International Journal of Engineering and Allied Sciences (IJEAS)
||Volume 2|| ||Issue 1|| ||2016||
ISSN: 2455-2054

Role of piRNAs in diseases propagation

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----------ABSTRACT----------

A new class of small-RNAs called PIWI-interacting RNAs (piRNAs) which binds with a special kind of protein called "PIWI proteins". Recently, it has been noted that the small piRNAs has a role in different diseases progression including cancer development. In this small communication, we emphasize on the discovery of piRNAs, PIWI protein subfamily, piRNAs clusters, responsibility of piRNAs in tumorigenesis and cancer. However, the piRNAs and their interacting proteins in different diseases including different cancers have yet to be fully explored. Therefore, more research is needed on the novel piRNA to understand its role in diseases propagation.

Keywords *- piRNAs; Cancer, PIWI proteins, PIWI-interacting RNAs, diseases propagation.*

I. INTRODUCTION

During 2006, a milestone discovery led to the identification of a new class of small-RNAs called PIWI-interacting RNAs (piRNAs). The researchers have identified micro-RNAs during the process of spermatogenesis in mammalian testes. They have found the expression of these micro-RNAs during the process of spermatogenesis [1–6]. It has been noted that piRNAs are lengthier than miRNAs and siRNAs (Figure 1.). The length of piRNAs is approximately 30 bases long (26–32 nt) whereas the length of miRNAs and siRNAs is 21–23 nt. During the biogenesis of this micro RNA, it binds with a special kind of protein called "PIWI proteins". As these small-RNAs bind with the PIWI proteins, therefore, these RNAs are called PIWI-interacting RNAs (piRNAs). The PIWI subfamily proteins belong to the Argonaute protein family [7-8].

II. DISCOVERY OF PIRNAS

The Five groups are accounted for the discovery of piRNAs which are expressed exclusively in mammalian testes (rat, mouse as well as human) and to bind MIWI (murine PIWI) or MILI proteins. The groups are Grivna et al. (2006)[1]; Lau et al. (2006)[3]; Girard et al. (2006)[4]; Aravin et al. (2006)[5]; Watanabe et al. (2006)[6].

III. PIWI PROTEIN SUBFAMILY

According Piwi protein subfamily plays a fundamental role in genome stability in germline cells. Piwi proteins are highly enriched in the gonads of all animals [9, 10]. These proteins are accountable to maintain differentiation in stem cells. This family protein provides the stability of cell division rates in germ cells [11]. Piwi proteins are highly conserved and present in both plants and animals. [12]. It is studied in several model organisms such as Caenorhabditis elegans, Drosophila, Zebrafish, and Mice [13]. It was illustrated that this family of proteins are paralogs of Argonaute proteins. This protein

family is sharing the same domain architecture with Argonaute proteins [14]. Conversely, the binding property or binding characteristics of Piwi proteins and Argonaute proteins with small noncoding RNAs are same [1-6]. Argonaute proteins bind to siRNAs or miRNAs and take part in the RNA interference (RNAi) and miRNA pathways. On the other hand, Piwi proteins bind to piRNAs and are involved in the piRNA pathway during gametogenesis [15-16]. There are two domains in Argonaute proteins which are PAZ domain and the PIWI domain. This is the main structural feature of Argonaute proteins. It has been noted that the study on PAZ domains from different organisms exposed that this domain enclosed a specific binding pocket. This pocketed anchors the feature two nucleotide 3' overhang that results from digestion of RNAs by RNase III and it is a step for the processing of small RNAs. [17-21]. Conversely, PIWI domains show wide homology to RNase H [22-26].

