NMR conformational dynamics of LAM, RRM1 and RRM2 domains of LA protein

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La/SSB (Lupus Antigen) is a multi-domain RNA binding protein. It was first described as an auto-antigen in patients suffering from rheumatic systematic lupus erythematosus and Sjogren's syndrome. La protein has a key role in tRNA molecules biogenesis by binding to their 3' end and guides accurate 5' end maturation of pre-tRNAs by RNase P, while protecting their 3'ends from degradation at the same time. Although La is located in the nucleus, it has been suggested that it also facilitates translation of certain cellular and viral-encoded m-RNAs, such as hepatitis B and C. La from the lower eukaryote *Dictiostelium discoideum* has four distinct domains, namely La motif (LAM), two RNA recognition motifs (RRM1 and RRM2) and a C-terminus region. So far the structure of the full-length La protein remains elusive. Only limited structural data of the La and RRM motifs from few eukaryotes exist (including human) with bound synthetic oligonucleotides providing inadequate information on the possible roles of La/SSB protein as a whole, in a more dynamic tRNA - dependent cellular network.

To elucidate the structural and biological role of its domain we initiated an extensive structural and functional characterization of a "domain library" of La/SSB, of different length and different structural signature. High resolution NMR spectroscopy revealed that all the domains are well-folded. LAM adopts a "winged-helix" structure, whereas both RRM1 and RRM2 domains are found to be classical RRM structures. In addition, the RNA binding properties of the La motif were investigated and the interaction interface was identified through chemical shift perturbation of amide groups in ^{1}H-^{15}N HSQC spectra. Interestingly, both NMR analysis and biochemical experiments indicate that LAM alone can mediate interaction with pre-tRNAs, an observation which raises questions on the actual role of La motif in combination with the RRM motifs, during tRNA biogenesis.

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