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Characterization of the Sheep Complement Factor B gene (*CFB*)

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Keywords: MHC; complement; SNP; polymorphism

21 **Abstract**

22 The Complement Factor B gene (*CFB*) of the alternative complement pathway has been
23 identified in the sheep Major Histocompatibility Complex (MHC) and its genomic
24 sequence determined. *CFB* is located approximately 600bp upstream of the complement
25 C2 gene, contains 18 exons, and manifests the domain signature characteristic of CFB
26 protein. Thirteen single nucleotide polymorphisms were identified in merino sheep and
27 interbreed variation was identified by comparison with International Sheep Genomics
28 Consortium data. Two predicted non synonymous substitutions were observed and *in-silico*
29 analysis indicates that these are likely to have a destabilising effect on the protein structure.
30 Sheep and cattle *CFB* were compared and shown to contain a common nine nucleotide
31 deletion in exon 18 relative to human *CFB*. Predicted CFB amino acid sequences for these
32 two species contain 761 aa relative to 764 aa in the human orthologue. Sequencing of the
33 cosmid and BAC clones used in this study permitted the relative positions of three adjacent
34 loci to be determined and showed that the previously described microsatellite locus (*BfMs*)
35 is located within *SKIV2L*.

36

37 **Keywords:** sheep, cattle, *CFB*, SNP, MHC

38

39 The MHC is the most important region in the vertebrate genome with respect to regulating
40 adaptive immunity, and many studies have identified diverse disease susceptibility loci
41 within this chromosomal region in a variety of mammals (Kumanovics, *et al.* 2003). The
42 MHCs of mammals also include numerous non histocompatibility genes, many of which
43 are closely associated with immune effector mechanisms. In the human MHC, many of
44 these genes occupy an approximately 1 Mb region between the well characterised class I
45 and class II regions and are generally referred to as the central or class III region. Similar
46 structures exist in other mammals including sheep and cattle (Schwaiger, *et al.* 1996),

47 although an inversion of central region genes has been reported in cattle (Liu *et al.*, 2006).
48 The description of a local inversion of the subregion containing sheep complement C4 and
49 the CYP21 loci has been reported previously (Qin *et al.*, 2008).

50

51 There is also evidence that the genomes of many species are comprised of blocks within
52 which recombination is restricted (Dawkins, *et al.*, 1999; Dawkins, *et al.*, 1983; Gabriel, *et*
53 *al.*, 2002). However, Subrahmanyam *et al.* (2001) have shown that sampling variance of the
54 genealogical process may result in linkage disequilibrium-identified block like structures
55 even in the presence of uniform recombination across the region under study. The presence
56 of block like structures in the human MHC has been supported by numerous haplotyping
57 studies (Daly, *et al.*, 2001), and through sperm genotyping which identified so called “hot
58 spots” of recombination (Jeffreys *et al.*, 2001). Therefore, in order to identify MHC
59 haplotypes for disease and productivity studies, it should be possible to genotype markers
60 characteristic of the blocks rather than typing multiple markers at greater cost that would
61 provide redundant information.

62

63 Complement Factor B is a single polypeptide that is an essential component of the
64 alternative pathway of complement activation. Polymorphisms in genes within the central
65 regions of mammalian MHCs, including *CFB*, should help to identify central region blocks
66 or sub-blocks characteristic of sheep MHC haplotypes. In this report, the genomic
67 sequences of sheep and cattle *CFB* are compared with their human orthologues. Single
68 nucleotide polymorphisms (SNP) in sheep *CFB* were identified and a panel of these is
69 reported herein.

70

71 A total of 35,000 colonies from a male sheep cosmid library (Clontec) were plated out and
72 transferred onto nylon membranes (Hybond N+, Amersham). Cosmid clones containing

73 sheep *CFB* sequence were identified through screening of these colonies using a ³²P
74 labelled human *CFB* cDNA clone as a probe (M. Carroll, Oxford). The insert from one of
75 the positive clones (BfC4.2.20) was digested with BamHI and subcloned into pGEM-4Z
76 vector (Promega Life Science).

77

78 Sequences were generated using Big Dye chemistry and a 3730 DNA Analyser (Applied
79 Biosystems). Primers were designed from first pass sequences and the remainder of the
80 *CFB* gene was sequenced progressively in both directions. Final sequence contigs were
81 generated using Vector NTI contig express (Invitrogen). The identification of putative
82 Factor B DNA was performed using BLAST software, while the intron/ exon organization
83 of genes was derived using servers for Twinscan (<http://mblab.wustl.edu/query.html>) (Hu
84 and Brent, 2003) and GAP (<http://deepc2.psi.iastate.edu/aat/align/align.html>) and also
85 DNA Strider software (cmarck@cea.fr) (Douglas, 1994). Multiple sequence alignments
86 were generated using ClustalX software (Thompson *et al.*, 1994).

87

88 Eleven pairs of oligonucleotide primers (Supplementary Table S1) were identified from
89 sheep *CFB* and used to amplify the entire genomic sequence in approximately 500bp
90 overlapping fragments. PCR products generated from at least five randomly selected
91 Australian Merino sheep were sequenced. SNPs were confirmed when at least two
92 heterozygotes and one of each homozygote were observed. SNP typing was performed
93 using PCR and pyrosequencing with Pyro Gold reagents on the PSQTM96MA System (see
94 supplementary Table 2). SNP allele frequencies and inferred haplotypes were determined
95 for two SNP loci (Sh*CFB* 4 and 7) in a panel of 58 merino sheep. The web server versions
96 of iPTree-STAB algorithm (Huang *et al.*, 2007) and 'iMutant' (Capriotti *et al.*, 2004;
97 Capriotti *et al.*, 2005; Capriotti *et al.*, 2008) were used to predict *in-silico* the effects of
98 amino acid substitutions on the stability of the protein.

100 Sequence at the 5' end of cosmid BfC4.2.20 (containing *CFB*) exhibited homology with
101 human *SKIV2L*, while the 3' end exhibited homology with the human complement C2
102 gene, thereby confirming the relative order and distance between these loci (Qin *et al.*,
103 2008). Further sequencing of overlapping subclones showed the presence of *RDBP* close
104 to *SKIV2L* (EF197843). The *RDBP* locus was on the complementary strand relative to the
105 other two loci. Furthermore, the previously described microsatellite locus (Groth and
106 Wetherall, 1995) was identified as being within an intron of the *SKIV2L*. Thus cosmid
107 BfC4.2.20 contained sequences for several genes present in the equivalent region of the
108 human MHC. A diagrammatic representation of the structure of this clone is shown in
109 Figure 1. Furthermore, a detailed map of this central region of the sheep MHC has
110 previously been published (Qin *et al.*, 2008; Liu *et al.*, 2006).

111

112 Sequence data from cosmid BfC4.2.20 showed that sheep *CFB* comprises 5857 bp with 17
113 introns separating 18 exons. The predicted coding sequence was 2283 bp encoding a
114 peptide of 761 aa. An annotated genomic and cDNA sequence of the cattle *CFB* locus was
115 available from GenBank (NW 930219 and XM 591873) together with a predicted *CFB*
116 peptide of 741 aa (XP 591873.2). Comparison of human and sheep *CFB* with the cattle
117 *CFB* showed the presence of an additional cytosine base at position 790 in the 2284 bp
118 *CFB* cattle sequence. Re-sequencing of a 224 bp PCR amplified segment of cattle *CFB*
119 spanning this region confirmed the error in the reported GenBank sequence. When the
120 corrected cattle sequence was aligned to the sheep and human *CFB*, the similarity of cattle
121 *CFB* (and its deduced CDS) became apparent (Supplementary Figure 1). Cattle and sheep
122 *CFB* both share a common nine nucleotide deletion in exon 18. An alignment of the
123 predicted *CFB* peptides from sheep and cattle with the known amino acid sequences of
124 mouse, chimpanzee and human *CFB* is shown in Figure 2. Both human and chimp *CFB*
125 proteins have 764 aa whereas the other three species have 761 aa each. Mouse *CFB* has a

126 nine bp deletion (three amino acids) near the amino terminal end of the peptide. It was
127 noted that the 3' UTR for *CFB* overlaps the 3' end of the sheep *RDBP*, indicating that
128 these two genes are located on opposing strands.

129

130 Nine SNPs were identified within sheep *CFB* (Table 1). Each SNP manifested a minimum
131 allele frequency of ≥ 0.05 and all three genotypes were observed. The availability of 454
132 raw sheep sequences from the International Sheep Genomics Consortium (ISGC -
133 <https://isgdata.agresearch.co.nz/>) permitted pairwise BLAST alignments with the *CFB*
134 sequence reported herein, thereby identifying additional SNPs. Five of the SNPs identified
135 in this study were present in the ISGC sequences, together with additional information
136 concerning the breed of sheep. Four additional SNPs were discovered in the ISGC
137 sequences although their frequency in unrelated sheep is unknown (Table 1). It was noted
138 that the ISGC sequences contained a C/T SNP at position 3147 in the *CFB* sequence which
139 was present in the Awassi, Texel and Poll Dorset sequences but not present in either of the
140 two Merino sheep sequences. This SNP was not observed in our study based on Merino
141 sheep, where its presence would be predicted to change the non-synonymous SNP at
142 position 3149 into a synonymous SNP. *In-silico* analysis of the two non-synonymous
143 SNPs was performed using iMutant (Huang et al., 2007) and iTREE-STAB (Capriotti et al.,
144 2004; Capriotti et al., 2005; Capriotti et al., 2008) and predicted that the mutations L423F
145 and the K544T are probably destabilising to the protein structure. The iMutant $\Delta\Delta$ Free
146 energy was calculated to be -1.54 kcal/mol and -0.28 kcal /mol respectively, with only high
147 confidence support for the L423F mutation. The effects of these mutations on the protein
148 function will require additional investigation.

149

150 It was also observed that for two of the genotyped SNPs present in sheep *CFB* (*ShCFB5*
151 and *ShCFB8*), all four possible haplotypic combinations were observed. Since double

152 recombination events at such a relatively close proximity within a gene are very rare, this
153 observation implies an ancestral inter-allelic gene conversion within the *CFB* locus. Direct
154 evidence for inter-allelic gene conversion has been described for *HLA-DPBI* haplotypes
155 using direct sperm analysis (Zangenberg *et al.*, 1995). Indirect evidence also occurs at the
156 human *ABO* locus (Yip, 2002) and within the class II region of the human MHC
157 (International Immunogenetics Project HLA database) where at least 500 *HLA-DRBI*
158 alleles have been reported. In the latter instance, most polymorphisms occur with exon 2,
159 which is associated with antigen recognition and therefore may be under positive selection.
160 The panel of sheep SNPs described in this report will assist in the identification of MHC
161 haplotypes associated with productivity traits (Bot, 2000; Stear *et al.*, 2009) and
162 supplement existing MHC microsatellite and SNP markers (Groth and Wetherall, 1994;
163 Groth and Wetherall, 1995; Siva Subramaniam *et al.* 2010; Worley *et al.*, 2006).

164

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166

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174

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Table 1: SNPs identified in the CFB gene in sheep.

SNP	Position*	Allele 1	Allele 2	Type*	Present in ISGC sequence & breed type
ShCFB1	757	A	G	Intronic	Yes Mer, Rom
ISGC_1	1358	A	G		Tex
ShCFB2	2245	C	T	Syn (S)	Yes Tex, SBF, AW, PD, Mer
ISGC_2	2320	A	C		Tex
ShCFB3	2423	A	G	Intronic	Yes Mer Rom
ISGC_3	2479	T	C		Rom
ShCFB4	2922	C (0.08)	T (0.92)	Intronic	Yes SBF, AW
ShCFB5	2985	C	T	Intronic	no
ISGC_4	3147	C	T		AW, Tex, PD
ShCFB6	3149	C	G	NS (F->L)	No
ShCFB7	4222	C (0.17)	T (0.83)	Intronic	Yes AW
ShCFB8	4413	A	C	NS (K->T)	No
ShCFB9	5515	C	G	Intronic	No

Notes: 'Position*' refers to base number in the genomic sequence described in this report. Allele frequencies in a panel of 58 unrelated sheep are shown in parentheses. ISGC refers to SNPs identified from the genomic sequence available from the International Sheep Genomics Consortium (<https://isgcdata.agresearch.co.nz/>). Syn = synonymous substitution. NS = non synonymous substitution. Breeds: SB Scottish blackface, AW Awassi, PD Poll Dorset, Tex Texel, Mer Merino, Rom Romney.

