

Transcription Factors as Targets for Cancer Therapy

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Many diseases are caused by dysregulated gene expression. The oversupply or overactivity of one or more transcription factors may be required for the survival, growth, and metastatic behavior of all human cancers.¹ Pyrrole-imidazole polyamides are synthetic molecules programmed to read the DNA double helix by a set of simple chemical principles.^{2,3} These cell permeable small molecules achieve affinities and specificities comparable to DNA-binding proteins. Research efforts are focused on the modulation of gene expression pathways in cell culture by disruption of transcription factor-DNA interfaces.⁴ An x-ray crystal structure of an eight-ring cyclic Py-Im polyamide•DNA complex reveals alteration of DNA conformation as a mechanism for disruption of transcription factor-DNA interfaces.

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