

## **ABSTRACT**

The cellular prion protein (PrP<sup>c</sup>) is essential for pathogenesis of fatal neurodegenerative prion diseases. Recently reported four cases of vCJD transmission by blood transfusion raise concerns about the safety of blood products. Proper understanding of PrP<sup>c</sup> in blood is necessary for development of currently unavailable blood screening tests for prion diseases. Flow cytometry is an attractive method for prion detection, however, the reports on the quantity of PrP<sup>c</sup> on human blood cells are contradictory.

We showed that the majority of PrP<sup>c</sup> in resting platelets is present in the intracellular pool and is localized in  $\alpha$ -granules. We demonstrated that both, human platelets and red blood cells (RBC) express significant amount of PrP<sup>c</sup> and thus may play an important role in the transmission of prions by blood transfusion. Our results suggest a unique modification of PrP<sup>c</sup> on human RBC. Such modification of pathological prion protein could distort the results of blood screening tests for prions. Further we showed that the storage of blood prior to analysis and the choice of anti-prion antibody greatly affect the detection of PrP<sup>c</sup> by flow cytometry and we identified platelet satellitism as a factor contributing to the heterogeneity of PrP<sup>c</sup> detection in blood cells. Moreover, we demonstrated existence of washable pool of PrP<sup>c</sup> on the leukocytes of cynomolgus monkeys. Next we studied the role of PrP<sup>c</sup> in erythropoiesis. We demonstrated that surface expression of PrP<sup>c</sup> on mouse erythroid precursors in bone marrow and spleen follows similar pattern during the cells' maturation. PrP<sup>c</sup> expression in differentiating MEL cells mimics the pattern seen *in vivo* suggesting PrP<sup>c</sup> importance in early stages of erythroid differentiation. Moreover, PrP<sup>c</sup> expression accelerated recovery from stress erythropoiesis in inbred mice.

In conclusion, this study contributes to knowledge about the PrP<sup>c</sup> distribution and function in blood cells which is important for development of blood screening test for prion disease.

### **Key words:**

cellular prion protein, flow cytometry, erythroid differentiation, physiological role