Figure1

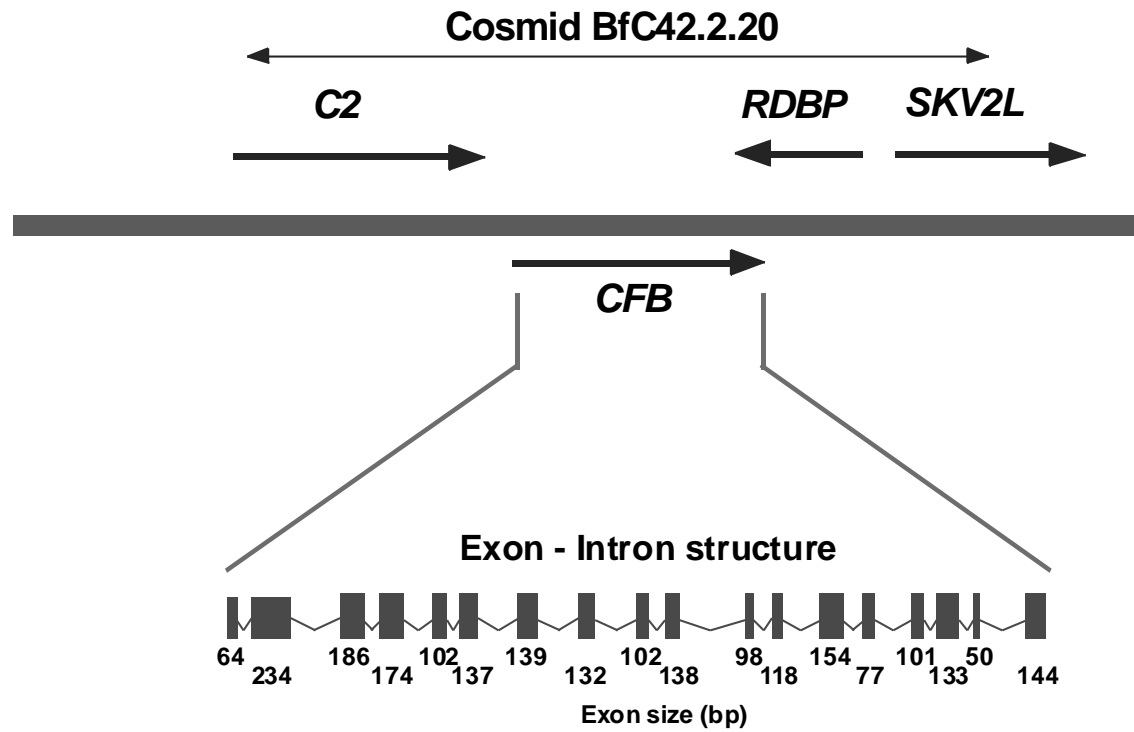


Figure 1: A diagrammatic representation of the cosmid clone and the intron and exon structure of *CFB*. The arrows represent the direction of transcription of the respective genes *C2*, *CFB*, *RDBP* and *SKIV2L*. The intron and exon structure of the *CFB* with exons being represented as shaded boxes and introns as lines between the exons.

Figure2

HosaFB764	MGSNLSPQLC	LMPFILGLLS	GGVTTTPWSL	ARPQGSLSLE	GVEIKGGSFR	LLQEQQALEY	60
PatrFB764P.	.Q.E.....	
MumuFB761	.E.---.....	.VLLV..FS.SA..VLEV.....Q.....G.....	
OvarFB761	.RIGHN.R..	.V.L.....C	..GM..LPE	.G..SP....KA..V...	
BotaFB761	..IGHN.R..	.V.L.....C	..GM..LPE	.G..SP....KA..V...	
HosaFB764	VCPSGFYYP	VQTRTCRSTG	SWSTLKTQDQ	KTVRKAECRA	IHCPRPHDFE	NGEYWPRSPY	120
PatrFB764V.	
MumuFB761	L.....D.Q.R..	.I.Q.....	.R...Q...	...F...F	
OvarFB761	L.....	..I.....	...Q...R	.I.KR...K.	.R...Q...	...AA.	
BotaFB761	L.....	T.I.....	...Q...R	.I.KR...K.	.R...Q...	...AA.	
HosaFB764	YNVSDEISFH	CYDGYTLRGS	ANRTCQVNGR	WSGQTAICDN	GAGYCSNPGI	PIGTRKVGSO	180
PatrFB764	
MumuFB761	..L.Q...QV....E...	.D.....DP....	
OvarFB761	..L.....RF...LG...	.D.E....DP....	.L.....	
BotaFB761	..L.....RG...	.D.E....D	..T..P....	.L.....	
HosaFB764	YRLEDSVTYH	CSRGLTLRGS	QRRTCQEGGS	WSGTEPSCQD	SFMYDTPQEV	AEAFLLSSLTE	240
PatrFB764	
MumuFB761I.....V....	.K.K.....S.....	
OvarFB761R...Y	.N.....V	.Q.....A..	
BotaFB761R...Y	.N.....	EQ...L...A..	
HosaFB764	TIEGVDAEDG	HGPGEQQKRK	IVLDPSGSMN	IYLVLDGSDS	IGASNFTGAK	KCLVNLIKVK	300
PatrFB764	
MumuFB761	...A.....	.S.....S.....	R..T.....	
OvarFB761S.....	V..H.....	N..RDF...	
BotaFB761S.....	V..H.....	N..RDF...	
HosaFB764	ASYGVKPRYG	LVTYATYPKI	WVKVSEADSS	NADWVTKQLN	EINYEDHKLK	SGTNTKKALQ	360
PatrFB764H...DP...	
MumuFB761R.....	.L...V..V	L.R..DER..	D.....EK..	Q.S.....R...	
OvarFB761K...E..V	LI..FDPK..	E.....E..V	R...A.....	A....R..L	
BotaFB761K...E..V	LIR..DPK..	E.....D...	Q...A.....	A....R..L	
HosaFB764	AVYSMMSWPD	DVPPEGWNRT	RHVIILMTDG	LHNMGGDPIT	VIDEIRDLLY	IGKDRKNPRE	420
PatrFB764I.....	
MumuFB761AG	.A.....I....N.V.	..QD..A..D	..R.P.....	
OvarFB761	E..N...RDI	NNLK.T....I....V.	..HD..Y..D	..RN.....	
BotaFB761	E..N...REV	NQFK.T....I....V.	..HD..Y..D	..RN.....	
HosaFB764	DYLDVYVFGV	GPLVNQVNIN	ALASKKDNEQ	HVFKVKDMEN	LEDVFYQMID	ESQSLSLCGM	480
PatrFB764	
MumuFB761DS...HD	..N.....	..TK.....	
OvarFB761	...I.....E...K...	...LQG...	...V..L.	..RT.G...	
BotaFB761	...I.....E...K.K	...LQG...	...V..L.	..RT.G...	
HosaFB764	VWEHRKGTDY	HKQPWQAKIS	VIRPSKGHES	CMGAVVSEYF	VLTAAHCFV	DDKEHSIKVS	540
PatrFB764	
MumuFB761	...K..N..T..L...TM.	..QK.....	
OvarFB761	...KD..P.H....I....EK.....	
BotaFB761	...KD..A.T.....	...I....EK.....	
HosaFB764	VGGEKRDLEI	EVVLFHPNIN	INGKKEAGIP	EFYDYDVALI	KLKNKLYGQ	TIRPICLPCT	600
PatrFB764A....	
MumuFB761	...QR.....	.E.....K..AE...VL.....	
OvarFB761	...KRQEW.V	.E.....	L.A..AK...TK...ET	
BotaFB761	L..QRKEW.V	KEI...K.D	L.A..AK...V	R..E...ET	
HosaFB764	EGTTRALRLP	PTTTCQQQKE	ELLPAQDIKA	LFSVEEEKKL	TRKEVYIKNG	DKKGSCERDA	660
PatrFB764	
MumuFB761	Q.A..K.H..	Q...VK.V..	...QG.S.A.....	
OvarFB761	..SIQ.....	RS.....MQ	...K..E.	...SK.T.	..A.....	...A.....	
BotaFB761	..SIQ.....	RS.....MQ	...K..E.	...SK.T.	..A.....	...A.....	

HosaFB764	QYAPGYDKVK	DISEVVTPRF	LCTGGVSPYA	DPNTRCGDSG	GPLIVHKRSR	FIQVGVISWG	720
PatrFB764	
MumuFB761	TK.Q..E...	.A.....D...K...	
OvarFB761	LH.....	.V.....A...K...I.....	
BotaFB761	LR....E...	.V.....D...K....I.....	
HosaFB764	VVDVCKNQKR	QKQVPAHARD	FHINLFQVLP	WLKEKLQDED	LGFL		764
PatrFB764		764
MumuFB761RD.R.	.QL..SY...D..K...		761
OvarFB761---	PQ...GY...YH...KN..		761
BotaFB761---	PQ...GY...Y....N..		761

Figure 2: Multiple sequence alignment for five mammalian CFB peptides. The reference peptide is human CFB (Accession No. gi67782358). Chimpanzee(Patr) Acc. No. gi29690185. Mumu Acc No. gi6996919. Ovar this study (Acc No. EF446375.1) and Bota Acc. No XP 591873.2 plus this study. The three amino acid deletions present in sheep, cattle and mouse CFB are highlighted as grey shaded dashes.

Supplementary Figure 1: Multiple sequence alignment of human, sheep and cattle *CFB* genomic DNA showing exons and SNPs

EXON 1

```

HumCFB_genDNA      ATGGGGAGCAATCTCAGCCCCAACTCTGCCTGATGCCCTTTATCTTGGGCCTCTGTCT 60
HumCFB_CDS         ATGGGGAGCAATCTCAGCCCCAACTCTGCCTGATGCCCTTTATCTTGGGCCTCTGTCT 60
ShCFB_genDNA       ATGAGGATGGTCAACAACCCCGACTCTGCCTGGTACCCTTGATCCTGGGCCTCTGTGT 60
SheepCFB_CDS       ATGAGGATGGTCAACAACCCCGACTCTGCCTGGTACCCTTGATCCTGGGCCTCTGTGT 60
BovCFB_genDNA      ATGGGGATGGTCAACAACCCCGACTCTGCCTGGTACCCTTGATCCTGGGCCTCTGTGT 60
BovCFB_CDS         ATGGGGATGGTCAACAACCCCGACTCTGCCTGGTACCCTTGATCCTGGGCCTCTGTGT 60
                    *** ** * ** * ** * ** * ** * ** * ** * ** * ** * ** * ** *

```

EXON 2

```

HumCFB_genDNA      GGAGGTAAGCGAGGGTAA-----CCTTCCCTTCCTGCTGTCTCCAGCATCCCTCCT 111
HumCFB_CDS         GGAG----- 64
ShCFB_genDNA       GGAGGTAAGTGAGATCACAGCCCTC-TCCCTCCACTCCTGCTTCCCCACAATCTGTCT 119
SheepCFB_CDS       GGAG----- 64
BovCFB_genDNA      GGAGGTAAGTGAGATCACAGCCCTCCTCCACTCCTGCTTCCCCACGATCCGTCT 120
BovCFB_CDS         GGAG----- 64
                    ****

```

EXON 3

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HumCFB_genDNA      TGGCCTTTTGGGGCCAGGCTTCATCAGCCTTTCTCTTCAGGTTGTGACCACCCTCCATGG 171
HumCFB_CDS         -----GTGTGACCACCCTCCATGG 84
ShCFB_genDNA       CGGCCTTGAGGCTGGGCCTCACCAACTTTTCTCTTTAGGTTGGGCATGACACCCTG 179
SheepCFB_CDS       -----GTGTGGGCATGACACCCTG 84
BovCFB_genDNA      CGGCCTTGAGGCTGGGCCTCACCAACTTTTCTCTTTAGGTTGGGCATGACGCCATTG 180
BovCFB_CDS         -----GTGTGGGCATGACGCCATTG 84
                    ***** ** ** ** *

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EXON 4

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HumCFB_genDNA      TCTTTGGCCCGGCCAGGGATCCTGCTCTCTGGAGGGGTAGAGATCAAAGCGGCTCC 231
HumCFB_CDS         TCTTTGGCCCGGCCAGGGATCCTGCTCTCTGGAGGGGTAGAGATCAAAGCGGCTCC 144
ShCFB_genDNA       CCTGAGGCTGGGCCTCAAAGCCCTGCTCTCTGGAGGGGTAGAGATCAAAGGTGGCTCC 239
SheepCFB_CDS       CCTGAGGCTGGGCCTCAAAGCCCTGCTCTCTGGAGGGGTAGAGATCAAAGGTGGCTCC 144
BovCFB_genDNA      CCTGAGGCTGGGCCTCAAAGCCCTGCTCTCTGGAGGGGTAGAGATCAAAGGTGGCTCC 240
BovCFB_CDS         CCTGAGGCTGGGCCTCAAAGCCCTGCTCTCTGGAGGGGTAGAGATCAAAGGTGGCTCC 144
                    ** ** * ** * ** * ** * ** * ** * ** * ** * ** * ** * ** *

