Summary

The conformational conversion of the cellular prion protein (PrPc) to the misfolded isoform (PrPsc) is the central pathogenic event in the transmissible neurodegenerative prion diseases. The recently shown transmissibility of variant Creutzfeldt-Jakob disease by blood transfusion emphasizes the need for better understanding of the PrPc in blood. In the current thesis, we focused on blood platelet PrPc, which has not been very well described so far.

In the first part of the thesis, platelet PrPc was characterized as glycosylphosphatidylinositol-anchored glycoprotein with dominant diglycosylated form. Platelet PrPc was shown to be sensitive to cleavage with proteinase K, which is a feature discriminating between cellular and pathological prion protein. We have confirmed that platelet PrPc binds copper ions by its N-terminal octapeptide repeat region. Regarding quantity of PrPc molecules expressed on blood elements we have proved that both platelets and red blood cells express considerable amount of PrPc and thus can not be neglected in the problematic of prions transmission by blood transfusion. The detailed study regarding PrPc localization in blood platelets is presented in the second part of the thesis. PrPc was shown to be expressed in α-granules as well as on the cytoplasmic membrane of platelets. Substantial amount of PrPc was found to localize in the lipid rafts. The majority of lipid raft associated PrPc was shown to be linked to platelet cytoskeleton. As for revealing the physiological role of PrPc in blood platelets further research needs to be done.

Taken together, blood platelets express indispensable amount of PrPc, which does not significantly differ from very well described neuronal PrPc. Thus, our results are support for next study of the role of platelet PrPc in the pathogenesis of prion diseases.