

A possible method of gene editing using Ni(II)-induced zinc finger nucleases

^aI. Bálint, ^aB. Csipak, ^aA. Czene, ^bA. Belczyk, ^bA. Sparavier, ^cM. N. Asaka, ^cK. Nagata,
^bW. Bal, ^bB. Gyuresik

^aDepartment of Inorganic and Analytical Chemistry, MTA-SzTE Bioinorganic Chemistry
Research Group, University of Szeged, Szeged, Hungary

^bInstitute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland

^cNagata Special Laboratory, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

† Dr. Béla Gyuresik; e-mail: gyuresik@chem.u-szeged.hu; Dóm tér 7, 6720 Szeged, Hungary

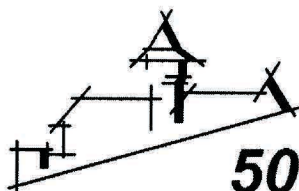
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The goal of our experiments was to design new type of artificial nucleases to specifically recognize, bind and cleave DNA for wide variety of purposes. Zinc finger proteins are modular specific DNA binders that can be designed to target any desired DNA base sequence. As such, they can control the function of genes, but they also can be turned into specific DNA manipulating agents. A hydrolytic reaction by means of which we can specifically cleave proteins by nickel(II) ions – results in a square planar metal complex at the N-terminus of the C-terminal cleavage product. The latter complex is known as ATCUN motif, which is able to cleave DNA. Based on these facts, the combination of the two experiments will, according to our expectations, will lead to the development of in situ prepared specific nucleases.

For this purpose, we established the optimal conditions of the specific cleavage of the zinc finger proteins both in the absence and presence of DNA. We elaborated a test system and a precise protocol to study the specific cleavage of the P-1MEY# zinc finger protein - which is modified to contain only one cleavage site for nickel(II) ions. Combined electrophoretic, HPLC, CD and MS measurements were applied to monitor the reaction and to determine the solution structure of the complexes formed.