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EXON 5

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HumCFB_genDNA      TTCCGACTTCTCAAGAGGGCCAGGCACCTGGAGTACGTGTGCTCTTCTGGCTTCTACCCG 291
HumCFB_CDS         TTCCGACTTCTCAAGAGGGCCAGGCACCTGGAGTACGTGTGCTCTTCTGGCTTCTACCCG 204
ShCFB_genDNA       TTCCGGCTTCTCAAGGGGGCCAGGTGCTGGAGTACTTGTGCTCTTCTGGCTTCTACCCA 299
SheepCFB_CDS       TTCCGGCTTCTCAAGGGGGCCAGGTGCTGGAGTACTTGTGCTCTTCTGGCTTCTACCCA 204
BovCFB_genDNA      TTCCGGCTTCTCAAGGGGGCCAGGTGCTGGAGTACTTGTGCTCTTCTGGCTTCTACCCA 300
BovCFB_CDS         TTCCGGCTTCTCAAGGGGGCCAGGTGCTGGAGTACTTGTGCTCTTCTGGCTTCTACCCA 204
                    ***** ** * ** * ** * ** * ** * ** * ** * ** * ** *

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EXON 6

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HumCFB_genDNA      TACCCTGTGCAGACAGTACCTGCAGATCTACGGGGTCTGGAGCACCTGAAGACTCAA 351
HumCFB_CDS         TACCCTGTGCAGACAGTACCTGCAGATCTACGGGGTCTGGAGCACCTGAAGACTCAA 264
ShCFB_genDNA       TATCCTGTGCAGATTCGCACCTGCAGATCCACAGGGTCTGGAGCACCTGCAGACTCAA 359
SheepCFB_CDS       TATCCTGTGCAGATTCGCACCTGCAGATCCACAGGGTCTGGAGCACCTGCAGACTCAA 264
BovCFB_genDNA      TACCCACGCAGATTCGCACCTGCAGATCCACAGGGTCTGGAGCACCTGCAGACTCAA 360
BovCFB_CDS         TACCCACGCAGATTCGCACCTGCAGATCCACAGGGTCTGGAGCACCTGCAGACTCAA 264
                    ** ** * ** * ** * ** * ** * ** * ** * ** * ** * ** * ** *

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EXON 7

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HumCFB_genDNA      GACCAAAGACTGTCAAGAGGGCAGAGTGCAGAGTTTGAGGGCAATGAGTGTGGCAGT 411
HumCFB_CDS         GACCAAAGACTGTCAAGAGGGCAGAGTGCAGAG----- 298
ShCFB_genDNA       GACAGAAAGATTGTCAAGAGGGCTGAATGCAAAGTTGGAGGGCAGTGAAGTGGGCATG 419
SheepCFB_CDS       GACAGAAAGATTGTCAAGAGGGCTGAATGCAAAG----- 298
BovCFB_genDNA      GACAGAAAGATTGTCAAGAGGGCTGAATGCAAAGTTGGAGGGCAGTGAAGTGGGCATG 420
BovCFB_CDS         GACAGAAAGATTGTCAAGAGGGCTGAATGCAAAG----- 298
                    *** ***** ** * ** * ** * ** * ** *

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EXON 8

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HumCFB_genDNA      GGCTAAGGCAGAAACAGGGCAGCGGCAGCAAGGTCAGGACTAGGAT----- 459
HumCFB_CDS         ----- 459
ShCFB_genDNA       GGCCGGCTGTGGGACGGAGCAGGTGGCAGCCAAGGTCAGACTTGAATAAGTCTAGGCTT 479
SheepCFB_CDS       ----- 479
BovCFB_genDNA      GGCTGGCTGTGGGACGGAGCAGGTGGCAGCCAAGGTCAGACTTGGATAAGTCTAGGCTT 480
BovCFB_CDS         ----- 480

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EXON 9

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HumCFB_genDNA      ----GAGACTAGGCAGGGTGACAAGGTGGGCTGACCGGGAGTAGGAGCAGTTTTAGGGT 514
HumCFB_CDS         ----- 514
ShCFB_genDNA       GAGTGGAGACCAGGCAGGCTGAAAAGTTGGGCTGAGCACGGGTGAGAGCTGAGCGAGGGT 539
SheepCFB_CDS       ----- 539
BovCFB_genDNA      GAGTGGAGACCAGGCAGGCTGACAAGTTGGGCTGAGCACGGGTGAGAGCTGAGCGAGGGT 540
BovCFB_CDS         ----- 540

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EXON 10

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HumCFB_genDNA      GGCAGGCGGAAAGGGGGCAAGAAAAGCGGAGTTAACCTTACTAAGCATTTACCTTGGG 574
HumCFB_CDS         ----- 574
ShCFB_genDNA       TGGAGGTGGGATGGAGAGAGAAGGAAGGGGAGCTAGACTTTACTAAGCATTTACCTTGTG 599
SheepCFB_CDS       ----- 599
BovCFB_genDNA      TGGAGGTGGGATGGAGAGAGAAGGAAGGGGAGCTAGACTTTACTAAGCATTTACCTTGTG 600
BovCFB_CDS         ----- 600

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HumCFB_genDNA	CTTCCAGGCAGCCCTGGAAGTCAAGAGAACAACACTCAGAAATGGGGAGGGAGAAGCAGTGG	634
HumCFB_CDS	-----	
ShCFB_genDNA	---TCAGGCAGCCCTGGCAGTTCAAAGAACAACCTTAGAAATGGGGAGGGAGCAGCAGT	656
SheepCFB_CDS	-----	
BovCFB_genDNA	---TCAAGCAGTCCCGGTAGTTCAAAGAACAACCTTAGAAATGGGGAGCGGGGAGCAGCAGT	657
BovCFB_CDS	-----	
HumCFB_genDNA	AATCCATATGGGTTGAGG-----AGTAGGTAAGATGCTGCTTCTGCGGGACTGGG	684
HumCFB_CDS	-----	
ShCFB_genDNA	ACTCCTTATGGGTGGAGGCTCCTCCAGGGTTCGAGGGTAGTAGCTATCCTGTGGGGCCCA	716
SheepCFB_CDS	-----	
BovCFB_genDNA	ACTCCTTATGGGTGGAGGTTCTCCAGGGTTCGAGGGTAGTAGCTATTCTGTGAGGCCCA	717
BovCFB_CDS	-----	
HumCFB_genDNA	AATGCGCTGTTTTCTCAGTGACATGGTCTCCGAGACCAGGAGGGATACACCTAAGG--CAG	742
HumCFB_CDS	-----	
ShCFB_genDNA	GAAGTTATATTTCTCAGTGACAGGGTCCCTGAGACCAGAAAGGTTATCCTAAAGGGGCAG	776
	(G)	
SheepCFB_CDS	-----	
BovCFB_genDNA	GAAGTGGTATTTCTCAGTGACAGGGTCCCTGAGACCAGAAAGGTTATCCTAAAGGG--CAG	776
BovCFB_CDS	-----	
	EXON 3	
HumCFB_genDNA	CCTTCCCTCTTGATGACTTCTACTTG-----TCCCCCTTCTCAAAGCAATCCACT	794
HumCFB_CDS	-----CAATCCACT	307
ShCFB_genDNA	CCCTTCCCTTCCAGTAACCTTCTACTTGGTTTCCACCTCCTTGCCCCAAAGCAATTCGCT	836
SheepCFB_CDS	-----CAATTCGCT	307
BovCFB_genDNA	CCCTTCCCTTCCAGTAACCTTCTACTTGGTCTCCACCCCTTGCCCCAAAGCAATTCGCT	836
BovCFB_CDS	-----CAATTCGCT	307
	**** * **	
HumCFB_genDNA	GTCCAAGACCACAGACTTCGAGAACGGGAATACTGGCCCCGGTCTCCCTACTACAATG	854
HumCFB_CDS	-----	367
ShCFB_genDNA	GTCCAAGACCACAGGATTTTGGAGATGGGGAGTACTGGCCCCGGCTGCTACTACAATG	896
SheepCFB_CDS	-----	367
BovCFB_genDNA	GTCCAAGACCACAGGATTTTGGAGATGGGGAGTACTGGCCCCGGCTGCTACTACAATG	896
BovCFB_CDS	-----	367
	***** ** * ***** ***** ***** ***** ** *****	
HumCFB_genDNA	TGAGTGATGAGATCTCTTCCACTGCTATGACGGTTACTCTCCGGGGCTCTGCCAATC	914
HumCFB_CDS	-----	427
ShCFB_genDNA	TGAGCGATGAGATCTCTTCCGCTGCTATGATGGCTACTCTTCCGGGGCTCTGCCAATC	956
SheepCFB_CDS	-----	427
BovCFB_genDNA	TGAGCGATGAGATCTCTTCCGCTGCTATGATGGCTACTCTTCCGGGGCTCTGCCAATC	956
BovCFB_CDS	-----	427
	***** ***** ***** ***** ** ***** * *****	
HumCFB_genDNA	GCACCTGCCAAGTGAATGGCCGATGGAGTGGGCAGACAGCGATCTGTGACAACGGAGTG	974
HumCFB_CDS	-----	484
ShCFB_genDNA	GCACCTGCCTAGGGAATGGTCCGTTGGGATGGGGAAACGGCCATCTGTGATGATGGAGTG	1016
SheepCFB_CDS	-----	484
BovCFB_genDNA	GCACCTGCCAAGGAATGGTCCGTTGGGATGGGGAAACGGCCATCTGTGATGATGGAGTG	1016
BovCFB_CDS	-----	484
	***** ** ***** ** ** ***** * ** * ***** * ****	
HumCFB_genDNA	AGAAGCATCCCCTC--CCCTACATTTGCTGTCTCCCTGACGGCGCCAGCCGAGGAGT	1031
HumCFB_CDS	-----	
ShCFB_genDNA	AGAACCGTCCCCCG--TCCACAACAGCTCCTTCTCCCTGACCACCTGCAGCCTGAGGAA--	1074
SheepCFB_CDS	-----	
BovCFB_genDNA	AGAACCGTCCCCCTGTCCACAACAGCTCCTTCTCCCTGACCACCGCAGCCTGAGGAA--	1075
BovCFB_CDS	-----	
HumCFB_genDNA	GGGCACTCGGCTCCGGACACTGTAACCTTTGCTCTTACCTTGTCTACGGGGCCTCAGGC	1091
HumCFB_CDS	-----	
ShCFB_genDNA	-----CCAGGGCCACAGCTCCTGGTGTCTGCTTGTGCTTTTGGCCCCAGGC	1122
SheepCFB_CDS	-----	
BovCFB_genDNA	-----CCAGTGCCACAGCTCTCGGTTCTTGTGCTTGTGCTTTTGGCCCCAGGC	1123
BovCFB_CDS	-----	
	EXON 4	
HumCFB_genDNA	TTCAGTGCTTACCTCGATGTCTCATACCTTGCAGCGGGGTACTGCTCCAACCCGGGCAT	1151
HumCFB_CDS	-----CGGGGTACTGCTCCAACCCGGGCAT	509
ShCFB_genDNA	TTTGGCCCTCACCAGTGTGTCTTACACTTCTGCAGCGGGGTACTGCCCCAACCCGGGCAT	1182
SheepCFB_CDS	-----CGGGGTACTGCCCCAACCCGGGCAT	509
BovCFB_genDNA	TTTGGCCCTCACCAGTGTGTCTTACACTTCTGCAGCGAGTACTGCCCCAACCCGGGCAT	1183
BovCFB_CDS	-----CGACGTACTGCCCCAACCCGGGCAT	509
	** ***** *****	
HumCFB_genDNA	CCCCATTGGCACAAGGAAGTTGGGCAGCCAGTACCGCCTTGAAGACAGCGTACCTACCA	1211
HumCFB_CDS	-----	569
ShCFB_genDNA	CCCCCTTGGCACGAGGAAGTTGGGCAGCCAGTACCGCCTTGAAGATCGTGTACCTACTA	1242
SheepCFB_CDS	-----	569
BovCFB_genDNA	CCCCCTTGGCACGAGGAAGTTGGGCAGCCAGTACCGCCTTGAAGACCGTGTACCTACTA	1243
BovCFB_CDS	-----	569

