Summary

The survival of patients with malignant diseases can be increased in the future using more individualized therapies. Malignancies are more heterogenous in their drug sensitivity than they are rated into different subgroups for cytostatic treatment. Using of effective drugs determined by in vitro drug sensitivity test might result in a better clinical outcome. The most frequently used chemotherapy regimes originate from the non-Hodgkin lymphoma protocols and there are no specific cytotoxic drugs that would have been specifically selected against EBV induced lymphoproliferative disorders. As lymphoblastoid cell lines (LCLs) are well established *in vitro* models for posttransplant lymphoproliferative disorders (PTLD), we have assessed 17 LCLs for cytotoxic drug sensitivity. The precise number of living and dead cells was determined using a custom made automated laser confocal fluorescent microscope. Independently from their origin, LCLs showed very similar drug sensitivity patterns against 29 frequently used cytostatic drugs. LCLs were highly sensitive for vincristine, methotrexate, epirubicin and paclitaxel. Our data suggest that the inclusion of epirubicin and paclitaxel into chemotherapy protocols against PTLD may be justified. We characterized the effect of 28 frequently used chemotherapeutic agents on the capacity of NK cells to kill target cells. We found that treatment of NK cells with the drugs:including vinblastine, paclitaxel, docetaxel, cladribine, chlorambucil, bortezomib, MG-132 effectively inhibited NK mediated killing, without affecting the viability of NK cells. On the other hand we found drugs that permitted efficient NK-mediated killing even at concentrations comparable to or higher than the maximally achieved therapeutic concentration *in vivo*, in humans. We suggest that these drugs which include asparaginase, bevacizumab, bleomycin, doxorubicin, epirubicine, etoposide, 5-fluorouracil, hydroxyurea, streptozocin and 6-mercaptopurine could be combined effectivelly with NK based adjuvant immunotherapy:. Using MTT assay we also investigated how G-CSF might influence the sensitivity of leukemic cells to daunorubicin induced cell death.. After pretreatment of KG-1 leukaemic cells with G-CSF a moderate increase in the resistance of the cells to daunorubicin could be observed. This may draw attention to the risk of G-CSF application as an adjuvant therapy of AML and childhood ALL. In summary, we show in this thesis possibble ways to use the in vitro drug sensitivity assay for the clinical practice. In case of some patients where no effective protocols by proved multicentric randomized studies are available, as well as in case of rare malignant diseases or in advanced tumors, our new in vitro drug sensitivity assay may lead to develop novel cytostatic protocols against these malignancies.