4 Conclusion

As discussed before, lysosomal disorders can provide clues about the function of a deficient protein and about important cellular mechanisms. Because of that it is worthwhile to study patients with these rare disorders and learn from complex disease manifestations at biochemical, morphological and molecular levels.

This thesis is accompanied with papers on sphingolipidoses, the most frequent group of lysosomal disorders, and a mucopolysaccharidosis. The core of the thesis is analysis of the molecular causes of diseases in relation to clinical manifestations. There is a practical application to that, because enzyme replacement therapy, an effective, but extremely expensive treatment, is available for several of lysosomal storage disorders. Prediction of the future severity of the disease can identify patients, who can benefit most from the treatment. There is a trend to preventive treatment which can stop development of irreversible changes in the patients tissues. Because of excessive costs of the treatment even the richest countries do not treat all patients with these diseases.

In Fabry disease we have shown for the first time that X-inactivation influences the severity of the disease in heterozygous females. Analysis of inactivation has a potential to become a predictive test in Fabry females – this, however, must be confirmed by further studies.

Another contribution of this thesis is the finding of the gene mutated in MPS IIIC. The gene encodes an unusual lysosomal membrane protein, N-acetyltransferase, belonging to a new protein family, members of which are in addition to N-acetyltransferase bacterial proteins carrying COG4299 domain.