THE STRUCTURE OF THE TWO CENTRAL DOMAINS OF KSRP REVEALS A FRAGMENTED RNA BINDING SURFACE

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K-homology Splicing Recognition Protein (KSRP) is a multi-functional RNA binding protein involved in pre-mRNA processing and mRNA decay. The protein binds an array of RNA targets using four K-Homology (KH) domains. As for other RNA binding proteins, the simultaneous use of several of KSRP RNA binding domains allows the recognition of more complex RNA targets, and inter-domain arrangement can play a crucial role in protein-RNA interaction and protein function. We show here that the two central domains of KSRP interact, sandwiching a largely structured inter-domain linker. The orientation of KH2 and KH3 is different from the KH-KH orientations observed in other regulatory proteins. Unusually, the linker does not participate in the recognition of the AU-rich RNA targets, but instead act as a pivot to position the domains. The inter-domain orientation creates a fragmented RNA binding surface with the two separate RNA binding grooves at a 90º angle.

This work has been carried out with financial aid of European Molecular Biology Organization (EMBO) and Wellcome Trust Grant.