Graphical Abstracts

Therapeutic Agents Based on DNA Sequence Specific Binding
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Targeting Transcription Factor Binding to DNA by Competing with DNA Binders as an Approach for Controlling Gene Expression
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Minor-Groove Binding Agents: Rational Design of Carboxamide Bond Isosteres
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Structural and Functional Diversity of Estrogen Receptor Ligands

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Crystal structures of LB domain of ERα in agonist-bound (a) and antagonist-bound (b) conformations. In each case, only one monomer of LB domain is shown in gray with the C-terminal H12 helix colored yellow for contrast. In (a), LB domain is bound to estradiol (E2) and a short helical peptide (colored brown), which is derived from the TIF2 transcriptional co-activator and harbors the canonical LXXLL motif. E2 is depicted as a ball-and-stick model with various atom types and associated bonds shown in green (C) and red (O). In (b), LB domain is bound to 4-hydroxytamoxifen (OHT), depicted as a ball-and-stick model with various atom types and associated bonds shown in green (C), red (O), and blue (N). Note the similarity in the mode of docking of TIF2 peptide to LB domain in response to E2 agonist (a), and that adopted by H12 helix in response to OHT antagonist (b). In (b), the red arrows indicate the unwinding of H3 and H11 helices by about one turn upon the binding of OHT. The structures shown in (a) and (b) were respectively rendered from atomic coordinates provided by PDB codes 1GWR and 3ERT using RIBBONS [141].

DNA Recognition by a Novel Bis-Intercalator, Potent Anticancer Drug XR5944

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Different DNA binding sites of XR5944, a bis-intercalator with major groove binding. (A)-(B) Schematic models of (A) 1:1 XR5944-DNA complex with d(ATGCAT)2 which contains the ideal drug binding site and (B) 2:1 XR5944-DNA complexes with the native TFF1-ERE sequence. The XR5944 molecules are shown in CPK model. Adenine, thymine, guanine and cytosine are red, blue, green and yellow, respectively. (C)-(E) Representative structures of each XR5944-DNA complex, viewed from the major groove (left) and the minor groove (right). (C) 1:1 XR5944 - d(ATGCAT)2 complex; (D) the first XR5944-DNA complex and (E) the second XR5944-DNA complex in the 2:1 XR5944-TFF1 complex. The XR5944 molecules are shown in CPK model. DNA sequences are labeled.
The Interaction of DNA-Binding Ligands with Trinucleotide-Repeat DNA: Implications for Therapy and Diagnosis of Neurological Disorders
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Potential Therapeutic Advantages of Doxorubicin when Activated by Formaldehyde to Function as a DNA Adduct-Forming Agent
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Formaldehyde acts as a molecular switch to change the mechanism of action of doxorubicin from topoisomerase II mediated to drug-DNA adduct formation.