HuR Binds to Long Noncoding RNAs in Renal Cancer Cells

Parreira, K.S.; Fachel, A.A.; Bagatelli, F.F.M., Verjovski-Almeida, S.

Departamento de Bioquímica, Institute de Química, Universidade de São Paulo, 05508-900 São Paulo, SP, Brazil.

RNA binding proteins (RBPs) play important roles in several aspects of post-transcriptional gene regulation. Human antigen R (HuR) is a ubiquitously expressed RBP that selectively binds to AU-rich elements (ARE) sites within mRNAs to stabilize them and prevent their degradation. Additionally, HuR has already been proposed to play major roles in cell proliferation and tumorigenesis (Dixon et al., 2001). Based on computational analysis, we were able to show that approximately 7% of intergenic and intronic long noncoding RNAs (IncRNA) contains at least one ARE in their sequences. We therefore postulate that HuR directly interacts with IncRNAs thereby stabilizing them. These IncRNAs may be involved in the establishment and progression of clear cell renal carcinoma. In order to identify putative long noncoding HuR targets, RIP-Chip assays were performed with a 244k microarray platform designed by our group to contain all IncRNAs identified at hg19 UCSC assembly. A renal tumor cell model (786-O) was employed. Total (input) and anti-HuR immunoprecipitated RNA were reverse transcribed, amplified, labeled with Cy3/Cy5 and hybridized against the microarray platform. We could find a huge number of IncRNAs with high HuR/Input enrichment (≥ 4 x): 2368 intronic antisense, 7959 intronic sense and 5506 intergenic IncRNAs. These promising sets of transcripts are candidates to interplay with HuR. Further assays will be performed to validate and also describe in depth these putative specific binding sites. The modulation of IncRNAs stability by RBPs may impinge significant consequences to cell biology considering the numberless functions already described for this emerging transcript class.

Keywords: cancer, HuR, IncRNA, RBP, RIP-Chip, post-transcriptional regulation

Supported by: FAPESP