Table 1. mAbs used for flow cytometry and Western blotting

Antibody	Subclass	Specificity	Epitope (aa)	Reference
FH11	IgG2b	PrP	54–57	C. R. Birkett & J. Langeveld (personal communication)
4F2	IgG2b	PrP	61–76	Krasemann *et al.* (1999)
8G8	IgG2a	PrP	95–110	Krasemann *et al.* (1999)
6H4	IgG1	PrP	144–152	Korth *et al.* (1997)
44-97	IgG1	CD4 (T-cell subset)	–	Maddox *et al.* (1985)
IL-A51	IgG1	CD8 (T-cell subset)	–	MacHugh & Sopp (1991)
86D	IgG1	γ/δ T-cell receptor	–	Mackay *et al.* (1989)
CC-G33	IgG1	CD14 (monocytes)	–	Sopp *et al.* (1996)
25-69	IgG1	sIgM (B cells)	–	Maddox *et al.* (1987)
CC125	IgG1	CD11b (B-cell subset)	–	Hall *et al.* (1993)
CC32	IgG1	CD62 (lymphocyte subsets)	–	Howard *et al.* (1992)
CC21	IgG1	CD21 (B cells)	–	Sopp (1996)
DU2-104	IgM	CD72 (B cells)	–	Young *et al.* (1997)
CAPP2A	IgG1	CD41/CD61 (platelets)	–	Mateo *et al.* (1996)
TD14	IgG1	CD45 (leukocytes)	–	Bembridge *et al.* (1993)

Analysis of PrP^C expression on blood-cell populations by flow cytometry. PBMCs, granulocytes, erythrocytes and platelets were analysed by flow cytometry using one-colour indirect immunofluorescence. PBMCs, granulocytes and erythrocytes were distributed at 10^6 cells per well and platelets at 10^7 per well in a 96-well microtitre plate. Each fraction was incubated with the primary antibodies 4F2 (1 μg ml^{-1}), TD14 (1:10 dilution of culture supernatant) and CAPP2A (5 μg ml^{-1}) for 10 min at room temperature. All antibodies used for flow cytometry were diluted in PBS containing 1% (w/v) BSA and 0·1% (w/v) sodium azide, except for the platelet studies, where the antibodies were diluted in platelet buffer. PBMCs, granulocytes and erythrocytes were washed three times in PBS containing 1% (w/v) BSA and 0·1% (w/v) sodium azide at 400 *g* for 2 min. Platelets were washed three times in platelet buffer at 1000 *g* for 2 min. Cells were incubated for 10 min at room temperature with secondary goat anti-mouse immunoglobulin conjugated to fluorescein isothiocyanate (FITC), diluted 1:200 (Southern Biotechnology Associates) and then washed twice, as above. Negative controls included samples in which primary and/or secondary antibodies had been omitted and samples in which the primary antibody was replaced with an isotype-matched antibody of irrelevant specificity.

In some experiments, platelets and PBMCs were permeabilized to demonstrate intracellular PrP^C. Briefly, 100 μl Perm-2 solution (diluted 1:10 in distilled water; Becton Dickinson) was added to the cells and incubated for 10 min at room temperature and the cells were washed twice as described above. Cells were then labelled for PrP^C, as above. To demonstrate that cells were permeabilized adequately, Alexa fluor 568 phalloidin (Molecular Probes Europe BV) at a dilution of 1:40 was used as a positive control to stain the actin cytoskeleton.

For two-colour indirect-immunofluorescence analysis of PrP^C expression on subsets of PBMCs, samples were incubated for 10 min at room temperature with 8G8 (1 μg ml^{-1}) and one of the following subset-specific markers: 44-97, IL-A51, 86D, CC-G33, 25-69, CC125, CC32, CC21 or DU2-104 (Table 1). Antibodies were supplied as hybridoma-culture supernatants and were diluted 1:10 as above, apart from Du2-104, which was used undiluted. After washing as above, samples were incubated with isotype-specific secondary antibodies (Southern Biotechnology Associates): either FITC-conjugated goat anti-mouse IgG1 (diluted 1:100) or FITC-conjugated goat anti-mouse IgM (diluted 1:100), together with phycoerythrin-conjugated goat anti-mouse IgG2a (diluted 1:200) for 10 min at room temperature, then washed as above.

