Zn^{2+} Dependent Peptide Nucleic Acids Probes

Andriy A. Mokhir, Roland Kraemer, Iris Boll

Anorganisch-Chemisches Institut, Ruprecht-Karls-Universitaet Heidelberg

ABSTRACT. Peptide nucleic acid (PNA) is a mimic of DNA, which has excellent binding affinity and sequence specificity towards oligonucleotides. Therefore, PNA has a strong potential as an antisense and antigene agent as it was established in cell-free systems and *in vivo*. In future therapeutical applications it might be of advantage if PNA can be activated only in specific cells, thus avoiding the risk of adverse side-effects in non-targeted cells. One of the approaches for this includes targeted delivery of PNA to specific cells using tethering PNA to the ligands recognised by cell receptors[1]. Another way is the activation of PNA by the component present in the cell. We have shown for the first time that Zn^{2+} can substantially increase binding affinity of terminally modified PNA to DNA targets *in vitro*[2]. Zn^{2+} is present at high concentration in brain, pancreas, and spermatozoa. In breast cancer, tissues zinc levels are increased by 72 %.

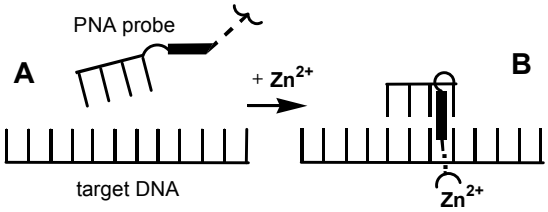

Figure 1. Zn^2 dependent binding of PNA to target DNA. Intercalator is shown as a thick line.

We have synthesized PNA, in which a Zn^{2+} chelating ligand is conjugated via an aromatic linker. Intercalation of the aromatic linker is regulated by the metal coordination to the ligand (Figure 1). In this poster we present results of optimization of structure of such conjugates to achieve the highest effect of Zn^{2+} on binding of PNA to DNA targets.

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2. A. Mokhir, R. Kraemer, H. Wolf, *J. Am. Chem. Soc.* **2004**, *126(20)*, 6208-6209.