Human regulatory Ki-1/57 is a novel intrinsically unstructured protein involved in mechanisms of pre-mRNA splicing

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The human protein Ki-1/57 was previously identified in malignant cells from Hodgkin's lymphoma. Recently, we characterized the interaction of Ki-1/57 with the regulatory proteins RACK1, p53 and several p53-associated proteins. Besides, we found that Ki-1/57 is methylated by the arginine methyltransferase PRMT1. Despite these studies, the functional role of Ki-1/57, as well its structural characteristics remained to be determined. Here, by using several approaches such as SAXS, analytical gel filtration, analytical ultracentrifugation and circular dichroism, we structurally characterized Ki-1/57 as new member of the growing list of intrinsically unstructured proteins. Furthermore, we demonstrated that Ki-1/57 binds to poly-U RNA and is associated with the splicing proteins SFRS9 and hnRNPQ in HeLa cells extracts. We found that Ki-1/57 can modify the splicing site selection of the adenoviral E1A pre-mRNA and also can partially restore the inhibitory effect of SFRS9 in generating a specific E1A mRNA isoform. Moreover, we verified that Ki-1/57 co-localizes to nuclear bodies involved in RNA/pre-mRNA processing and/or snRNP-assembling, dependently of the cellular methylation status and its N-terminal region. Similarly to Ki-1/57 and hnRNPQ, we observed that SFRS9 is also methylated by PRMT1 and has its sub-nuclear localization affected by methylation. In summary, our findings suggest that Ki-1/57 is a novel intrinsically unstructured protein involved in cellular events related to pre-mRNA splicing.
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