Structure of the Human SBDS Protein and Elucidation of its RNA Binding Site

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Nuclear Magnetic Resonance Spectroscopy is being employed in the elucidation of the structure of the H. sapiens SBDS protein, and in the study of its interaction with RNA. The SBDS protein is a member of a highly conserved protein family with orthologs in organisms ranging from plants, Archaea and yeast to vertebrate animals, suggesting that it may have a fundamental, conserved biochemical role. Several lines of evidence suggest that SBDS has a role in RNA metabolism. Mutations were described in the SBDS gene related to Shwachman-Diamond Syndrome (SDS; OMIM 260400), an autosomal recessive disorder characterized by clinical features that include hematological dysfunction, pancreatic exocrine insufficiency and skeletal abnormalities. SDS patients are significantly predisposed to the development of hematological abnormalities, including leukemia. SDS therefore represents an important model for understanding the genetic determinants underlying the multi-step progression to leukemia. For the structure elucidation, experiments were carried for the recombinant protein at the LNLS NMR laboratory and are in final phase of refinement. Titration of SBDS protein with RNA were followed by NMR recording the ¹⁵N-HSQC spectra and allowed the identification of the RNA-binding sites.

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