A dicing protein (Dicer-2): Looking for a specific target for cleavage in RNA interference pathway

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Genes are the information carriers what makes us human. Everything we have is basically encoded in our genes. But there is an amazing regulation from genes to an organism. First of all, genes are transcribed into RNA which can be thought as an intermediate. After this step, RNA molecule is translated into proteins which are small building blocks form cells, organs, our eye, hair colors. Sometimes those proteins can result some diseases if they are in bad shaped, falsely encoded or maybe in huge number. This information transfer between genes to protein is called "*the Central Dogma*". Last century it has been found that there are some other transfers like RNA to RNA, RNA to DNA and this pathway is not directly from gene to RNA then protein. Also some regulatory RNAs have been shown that they can regulate their own synthesis or replication.

RNA interference is another regulatory mechanism found in all eukaryotic cells and plays significant role in RNA step. Basically, RNA interference pathway acts as a cop that detects and controls the double-stranded RNAs (dsRNA). dsRNAs can be encoded in our genome like a normal gene, or can be introduced into a cell by virus or moving genetic elements. After they become RNA, they are not translated into protein so they stay as RNA and they processed by various proteins. After they are processed into small RNAs that can be called microRNA, small interfering RNA or Piwi-interacting RNA; those small RNAs start to search for their target which has same or similar sequence. When they found their targets, by the aid of some proteins they can cut, inhibit the translation of their targets into a protein. As it is called RNA is interfering, this mechanism is basically called RNA interference (RNAi) and Andrew Fire and Craig Mello won the Nobel Prize for the discovery of this amazing mechanism in 2006.

In this RNAi pathway, even though the whole pathway is not crystal clear yet, scientists have been finding different proteins, properties of those proteins, their regulation mechanism etc. One of those proteins is called Dicer (There are 2 Dicer proteins in *Drosophila*, Fruit flies, Dicer-1 and Dicer-2). As it is called, it dices long dsRNA into small pieces of dsRNA which then can find its target. This dicing mechanism is highly regulated and this specific cleavage by Dicer protein is a hallmark of RNAi pathway. Dicer proteins cut their target from a specific place which can be different for various small RNAs. Simply, Dicer protein binds to its target long dsRNA and it rules from one end then it cleaves from a specific distance from the end it ruled.

In our project, we have tried to figure out, how this Dicer-2 protein cuts its target, and why this protein wants to bind some long dsRNA more eagerly rather than binding other ones. What is its specificity for binding and at the same time what kind of factors can affect the cleavage of long dsRNA by this protein? Some properties of dsRNA might be more favorable for Dicer-2 protein as well as some conditions might affect the cleavage by Dicer-2 positively or negatively.

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