BovCFB_CDS CCCCCTTGGCACGAGGAAGGTGGGCGAGCCAGTACCGCCTTGAAGACCGTGTACCTACTA 569
**** *
HumCFB_genDNA CTGCAGCCGGGGCTTACCCTGCGTGGCTCCCAGCGGCAGCGTGTGAGGAAGGTGGCTC 1271
HumCFB_CDS CTGCAGCCGGGGCTTACCCTGCGTGGCTCCCAGCGGCAGCGTGTGAGGAAGGTGGCTC 629
ShCFB_genDNA CTGCAACCGGGGCTCACTCTACGTGGTTCCAGCAGCGAACATGCCAGGAAGGTGGCTC 1302
SheepCFB_CDS CTGCAACCGGGGCTCACTCTACGTGGTTCCAGCAGCGAACATGCCAGGAAGGTGGCTC 629
BovCFB_genDNA CTGCAACCGGGGCTCACTCTACGTGGTTCTGAGCAGCGAACATGCCTGGAAGGTGGCTC 1303
BovCFB_CDS CTGCAACCGGGGCTCACTCTACGTGGTTCTGAGCAGCGAACATGCCTGGAAGGTGGCTC 629
**** *
HumCFB_genDNA TTGGAGCGGGACGGAGCCTTCCTGCCAAGGTGACCTTTG---ACCTGTACCCCCAGGTCA 1328
HumCFB_CDS TTGGAGCGGGACGGAGCCTTCCTGCCAAG--- 658
ShCFB_genDNA TTGGAGTGAACAGAGCCTTCCTGCCAAGGTGACCTTACTTATCTGTACCCTCAGGTCA 1362
SheepCFB_CDS TTGGAGTGAACAGAGCCTTCCTGCCAAG--- 658
BovCFB_genDNA TTGGAGTGAACGGAGCCTTCCTGCCAAGGTGACCTTA---TCTGTACCCTCAAGTCA 1359
BovCFB_CDS TTGGAGTGAACGGAGCCTTCCTGCCAAG--- 658
***** *
HumCFB_genDNA GATCCTGGTCTTCCATCCTACTGTCTTCTCTCCCACCTCAACCCTGCTCTTTCCTCACT 1388
HumCFB_CDS -----
ShCFB_genDNA GACCCTGTCTCCCATCCGCACATCCCCCAGGAGCATACTGCCATCTCCCGCTGCCACC 1422
SheepCFB_CDS -----
BovCFB_genDNA GACCCTGTCTCCCATCTGCACATCCCCCTCAGGAGCGCACTGCCTTCTCTCACTGCCACC 1419
BovCFB_CDS -----
HumCFB_genDNA TTGTTTAAACCTCCCTGTACAATATCTCACTTCTGAGCCTTTTATACCCTGGAAACCCA 1448
HumCFB_CDS -----
ShCFB_genDNA ATCCAGCTCCTTCTCCCTTCTTAAATCTCCCCGAAGAGCTTCTGAGCCTTCCGCCCCA 1482
SheepCFB_CDS -----
BovCFB_genDNA ATCCAGCTCCTTCTCCCTTCTTAAATCTCCCAGAAGACTTCTAAGCCCTTCCCGCCC 1479
BovCFB_CDS -----
HumCFB_genDNA TGATCCCCGCTCTTTGGTCACTGTATCCCTGACACTCCAGACATTTGACCTCATTTT 1508
HumCFB_CDS -----
ShCFB_genDNA GAAGCCCACCACTCCTGT---CAGTGTCCCTGACCCTCCAGACATTTGACCTGCTCTC 1539
SheepCFB_CDS -----
BovCFB_genDNA CTGAAGCCACCACTCTCGTGT---CAGTGTCCCTGACCCTCCAGACATTTGACCTGCTCTC 1538
BovCFB_CDS -----
EXON 5
HumCFB_genDNA TGAC-TCTCCAG-ACTCCTTATGTACGACACCCTCAAGAGGTGGCCGAAGCTTTCCT 1566
HumCFB_CDS -----ACTCCTTATGTACGACACCCTCAAGAGGTGGCCGAAGCTTTCCT 704
ShCFB_genDNA TGACCTCTCCAG-ACTCCTTATGTACGACACTCCTGCAGAGGTGGCCGAAGCTTTCCT 1598
SheepCFB_CDS -----ACTCCTTATGTACGACACTCCTGCAGAGGTGGCCGAAGCTTTCCT 704
BovCFB_genDNA TGATCTCTCCAG-ACTCCTTATGTACGACACTCCTGCAGAGGTGGCCGAAGCTTTCCT 1598
BovCFB_CDS -----ACTCCTTATGTACGACACTCCTGCAGAGGTGGCCGAAGCTTTCCT 704
***** *
HumCFB_genDNA GTCTTCCCTGACAGAGACCATAGAAGGAGTGCATGCTGAGGATGGGCACGGCCAGGTTT 1626
HumCFB_CDS GTCTTCCCTGACAGAGACCATAGAAGGAGTGCATGCTGAGGATGGGCACGGCCAG---- 760
ShCFB_genDNA GTCTTCCCTGACAGAGACCATAGAAGGAGTTGATGCCGAGGATGGACACAGCCAGGTTT 1658
SheepCFB_CDS GTCTTCCCTGACAGAGACCATAGAAGGAGTTGATGCCGAGGATGGACACAGCCAG---- 760
BovCFB_genDNA GTCTTCCCTGACAGAGACCATAGAAGGAGTTGATGCCGAGGATGGACATAGCCAGGTTT 1658
BovCFB_CDS GTCTTCCCTGACAGAGACCATAGAAGGAGTTGATGCCGAGGATGGACATAGCCAG---- 760
***** *
HumCFB_genDNA GAAGACAGAGA----AGGGAGGCAGGGCAGGGAAGTGGGGAAAATGGAGAAGGGACAGA 1682
HumCFB_CDS -----
ShCFB_genDNA GAAGGCAGAGGGG--AGGCAGGGGAGTTGGGCCTGGGGTGGAGAAGGGGCAGGAGA 1716
SheepCFB_CDS -----
BovCFB_genDNA GAAGGCAGAGAGGGGAGGCGGGCAGGGAGTTGGGCATGGGGTGGAGAAGGGGCAGGAGA 1718
BovCFB_CDS -----
EXON 6
HumCFB_genDNA ACTGTTAATGCTGGAGCCTGAGCCACTCTCTGGCACCCAGGGGAACAACAGAAGCGGAA 1742
HumCFB_CDS -----GGGAACAACAGAAGCGGAA 779
ShCFB_genDNA CCTATTTGTTCTGGAGCCTGAGCCTCTCTGATGGCATCCAGGGGAACAACAGAAGAGAAA 1776
SheepCFB_CDS -----GGGAACAACAGAAGAGAAA 779
BovCFB_genDNA CCTCTTTGTTCTGGAGCCTGAGCCTCTCTGGTGACATCCAGGGGAACAACAGAAGAGAAA 1778
BovCFB_CDS -----GGGAACAACAGAAGAGAAA 779
***** *
HumCFB_genDNA GATCGTCTGGACCCCTCAGGCTCCATGAACATCTACCTGGTGTAGATGGATCAGACAG 1802
HumCFB_CDS GATCGTCTGGACCCCTCAGGCTCCATGAACATCTACCTGGTGTAGATGGATCAGACAG 839
ShCFB_genDNA GATTTCCCTGGACCCCTCAGGCTCCATGAACATCTACCTGGTATTGGATGGATCAGACAG 1836
SheepCFB_CDS GATTTCCCTGGACCCCTCAGGCTCCATGAACATCTACCTGGTATTGGATGGATCAGACAG 839
BovCFB_genDNA GATTTCCCTGGACCCCTCAGGCTCCATGAACATCTACCTGGTATTGGATGGATCAGACAG 1838
BovCFB_CDS GATTTCCCTGGACCCCTCAGGCTCCATGAACATCTACCTGGTATTGGATGGATCAGACAG 839
*** *
HumCFB_genDNA CATTTGGGGCCAGCAACTTCACAGAGCCAAAAGTGTCTAGTCAACTTAATTGAGAAGGT 1862
HumCFB_CDS CATTTGGGGCCAGCAACTTCACAGAGCCAAAAGTGTCTAGTCAACTTAATTGAGAAG-- 897
ShCFB_genDNA CGTGGGGGCCCAACTTCACAGGGCCAAAAGTGTCTCAGAGATTTCAATTGAGAAGGT 1896
SheepCFB_CDS CGTGGGGGCCCAACTTCACAGGGCCAAAAGTGTCTCAGAGATTTCAATTGAGAAG-- 897
BovCFB_genDNA CGTGGGGGCCCAACTTCACAGGGCCAAAAGTGTCTCAGAGATTTCAATTGAGAAGGT 1898

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BovCFB_CDS      CGTGGGGGCCCAACTTCACAGGGGCCAAGAATGTCTCAGAGATTTTCATCGAGAAG-- 897
* * * * *          * * * * *          * * * * *          * * * * *          * * * * *

HumCFB_genDNA   GGAATCCTCCTATCCCTGAACCTCGGGGGAATGGAA---TCTCGTGATCTTCCAGGACTA 1919
HumCFB_CDS      -----
ShCFB_genDNA   GGGGCCCTCCCTTGAAGGTGGGAAC----- 1924
SheepCFB_CDS   -----
BovCFB_genDNA  GGGGCCCTCCCTTGAAGGTGGGAACCTTGAAGGACCTCACTGCCCTGCCAGGACTA 1958
BovCFB_CDS     -----

HumCFB_genDNA   GCTCCCTGATCATTCAGCCCCTCTGAACAACAGGGCCCCAGGAAAATCTCCAGGTCCTA 1979
HumCFB_CDS     -----
ShCFB_genDNA   -----TCCAGCCCCTCTGAGCCACAGGGTCCAG-AAAATCTCCAGGTCCCA 1971
SheepCFB_CDS   -----
BovCFB_genDNA  GTTCCCAAATACCTCCAGCCCCTTGGAGCCACAGGGTCCAG-AAAATCTCCAGGTCCCTA 2017
BovCFB_CDS     -----

HumCFB_genDNA   TTCTGTCTCCTTCCCTTTTACTTGAAGCAGTTTCTTGACTGGTAATTCCTCCATGAACC 2039
HumCFB_CDS     -----
ShCFB_genDNA   TTGTGTCTCCTTTCCTTTTACTTGAACCTTTAACTTGGACTCCTCCATGACCCCAGGGTG 2031
SheepCFB_CDS   -----
BovCFB_genDNA  TTGTGTCTTCTTTCCTTTTACTTGAACCTTTAACTTGGACTCCTCCATGACCTCAGGGTG 2077
BovCFB_CDS     -----

HumCFB_genDNA   -----TCAGCCCTGAGCCTCTTACTGAGAGCCTCCCT----GTCCCAGCAAAGTCGCTG 2090
HumCFB_CDS     -----
ShCFB_genDNA   ATGAGTCAGTCTTGAGTCTCTTACTAAGGACTTTCCTATCTGTCTCAGCCAAGTGCTG 2091
SheepCFB_CDS   -----
BovCFB_genDNA  ATGAGTCAGTCTTGAGTCTCTTACTAAGGACTTTCCTATCTGTCTCAGCCAGTGCTG 2137
BovCFB_CDS     -----

HumCFB_genDNA   AAATCTCCAATCAGTATTCTATTTTCAATGCCATGGCGCCTTGTTCTCCTCACCAC 2150
HumCFB_CDS     -----
ShCFB_genDNA   AATCTCCAATCGTA-TATTCTACTTTTGATGCTGTGACCTATTGCTTCCCTTGCCCAC 2150
SheepCFB_CDS   -----
BovCFB_genDNA  AATCTCCAACCGTA-TATTCTCTTTTGATGCTGTGACCTATTGCTCCTCAGCCCAC 2196
BovCFB_CDS     -----

                    EXON 7

HumCFB_genDNA   AGGTGGCAAGTTATGGTGTGAAGCCAAGATATGGTCTAGTGACATATGCCACATACCCCA 2210
HumCFB_CDS     --GTGGCAAGTTATGGTGTGAAGCCAAGATATGGTCTAGTGACATATGCCACATACCCCA 955
ShCFB_genDNA   AGGTGGCAAGCTACGGGGTGAAGCCAAAATATGGGCTAGTGACATATGCCACAGAACCCA 2210
SheepCFB_CDS   --GTGGCAAGCTACGGGGTGAAGCCAAAATATGGGCTAGTGACATATGCCACAGAACCCA 955
BovCFB_genDNA  AGGTGGCAAGCTATGGGGTGAAGCCAAAATATGGTCTAGTGACATATGCCACAGAACCCA 2256
BovCFB_CDS     --GTGGCAAGCTATGGGGTGAAGCCAAAATATGGTCTAGTGACATATGCCACAGAACCCA 955
                    * * * * *          * * * * *          * * * * *          * * * * *          * * * * *

HumCFB_genDNA   AAATTTGGGTCAAAGTGTCTGAAGCAGACAGCAGTAATGCAGACTGGGTCACGAAGCAGC 2270
HumCFB_CDS     AAATTTGGGTCAAAGTGTCTGAAGCAGACAGCAGTAATGCAGACTGGGTCACGAAGCAGC 1015
ShCFB_genDNA   AAGTTTGTGATCAAAGTGTTCGATCCAAAGAGCAGTGAAGCAGACTGGGTCACGAGCAGC 2270
                    C [AGT/S -> AGC/S]

