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Potential of the Aptamers to fill therapeutic gaps to fight RNA viruses

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Abstract

The current global pandemic caused by SARS-Cov-2 has revealed the lack of an effective therapeutic treatment, among other major deficiencies. This lack of an effective drug to fight it is a common deficiency in dealing with many other infections caused by RNA viruses, e.g. HIV, HCV, SARS, and Dengue, Zika or Ebola viruses, among others. In addition to the information that encodes the viral proteins, RNA genomes carry all other information required for the successful completion of the viral cycle. It includes the information required to efficiently sequester and utilize the cellular machinery and all the information involved in the regulation of the essential viral processes. To bear all the information RNA viruses have developed different molecular strategies to compact it in different levels of coding within the RNA genomes. Thus the nucleotide sequence stores essential information in highly conserved structural RNA domains composed of discrete structural units. The different structural genomic RNA domains play essential functions, and the preservation of their structure is essential for their proper functioning. Therefore interfering with the activity of these essential domains, by competing the interactions they are involved in or by modifying their structure, offers an excellent scenario for fighting infections caused by RNA viruses. It represents a clear alternative to the traditional therapeutic strategies aimed to target viral proteins. Aptamers are short oligonucleotides that efficiently bind to a specific target molecule. The recognition of their target strictly depends on the conformational distribution of specific functional groups in the global structure of the substrate molecule. Therefore aptamers offer a potential means for the development of efficient therapeutic drugs recognizing specific structural features of the viral RNA genome. Numerous studies have reported the potential of aptamers to act as efficient drugs against a variety of RNA viruses being HIV and HCV some of the favorite targets. We have demonstrated that RNA aptamers targeting different essential structural elements of the HIV and HCV RNA genomes efficiently inhibited their replication, reaching up to 85 and 95% inhibition rates, respectively. These results and those from other authors indicate the potential of the aptamers to fill therapeutic gaps in the fight against RNA viruses.

Biography:

Alfredo Berzal-Herranz has devoted his career to the RNA Biology. Got his PhD in the CIB-CSIC Madrid, then moved first to BMC (Sweden), University of Vermont (US) and finally to the Instituto de Parasitología y Biomedicina "López-Neyra" (IPBLN-CSIC) (Granada, Spain). Since 2005 to 2014 he was Director of the IPBLN. His contributions to the field include an unique in vitro selection procedure to study the sequence and structural requirements of the hairpin ribozyme/substrate complex. More recently, the identification of a long range RNA-RNA interaction sufficient to promote the HCV RNA genome circularization. Currently, his group is mainly focusing in the structure/function of viral genomic RNA domains and characterization of antiviral RNA molecules.

Speaker Publications:

1. Romero-López, Cristina & Berzal-Herranz, Alfredo. (2020). The Role of the RNA-RNA Interactome in the Hepatitis C Virus Life Cycle. International Journal of Molecular Sciences. 21. 1479. 10.3390/ijms21041479.
2. Berzal-Herranz, Alfredo & Romero-López, Cristina. (2019). RNA aptamers: antiviral drugs of the future. 6415. 10.3390/ECMC2019-06415.
3. Castillo, Jesús & Ovejero, Tamara & Romero-López, Cristina & Sanmartin, Isaias & Berzal-Herranz, Alfredo & Oltra, Elisa & Gallego, Jose. (2019). Structure and function analysis of the essential 3'X domain of hepatitis C virus. RNA. 26. rna.073189.119. 10.1261/rna.073189.119.

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