Cells were resuspended in 100 μl 1% (w/v) paraformaldehyde in PBS and stored overnight at 4 °C before analysis. As described previously (Barclay *et al.*, 2002), samples were analysed on a flow cytometer (FACSCalibur; Becton Dickinson) equipped with a previously calibrated 488 nm argon laser. Software used for analysis was WinMDI 2.8 (The Scripps Research Institute, CA, USA). For each sample studied, at least 10 000 cells of interest were acquired by appropriate gating based on light-scattering characteristics and/or expression of cell-specific markers.

Mean fluorescence intensity (MFI) was calculated by the WinMDI software as either the geometric mean of total PrP fluorescence for one-colour staining or the geometric mean of the PrP fluorescence in the gated cell subset for two-colour staining. The MFI for negative controls (PrP-specific mAbs omitted) was calculated for comparison. The negative-control values were subtracted from the mean PrP fluorescence to give a value corresponding to PrP-specific fluorescence.

Analysis of PrP^C expression in blood-cell populations by Western blotting. Fractions were prepared by using Histopaque-1083, as described above. All pellets were stored at −80 °C until required. Samples were thawed and diluted to an appropriate volume with PBS. An equal volume of 2× NuPAGE lithium dodecyl sulphate sample buffer (Invitrogen) was added to the sample, mixed and a 1:10 final dilution of NuPAGE sample reducing agent (Invitrogen) was added and mixed. All samples were heated for 5 min at 100 °C on a heating block before electrophoresis on 10% Bis/Tris NuPAGE Novex gels (Invitrogen) using standard protocols. NuPAGE antioxidant (Invitrogen) was added to the running buffer at a 1:400 dilution. Gels were electroblotted onto an Immobilon-P transfer membrane (Millipore) and blocked for 1 h in 5% (w/v) milk powder prepared in PBS containing 0·05% (v/v) Tween 20 (PBST). PrP was detected by probing the membrane with 4F2 [1 μg ml^{-1} in PBST containing 0·5% (w/v) milk powder] overnight at 4 °C. The membrane was then washed with PBST for 30 min (with six changes of buffer) and subsequently incubated for 1 h with goat anti-mouse IgG conjugated to horseradish peroxidase [diluted 1:7500 in PBST containing 0·5% (w/v) milk powder]. Blots were

washed as before and developed by using Supersignal West Pico chemiluminescent substrate (Perbio Science UK) and visualized on Hyperfilm ECL (Amersham Biosciences).

RESULTS

Expression of PrP^C in cellular components of blood

Expression of PrP^C on the surface of sheep granulocytes, PBMCs, platelets and erythrocytes was analysed by flow cytometry using a variety of PrP-specific mAbs (FH11, 8G8, 6H4 and 4F2) that bound to different epitopes on PrP (see Table 1). All cells were gated according to their light-scattering characteristics (data not shown).

The efficiency of the separation of different fractions was confirmed by staining with antibodies TD14 (CD45) and CAPP2A (CD41/CD61). CD45 was expressed on 100% of leukocytes (granulocytes and PBMCs), but not on platelets or erythrocytes (red blood cells) (Fig. 1a).

