1.2. SUMMARY

Antibodies can recognize tumor specific antigens expressed on the cell membrane. An increasing number of monoclonal antibodies is already in clinical use for therapy of malignant diseases. IgG-antibodies have been very successful for tumor therapy, e.g. the treatment of Non-Hodgkin's-lymphoma with the monoclonal anti-CD20-antibody Rituximab. One major goal of tumor immunologic research is the improvement of monoclonal antibodies to maximize therapeutic efficacy. Apart from antibody-dependent cellular cytotoxicity (ADCC) and direct antibody effects on the malignant cells (e.g. induction of apoptosis, bockade of important signaling pathways), complement activation (CDC) is an important mechanism of antibody triggered anti-tumor effects. The efficacy of complement derived tumor cell lysis is dependent on the antibody-class or –subclass, respectively. As IgM-antibodies are much more potent than IgG-antibodies in activating the complement system, the use of IgM-antibodies could contribute to improved tumor therapy.

Acute myeloid leukemia is the most frequent type of acute leukemias in adults. The CD33 antigen represents a good therapeutic target, because approximately 85% of all leukemia patients express this antigen on the surface of leukemic blasts but not on normal pluripotent hematopoietic stem cell.

In this thesis, the efficacy of an anti-CD33-IgG is compared with an anti-CD33-IgM antibody with respect to complement activation. Eukaryotic expression vectors encoding IgM light- and heavy chains were cloned and sequence verified. A transient expression system, based on HEK 293-EBNA-cells, allowed for the rapid production of limited amounts of recombinant protein (IgM-hexamer), which was purified thereafter using a two step chromatographic procedure.

Both antibody formats were correctly expressed and demonstrated by flow cytometry no relevant differences with respect to affinity. In the cytotoxicity assay, the IgM antibody format was more effective in terms of complement dependent cell lysis. This difference was already evident when using the same antibody concentrations and was even more pronounced at isomolar concentrations of both formats.

As depicted in this thesis, the IgM antibody-format is an interesting starting point for the improvement of antibody based tumor therapy. Whether these *in vitro* results also translate into a more efficient *in vivo* tumor therapy should be tested next in an animal model.