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A gene-expression inhibitor that targets an alpha-helix-mediated protein interaction.

Asada S, Choi Y, Uesugi M

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Selected by | Thomas Kodadek / John Koh
First evaluation 9 May 2003 | Latest evaluation 16 May 2003
Relevant Sections

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Thomas Kodadek University of Texas Southwestern Medical Center, United States CHEMICAL BIOLOGY New Finding	**The isolation of small molecules that block protein-protein interactions is a potentially attractive route to manipulate biological pathways, but there is a bias, particularly in the pharmaceutical industry, that protein-protein interactions are difficult drug targets. A screen of 2422 small molecules in a cell-based assay uncovered inhibitors of the interaction between ESX (an epithelial-specific transcription factor) activation domain and the SRIP130 (a Ras-linked subunit of the human mediator complex) coactivator.** It was shown that this effect resulted in downregulation of ESX-activated genes without affecting genes activated by other transcription factors. Thus, this study provides an interesting example of manipulating protein-protein interactions between transcription factors to manipulate the level of expression of specific genes. Evaluated 16 May 2003
John Koh University of Delaware, United States CHEMICAL BIOLOGY Tech Advance	**This paper describes the discovery and characterization of a small (drug-like) molecule capable of disrupting protein-protein interactions between ESX (an epithelial-specific transcription factor) and Sur-2 by mimicking the alpha-helical activation domain of ESX.** The ESX-Sur-2 interaction is associated with the over expression of the Her2 oncogene in breast cancer and blocking this interaction may represent a new therapeutic target. Protein-protein interactions are notoriously difficult interactions to disrupt by small molecules. This study represents a successful design strategy applied to an important biomedical target. Evaluated 9 May 2003

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