One of the key features of cancer cells is the ability to escape programmed cell death (apoptosis). As a mechanism of apoptosis inactivation in cancer cells, somatic mutations of pro-apoptotic genes have been reported in many cancers.
Caspase 10 is an initiator caspase whose physiological function remains poorly understood. Also the ability of caspase 10 to substitute for caspase 8 in the death receptors apoptotic pathway is still controversial. However, the fact that some of the mutations found in CASP10 gene was associated with apoptosis defects (79, 81) suggest that caspase 10 could be also important in apoptosis initiation.
In our lab, there was found a heterozygous mutation in CASP10 gene of Jurkat (human T-acute lymphoblastic leukemia) clone resistant to TRAIL (J-TR1). This mutation influence the amino acid composition close to the active site of the enzyme.
The aim of this thesis was to confirm the mutation by ARMS-PCR and to determine if an overexpression of normal (unmutated) or mutated caspase 10 D in TRAIL sensitive and/or TRAIL resistant Jurkat cells (J-WT and/or J-TR1) will influence TRAIL induced apoptosis.
Mutation was confirmed. We created J-WT and J-TR1 stable clones transfected by vector with unmutated or mutated CASP10 D (CASP10 D WT or CASP10 D MUT). CASP10 D MUT overexpression in J-WT clones didn't influence a total caspase 10 activity and didn't influence TRAIL induced apoptosis. Thus, the mutation don't play a role in resistance of J-TR1 cells to TRAIL.
CASP10 D WT wasn't overexpressed on protein level in majority of clones (expression only on mRNA level).