SheepCFB_CDS   AAGTTTGTGATCAAAGTGTTCGATCCAAAGAGCAGTGAAGCAGACTGGGTCACGAGCAGC 1015
BovCFB_genDNA  AAGTTTGTGATCAGAGTGTCCGACCCAAAGAGCAGCGAAGCAGACTGGGTCACGAGCAGC 2316
BovCFB_CDS     AAGTTTGTGATCAGAGTGTCCGACCCAAAGAGCAGCGAAGCAGACTGGGTCACGAGCAGC 1015
                    ** * * * * *          * * * * *          * * * * *          * * * * *          * * * * *

HumCFB_genDNA   TCAATGAAATCAATTATGAAGGTCAGAGGTTAGGGAATGGTGGGAGGTTCACTTTGGGGT 2330
HumCFB_CDS     TCAATGAAATCAATTATGAAG----- 1036
ShCFB_genDNA   TCAACCGAATCAACTACGAGGTCAGAAGTCAGGGAAGGGTGGGAGGTTCACTTTAGGGT 2330
SheepCFB_CDS   TCAACCGAATCAACTACGAG----- 1036
BovCFB_genDNA  TCAACCAAATCAACTACGAGGTCAGAAGTCAGGGAAGGGTGAAGGTTCACTTTGGGGT 2376
BovCFB_CDS     TCAACCAAATCAACTACGAG----- 1036
                    ****          *****          * * * * *

HumCFB_genDNA   CAGGAGGTTTCAGG----- 2343
HumCFB_CDS     -----
ShCFB_genDNA   CAGAGAGGTCAGAAGTCAGGGAAGGGTGGGAGGTTCACTTTGGTCTGAAGTTTCAGAAGT 2390
SheepCFB_CDS   -----
BovCFB_genDNA  CAGAGAGTCTGAAGT-----TTCAGGAGT 2401
BovCFB_CDS     -----

HumCFB_genDNA   ---GTGGAGGGGGTCATGAGACTACCTTGAGGGCGACAGGGAGGACCACCTTTGTAGTCAA 2400
HumCFB_CDS     -----
ShCFB_genDNA   GTTGTGGGAGGGTGTAGTGAGACCATGTGGGGAAGGCAGGAGGACTACGTTTTTAATCCA 2450
                    G
                    A

SheepCFB_CDS   -----
BovCFB_genDNA  GTCGTGGGAGGGTGTAGTGAGACCATGTGGTGGGCGAGGAGGACTACTTTTTAATCCA 2461
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BovCFB_CDS	-----	
HumCFB_genDNA	AAGTTGAACAGCAGGATCGTTGGCAATGGAGGTTAGTGGGAACCTGTTGGGGCTGGAA	2460
HumCFB_CDS	-----	
ShCFB_genDNA	TGGTTGGACAGCAGGGTCATTGGAAAATGTGGTTTGGTGGGAATCCTTTGGAA-CTGAGA	2509
SheepCFB_CDS	-----	
BovCFB_genDNA	CGGTTGGACAGCAGGGTCATTGGAAAATGGGGTTTGGTGGGAACCTTTGGAA-CTGAGA	2520
BovCFB_CDS	-----	
HumCFB_genDNA	GGGCCACTTTGTGGTCAAAGGGAAGTCCGTGTAATGATGATTAACCTTAAAAAGTTGAAAG	2520
HumCFB_CDS	-----	
ShCFB_genDNA	GGGGTACTTTGTGGTCAAAGGGAAGACAGTGGGGTAACAACCTCA-----AGTTGACAG	2562
SheepCFB_CDS	-----	
BovCFB_genDNA	GGGGCACTTTATTTGTCAAAGAAAAGACAATGGGGTGACAACCTCA-----AGTTGACAG	2573
BovCFB_CDS	-----	
HumCFB_genDNA	ATGTGGGATTTTCAGTTGCAGATTGGTCTCTGGGGTTAAAAGATGGCTTGGAAGACCAGGT	2580
HumCFB_CDS	-----	
ShCFB_genDNA	ATGTGGGATGCCAGTTGCTGCCAGACCTCTGGGGTCAAG-GATGGCTTGGGAGACCAGG-	2620
SheepCFB_CDS	-----	
BovCFB_genDNA	ATGTGGGAACCCAGTTGCCGCTGGACCCTGGGGTCAAG-GACGGGTTGGGAGACCAGGC	2632
BovCFB_CDS	-----	
	EXON 8	
HumCFB_genDNA	GAGGTGATGGTCTCTCCCTCTCCACAGACCACAAGTTGAAGTCAGGGACTAACACCAAG	2640
HumCFB_CDS	-----ACCACAAGTTGAAGTCAGGGACTAACACCAAG	1068
ShCFB_genDNA	-----TGATGACATCTTCCCTGTTTCCAGATCACAACTGAAAGCAGGGACCAACACCAAG	2676
SheepCFB_CDS	-----ATCACAACTGAAAGCAGGGACCAACACCAAG	1068
BovCFB_genDNA	GAGGTGACGACACCTTCCCTGTTTCCAGATCACAACTGAAAGCAGGGACCAATACCAAG	2692
BovCFB_CDS	-----ATCACAACTGAAAGCAGGGACCAATACCAAG	1068
	* *	
HumCFB_genDNA	AAGGCCCTCCAGGCAGTGTACAGCATGATGAGCTGGCCAGATGACGTCCCTCCTGAAGGC	2700
HumCFB_CDS	-----AAGGCCCTCCAGGCAGTGTACAGCATGATGAGCTGGCCAGATGACGTCCCTCCTGAAGGC	1128
ShCFB_genDNA	AGGGCTCTCCTGGAAAGTGTACAACATGATGAGCAGAGATATAAACAACCTCAAAGAGACC	2736
SheepCFB_CDS	AGGGCTCTCCTGGAAAGTGTACAACATGATGAGCAGAGATATAAACAACCTCAAAGAGACC	1128
BovCFB_genDNA	AGGGCTCTCCTGGAAAGTGTACAACATGATGAGCAGGGAAGTAAACCAGTTCAAAGAGACC	2752
BovCFB_CDS	AGGGCTCTCCTGGAAAGTGTACAACATGATGAGCAGGGAAGTAAACCAGTTCAAAGAGACC	1128
	* *	
HumCFB_genDNA	TGGAACCGCACCCGCCATGTCATCATCTCATGACTGATGGTCAGAAGGGACCTCTCTCC	2760
HumCFB_CDS	-----TGGAACCGCACCCGCCATGTCATCATCTCATGACTGATG-----	1168
ShCFB_genDNA	TGGAACCGCACCGCCACGTCATTATCATGACTGATGGTAAGAGGGG---CTTTTCT	2793
SheepCFB_CDS	-----TGGAACCGCACCGCCACGTCATTATCATGACTGATG-----	1168
BovCFB_genDNA	TGGAACCGCACCGCCACGTCATTATCATGACTGACGGTAAGAGGGG---CTTTTCT	2809
BovCFB_CDS	-----TGGAACCGCACCGCCACGTCATTATCATGACTGACG-----	1168
	***** *	
HumCFB_genDNA	TGTCCCAGCTCCCACCTTCTCAGACCAGCATGTGGCCCTTAAGTCCACTTGTAAACT	2820
HumCFB_CDS	-----	
ShCFB_genDNA	CCTGCCTGACTCCCACCTTCTCAAATCAGCTCGTGGCCCC-GAGCCCACACATAGCAC-	2851
SheepCFB_CDS	-----	
BovCFB_genDNA	CCTGCCTGACTCCCACCTTCTCAAACCAGCCCCGTGGCCCC-AAGTCCACATGTAAACT	2868
BovCFB_CDS	-----	
HumCFB_genDNA	ATACCCATGGTTGGGGCCCTGAATGTGACTCATAGCTGGCTGTTTTCATCTCTCCTGTGACC	2880
HumCFB_CDS	-----	
ShCFB_genDNA	AGACTTGTGGCTGGGGATGGCGTGTCTTCCAGTGCCTTTACAAGGAGGGCCCTC	2911
SheepCFB_CDS	-----	
BovCFB_genDNA	GGACTTGTGGTGGGGATGGCGTGTCTTCTTGTGCCTTTACAAGGAGGGACCCTC	2928
BovCFB_CDS	-----	
HumCFB_genDNA	CTTCATAAGGAATTTCTTCCCTAAAGCCCTGTGATCAACTATCTTAACCCTTCTCAACTTG	2940
HumCFB_CDS	-----	
ShCFB_genDNA	CACTCCATGACCTCTCACTCATGGTCTCTCCCAACCTGCTCACTCAGCCCTGTAC---	2968
	H	
SheepCFB_CDS	-----	
BovCFB_genDNA	CACTCCGTGATCTCTCACTCATGATCTCTCTCCAACCTGCTCACTCAGCCCTGTAT---	2985
BovCFB_CDS	-----	
HumCFB_genDNA	CTCACCCGTCATGTTGATTCCTTGCCTTTAGCCAGTTTATCTTCTTATCTCCTACCCTC	3000
HumCFB_CDS	-----	
ShCFB_genDNA	GTCATTCTTCCAGCCCTTTTGTCTTCTTGGACCCTCTCCCTTACGCTCTTCCACCCTC	3028
	H	
	C	
SheepCFB_CDS	-----	
BovCFB_genDNA	GTCATTCTTCCAGCCCTTTTGTCTTCTTGGACCCTCTCTCTTATGCTCTCCACCCTC	3045
BovCFB_CDS	-----	
	EXON 9	
HumCFB_genDNA	ATGGTCTGTCTCTTCTGCAGATTGCACAACATGGGCGGGGACCAATTACTGTGATTG	3060
HumCFB_CDS	-----GATTGCACAACATGGGCGGGGACCAATTACTGTGATTG	1207
ShCFB_genDNA	ACGGTCC-GTCTCTCCTGCAGGTTTGCACAACATGGGTTGGGATCCAGTCACTGTGATTG	3087

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SheepCFB_CDS -----GTTTGCACAACATGGGTGGGGATCCAGTCACTGTCATT 1207
BovCFB_genDNA ACTGTCC-GTCTCTCCTGCAGGTTTGCACAACATGGGTGGGGATCCAGTCACTGTCATT 3104
BovCFB_CDS -----GTTTGCACAACATGGGTGGGGATCCAGTCACTGTCATT 1207
* * * * *

HumCFB_genDNA ATGAGATCCGGGACTTGCTATACATTGGCAAGGATCGCAAAAACCAAGGGAGGATTATC 3120
HumCFB_CDS ATGAGATCCGGGACTTGCTATACATTGGCAAGGATCGCAAAAACCAAGGGAGGATTATC 1267
ShCFB_genDNA ATGATATTCGGTACTTGCTAGACATTGGTAGAAATCGCAAAAACCCAGGGAGGATTAT 3147
SheepCFB_CDS ATGATATTCGGTACTTGCTAGACATTGGTAGAAATCGCAAAAACCCAGGGAGGATTAT 1267
BovCFB_genDNA ACGATATTCGGTACTTGCTAGACATTGGTAGAAATCGCAAAAACCCAGGGAGGATTATC 3164
BovCFB_CDS ACGATATTCGGTACTTGCTAGACATTGGTAGAAATCGCAAAAACCCAGGGAGGATTATC 1267
* * * * * T/C

HumCFB_genDNA TGGGTGAGTAAC-CTGCCTAGGACCCAGCACCCCACTTCTCAGGGCTTGGACCCTCA-- 3177
HumCFB_CDS TGG----- 1270
ShCFB_genDNA TGGGTGAGTTTTACTGCCTAGGACCCAGCACCCCACTTTATTAGCTTCTTGCCTGTGCCA 3207
SheepCFB_CDS TGG----- 1270
C TTG/L -> TTC/F

BovCFB_genDNA TGGGTGAGTTTTACTGCCTAGGACCCAGCACCCCACTTTACTAGCTTCTTGCCTGCGCCA 3224
BovCFB_CDS TGG----- 1270
***

EXON 10

HumCFB_genDNA -----TCCTTCCTTTTATCCCTCAGATGCTATGTGTTTGGGGTGGGCC 3223
HumCFB_CDS -----ATGCTATGTGTTTGGGGTGGGCC 1295
ShCFB_genDNA GGGCCAAGATAC--TCACTGTTTTTCTCTCTCAGACATCTATGTGTTTGGGGTGGACC 3265
SheepCFB_CDS -----ACATCTATGTGTTTGGGGTGGACC 1295
BovCFB_genDNA GGGCCAAGACTCTCACTCTGTTTTTCTCTCTCAGATATCTATGTGTTTGGGGTGGACC 3284
BovCFB_CDS -----ATATCTATGTGTTTGGGGTGGACC 1295
* * * * *