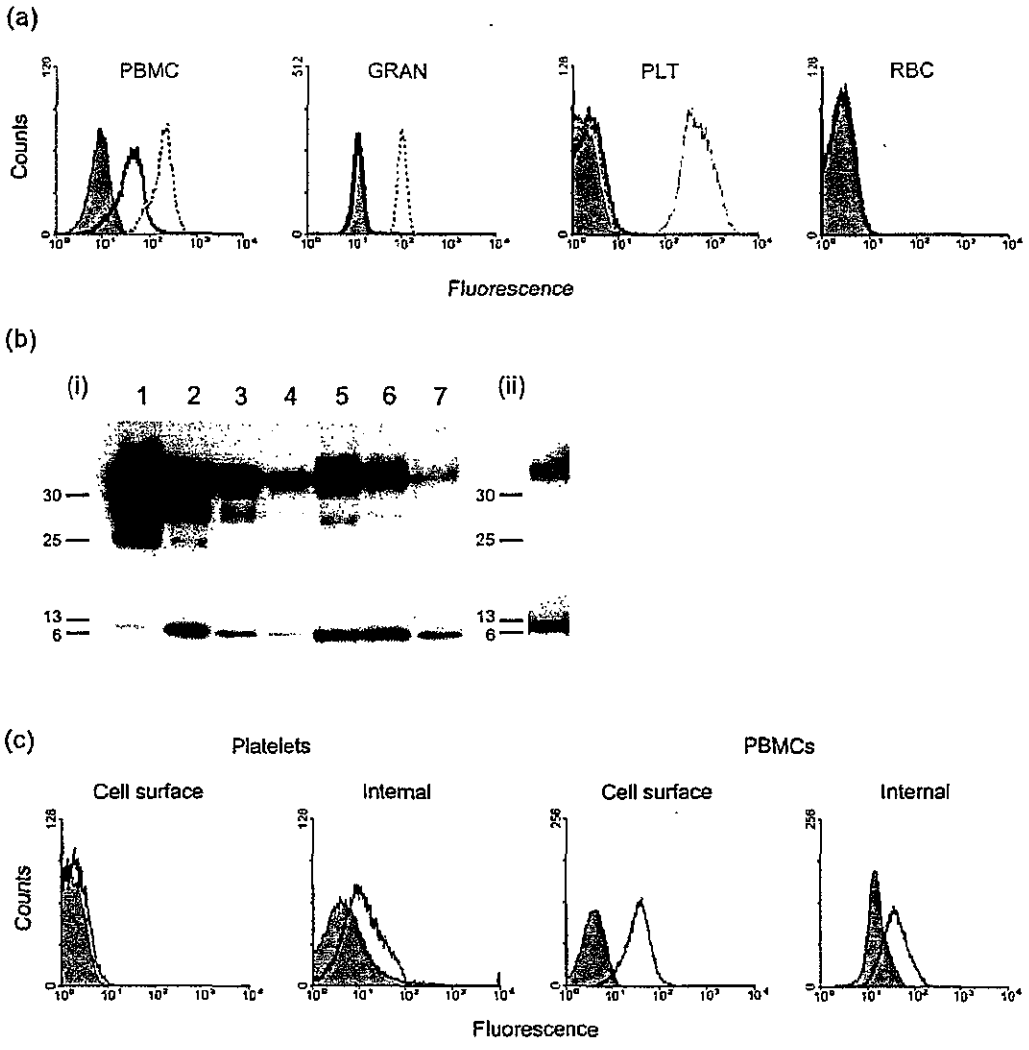

Fig. 1. Cellular distribution of PrP^C in uninfected sheep blood. (a) Cell-surface PrP^C expression on PBMCs, granulocytes (GRAN), platelets (PLT) and red blood cells (RBC) analysed by flow cytometry. Cells were stained by using antibodies to PrP (4F2, black line), CD45 (TD14, dashed line) and CD41/CD61 (CAPP2A, grey line). Filled area, negative controls (no antibodies). (b) Western blot analysis of PrP^C expression in sheep-blood cells, probed with mAb 4F2. (i) Lane 1, normal sheep-brain homogenate (equivalent to 80 ng tissue); lane 2, PBMCs ($\sim 1{\cdot}6 \times 10^6$ cells); lanes 3 and 4, doubling dilutions of PBMCs; lane 5, platelets ($\sim 3{\cdot}2 \times 10^8$ cells); lanes 6 and 7, doubling dilutions of platelets. Exposure time, 5 min. (ii) Red blood-cell membranes (equivalent to $\sim 1{\cdot}6 \times 10^8$ cells). Exposure time, 4 h. (c) Flow-cytometry analysis of intracellular PrP^C in platelets and PBMCs. Cells were stained with 4F2 (thick line) with or without permeabilization. Filled area, isotype-matched negative controls.

