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Loss of ADAR1 protein induces changes in small RNA landscape in hepatocytes

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Abstract

In recent years, numerous evidence has been accumulated about the extent of A-to-I editing in human RNAs and the key role ADAR1 plays in the cellular editing machinery and cellular antiviral response. It has been shown that A-to-I editing occurrence and frequency are tissue specific and essential for some tissue development, such as liver. To study the effect of ADAR1 function in hepatocytes, we have created Huh7.5 ADAR1 KO cell lines. Upon IFN treatment, the Huh7.5 ADAR1 KO cells show rapid arrest of growth and translation, from which they do not recover. We developed a new method for translatome analysis based on sequencing of separate polysome profile RNA fractions and a novel bioinformatical approach. We found significant changes in transcriptome and translatome of the Huh7.5 ADAR1 KO cells. The most prominent changes include negatively affected transcription by RNA polymerase III and the deregulation of snoRNA and Y RNA levels. Furthermore, we observed that ADAR1 KO polysomes are enriched in mRNAs coding for proteins pivotal in a wide range of biological processes such as RNA localization and RNA processing, whereas the unbound fraction is enriched mainly in mRNAs coding for ribosomal proteins and translational factors. This indicates that ADAR1 plays more relevant role in small RNA metabolism and ribosome biogenesis. Supported by the project National Institute of virology and bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) - Funded by the European Union - Next Generation EU

Topic category

RNA & Cellular Immunity

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