Fabry disease is an inherited defect of lysosomal α-galactosidase A (α-GALA), causing progressive accumulation of glycosphingolipids with terminal α-galactosyl moieties, especially globotriaosylceramide (Gb_3Cer) and in to a small extent also galabiosylceramide (Ga_2Cer) and blood group B glycolipids, in most tissues and body fluids.

This diploma thesis is an extension of previous laboratory studies and intends to contribute to clarification of some specific features of catabolic pathways of glycolipids substrates in lysosomal storage disorders, especially blood group B glycolipids. Therefore, analysis of human pancreas and lungs tissues was performed using TLC imunodetection and immunohistochemical analysis of these glycolipids. The most striking observation was massive accumulation of B-6-2 glycolipid and of others complex B-glycolipids in the pancreas of the patient with Fabry disease with blood group B. The level of blood group B substrates exceeded significantly storage of Gb_3Cer substrate.

An important part of this work were metabolic experiments in cell cultures in order to answer the question about participation of related glycosidases – α-galactosidase A and α-N-acetylgalactosaminidase (α –NAGA) in the lysosomal degradation of glycosphingolipids with terminal α-galactose.

Loading experiments were performed using labeled [^{3}H]B-6-2 glycolipid in the cultures of skin fibroblasts of patients with α-GALA, α-NAGA deficiencies, with prosaposin and saposin B deficiencies. In the cells with deficient activity of α-GALA, block in the first stage of degradation of the substrate B-6-2 glycolipid (cleavage of terminal α-galactose), was not found. This result may suggest the participation of α-NAGA in the cleavage of natural substrates of α-GALA. Similarly, when activities of α-GALA and α-NAGA were measured *in vitro* with fluorogenic substrate, residual activity was observed. This activity was inhibited using N-acetylgalactosamine and is attributable to α-NAGA.

In the cells with the deficiency of prosaposin, first steps of B-6-2 glycolipid degradation were normal. Expected blocks in the degradation pathway were observed at the level of oligosaccharide chain with four and two sugars containing (β1→4) galactose.

Finally, a preparation procedure of non-radioactively labeled Gb_4Cer (C19:0 Gb_4Cer) was designed using commercial SCDase. This compound would replace radioisotope-labeled substrate [^{3}H]Gb_4Cer in future metabolic studies.