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HumCFB_genDNA TTTGGTGAACCAAGTGAACATCAATGCTTTGGCTTCCAAGAAAGACAATGAGCAACATGT 3283
HumCFB_CDS TTTGGTGAACCAAGTGAACATCAATGCTTTGGCTTCCAAGAAAGACAATGAGCAACATGT 1355
ShCFB_genDNA TCTAGTGAACCAAGAGAATCAATGCTTTGGCTTCCAAGAAGGATAAAGAGCAACACGT 3325
SheepCFB_CDS TCTAGTGAACCAAGAGAATCAATGCTTTGGCTTCCAAGAAGGATAAAGAGCAACACGT 1355
BovCFB_genDNA TCTAGTGAACCAAGAGAATCAATGCTTTGGCTTCCAAGAAGGATAAAGAGAAACACGT 3344
BovCFB_CDS TCTAGTGAACCAAGAGAATCAATGCTTTGGCTTCCAAGAAGGATAAAGAGAAACACGT 1355
* * * * *

HumCFB_genDNA GTTCAAAGTCAAGGATATGAAAACCTGGAAGATGTTTTCTACCAAATGATCGGTAGGGA 3343
HumCFB_CDS GTTCAAAGTCAAGGATATGAAAACCTGGAAGATGTTTTCTACCAAATGATCG----- 1408
ShCFB_genDNA GTTCAAAGTCAAGGATATGAAAACCTGGAAGATGTTTTCTCGTCCAAATGCTTGTAAGAA 3385
SheepCFB_CDS GTTCAAAGTCAAGGATATGAAAACCTGGAAGATGTTTTCTCGTCCAAATGCTTG----- 1408
BovCFB_genDNA GTTCAAAGTCAAGGATATGAAAACCTGGAAGATGTTTTCTCGTCCAAATGCTTGTAAGAA 3404
BovCFB_CDS GTTCAAAGTCAAGGATATGAAAACCTGGAAGATGTTTTCTCGTCCAAATGCTTG----- 1408
***** * * * *

HumCFB_genDNA GATACA-----AGGGAATAAAGAACAACACTCTCCTCAGGTTCCCTGAAGT 3390
HumCFB_CDS -----
ShCFB_genDNA GCTATGGAAGCTATAAGGAGATGGTCAGGAAACTCAGCTCTCCCGAGCCCTCAAGGT 3445
SheepCFB_CDS -----
BovCFB_genDNA GCTATGGAAGCTATAAGGAGATGGTCAGGAAACTCAGCTCTCCCGAGCCCTCAAGGT 3464
BovCFB_CDS -----

HumCFB_genDNA AATTCATTCTTCTTACACCTGAAGCTCTAGTTGCCCTGGAAAGCCTTCTTTCATTCCTCC 3450
HumCFB_CDS -----
ShCFB_genDNA CACTCATTCTTCCACTCCTTCTAAAGCCCTGGAAAGCTTGGAAAGCCCTTTC----TCTCC 3501
SheepCFB_CDS -----
BovCFB_genDNA CACTCATTCTTCCACTCCTCCTAAAGCCCTGGAAAGCTTGGAAAGCCCTTTC----TTTCC 3520
BovCFB_CDS -----

HumCFB_genDNA TTCTCTACCTCAGTGTACTATTCTTGTTCCTGGCACGTTCCTACT---TAACCTTAGAA 3507
HumCFB_CDS -----
ShCFB_genDNA TCCTCTACCTCAGGTACTATTCTTGTTCCTGGTACTTTCCACTCCCTGATCTCAGAA 3561
SheepCFB_CDS -----
BovCFB_genDNA TCCTCTACCTCAGGTACTATTCTTGTTCCTGGTACTTTCCACTCCCTGATCTCAGAA 3580
BovCFB_CDS -----

HumCFB_genDNA TCACAGAGCTCTGAGCACTTCAGAGATCTTCTATAGTCTACATTTGACA--CGTGGAA 3565
HumCFB_CDS -----
ShCFB_genDNA TCACAAGTCTGAAATGATGAGACACCTTCTCAAGTCCCTCCTTTTACAGATATGGAA 3621
SheepCFB_CDS -----
BovCFB_genDNA TCATGAGTCTGAAATGATGCCGAGACCTTCTCAAGTCCCTCCTTTTACAGATATGGAA 3640
BovCFB_CDS -----

HumCFB_genDNA ACAGAAGCCAAAGGAGGTCAAGGACAGCAAGTTAGCAACAAGGTTGGGCTTGAAAACAG 3625
HumCFB_CDS -----
ShCFB_genDNA GCTGGGGCCAACAGTGGTCAAGAAATGGCAAGTTAGCAGGA--GTTGGGCTGAAAATGC 3679
SheepCFB_CDS -----
BovCFB_genDNA GCTGGGGCCAAAAGGAGGTCAAGAAATGGCAAGTTAGCAGGA--GTTGGGCTGAAAATGC 3698
BovCFB_CDS -----

HumCFB_genDNA CCAGGCCCTGACAGCTTGATCCCAAGTCTTTCCCTTTTTCAGTCCACCATAGCAGTTTT 3685
HumCFB_CDS -----
ShCFB_genDNA CCAGGTCTCTGAGTT-----TAGT 3698
SheepCFB_CDS -----
BovCFB_genDNA CCAGGTCTCTGAGCT-----TAGT 3717
BovCFB_CDS -----

HumCFB_genDNA CTCCTAACACGAGGAAACAAATACCCGTGGTCTTTCCTTTCTCCTTTTGGGCCTTTGCT 3745
HumCFB_CDS -----
ShCFB_genDNA CTCATGATFCCAGTGGTTCCTTGCTTCCTTCCCTCTGTGGGCATCTGCTCCCCACAG 3758
SheepCFB_CDS -----
BovCFB_genDNA CCCATGATFCCAGTGGTTCCTTGCTTCCTTCCCTCTTTTGGGCATCTGCTCCCCACAG 3777
BovCFB_CDS -----

HumCFB_genDNA CCCCATAGACTCCTACCCAAAAGGCTGCTGCCATTTGGGAATGAAGTGTCCGAGTTTT 3805
HumCFB_CDS -----
ShCFB_genDNA ACACACTGGCGTCTTCCCAAGACAGCTGCCATTTGGGAATGAAGTGTCCGAGTTTT 3817
SheepCFB_CDS -----
BovCFB_genDNA ACACACTGGCCTCCCTCCGCAAGACAGCTGCCATTTGGGAATGAAGTGTCCGAGTTTT 3836
BovCFB_CDS -----

EXON 11
HumCFB_genDNA AGCACATCTCCTTCTGTCAGATGAAAGCCAGTCTCTGAGTCTCTGTGGCATGGTTTTG 3865
HumCFB_CDS -----ATGAAAGCCAGTCTCTGAGTCTCTGTGGCATGGTTTTG 1445
ShCFB_genDNA AGCACAACTCCTTTCTTCCAGATGAAAGCCGACACTGGGTCTCTGTGGCATGGTTTTG 3877
SheepCFB_CDS -----ATGAAAGCCGACACTGGGTCTCTGTGGCATGGTTTTG 1445
BovCFB_genDNA AGCACAACTCCTTTCTTGTGATGAAAGCCGACACTGGGTCTCTGTGGCATGGTTTTG 3896
BovCFB_CDS -----ATGAAAGCCGACACTGGGTCTCTGTGGCATGGTTTTG 1445
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HumCFB_genDNA GGAACACAGGAAGGGTACCATTACCACAAGCAACCATGGCAGGCCAAGATCTCAGTCAT 3925
HumCFB_CDS GGAACACAGGAAGGGTACCATTACCACAAGCAACCATGGCAGGCCAAGATCTCAGTCAT 1505
ShCFB_genDNA GGAGCACAGGATGGTACTCCCTACCACAAGCAACCATGGCAGGCCAAGATCTCAGTCAT 3937
SheepCFB_CDS GGAGCACAGGATGGTACTCCCTACCACAAGCAACCATGGCAGGCCAAGATCTCAGTCAT 1505
BovCFB_genDNA GGAGCACAGGATGGTACTGCCCTACCACAAGCAACCGTGGCAGGCCAAGATCTCGGTAC 3956
BovCFB_CDS GGAGCACAGGATGGTACTGCCCTACCACAAGCAACCGTGGCAGGCCAAGATCTCGGTAC 1505
*** **

HumCFB_genDNA TGTAAAGCAGAAATCCCAGTAGTGGGGACTTGGGGAGGTGAGGTCAAGGTGAAATGGGA 3985
HumCFB_CDS T----- 1506
ShCFB_genDNA TGTAAAGTGCAGTGTCTGGTGGTGGAACTTAGGGGAGGGGAAGTCAGGGTGAATAAAG 3997
SheepCFB_CDS T----- 1506
BovCFB_genDNA TGTAAAGTGCAGTGTCTGGTGGTGGAACTTAGAGGAAGGGAGGTGAGGGTGAATGAAG 4016
BovCFB_CDS T----- 1506
*

HumCFB_genDNA GTAGGGGAAGGAAAAATGGCCATAAGAGATGGTGGTTTGTGAAAGTTGAGCTTTCCTC 4045
HumCFB_CDS -----
ShCFB_genDNA GTCAGAGGAAGGGCAAGGCACTCTTGATCAGACTGTGATATTTGTGAAAGCTGAGCTTTC 4057
SheepCFB_CDS -----
BovCFB_genDNA GTCGGAGGAAGGGCAAGGCACTCTTGATCAGATTGTGAGATTTGTGAAAGCTGAGCTTTC 4076
BovCFB_CDS -----

EXON 12

HumCFB_genDNA TCTACTGTGTGTCCTCCAGCGCCCTCAAAGGGACACGAGAGCTGTATGGGGGCTGTGGT 4105
HumCFB_CDS -----CGCCCTCAAAGGGACACGAGAGCTGTATGGGGGCTGTGGT 1547
ShCFB_genDNA CCTCTGCTGCTGCCAGCGCCCTCAAAGGGGATGAGAGCTGTATGGGTGCTATCGT 4117
SheepCFB_CDS -----CGCCCTCAAAGGGGATGAGAGCTGTATGGGTGCTATCGT 1547
BovCFB_genDNA CCTCTGCTGCTGCCAGCGCCCTCAAAGGGGATGAGAGCTGTATGGGTGCTATTTGT 4136
BovCFB_CDS -----CGCCCTCAAAGGGGATGAGAGCTGTATGGGTGCTATTTGT 1547
***** **

HumCFB_genDNA GTCTGAGTACTTTGTGCTGACAGCAGCACATTGTTTCACTGTGGATGACAAGGAACACTC 4165
HumCFB_CDS GTCTGAGTACTTTGTGCTGACAGCAGCACATTGTTTCACTGTGGATGACAAGGAACACTC 1607
ShCFB_genDNA GTCTGAGTACTTCGTGCTGACGGCTGCACACTGTTTCACTGTGGATGATGAGAAACACTC 4177
SheepCFB_CDS GTCTGAGTACTTCGTGCTGACGGCTGCACACTGTTTCACTGTGGATGATGAGAAACACTC 1607
BovCFB_genDNA GTCTGAGTACTTTGTGCTGACGGCTGCACACTGTTTCACTGTGGATGATGAGAAACACTC 4196
BovCFB_CDS GTCTGAGTACTTTGTGCTGACGGCTGCACACTGTTTCACTGTGGATGATGAGAAACACTC 1607
***** **

HumCFB_genDNA AATCAAGGTCAGCGTAGGTAAGGATGCAACTGAAG-GTCTGGGCTGCACCTATGCTCTC 4224
HumCFB_CDS AATCAAGGTCAGCGTAG----- 1624
ShCFB_genDNA AATCAAGGTCAGCGTGGTAAGGATGCAATCCATCCATTCTGAGCTTCTGCAAGTGCCTC 4237

SheepCFB_CDS AATCAAGGTCAGCGTGG----- 1624
BovCFB_genDNA AATCAAGGTCAGCGTGGTAAGGATGCAACCCATCAATTCTGAGCTTCTGCGGTGCCCTC 4256
BovCFB_CDS AATCAAGGTCAGCGTGG----- 1624
***** **

HumCFB_genDNA CAGGCAACACCTCCACTTTCTACAGATCTTACACTCCACCCATCCTCAATGCAGCCCCA 4284
HumCFB_CDS -----
ShCFB_genDNA TGGGCAACACTGCC-----TCCAGGGCCACTTCCCAACTGTCTCATCGCAGCCCT- 4289
SheepCFB_CDS -----
BovCFB_genDNA TGGGCAACACTGCC-----TCCAGGGCCACTTCCACTGTCTCATCGCAGCCCT- 4308
BovCFB_CDS -----

