特別講演 1**II-1 Platelet room temperature storage versus platelet refrigeration.**

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Refrigeration of platelets results in their rapid clearance after transfusion. One pathway that mediates the rapid removal of transfused platelets exposed to cold for short periods (≤ 4 h) is the clustering of the von-Willebrand factor (VWF) receptor complex. Clustered VWF receptors are recognized by the α M β 2 integrin on hepatic macrophages, which, through its lectin domain (J. Biol. Chem. 280 : 18025, 2005), binds exposed β N-acetylglucosamine (β GlcNAc) residues on the clustered GPIb α subunits (Cell 112 : 87, 2003). Blocking s-GlcNAc residues of the clustered GPIb α with galactose prevents binding of mouse platelets to macrophages, prolonging circulation times of refrigerated platelets. Platelet-associated surface galactosyltransferase efficiently galactosylates chilled platelets when UDP-galactose is added to platelet-rich plasma (Science 301 : 1531, 2003).

Because an externally-exposed glycosyltransferase activity contradicts the dogma that such enzymes reside solely within the Golgi apparatus, we explored the origin of this enzyme in murine megakaryocytes and its mechanism of delivery to platelets. In immature megakaryocytes, the Golgi organizes into perinuclear arrays. However, once proplatelet extension begins, the perinuclear apparatus disassembles, and Golgi-associated proteins, such as GM130 and an YFP tagged Golgi marker construct based on the polypeptide transferase GalNAc-T2, are transported through the proplatelets in vesicular/granular structures. Labeling with platelet granule markers reveals correspondence of Golgi markers with predominantly dense granules, suggesting that Golgi membrane becomes packaged into granules, which deliver Golgi-associated glycosyltransferases and other "immature" glycoproteins into the nascent platelets and from there to the platelet surface.

Using an array of monoclonal antibodies towards the VWF receptor complex and fluorescence resonance energy transfer (FRET), we have shown that refrigeration of platelets in plasma for ≥ 48 h induces both conformational changes and clustering of the VWF complex, to prime it for activation by inducing VWF binding. To characterize the hemostatic function of refrigerated and galactosylated random human platelets processed in the blood bank, we studied platelet aggregation in vitro under static and flow conditions and expression of integrin $\cdot$ 3 (CD61), P-selectin (CD62P), GPIb $\cdot$ (CD42b) using flow cytometry, as well as annexin V binding and integrin $\cdot$ II $\cdot$ 3 activation. Circulatory ability of galactosylated, refrigerated platelets was evaluated using THP1 macrophages, which recognize and phagocytize refrigerated platelets. Platelets refrigerated and galactosylated for 14 days 1) maintained their ability to aggregate when exposed to agonists ; 2) showed less pronounced changes in surface expression of GPIb $\cdot$ compared to room temperature stored platelets ; 3) increased P-selectin expression ; and 4) were poorly phagocytised by differentiated THP1 cells in vitro. In addition, refrigerated (≤ 14 days) platelets still adhere well to collagen-coated surfaces under flow (1000 seconds $^{-1}$ for 2 min), demonstrating that VWF receptor function remains intact.

We propose that galactosylation is an efficient method to preserve refrigerated platelet function and to prevent recognition by macrophages in vitro.

特別講演 2

II-2 "The Blood Programme for vCJD in the UK"

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vCJD, described less than 10-years ago by the National CJD Surveillance Unit (Edinburgh), has already had a significant impact on the UK blood supply. Precautionary measures already taken in chronological order are :

- 1977 Withdrawal and recall of any blood components, plasma derivatives or tissues obtained from any individual who later develops vCJD ;
- 1998 Importation of plasma from countries other than the UK (mainly from the US) for fractionation to manufacture plasma derivatives (announced May 1998, fully implemented October 1999) ;
- 1998 Decision announced to leucodeplete all blood all blood components ; fully implemented October 1999 ;
- 2002 Department of Health (DH) purchased a US plasma collection facility to secure long-term supplies of non-UK blood plasma for the benefit of UK patients ;
- 2003 Individuals who had received a transfusion of blood components in the UK since 1980 were excluded from donating blood
- 1998 et seq. Promotion of appropriate use of blood and tissue products and use of alternatives throughout the National Health Service (reduction in red cell use over the last 5-years = 15%).

Key events :

- 2004 December—first possible transmission of vCJD by blood transfusion ;
 - 2005 January—all known recipients of "vCJD" donors notified of their risk ;
 - 2004 June—second possible transmission of vCJD ;
 - 2005 July—notification of donors whose blood had been transfused to individuals who developed vCJD
- Impact of vCJD on blood donors : reduction in donor pools—whole blood and apheresis donors
Potential future impact when a vCJD blood-screening test becomes available
Preparatory Initiatives : —evaluation of PRION removal filters
—test assessment facility for vCJD blood test when available
Risk Assessments and Contingency Planning
Market Research and Donor Surveys to predict some of the impacts of vCJD on the blood supply