Deciphering the information coded by the functional RNA domains of the Hepatitis C virus genome

RNA viruses have developed a coding information system that complements the protein-coding one. It consists in storing information in discrete, highly conserved structural units termed functional RNA domains. The hepatitis C virus (HCV) genome is a (+)ssRNA, which shows a high sequence variability. It contains a single open reading frame (ORF) flanked by complexly structured untranslated regions (UTRs). Besides the high structural conservation of the UTRs among different virus isolates a structural conservation analysis of the HCV RNA genome has identified the existence of highly conserved structural elements all throughout the genome. These conservations reflect that they store important information for the virus. Structural analysis of the HCV genome, using the SHAPE technology, has revealed that the two ends of the genome mutually modify each other structure. These conformational changes modulate the essential functioning of these genome regions. In particular we have shown that the highly conserved 5’BSL3.2 domain, within the region termed CRE (cis-replication element) at the 3’ end of the ORF, which plays an essential role in replication is also involved in controlling the viral translation. Further we have shown that the HCV genome dimerization is affected by RNA elements outside of the 3’X domain. We have identified essential nucleotides and structural elements within the IRES region and within the CRE region that are involved in the genome dimerization efficiency. We have demonstrated the existance of a complex network of RNA-RNA interactions where the 5BSL3.2 element seems to play a central role connecting different regions of the HCV RNA genome.

Biography

Alfredo Berzal Herranz got his PhD from the Autónoma University of Madrid (1990). After a Postdoctoral stay at the University of Vermont (US), in 1993 he moved to the Instituto de Parasitología y Biomedicina “López-Neyra” (IPBLN; Spain) belonging to the Spanish National Research Council (CSIC) to lead his research group. Since November 2005 to March 2014 he was the Director of IPBLN-CSIC. He has published more than 80 papers, and serves as Editorial Board Member of 15 journals. He is interested in the biological activity of the RNA, mainly focusing in the structure/function of viral genomic RNA domains and characterization of antiviral RNA molecules.

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