

The Solution Structure of the Human ETS1-DNA Complex Reveals a Novel Mode of Binding and True Side Chain Intercalation. (1995). Cell 83, 761-771.

Erratum

Milton H. Werner,* G. Marius Clore,*
Constance L. Fisher,† Robert J. Fisher,†
Loc Trinh,‡ Joseph Shiloach,‡
and Angela M. Gronenborn*

*Laboratory of Chemical Physics
Building 5

National Institute of Diabetes and
Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland 20892-0520

†Frederick Cancer Research
and Development Center

National Cancer Institute
Frederick, Maryland 21707

‡Laboratory of Cellular
and Developmental Biology
National Institute of Diabetes and
Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland 20895-0520

Comparison of the published three-dimensional structures of the DNA binding domain (DBD)/DNA complexes of ETS1 by NMR (Werner et al., 1995) and the related Pu.1 by X-ray crystallography (Kodandapani et al., 1996) revealed an apparent discrepancy in which the protein domains bind with opposite polarity to their target sequences. This surprising and highly unlikely result caused us to reexamine our NMR structure. Further NMR experiments have revealed an unfortunate error in the original interpretation of the spectra defining the orientation of the ETS1-DBD on DNA. It was originally concluded that the ETS1-DBD bound to DNA with a bipartite motif involving major groove recognition via a helix-turn-helix (HTH) element and minor groove recognition via protein sidechain intercalation. The presence of intercalation was deduced on the basis of numerous nuclear Overhauser enhancements (NOEs) between several amino acids in the protein and a resonance at 12.33 ppm originally assigned to a DNA imino proton. New NMR experiments (specifically, a one-dimensional heteronuclear spin-echo difference spectrum and a three-dimensional ^{13}C -edited NOE spectrum recorded in water) demonstrate that this resonance, which is located within the imino proton region of the DNA spectrum, arises from the hydroxyl proton of Tyr-86. The misassignment of the resonance at 12.33 ppm was the crucial error which resulted in the incorrect orientation of the ETS1-DBD on the DNA. Confounding the original analysis in this particular case was the fact that ~90% of the intermolecular NOEs involved sugar H3', H4', H5', and H5'' protons whose resonances are located in a very crowded region of the spectrum with near degeneracies for almost all H3' and H4' protons and many complete degeneracies for the H5' and H5'' protons. Following the subsequent reanalysis of the intermolecular NOEs, the structure of the ETS1-DBD/DNA complex was recalculated (on the basis of 2118 experimental NMR restraints, including 35 intermolecular NOEs) and found

to be similar to the X-ray structure of the Pu.1-DBD/DNA complex (Kodandapani et al., 1996), thereby resolving the previous controversy in the literature. A schematic diagram of the revised structure of the ETS1-DBD/DNA complex (obtained by averaging the coordinates of 25 simulated annealing structures) is shown in Figure 1. A full description of the revised structure will be published elsewhere, and the coordinates and experimental restraints have been deposited in the Brookhaven Protein Data Bank (accession numbers 2STT, 2STW, and 2STW_MR).

References

Werner, M.H., Clore, G.M., Fisher, C.L., Fisher, R.J., Trinh, L., Shiloach, J., and Gronenborn, A.M. (1995). The solution structure of the human ETS1-DNA complex reveals a novel mode of binding a true side chain intercalation. *Cell* 83, 761-771.

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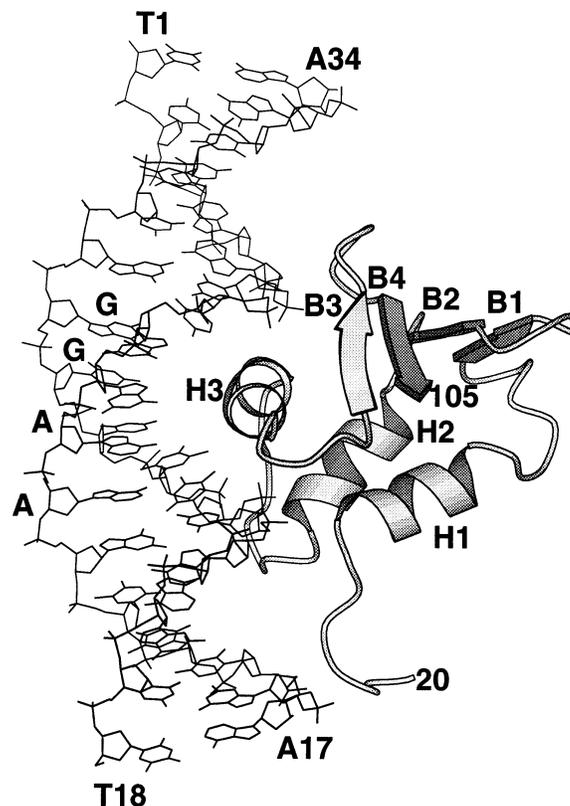


Figure 1. The NMR Structure of the ETS1/DBD DNA Complex
ETS1 is depicted as a ribbon diagram.