Identification of novel Z-DNA binding proteins by computational approaches

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Z-DNA has a role in controlling various cellular processes such as chromatin remodeling, gene expression, and genome stability [1]. The structure and function of Z-DNA are tightly regulated by proteins containing Z-DNA binding motifs, but the species of Z-DNA binding proteins are limited. However, considering the role of Z-DNA in key cellular processes, it is expected that many Z-DNA binding proteins must be present in cells. To answer this question, we employed computational methods to predict a novel Z-DNA binding protein present in nature. First, atomic structures or predicted models of proteins were prepared from the Protein Data Bank (PDB) or Alphafold. Their structural similarities to the known Z-DNA were predicted using various available structural comparison programs. The 17 highly-ranked proteins were considered as the first candidates and their Z-DNA binding activity was predicted using the HDOCK server [2]. In addition, their DNA binding properties were also expected using a machine learning process. Finally, the B- and Z-DNA binding activity of the final seven candidates were estimated by molecular dynamic simulation and their binding energies. The experimental validation of this novel Z-DNA binding protein and its biological implications will be further investigated.

Figure 1. The binding mode of a novel Z-DNA binding protein identified in this study