Editorial

RNA Interference: Current State and Perspectives

Transcription is the process whereby genetic information in some DNA sequences specifies the synthesis of RNA. Recent studies demonstrate that most of the human genome is transcribed[1] and only a small proportion (~1%) is translated. These transcripts, which are not translated, include a large series of RNAs such as rRNA, tRNA, snRNA, mRNA variants, and a number of long and short non-coding RNA (ncRNA). The sense and antisense transcripts from many genes or genomic regions may form double stranded molecules, which may or may not interfere with normal cellular processes. Overall, this complex system apparently is implicated in the regulation of most genes during the development or in response to cellular alterations.

Twelve years later, Fire et al [2] (Nobel Prize in 2006) described a process in the nematode Carenorhabditis elegans, in which long double-stranded RNA (dsRNA) caused a suppression of complementary genes called RNA interference (RNAi). RNAi and related gene-silencing pathways are initiated by the production of small RNAs with ~20-30 nucleotides (siRNA) presenting complementarities with the transcripts that they regulate.

The introduction of RNAi and related small-RNA in the scenario of expression gene regulation has modified the understanding of biomedical research. In the last years, RNAi has become the standard method for in vitro knockdown of any target gene of interest. In addition, RNAi has been considered as a powerful tool to study the cellular processes and to silence genes implicated in several human diseases, such as cancer. The potential of this methodology has also been explored to develop novel therapeutic strategies. The efficient delivery of target gene-specific siRNA has been one major challenge in the establishment of therapeutic RNAi-based. In this issue, Belizário and Moreira presents a review with the recent advances and siRNA delivery and targeting in human cancer by RNA interference approach. In cancer treatment, target molecules represent, in general, genes that have been shown previously to be relevant or rate limiting for growth factors and receptors, antiapoptotic proteins or downstream signal transduction factors.

Although much is known about the mechanisms of RNAi, there are still many barriers to be crossed, including: (1) RNAi is a self regulatory mechanism of the cell and side effects of the treatment must be considered; (2) The specificity across tissues and cell types remains an unresolved issue; (3) It is essential to clarify the controversial facts regarding the immunostimulatory siRNA features; (4) The toxic effects caused by genetic vectors used to express siRNA or miRNA must be considered, and; (5) Large scale functional studies and proteomics approaches will be necessary to identify non-specific responses to foreign RNA in human cells (Olejniczak et al, 2010).[3] Despite these considerations, RNAi approach is already being used therapeutically in human clinical trials and the pharmaceutical companies are officially involved in the process.

Reference

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Silvia Regina Rogatto, PhD