with the sheep genomes by use of human chromosome-specific painting probes. *Mammal Genome* 10:719-723 (1999).
- International Human Genome Sequencing Consortium. *Nature* 409:860-921 (2001).
- ISCNDB (2000): International System for Chromosome Nomenclature of Domestic Bovids, Cribriu EP, Di Bernardino D, Di Meo GP, Eggen A, Gallagher DS, Gustavsson I, Hayes H, Iannuzzi L, Popescu CP, Rubes J, Schmitz S, Stranzinger G, Vaiman A, Womack J: *Cytogenet Cell Genet* 92:283-99 (2001).
- Karall-Albrecht C, Groenen MA, van der Poel JJ, Barendse W, Womack JE, Kalm E, Looft C: Mapping of 16 ESTs expressed in the bovine mammary gland during lactation. *Mammal Genome* 11:320-255 (2000).
- Laurent P, Elduque C, Hayes H, Saunier K, Eggen A, Leveziel H: Assignment of 60 human ESTs in cattle. *Mammal Genome* 11:748-754 (2000).
- Libert F, Lefort A, Okimoto R, Womack J, Georges M: Construction of a bovine genomic library of large yeast artificial chromosome clones. *Genomics* 18:270-276 (1993).
- Ma RZ, van Eijk MJ, Beaver JE, Guerin G, Mummery CL, Lewin HA: Comparative analysis of 82 expressed sequence tags from a cattle ovary cDNA library. *Mammal Genome* 9:545-549 (1998).
- Masabanda J, Wigger G, Eggen A, Stranzinger G, Fries R: The bovine glutamine synthase gene (GLUL) maps to 10q33 and a pseudogene (GLULP) to 16q21. *Mammal Genome* 8:794-795 (1997).
- Monteagudo LV, Arruga MV, Tejedor MT, Savva D, Skidmore CJ: Mapping of six genes in cattle using a panel of interspecific hamster X cattle hybrid clones. *Anim Genet* 23(suppl 1):82 (1992).
- Mouse Genome Sequencing Consortium: Initial sequencing and comparative analysis of the mouse genome. *Nature* 420:520-562 (2002).
- Ozawa A, Band MR, Larson JH, Donovan J, Green CA, Womack JE, Lewin HA: Comparative organization of cattle chromosome 5 revealed by comparative mapping by annotation and sequence similarity and radiation hybrid mapping. *Proc natl Acad Sci, USA* 97:4150-4155 (2000).
- Pinton P, Schibler L, Cribriu E, Gellin J, Yerle M: Localization of 113 anchor loci in pigs: improvement of the comparative map for humans, pigs, and goats. *Mammal Genome* 11:306-315 (2000).
- Rat genome project: <http://www.hgsc.bcm.tmc.edu/projects/rat/assembly.html> (2003).
- Roncoleta M, Kata SR, Womack JE, Amaral ME: Mapping the prostaglandin-D synthase gene (PTGDS) to bovine chromosome 1. *Anim Genet* 33:322-323 (2002).
- Schibler L, Vaiman D, Oustry A, Giraud-Delville C, Cribriu EP: Comparative gene mapping: a fine-scale survey of chromosome rearrangements between ruminants and humans. *Genome Res* 8:901-915 (1998).
- Schläpfer J, Kata SR, Amarante MR, Womack JE: Syntenic assignment of thrombomodulin (THBD) and phosphatidylinositol-specific phospholipase C (PLC-II) to bovine chromosome 13. *Anim Genet* 28:308-309 (1997).
- Solinas-Toldo S, Lengauer C, Fries R: Comparative genome map of human and cattle. *Genomics* 27:489-496 (1995).
- Sonstegard TS, Garrett WM, Ashwell MS, Bennett GL, Kappes SM, Van Tassel CP: Comparative map alignment of BTA27 and HSA4 and 8 to identify conserved segments of genome containing fat deposition QTL. *Mammal Genome* 11:682-688 (2000).
- Schmutz SM, Moker JS, Berryere TG: In situ hybridisation of five loci to cattle chromosome 1. *Cytogenet Cell Genet* 81:51-53 (1998).
- Vaiman D, Schibler L, Bourgeois F, Oustry A, Amigues Y, Cribriu EP: A genetic linkage map of the male goat genome. *Genetics* 144:279-305 (1996).
- Venter JC, Adams MD, Myers EW, Li PW, Mural RJ, Sutton GG, Smith HO, Yandell M, Evans CA, Holt RA, et al: *Science* 291:1304-1351 (2001).
- Womack JE, Moll YD: Gene map of the cow: conservation of linkage with mouse and man. *J Hered* 77:2-7 (1986).