

FIGURE LEGENDS

Supplementary Figure 1. Sequence-specific base contacts in all classical ZNF:DNA complexes. (A) The canonical model. (B) ZNF217_F67 (PDB ID:4IS1), (C) Tramtrack_F12 (PDB ID: 2DRP) (1), (D) TFIIIA_F23_F5 (PDB_ID: 1TFG) (2), (E) Zif268_F123 (PDB ID: 1AAY) (3), (F) GLI_F45 (PDB ID: 2GLI) (4), (G) Gfi-1_F345 (PDB ID: 2KMK) (5), (H) KLF-4_F123 (PDB ID: 2WBS) (6), (I) GAGA (PDB ID: 1UYI) (7), (J) Aart_F123456 (PDB ID: 2I13) (8), (K) TATA_F123 (PDB ID: 1G2D) (9), (L) Designed ZNF protein F123 (PDB ID: 1MEY) (10). Zif268-like protein-DNA interactions are represented by black arrows. Non-canonical interactions are represented in red.

Supplementary Figure 2. Comparison of the two crystal forms of the ZNF217_F67-DNA complex. (A) Overlay of the C2 crystal form (magenta) and the P6₅22 form (blue). (B) Helical axis of the DNA helices of both crystal forms calculated using the software *Curves+* (11). Structures were overlaid over all heavy atoms.

Supplementary Figure 3. Fluorescence anisotropy titration data showing the DNA binding properties of ZNF217_F67. Binding of the GST-ZNF217_F67 construct (A), the ZNF217_F67 domain alone (B) and two ZNF217_F67 mutants (R481A and Y516A) in which one of the residue that contacts DNA in the structure has been substituted by an alanine (C) to three different 5'-fluorescein-tagged dsDNA oligonucleotides (sequences are detailed in Materials and Methods section 2.6). The association constants for the indicated interactions are specified on each graph, each value is the average of three measurements, and error bars indicate standard deviations from the mean.

Supplementary Figure 4. Overlay of ¹⁵N-HSQC spectra of ZNF217-F67 recorded in the absence (red) and presence (blue) of 1.5 molar equivalents of the specific (A) or nonspecific (B) DNA oligonucleotide. Sequences of the used oligonucleotides are detailed in Material and Methods.

Supplementary Figure 5. NMR spectroscopy titration data showing the DNA binding of ZNF217_F67 to the specific (A) or nonspecific (B) DNA sequences. ¹⁵N-HSQC spectra of the free protein (red) and bound to 0.8 (purple) and 1.5 (blue) molar equivalents of DNA.

