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Probing the Structure of the "Unstructured" (Proteins)

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It has been over 20 years since the NMR spectroscopy began to be recognized as an important tool for studying protein structures. In 1987 the first high-resolution NMR protein structure was published and met with a great enthusiasm by NMR spectroscopists as well as by many biochemists. With completion of the human genome project, however, more and more NMR spectroscopists are becoming aware of the fact that NMR may not turn out to be as powerful as one might originally expected in terms of structural genomics, the "high-speed" structure determination of proteins. Even with all the available isotope labeling and multi-dimensional NMR techniques along with the ultra-high field spectrometers the "size limitation" in NMR protein structure determination still remains as an obstacle against the "high-throughput". Over the last few years an interesting concept in terms of protein structure has been emerging associated with the so-called "unstructured proteins". These proteins are devoid of the typical "globular" shape (the tertiary structure) and hence cannot be crystallized. NMR methods have been proven to be extremely useful or to be even the method-of-choice for obtaining structural information on these proteins. In this talk we present structural information, both in the absence and in the presence of its target protein, on the transcriptional activation domain of human p53, an important tumor suppressor protein that belongs to such a "loosely-folded" protein family.