1. Summary

In vitro selection of DNA molecules has become an extremely useful technique to investigate the interaction of proteins with DNA. In my thesis, I have extended the technique of *in vitro* selection to DNA molecules under torsional strain. Libraries of negatively supercoiled plasmids or minicircles, containing a block of randomized sequence, were prepared and used to *in vitro* select double-stranded DNA ligands of the Zα domain of the human ADAR1 protein.

Under physiological conditions sequences of alternating purine and pyrimidine bases can adopt the Z-DNA conformation in the presence of negative supercoiling. The Zα domain is the only known high affinity protein ligand for Z-DNA. Until know now definite proof existed whether binding of Zα to DNA in addition to conformation specificity involves sequence specificity

Both the plasmid and minicircle libraries were successfully used in *in vitro* selection experiments with the Zα domain. The common sequence motif of the selected DNA sequences were stretches of alternating purine and pyrimidine sequences, especially those rich in CG and GC dinucleotides. Formation of the Z-DNA conformation by the selected sequences was shown by DEPC footprinting. The calculated propensity of the selected sequences to form Z-DNA was significantly higher than would be expected for random sequences.

The analysis of the selected sequences did not indicate any sequence specificity of DNA binding by the Zα peptide other than a preference for those sequences that most easily adopt the Z-DNA conformation. Similar results were obtained with Bandshift assays. I therefore propose that the Zα domain binds to DNA conformation specific and has negligible or no sequence specificity.