S31-3 Regulation of Gene Transcription by Small Synthetic Molecules

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Naturally occurring transcription factors usually have two independent domains, a DNA-binding domain and an activation domain. Here we show that derivatives of wrenchnolol, a synthetic molecule we previously discovered to interact with Sur-2 co-activator, serve as activation modules and stimulate gene transcription in vitro and in cells when tethered to a DNA-binding molecule. Thirteen derivatives of wrenchnolol were chemically synthesized and tested for their ability to activate transcription in vitro and in cells. One derivative activated transcription of a GAL4-responsive reporter gene 9 folds in cells when tethered to the GAL4 DNA-binding domain. This optimized derivative also induced myogenesis of C2C12 cells up to 45% when tethered to the DNA-binding domain of myogenic transcription factor MyoD.