

7 Summary

Although the cause of the Alzheimer's disease is still unknown, it is supposed to be closely related with the deposition of amyloid peptides in the brain of patients. The amyloid is thus a major target in the search for novel diagnostics and therapeutic approaches. This work employs RNA-technologies to develop new tools for the study of the Alzheimer's disease. The *in vitro* selection enables the design of specific nucleic acids (aptamers) against almost any target molecule. The aptamers have similar properties as monoclonal antibodies, but several advantages. The chemical synthesis of these nucleic acids enables tailor-made modifications. By introduction of specific reporter groups these RNAs become suitable tools for analytical and diagnostic purposes. Since a change of the amyloid concentration has been reported in the blood of Alzheimer's disease patients, the use of amyloid-specific aptamers for diagnosing the disease seems conceivable. Moreover, antibodies have been reported that prevent the aggregation of amyloid into senile plaques. This points towards a potential therapeutic application of the amyloid-specific aptamers.

High affinity RNA aptamers against the β A4(1-40) and a fragment β A4(1-16) were isolated from a combinatorial library of 10^{15} different molecules by using *in vitro* selection. For this purpose a DNA library containing 70 randomised nucleotides was chemically synthesised and transcribed into RNA. Affinic molecules were isolated after 8 rounds of selection and amplification. The apparent dissociation constants of these aptamers were 29-48 nM for the long peptide and 758 nM for the short β A4(1-16) fragment. The binding constants for the aptamers against the amyloid are within the range of the highest affinities so far described for peptide-specific aptamers.

This work introduces a new approach for the study and diagnosis of the Alzheimer's disease. In future experiments, the efficacy of the aptamers needs to be tested. In addition, identifying the minimal binding motifs and enhancing the stability of the aptamers against RNase degradation are necessary steps to render these aptamers into reliable tools.