The Discovery of Riboswitches

Wei Liu

Riboswitches are the non-coding portions of mRNAs that can fold complex structure and serve as receptors of specific metabolites. When they bind to their specific metabolite, their three-dimensional structures will change allosterically and therefore regulate the process of transcription and/or translation. Riboswitch was first named by Dr. Ronald Breaker in 2002, but before that, some scientists already noticed this phenotype of mRNA. Dr. Tina Henkin may be the first one who observed this special gene control system. She found that there was a conserved sequence in the 5' leader region of S-box gene family which involved in the biosynthesis of methionine and cysteine. This conserved sequence can form a secondary structure or possibly tertiary structure as the computer predicted. Based on experiments, Dr. Henkin showed that this structure would change when the leader region bound to a negative regulatory factor. The No.5 and No. 1 region of the conserved sequence paired with each other when lacking of the factor; however, when the factor bound to mRNA, No. 5 region would separate from No.1 region and form a hairpin structure, which stop the gene expression, but they don’t know what kind of factor the structure change needs and there are still a lot of questions unknown.

Until 2002, Dr. Breaker first demonstrated that mRNAs can bind metabolites directly in the absence of proteins and he also developed a useful method, in-line probing to detect the conformational change of mRNA. He found that the conformational change of the riboswitch in btuB gene, whose product is a membrane protein for the transportation of coenzyme B₁₂, is regulated by coenzyme B₁₂ (AdoCbl), and this binding recognition was very specific.

Right now, the development of riboswitches research is very fast. Two main mechanism of riboswitch regulation have been found. First, riboswitch can regulate the transcription. Like riboswitch in s-box genes, when the riboswitch bind its specific metabolite, its structure will change allosterically from antiterminator to terminator (hairpin structure) and therefore control the transcription. Now it is known that the factor regulated the riboswitch is s-adenosylmethionine (SAM) and the sequences involved in metabolite binding and terminator control system have been fully studied. The second mechanism of riboswitch regulation is the regulation of translation initiation. There is a conserved riboswitch called Sₘₖ-box in metK gene which encodes SAM synthetase. In Sₘₖ-box, there is a pair of Shine-Dalgarno (SD) anti-Shine-Dalgarno (ASD) sequences. SD sequence is important for the mRNA binding to 30S subunit of ribosome. By regulation of the SD sequence, riboswitch can regulate the initiation of translation.

There are totally seven classes of riboswitches now, but scientists also found some mRNA regulatory elements that share some features of riboswitches, like thermosensor RNA and T-box RNA. Whether they belong to riboswitch or not is still debated by many scientists and how to draw a clear distinctions between riboswitch and other gene-control system is still a question.

2. Ryan T. Fuchs, Frank J. Grundy and Tina M. Henkin. S-adenosylmethionine Directly Inhibits Binding of 30S Ribosomal Subunits to the $S_{MK}$ Box Translational Riboswitch RNA. PNAS, 2007(104): 4876-4880;