CD41/CD61 was expressed on >95% of ovine platelets. The erythrocyte population was negative for CD41/CD61, but a small percentage of leukocytes was positive. This has been observed previously (Mateo *et al.*, 1996; Sopp & Howard, 1997) and may be due to adherence of activated platelets or platelet fragments to the cells. No erythrocyte-specific markers were available; however, as the isolated population was negative for CD45 and CD41/CD61, it was assumed to be pure. Polymorphprep did not give a complete separation of granulocytes and PBMCs, presumably because sheep leukocytes have slightly different densities from the human equivalents. However, these two populations could also be distinguished readily by their light-scattering characteristics during flow cytometry.

Regardless of the mAb used, significant amounts of PrP^C were found only on PBMCs and not on the other cell populations (Fig. 1a). These results have been reported previously (Barclay *et al.*, 2002) and are in agreement with the findings of other investigators (Herrmann *et al.*, 2001). However, when the same cell populations were analysed by Western blotting, significant levels of PrP^C were detected in platelets (Fig. 1b), suggesting that it is in a predominantly intracellular location in these cells. The three bands representing diglycosylated, monoglycosylated and unglycosylated PrP^C were clearly visible at the highest concentration of PBMCs (as for brain-derived PrP^C). In both platelets and PBMCs, the diglycosylated form of PrP^C was predominant, but in platelets, there appeared to be much less of the mono- and unglycosylated forms. In addition, migration of the monoglycosylated protein appeared to be slightly faster in platelets than in PBMCs. This suggested that there are cell type-specific differences in the glycosylation pattern of PrP^C. A band with a molecular mass equivalent to that of diglycosylated PrP^C was also detected on erythrocyte membranes after prolonged exposure times [Fig. 1b(ii)], suggesting that this cell type may also express low levels of PrP^C. No PrP^C was detected in sheep granulocytes (data not shown), in line with the flow-cytometry results. In all lanes, a lower-molecular-mass band of approximately 9–10 kDa was seen, faintly in the brain sample but more prominently in platelet and PBMC samples. As mAb 4F2 binds to an epitope spanning residues 61–76 (octarepeat region) of PrP, this could represent an N-terminal cleavage fragment of the protein.

To confirm the intracellular location of PrP^C in platelets, both platelets and PBMCs were permeabilized and analysed by flow cytometry using mAbs 4F2, 8G8 and 6H4. PrP^C was detected in both permeabilized platelets and permeabilized PBMCs (Fig. 1c). To confirm that permeabilization had occurred, staining with Alexa-fluor 568 phalloidin marker, which binds specifically to F-actin, was used as a positive control (data not shown). The platelets were contaminated with a small percentage of leukocytes ($CD45^+$), but these were excluded from the analysis by gating using light-scattering characteristics.

Influence of PrP genotype on PrP^C expression by PBMCs

Susceptibility or resistance to scrapie in sheep is controlled to a large extent by coding polymorphisms of the PrP gene. The polymorphisms with the most significant effects are located at codons 136, 154 and 171, and alleles are designated by a three-letter code indicating the amino acids encoded at these positions. VRQ and ARQ alleles are associated with susceptibility to scrapie, whereas the ARR allele is associated with resistance. We examined the level of PrP^C expression on PBMCs from healthy sheep of three PrP genotypes (VRQ/VRQ, ARQ/ARQ and ARR/ARR; $n=7$ for each genotype) by indirect-immunofluorescence flow cytometry using mAbs FH11, 6H4 and 8G8, which bind to different epitopes on PrP, including the N-terminal and the more structured C-terminal domains of the protein. The MFI was calculated for each antibody as a measure of the amount of antibody bound to cell-surface PrP^C (Fig. 2a). Regardless of the mAb used, PBMCs from VRQ/VRQ sheep expressed higher levels of PrP^C than those from ARR-homozygous sheep, and these differences were statistically significant in pairwise comparisons using the Student's *t*-test ($P<0{\cdot}05$). PBMCs from ARQ/ARQ sheep had a level of PrP^C expression intermediate between those from VRQ/VRQ and ARR/ARR sheep, but the differences were not statistically significant. All three mAbs produced a monophasic staining pattern in each PrP genotype (Fig. 2b), so the differences could not be explained by the biphasic staining pattern seen in ARQ and ARR homozygotes by other investigators using different antibodies (Thackray *et al.*, 2004).

Level of PrP^C expression on different lymphocyte subsets varies and is highest on a subpopulation of B cells

The level of PrP^C expression on different PBMC subsets was examined by using two-colour indirect immunofluorescence on uninfected sheep with genotypes VRQ/VRQ and VRQ/ARQ ($n=4$ for each genotype). The PrP-specific mAb 8G8 was used in combination with a panel of mAbs identifying different PBMC subsets. Comparison of the MFI calculated for each subset indicated that PrP^C expression was detected at varying levels on all major subsets of PBMCs, including $CD4^+$, $CD8^+$ and γ/δ T cells, B cells and monocytes (Fig. 3). Levels of expression showed a consistent pattern of variation, depending on cell type. There did not appear to be significant differences between VRQ/VRQ and VRQ/ARQ sheep in the amount of PrP^C expressed on PBMC subsets, except in $CD21^+$ and $CD72^+$ B cells, where expression levels were much lower in VRQ/VRQ sheep. The reason for this difference is not clear. In both genotypes, high levels of PrP^C expression were seen on $CD62^+$ (L-selectin) cells, and PrP^C was expressed at higher levels on $CD21^+$ B cells than on $CD72^+$ B cells.

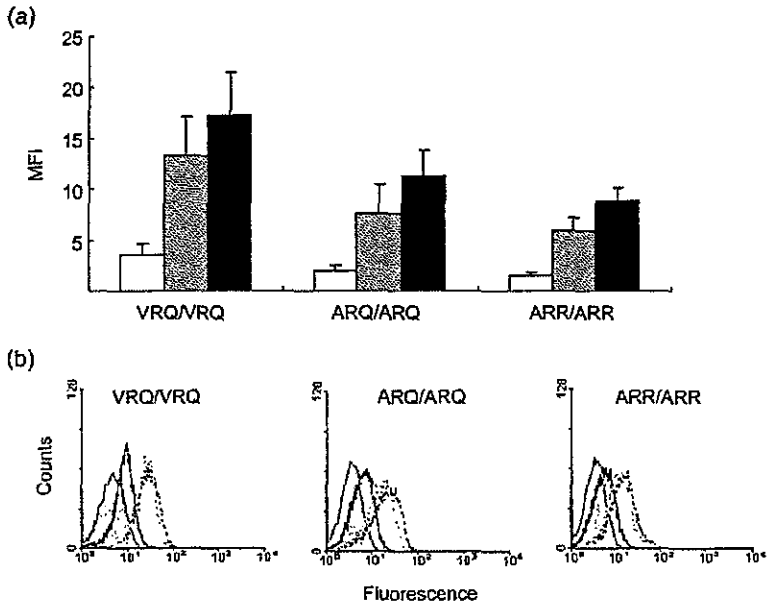

Fig. 2. Effect of PrP genotype on the PrP^C expression level of sheep PBMCs. (a) MFI values (mean ± SD; $n=7$) are shown for PBMCs from uninfected sheep homozygous for VRQ, ARQ and ARR, incubated with FH11 (open bars), 6H4 (hatched bars) and 8G8 (filled bars). (b) Representative flow-cytometry staining profiles for each antibody: FH11 (black line), 6H4 (grey dashed line) and 8G8 (black dashed line). Filled area, isotype-matched negative controls.

Expression of PrP on PBMCs of scrapie-infected sheep

The level of PrP^C expression on PBMC subsets was examined in scrapie-infected sheep with the PrP genotypes VRQ/VRQ (Fig. 4a) and VRQ/ARQ (Fig. 4b) and compared with uninfected sheep of the same genotypes ($n=4$ for each group). In general, scrapie infection appeared to result in higher levels of PrP being detected on the surface of PBMC subsets. Principal-component analysis revealed that the PrP-specific MFI values for $CD62^+$ and $CD21^+$ subsets provided the greatest significance in separating scrapie-infected from uninfected sheep (data not shown). These results suggested that there are increased levels of PrP on PBMCs from some scrapie-infected sheep, particularly on the $CD21^+$ and $CD62^+$ subsets, which warrants further investigation. As antibodies that distinguish PrP^C and PrP^{Sc} (or other disease-associated isoforms) are not readily available, we could not tell whether the increase in cell-surface PrP was a result of accumulation of PrP^{Sc} or altered turnover of PrP^C.

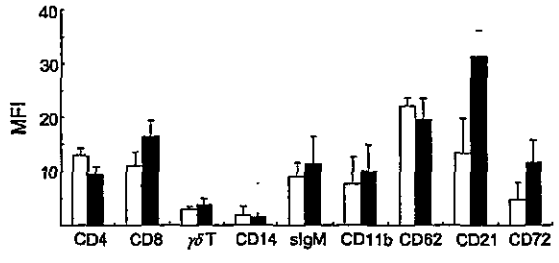

Fig. 3. PrP^C expression on PBMC subsets from uninfected sheep. PBMCs from VRQ/VRQ (open bars) and VRQ/ARQ (filled bars) sheep were analysed by two-colour immunofluorescent staining, using subset-specific mAbs and 8G8. Each bar represents the MFI (mean ± SD; $n=4$) in the FL2 channel (PrP) for each subset.

DISCUSSION

PrP^C is expressed widely in tissues other than the nervous system, although its precise function(s) remains obscure.

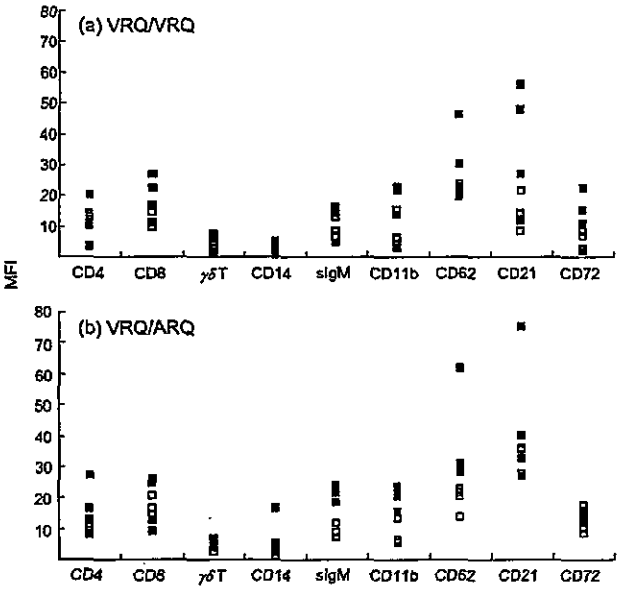

Fig. 4. Comparison of PrP^C expression on PBMC subsets from uninfected and scrapie-infected sheep. (a) VRQ/VRQ sheep; (b) VRQ/ARQ sheep. Individual values for MFI in the FL2 channel (PrP) are shown for uninfected (□) and scrapie-infected (■) sheep ($n=4$ for each group).

The distribution of PrP^C on cellular components of blood shows species-specific variation and our results confirm previous work demonstrating that, in sheep, cell-surface expression of PrP^C is confined to PBMCs. However, in follow-up studies using Western blotting, we have now demonstrated that sheep platelets contain significant amounts of PrP^C in an intracellular location. This is surprising, as sheep platelets have been reported not to express *mRNA for PrP (Herrmann et al., 2001). However, it is* possible that, in sheep, all PrP^C synthesis takes place in the megakaryocytes from which the platelets are derived. Human platelets have been shown to contain PrP^C in intracellular granules and, after activation, they both up-regulate surface PrP^C expression and release soluble PrP^C (Holada *et al.*, 1998; Perini *et al.*, 1996). The latter is thought to be the source of the large amounts of soluble PrP^C found in human plasma (MacGregor *et al.*, 1999). However, the functional significance of platelet-associated PrP^C remains unclear.

PrP^C expression alone does not appear to be sufficient to render a particular tissue or cell type susceptible to TSE infection, as it is expressed in many tissues that do not become infected during disease (Bendheim *et al.*, 1992). Conversely, although hamster PBMCs do not express PrP^C, infectivity is associated with these cells in hamsters infected experimentally with scrapie (Holada *et al.*, 2002). In this case, it is possible that hamster PBMCs act as carriers of the infectious agent, without being actively infected themselves. Here, we have shown that the level of PrP^C expression on sheep PBMCs correlates with PrP genotype, with the highest levels found on PBMCs from sheep that are highly susceptible to scrapie (PrP genotype VRQ/VRQ) and the lowest levels on scrapie-resistant sheep (PrP genotype ARR/ARR). These results disagree with those published recently by Thackray *et al.* (2004), who concluded that PBMCs from scrapie-susceptible and -resistant sheep expressed similar levels of cell-surface PrP^C. The reason for the discrepancy is not clear, but probably relates to the different mAbs used in their experiments. They measured the binding of two N-terminal mAbs with predicted epitopes between residues 25 and 89 of sheep PrP and one of these mAbs did in fact stain a significantly higher percentage of PBMCs from VRQ-homozygous sheep compared with ARQ and ARR homozygotes. In our experiments, we used three PrP-specific mAbs with epitopes in different regions of the molecule at residues 54–57 (FH11), 95–110 (8G8) and 144–152 (6H4), which did not include the polymorphic residues at positions 136 and 171. The genotype-specific differences in PrP^C staining were observed consistently with each of these antibodies, making it unlikely that the results can be explained by differences in antibody affinity for the variant PrP proteins or subtle differences in protein conformation that might influence the accessibility of certain epitopes to antibody binding. The much lower levels of binding of FH11 compared with the other two mAbs may possibly be explained by expression of an N-terminally truncated form of PrP^C on PBMCs, which would lack the FH11 epitope. Further work will be required to determine whether PrP-dependent differences in PrP^C expression levels extend to other tissues and to elucidate the mechanisms controlling protein levels expressed by different PrP alleles. These could operate at the level of gene transcription and translation, or result from differences in the rate of turnover of different PrP proteins. Thermal-denaturation studies with recombinant ovine PrP proteins *have shown that the formation of unfolding intermediates* of VRQ and ARQ proteins requires higher activation energy than in the case of ARR proteins, implying that susceptibility-associated PrP variants are intrinsically more stable than the ARR protein (Rezaei *et al.*, 2002). In addition, it has been found that recombinant ARR protein is degraded more rapidly by proteasomes than VRQ protein (Tenzer *et al.*, 2004). Factors such as these might contribute to a more rapid turnover of ARR PrP, leading to reduced cell-surface levels. It is possible to speculate that this could contribute to disease resistance by reducing the opportunity for conversion of ARR protein to the disease-associated isoform.

PrP^C was found on the cell surface of all subsets of PBMCs and there was considerable variation in expression levels between the different subsets. In both VRQ/VRQ and VRQ/ARQ genotypes, PrP^C expression was increased on $CD21^+$ B cells in comparison with cells expressing CD72, a pan-B-cell marker. In peripheral blood of adult sheep, there are two distinct subsets of B cells, which can be distinguished by their expression of the markers CD21, CD62 (L-selectin) and CD11b (Gupta *et al.*, 1998; Young *et al.*, 1997). The $CD21^+CD62^+CD11b^{lo}$ subset recirculates through secondary lymphoid tissues, whereas the $CD21^-CD62^-CD11b^{hi}$ subset is confined to blood and the marginal zone of the spleen. These subsets have been compared with the B1 and B2 cell subsets found in mice, but they do not share all their characteristics and it is unclear whether they represent distinct cell lineages or different maturation stages of B cells. Our results showing high levels of PrP^C expression on $CD21^+$ cells and lower levels on surface IgM^+, $CD72^+$ and $CD11b^+$ cells suggest that the recirculating B-cell subset expresses much more PrP^C at the cell surface than the non-recirculating subset. In addition, high levels of PrP^C expression were found on $CD62^+$ cells, which include α/β and γ/δ T cells as well as $CD21^+$ B cells and also recirculate preferentially through lymph nodes and *Peyer's patches.*

Further work is required to determine whether PBMC subsets expressing higher levels of PrP^C are more susceptible to scrapie infection and the implications for the peripheral pathogenesis of scrapie. However, a preliminary comparison of PrP expression levels in uninfected and scrapie-infected sheep suggested that, in some infected sheep, very high levels of PrP were found on $CD21^+$ B cells and $CD62^+$ lymphocytes. As we did not have access to mAbs that can distinguish PrP^{Sc} from PrP^C, it is not possible to say whether the apparent increase in protein levels is a result of

PrP^{Sc} *accumulation or upregulation of* PrP^{C} *expression in* response to infection. Further investigations using larger numbers of scrapie-infected sheep will be necessary to establish whether this observation is consistent enough to demonstrate statistical significance and whether it reflects the distribution of infectivity.

Following the reports of transmission of TSEs by blood transfusion in sheep (Houston *et al.*, 2000; Hunter *et al.*, 2002) and recent reports of two transfusion-associated cases of vCJD (Llewelyn *et al.*, 2004; Peden *et al.*, 2004), there is considerable interest in using sheep as a model for transmission of vCJD by blood products in humans. To characterize sheep fully as a model species, it is important to establish PrP^{C} expression patterns in the blood of uninfected sheep, as there are marked differences between species in the distribution of PrP^{C} in blood components. The results presented in this paper provide a more detailed picture of PrP^{C} expression on cellular components of sheep blood. In particular, platelets have been shown to contain intracellular PrP^{C}, although it cannot be detected at the cell surface, and in PBMCs, the highest levels of PrP^{C} expression were found on subsets of cells that recirculate preferentially through lymph nodes and Peyer's patches. In addition, expression of PrP on these particular subsets was upregulated dramatically in some scrapie-infected sheep. These findings provide valuable baseline data for studies on the distribution of infectivity and PrP^{Sc} in the blood of TSE-infected sheep and suggest that B-cell subsets may play a significant role in the peripheral pathogenesis of scrapie in sheep.

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研究報告の概要

背景：非常に高感度な dissociation-enhanced lanthanide fluoroimmunoassay （DELFIA）及びフローサイトメトリーが開発され、健常成人供血者の全血及び分離成分における可溶性細胞プリオンタンパク質（PrP^C）発現の特性を明らかにするために用いられている。これまでに、これらの手法を用いて変異型クロイツフェルト・ヤコブ病（vCJD）患者の血液中の PrP 発現及び濃度を評価した研究はない。

試験デザイン及び方法：vCJD 患者、孤発性クロイツフェルト・ヤコブ病（sCJD）患者、非 CJD 神経疾患対照、健常成人の血液について DELFIA を用いて PrP^C を、フローサイトメトリーを用いて細胞由来 PrP を測定した。

結果：DELFIA 解析により、健常成人と比較して全血中の PrP^C 濃度の有意な低下が vCJD 患者（p=0.012）と非 CJD 神経疾患患者（p=0.0004）で認められた。健常成人（p=0.022）及び神経疾患対照（p=0.050）と比較して sCJD 患者で血漿中 PrP^C における有意な上昇が認められた。フローサイトメトリーでは、血小板やリンパ球における PrP の発現や細胞内 PrP のプロテイナーゼ K に対する感受性に有意な差異は認められなかった。健常成人と比較して赤血球中の PrP は、神経疾患対照で有意に低値であった。

結論：CJD 患者と対照群の血液中に認められる細胞遊離型及び細胞由来 PrP には差があり、診断の一助として疾患を分析する上でその他の検査に有用となる可能性がある。

報告企業の意見	今後の対応
Dissociation-enhanced lanthanide fluoroimmunoassay（DELFIA）及びフローサイトメトリーを用いて変異型クロイツフェルト・ヤコブ病（vCJD）患者の血液中の PrP 発現及び濃度を評価したとの報告である。	今後も引き続き、プリオン病に関する新たな知見及び情報の収集に努める。

使用上の注意記載状況・その他参考事項等

赤血球M・A・P「日赤」
照射赤血球 M・A・P「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD 等の伝播のリスク