HumCFB_genDNA TTCCTTGACCCAGACCAGTACAGGATGGGGGAAGACGTGAAGTTAGGAATGACACGGG 4344
HumCFB_CDS -----
ShCFB_genDNA TCCCTTGATGCTGGACCAGTTAAGGATGGGGAAGATTTGGGTAGGGATGACATGCAGG 4349
SheepCFB_CDS -----
BovCFB_genDNA TCCCTTGATGCTGGACAAGTTAGGATGGGGAAGATTTGGGTAGGGATGACATGCAGG 4368
BovCFB_CDS -----

EXON 13

HumCFB_genDNA GCCAGAGGC---AGGAAGCTGCCACAAAGAGGTGGTACCTACTCTCTACTTTCAGGAG 4400
HumCFB_CDS -----GAG 1627
ShCFB_genDNA AAGGAGGCTGCCTACACAGACATCGGTCTAGAGGGACTCCCTCTCTACTTTCAGGAG 4409
SheepCFB_CDS -----GAG 1627
BovCFB_genDNA CAGGAGGCTGCCTACACAGATTTAGTGGTCTAGAGGAACCCCTTCTTGTACTTTCAGGAG 4428
BovCFB_CDS -----GAG 1627

HumCFB_genDNA GGGAGAAGCGGGACCTGGAGATAGAAGTAGTCTATTTACCCCCAACTACAACATTAATG 4460
HumCFB_CDS GGGAGAAGCGGGACCTGGAGATAGAAGTAGTCTATTTACCCCCAACTACAACATTAATG 1687
ShCFB_genDNA GAAAGGAGGAGGAGTGGGAGGTAGAAGAAGTCTATTTCACTCAAACTACAACCTCAATG 4469
SheepCFB_CDS GAAAGGAGGAGGAGTGGGAGGTAGAAGAAGTCTATTTCACTCAAACTACAACCTCAATG 1687
C [AAG/K -> ACG/T]

BovCFB_genDNA GACAGAGGAAGGAGTGGGAGGTAAGAAATCCTATTTTCATCCGAAGTACGACCTCAATG 4488
BovCFB_CDS GACAGAGGAAGGAGTGGGAGGTAAGAAATCCTATTTTCATCCGAAGTACGACCTCAATG 1687
* **

HumCFB_genDNA GGAAAAAGAAGCAGGAATTCCTGAATTTTATGACTATGACGTTGCCCTGATCAAGCTCA 4520
HumCFB_CDS GGAAAAAGAAGCAGGAATTCCTGAATTTTATGACTATGACGTTGCCCTGATCAAGCTCA 1747
ShCFB_genDNA CAAAAAAGCAAAGGCATTCCTGAGTTTTATGACTATGACGTTGCCCTCATCAAGCTCA 4529
SheepCFB_CDS CAAAAAAGCAAAGGCATTCCTGAGTTTTATGACTATGACGTTGCCCTCATCAAGCTCA 1747
BovCFB_genDNA CAAAAAAGCAAAGGCATTCCTGAGTTTTATGACTATGACGTTGCCCTCATCAAGCTCA 4548
BovCFB_CDS CAAAAAAGCAAAGGCATTCCTGAGTTTTATGACTATGACGTTGCCCTCATCAAGCTCA 1747

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HumCFB_genDNA      AGAATAAGCTGAAATATGGCCAGACTATCAGGTGAGAGCGTCCAGATCCCTGAGGAAAGG 4580
HumCFB_CDS         AGAATAAGCTGAAATATGGCCAGACTATCAG----- 1778
ShCFB_genDNA      CAAAGAAGCTCAAGTATGAGACCACCATCAGGTGAGCCATCTGGATTCCGAGAGAAAAGG 4589
SheepCFB_CDS      CAAAGAAGCTCAAGTATGAGACCACCATCAG----- 1778
BovCFB_genDNA     AGGAAAAGCTCAAGTATGAGACCACCATCAGGTGAGCCATCTGGATTCTGAGAGAAAAGG 4608
BovCFB_CDS        AGGAAAAGCTCAAGTATGAGACCACCATCAG----- 1778
                   * ***** ** **** * ** *****
HumCFB_genDNA     CTGGGAAAGGCTGGA-----GGACTGGGGTGAGGAGCAGGCCTGGTTTGTCTGTCT 4631
HumCFB_CDS        CTGGGAAAGGCTGGA-----GGACTGGGGTGAGGAGCAGGCCTGGTTTGTCTGTCT
ShCFB_genDNA     CTGGGAGAGGCAGAACTGAGACGGGAGCAGGCCAGGGTTCACGATCCTTGAATTCCCC 4649
SheepCFB_CDS     CTGGGAGAGGCAGAACTGAGACGGGAGCAGGCCAGGGTTCACGATCCTTGAATTCCCC
BovCFB_genDNA     CTGGGAGAGGCAGAACTGAGACAGTAGCAGGCCAGGGTTCACGATCCTTGAATTCCCC 4668
BovCFB_CDS       CTGGGAGAGGCAGAACTGAGACAGTAGCAGGCCAGGGTTCACGATCCTTGAATTCCCC
                   -----
                                EXON 14
HumCFB_genDNA     CCTGTCTCTTTATAGGCCATTTGTCTCCCCTGCACCGAGGGAACAACCTCGAGCTTTGAG 4691
HumCFB_CDS        CCTGTCTCTTTATAGGCCATTTGTCTCCCCTGCACCGAGGGAACAACCTCGAGCTTTGAG 1823
ShCFB_genDNA     ATCTCTCTCAACAGGCCATTTGTCTCCCCTGCACCTGAGGGATCGATTCAAGCCTTGAG 4709
SheepCFB_CDS     ATCTCTCTCAACAGGCCATTTGTCTCCCCTGCACCTGAGGGATCGATTCAAGCCTTGAG 1823
BovCFB_genDNA     ATCTCTCTCAACAGGCCATTTGTCTCCCCTGCACCTGAGGGATCGATTCAAGCCTTGAG 4728
BovCFB_CDS       ATCTCTCTCAACAGGCCATTTGTCTCCCCTGCACCTGAGGGATCGATTCAAGCCTTGAG 1823
                   -----
                   ***** * * * * *
HumCFB_genDNA     GCTTCCTCCAAC TACCAC TTGCCAGCAACAAGTAAGACATAC TTGGCAAGAGGA----T 4747
HumCFB_CDS        GCTTCCTCCAAC TACCAC TTGCCAGCAACAAGTAAGACATAC TTGGCAAGAGGA----T 1855
ShCFB_genDNA     GCTTCCAAGATCAACTACGTGCCAGCAACAGAGTAAGACACGTT CAGGGAGAGCGGCT-T 4768
SheepCFB_CDS     GCTTCCAAGATCAACTACGTGCCAGCAACAAGTAAGACATAC TTGGCAAGAGGA----T 1855
BovCFB_genDNA     GCTTCCAAGGTCAACCACATGCCAGCAACAGAGTAAGAGACATTCAGGGAGAGCAGCTTG 4788
BovCFB_CDS       GCTTCCAAGGTCAACCACATGCCAGCAACAAGTAAGAGACATTCAGGGAGAGCAGCTTG 1855
                   -----
                   ***** * * * * *
HumCFB_genDNA     AAGGATGAGATCCCAAGAGACAAGTGGGCATGAGAGGGAGGTGCAATAGGAAGAGATGA 4807
HumCFB_CDS        AAGGATGAGATCCCAAGAGACAAGTGGGCATGAGAGGGAGGTGCAATAGGAAGAGATGA
ShCFB_genDNA     GTAAGGGTGAAGTTCTGAGACAAGGAAGGGACGAGGGGGCG-TAGAGGGAGAACAGGTGA 4827
SheepCFB_CDS     GTAAGGGTGAAGTTCTGAGACAAGGAAGGGACGAGGGGGCG-TAGAGGGAGAACAGGTGA
BovCFB_genDNA     TTAAGGGTGAAGTTTGTGAGACAAGGAAGGGATGAGGGGGAG-----GGAGAGCAGGTCA 4842
BovCFB_CDS       TTAAGGGTGAAGTTTGTGAGACAAGGAAGGGATGAGGGGGAG-----GGAGAGCAGGTCA
                   -----
HumCFB_genDNA     TGCCTGGCCCAGAACCTAGCTCTAGAAGGGCTTAGGGGACATCTACTGAGTGACAAAGGC 4867
HumCFB_CDS        TGCCTGGCCCAGAACCTAGCTCTAGAAGGGCTTAGGGGACATCTACTGAGTGACAAAGGC
ShCFB_genDNA     TGCCTGGCCCAGCCGCCAGCTCACAGGAAGGAGTGAGGGGCCACTTGATGACAAGCATGA 4887
SheepCFB_CDS     TGCCTGGCCCAGCCGCCAGCTCACAGGAAGGAGTGAGGGGCCACTTGATGACAAGCATGA
BovCFB_genDNA     TGCCTGGCCCAGCCGCCAGCTCACGGGAAGGAGTGAGGGGCCACTTCGATGACAAGCACGA 4902
BovCFB_CDS       TGCCTGGCCCAGCCGCCAGCTCACGGGAAGGAGTGAGGGGCCACTTCGATGACAAGCACGA
                   -----
                                                                EXON 15
HumCFB_genDNA     AATGGGGAGATGACAGTGGTGGGAGCAGCTGAAGTGAC--GCAGTCTATTCGTCCAGAGG 4925
HumCFB_CDS        AATGGGGAGATGACAGTGGTGGGAGCAGCTGAAGTGAC--GCAGTCTATTCGTCCAGAGG 1858
ShCFB_genDNA     GGCGGGGAGGGGAGGGGAGGGGAGAGTGCTGCAATGACCCGCTATCCATCTGTAAAGTGC 4947
SheepCFB_CDS     GGCGGGGAGGGGAGGGGAGGGGAGAGTGCTGCAATGACCCGCTATCCATCTGTAAAGTGC 1858
BovCFB_genDNA     GGCGGGGAGGGGAGGGGAGAGTGCTGCAATGACCCAGTC---TATCCATCTGTAAAGTGC 4958
BovCFB_CDS       GGCGGGGAGGGGAGGGGAGAGTGCTGCAATGACCCAGTC---TATCCATCTGTAAAGTGC 1858
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HumCFB_genDNA AAGAGCTGCTCCCTGCACAGGATATCAAAGCTCTGTTTGTGCTGAGGAGGAGAAAAAGC 4985
HumCFB_CDS AAGAGCTGCTCCCTGCACAGGATATCAAAGCTCTGTTTGTGCTGAGGAGGAGAAAAAGC 1918
ShCFB_genDNA AAGAGCTACTCCCTGCCAAGGACATCGAAGCTCTGTTTGTGCTGAGTCTAAGAAGACCC 5007
SheepCFB_CDS AAGAGCTACTCCCTGCCAAGGACATCGAAGCTCTGTTTGTGCTGAGTCTAAGAAGACCC 1918
BovCFB_genDNA AAGAGCTACTCCCTGCAAAGGACATTGAAGCTCTGTTTGTGCTGAGTCTAAGAAGACCC 5018
BovCFB_CDS AAGAGCTACTCCCTGCAAAGGACATTGAAGCTCTGTTTGTGCTGAGTCTAAGAAGACCC 1918

HumCFB_genDNA TGACTCGGAAGGAGGTCTACATCAAGAATGGGGATAAGGTGAGAAACGGGCATCCTAAGG 5045
HumCFB_CDS TGACTCGGAAGGAGGTCTACATCAAGAATGGGGATAAG----- 1956
ShCFB_genDNA TGACTCGGAAGGCAGTCTACATCAAAAATGGGGACAAGGTGAGGAAGGTGGGATCCT--G 5065
SheepCFB_CDS TGACTCGGAAGGCAGTCTACATCAAAAATGGGGACAAG----- 1956
BovCFB_genDNA TGACTCGGAAGGCAGTCTACATCAAGAATGGGGACAAGGTGAGGAATGTGGGATCCT--G 5076
BovCFB_CDS TGACTCGGAAGGCAGTCTACATCAAGAATGGGGACAAG----- 1956

HumCFB_genDNA AGGCACTCTAGGCCCAATCCTTCTTAAGCCACTTCTGTTCATTACTTCTCCATGC---- 5101
HumCFB_CDS -----
ShCFB_genDNA AGGTCCTTTAGGCCCCAGTCTTCTTAAGCAAGCTTTGTTCCTCATGCCCTCTCTCCACAC 5125
SheepCFB_CDS -----
BovCFB_genDNA AGGTCCTTTAGGCCCCAGTCTTCTTAAGCAAGCTTTGTTCCTCACACCTCTCTCCACAC 5136
BovCFB_CDS -----

