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Structural Studies of SHOX-DNA Complex Involved in Growth Processes. N. Narayana, Dept. of Biochemistry, Case Western Reserve Univ., Cleveland, OH 44106 USA.

SHOX (short-stature homeobox-containing gene) protein, a transcription factor, highly expressed in bone marrow is shown to be involved in growth processes. The human SHOX (~300 amino acid residues), a multi-modular protein is characterized by an amino terminal nuclear localization signal, followed by homeodomain, putative SH3 binding site, and an OAR domain involved in the transcriptional activity. The nuclear SHOX protein binds to DNA in a sequence-specific manner. SHOX mutations are involved in skeletal abnormalities in Turner syndrome – intrauterine growth retardation, growth failure during childhood, reduced adult height, heart and renal developmental abnormalities. Therefore, interactions of SHOX with DNA are of physiological importance.

We have crystallized a fragment of human SHOX containing the homeodomain in complex with its target DNA duplex. The crystals diffract to at least 3Å resolution at a synchrotron facility. The SHOX-DNA crystals belong to the space group $P6_2$ (or $P6_4$), with $a = b = 67 \text{ \AA}$, and $c = 127 \text{ \AA}$. There exist two molecules of protein bound to one DNA duplex in the asymmetric unit. Acquisition of heavy atom derivative data sets in parallel with the structure determination trials by molecular replacement using atomic models from related complexes are underway.