Mauro Safir Filho et al., Med Chem (Los Angeles) 2017, 7:8(Suppl)
DOI: 10.4172/2161-0444-C1-033

Rational Design and Synthesis of Innovative RNA Ligands to Target HCV Internal Ribosome Entry Site

Mauro Safir Filho, Anthony R Martin and **Rachid Benhida**
Universite Côte d'Azur, France

Targeting RNA by using small molecules is one of the most intriguing challenges of current medicinal chemistry because, even if a large number of RNA-binding agents have already been identified, the rational design of synthetic molecules that would be specific for a particular RNA structure remains extremely difficult. Recently, this research field raises to an even greater interest since the discovery of new roles of non-coding RNA molecules, including the regulation of a wide number of biological processes as gene expression, tumorigenese and viral translation in chronic diseases, making them potential and important druggable targets. In this context, our research group devoted a lot of effort to develop small-sized organic molecule targeting RNAs. Our ligand design consisted in the combination of molecular recognition elements to enhance site specificity with electrostatic interactions to strengthen the complex stability. The preparation of these multimodal ligands was accomplished by assembling artificial nucleobases, able to form triplets through Hoogsteen interactions with A:U and G:C base pairs, with basic amino acid residues. The affinity and specificity of our ligands were evaluated towards the IIId loop of HCV Internal Ribosome Entry Site (IRES) as RNA model. Low micromolar dissociation constants could be obtained for our best ligand with two-fold higher affinity compared with the non-specific RNA binder neomycin used as positive control. Furthermore, high site specificity to target the single U:A base pair besides the bulge was also observed. Moreover, great selectivity to target the HCV IRES IIId loop instead natural tRNA was achieved. This work is supported by CAPES (fellowship to MSF, process number 99999.0011495/2015-01)

Biography

Mauro Safir Filho has a degree in Industrial Chemistry and a master's degree in Chemistry from the Federal University of Rio Grande do Sul (UFRGS), Brazil. Now he is PhD student at University Côte d'Azur, in Nice, France. He has experience in organic synthesis and photochemistry and now has been working on methodologies of post-synthetic modifications of oligonucleotides.

mauro.safir@hotmail.com

Notes: