Abstract

The cellular prion protein (PrP^C) is evolutionary conserved protein expressed in cells of various origins. Although PrP^C plays a basic role in the pathogenesis of the fatal neurodegenerative prion disorders, its physiological role remains enigmatic. Prion diseases are characteristic by long latency period during which they are not identifiable by any conventional methods. Although the blood is an ideal material for developing of screening tests, little is known about traits of PrP^C and its role in blood cells. We showed that human erythrocytes express low amounts of PrP^C per cell, but due to the high numbers of erythrocytes, they are major contributors to the pool of blood cell-associated PrP^C. Based on our biochemical characterization we propose that PrP^C on human erythrocytes is uniquely modified. Such a modification in abnormal prion protein may complicate screening tests for prion diseases in blood. It was reported that prion diseases deregulate the transcription of erythroid genes, and $PrP^{-/-}$ mice demonstrate a defective response to experimental anemia. To investigate the role of the PrP^C in erythropoiesis, we studied the protein's expression on mouse erythroid precursors *in vivo* and *in vitro*. We showed that surface expression of PrP^C on erythroid precursors in bone marrow and spleen follows similar pattern as the cells mature. We demonstrated that the regulation of PrP^C expression in differentiating murine erythroleukemia cells (MEL) cells resembles its regulation seen *in vivo*. Using RNA interference (RNAi) we created MEL lines with stably silenced expression of PrP^C, which showed that under normal conditions PrP^C seems dispensable for erythroid differentiation of MEL cells. We further used RNAi methodology to study the effect of PrP^C silencing on the propagation of prion infection and its influence on neuronal CAD5 cell culture.