Death receptor-6 (DR6/TNFRsf21/CD358) is a receptor from the TNFR superfamily that likely participates in the regulation of proliferation and differentiation of T- and B-lymphocytes and neural cells. The 655-amino acid human DR6 is a type I transmembrane protein containing four cysteine-rich domains in its extracelular part and a death domain followed by the CARD-like region in its cytoplasmic part. Overexpression of DR6 in some cell lines leads to apoptosis, and/or to activation of nuclear factor NF-κB and stress kinases of the JNK family.

In the first part of our work we focused on molecular characterization of DR6, including the analysis of its posttranslational modifications. We found that DR6 is an extensively posttranslationally modified protein including *S*-palmitoylation and both *N*- and *O*-glycosylation. Six *N*-glycosylation and one *S*-palmitoylation sites were precisely mapped to appropriate asparagines and cysteine respectively. The juxtaposed linker region (between cystein-rich domains and the transmembrane part), which also contains Ser/Thr/Pro-rich region with clustered putative *O*-glycosylation sites, is required for the plasma membrane localization of DR6. *N*-glycosylation, but interestingly not *S*-palmitoylation, may play a role in targeting of DR6 into detergent-resistant glycosphingolipid-enriched microdomains.

In the next part of this work we cover our studies analyzing the regulation of DR6 expression in human hematopoietic cells. We found that DR6 is not expressed in resting peripheral blood T and B cells, but is significantly upregulated in activated both CD4+ and CD8+ T lymphocytes upon TCR-mediated stimulation in a NF-κB- and NF-AT-dependent manner. Unlike primary lymphocytes, Jurkat lymphoblastic leukemia T cells already express DR6 likely via constitutive activation of PI3K pathway and strongly downregulate DR6 expression upon stimulation via suppression of its transcription. Furthermore, we have analysed the role of predicted NF-κB- and NF-AT-binding sites in the DR6 promoter in the expression of DR6.

Studies and results presented in this thesis should contribute both to the molecular characterization of DR6 as well as to to the elucidation of the role of DR6 in the immune system.