EXON 16

HumCFB_genDNA -TTCCACCTCCCTACAGAAAGCAGCTGTGAGAGAGATGCTCAATATGCCCCAGGCTA 5160
HumCFB_CDS -----AAAGGCAGCTGTGAGAGAGATGCTCAATATGCCCCAGGCTA 1997
ShCFB_genDNA TTCCCATCTCACCTACAGAAAGCCAGCTGTGAGAGAGACGCTCTGCATGCCCCAGGTTA 5185
SheepCFB_CDS -----AAAGCCAGCTGTGAGAGAGACGCTCTGCATGCCCCAGGTTA 1997
BovCFB_genDNA TTCCCTATCTCACCTACAGAAAGCCAGCTGTGAGAGAGATGCTTACGCCCCAGGTTA 5196
BovCFB_CDS -----AAAGCCAGCTGTGAGAGAGATGCTTACGCCCCAGGTTA 1997

HumCFB_genDNA TGACAAAGTCAAGGACATCTCAGAGGTGGTCACCCCTCGGTTCTTTGTACTGGAGGAGT 5220
HumCFB_CDS TGACAAAGTCAAGGACATCTCAGAGGTGGTCACCCCTCGGTTCTTTGTACTGGAGGAGT 2057
ShCFB_genDNA TGACAAAGTCAAGGACGCTCTCAGAGGTAGTCACCCCCAGGTTCTCTGCCTGGAGGTGT 5245
SheepCFB_CDS TGACAAAGTCAAGGACGCTCTCAGAGGTAGTCACCCCCAGGTTCTCTGCCTGGAGGTGT 2057
BovCFB_genDNA TGAAAAAGTCAAGGACGCTCTCAGAGGTAGTCACCCCCAGGTTCTCTGCCTGGAGGTGT 5256
BovCFB_CDS TGAAAAAGTCAAGGACGCTCTCAGAGGTAGTCACCCCCAGGTTCTCTGCCTGGAGGTGT 2057

HumCFB_genDNA GAGTCCCTATGCTGACCCCAATACTTGCAGAGGTGAGAGAATGCTCTTTGGTTGTGCTAC 5280
HumCFB_CDS GAGTCCCTATGCTGACCCCAATACTTGCAGAG----- 2089
ShCFB_genDNA GGCTCCCTACGCTGACCCCAACTTGCAAAGGTGAGAGAAGGCTCTTTGGTTGTGATGT 5305
SheepCFB_CDS GGCTCCCTACGCTGACCCCAACTTGCAAAG----- 2089
BovCFB_genDNA GGATCCCTACGCTGACCCCAACTTGCAAAGGTGAGAGAAGGCTCTTTGGTTGTGATGT 5316
BovCFB_CDS GGATCCCTACGCTGACCCCAACTTGCAAAG----- 2089
* *****

EXON 17

HumCFB_genDNA AAGTGCCCAAGGCCAACAGTCTTTTCTTACAGCTTCTCTCTCTCTGAGGTTGATTTC 5340
HumCFB_CDS -----GTGATTTC 2096
ShCFB_genDNA GAGTTCTGAGGCCTAAGT-----CTTTGCCTACAGCATCTCCTCCCCT--GCAGGTGATTTC 5359
SheepCFB_CDS -----GTGATTTC 2096
BovCFB_genDNA GAGTTCTGAGGCCTAAGT-----CTTTTCTACAGCATCTCCTCCCCT--GCAGGTGATTTC 5370
BovCFB_CDS -----GTGATTTC 2096

HumCFB_genDNA TGGCGGCCCTTGATAGTTTACAAAGAGAGTTCGTTTCAATCAAGTGAGTCTCCCTTTCC 5400
HumCFB_CDS TGGCGGCCCTTGATAGTTTACAAAGAGAGTTCGTTTCAATCAA----- 2139
ShCFB_genDNA TGGTGGCCCCCTGATTATTACAAAGAGGAGCCGCTTCAATCAAGTGAGTCTTCTCTTTCC 5419
SheepCFB_CDS TGGTGGCCCCCTGATTATTACAAAGAGGAGCCGCTTCAATCAA----- 2139
BovCFB_genDNA TGGTGGCCCCCTGATTATTACAAAGAGGAGTTCGTTTCAATCAAGTGAGTCTTCTCTTTCC 5430
BovCFB_CDS TGGTGGCCCCCTGATTATTACAAAGAGGAGTTCGTTTCAATCAA----- 2139

HumCFB_genDNA TATCT--GGGAGATGCCAAGTGGTCAGCATGGGCCCAAGCAGGAAAGCTCAATGCAT 5458
HumCFB_CDS -----
ShCFB_genDNA TCTCTCTGGAGAGATGCTGAGTGGTCAGCATGGGCCCAAAACAAGAAAGCTCACTGCAT 5479
SheepCFB_CDS -----
BovCFB_genDNA TTTCTCTGGAGAGATGCTGAGTGGTCAGCGTGGGCCCAAAACAGGAAAGCTCACTGCAT 5490
BovCFB_CDS -----

HumCFB_genDNA GTGGCTAGTAATTCGAGGTA-----GGCAGAGCCTGCCTCACCTT----- 5498
HumCFB_CDS -----
ShCFB_genDNA GTGGCTGAAAAGAGGTGGGGTGGGGCAGAGCCTGCTCACCTTCAGATTCTTCTTTGA 5539

SheepCFB_CDS -----
BovCFB_genDNA GTGGCTGAAAAGAGGTGGGGTGGGGCAGAGCCTGCCTCACCTTCAGACTCTTCTTTGA 5550
BovCFB_CDS -----

HumCFB_genDNA -----AGGACCGCATGCTTGGCTGCGTGTGTCAGAACGAGGCTGAGCTGGG 5546
HumCFB_CDS -----
ShCFB_genDNA ACTGGCCAATTTAGGGCCATGTGTCTGGTCTGTGTGC--CAGGGACAGAACTGAACTGGG 5598
SheepCFB_CDS -----
BovCFB_genDNA ACTGGCCAATTCAGGGCCATGTGTCTGGTCTGTGTGC--CAGGGACAGAACTGAACTGGG 5609
BovCFB_CDS -----

HumCFB_genDNA TCCCTAGTCTGATTCT-----TTAGGTCAGCTAAGACACAAGCAGGAACAGCCATGCTT 5601

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HumCFB_CDS -----
ShCFB_genDNA GCCCTAGTCTAGTCCCTCCAGGTCAGGTCAGTTCAGGTGCAACTGGTGGTAGTTGTGCTT 5658
SheepCFB_CDS -----
BovCFB_genDNA TCCTAGTCTCCAGG-----TCAGGTCAC TTCAGATGCAACTGGCAGTAGCTGTGCTT 5664
BovCFB_CDS -----

                                           EXON 18
HumCFB_genDNA CCAGGATT--AGGAATTC TACTGAATGATCCATGGCACCCCACTGC-CTCTGCAGGTTGG 5658
HumCFB_CDS -----GTTGG 2144
ShCFB_genDNA CCTGGGATTAAGGAGTTCTACCAAATGATTCCTGGCAACCCTCGCTCTTCCAGGTTGG 5718
SheepCFB_CDS -----GTTGG 2144
BovCFB_genDNA CCTGGGATTAAGGAGTTCTACTAAATGATTCCTGGCAACCCTCGCTCTCTCCAGGTTGG 5724
BovCFB_CDS -----GTTGG 2144
                                           *****
HumCFB_genDNA TGTAAATCAGCTGGGGAGTAGTGGATGTCTGCAAAAACCAGAAGCGGCAAAAGCAGGTACC 5718
HumCFB_CDS TGTAAATCAGCTGGGGAGTAGTGGATGTCTGCAAAAACCAGAAGCGGCAAAAGCAGGTACC 2204
ShCFB_genDNA CGTGATCAGCTGGGGCGCTCGTGGACGTTTGCAA-----GCGGCCACAGCAAGTACC 5769
SheepCFB_CDS CGTGATCAGCTGGGGCGCTCGTGGACGTTTGCAA-----GCGGCCACAGCAAGTACC 2195
BovCFB_genDNA CGTGATCAGCTGGGGCGCTCGTGGATGTTTGCAA-----GCGGCCACAGCAAGTACC 5775
BovCFB_CDS CGTGATCAGCTGGGGCGCTCGTGGATGTTTGCAA-----GCGGCCACAGCAAGTACC 2195
** ***** ** ***** ** ***** 9n INDEL ***** * **** *****

HumCFB_genDNA TGCTCAGC CCGAGACTTTCACATCAACCTCTTTCAAGTGCTGCCCTGGCTGAAGGAGAA 5778
HumCFB_CDS TGCTCAGC CCGAGACTTTCACATCAACCTCTTTCAAGTGCTGCCCTGGCTGAAGGAGAA 2264
ShCFB_genDNA TGGTTATGCTCGAGACTTTCACATCAACCTCTACCACGTGCTGCCCTGGCTCAAGGAAAA 5829
SheepCFB_CDS TGGTTATGCTCGAGACTTTCACATCAACCTCTACCACGTGCTGCCCTGGCTCAAGGAAAA 2255
BovCFB_genDNA TGGTTATGCTCGAGACTTTCACATCAACCTCTACCAGGTGCTGCCCTGGCTCAAGGAAAA 5835
BovCFB_CDS TGGTTATGCTCGAGACTTTCACATCAACCTCTACCAGGTGCTGCCCTGGCTCAAGGAAAA 2255
** * * * ***** ***** ** ***** ***** **

HumCFB_genDNA ACTCCAAGATGAGGATTTGGGTTTTCTATAAGGGTTTTCTGCTGGACAGGGGCGTGGGA 5838
HumCFB_CDS ACTCCAAGATGAGGATTTGGGTTTTCTA----- 2292
ShCFB_genDNA ACTCAAAAATGAGGATCTGGGTTTTCTATAAGGGTTTTCTGCTGGAAAGGGGCATGAGA 5889
SheepCFB_CDS ACTCAAAAATGAGGATCTGGGTTTTCTA----- 2283
BovCFB_genDNA ACTCCAAAAATGAGGATCTGGGTTTTCTATAAGGGTTTTCTGCTGGAAAGGGGCATGAGA 5895
BovCFB_CDS ACTCCAAAAATGAGGATCTGGGTTTTCTA----- 2283
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HumCFB_genDNA TTGAATTA AACAGCTGCGACAAC 5862
HumCFB_CDS -----
ShCFB_genDNA CCAAATTA AACATCTGCGACAAC 5913
SheepCFB_CDS -----
BovCFB_genDNA CCAAATTA AACAGCTGCG----- 5914
BovCFB_CDS -----

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Note: Human CFB (Ensembl ENSG00000204359), Sheep CFB (GB EF446375) and Bovine CFB (GB GI:76650941)

Supplementary Table 1: Sequencing primers for *CFB*

Locus	Forward (5'-3')	Reverse (5'-3')
Bf1	CTTTAGGTGTGGGCATGA	GGACCCTGTCACTGAGAAAT
Bf2	GAAGTTATATTTCTCAGTGACAGG	TCTGACCTGAGGGTACAGAT
Bf3	CTTATCTGTACCCTCAGGTCA	CCACCTTCTCAATGAAATCT
Bf4	TCAGAGATTTTCATTGAGAAGG	CCTCTCAGTTCCAAAGGATT
Bf5*	GGAACCTGAGAGGGGTACTTT	CAAACCTGCAGGAGAGAC
Bf6	CGTCTCTCCTGCAGGTTT	GCCCCAGCTTCCATATCT
Bf7	CCTTTTACAGATATGGAAGCTG	ATCCTTACCCACGCTGAC
Bf8*	GTCAGCGTGGGTAAGGAT	ACCCTTACAAGCCGCTCT
Bf9	GCTTGTAAGGGTGAAGTTCT	GAACCTGGGGGTGACTAC
Bf10	GTAGTCACCCCCAGGTTC	TGTCGCAGATGTTTAATTTG
Bf11	CAAATTAACATCTGCGACA	AAAGGGCTATGGAGATTTTC

*Bf5 and Bf8 were used for PCR-RFLP and their products were digested with Sau3A and Alu1 (Promega Life Science) respectively.

Supplementary Table 2: Primers for SNP typing by pyrosequencing.

Locus	PCR primers (5'-3')	Pyrosequencing Primers
<i>CFB</i>	F: TCTGTGTAGGCAGCCTCCTT R: GGGACACCGCTGATCGTTTAATCAAGGTCAGCGTGGGTAA	GAGGGCACTGCAGAA
C2	F: GGGACACCGCTGATCGTTTACCGATGGCATAGATGTCTGA R: AAGGGGAGGAGTGGTAGGAA	GGAGGGGAGCGGA
Univ2_B	5'- Biotin- GGGACACCGCTGATCGTTTA -3'	