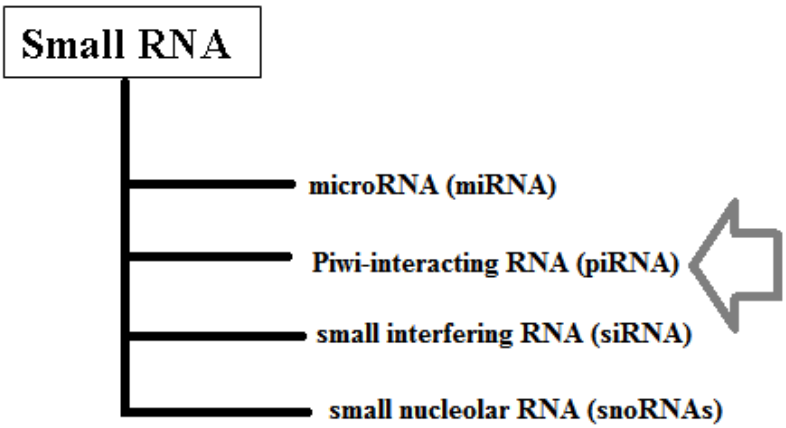

Figure 1. Different types of small RNAs

Three major PIWI-class proteins have been noted which are PIWIL1, PIWIL2 and PIWIL4. These protein are involved in a so-called 'ping-pong' amplification cycle and creating antisense piRNAs that are capable of repressing the transcript of origin [27]. Interestingly, PIWI proteins

IV. PIRNAS CLUSTERS

Transposable Elements (TEs) are most significant structural machinery of eukaryotic genomes which are repetitive DNA elements that can mobilize to take up new chromosomal locations within a genome. TEs act as insertional mutagens that can alter gene expression or rearrange chromosomes. Most piRNAs are derived from particular genomic sites termed piRNA clusters, which contain a large number and various types of TEs. Thus, the sequences of piRNAs derived from these clusters are homologous not only to TEs in the clusters, but also to related TEs located elsewhere in the genome and can therefore act as guide molecules to repress TEs in trans. Thus, piRNA clusters are genetic elements that regulate the activity of TEs. However, relatively little is known about how piRNA clusters are formed. In the Drosophila genome, 142 regions have been identified as piRNA clusters [22]. Although these sites account for less than 5% of the assembled genome, over 90% of all sequenced piRNAs can be derived from these regions [25]. The piRNA clusters cover chromosomal

regions of several to hundreds of kilobases, and they contain TEs that are mostly inactive copies or truncated fragments, arranged in a nested fashion [22].

It was noted that 81% to 96% of piRNAs is organized in clusters. Clusters ranges from 1 to 127 kb in size which are found predominantly in autosomes. A few of the clusters are organized in a bipartite in a manner with a stretch of piRNAs on one strand adjacent to a second stretch of piRNAs on the opposing strand.

V. RESPONSIBILITY OF PIRNAS IN TUMORIGENESIS AND CANCER

It has been noted that Piwi proteins and Piwi-associated piRNAs has a role in gametogenesis in Drosophila, Zebrafish as well as mice. Mutations are important for cancer development [36-38].Taubert et al have stated that Silencing of PiwiL2 can considerably decrease tumor cell propagation [39]. In general, it has been noted that PiwiL2 was extensively expressed in tumors. Lee et al reported that piRNAs can suppress transposon. Actually, transposable elements have been recorded in multiple tumor categories [40].

It has been noted that several piRNAs are associated with cancer. piR-651 is an important piRNAs. Cheng et al. noted that in gastric cancer, piR-651 was linked with tumor-node-metastasis stage [41] On the other hand, in breast cancer; piR-4987 expression was connected with lymph node [42]. However, we have to understand more about the role of piRNAs in Tumorigenesis and Cancer.

VI. CONCLUSION

piRNAs and their interacting proteins have a great role to play in various cellular processes. In recent years, advances of piRNAs have significantly started to comprehend the role in various cellular processes and to understand the role of piRNAs in different diseases including cancer. The piRNAs and their interacting proteins in different diseases including different cancers have yet to be fully discovered. Understanding the different biochemical pathway related to piRNAs will help in the discovery of the many other regulatory of piRNAs on the new possibility. This will help in understanding more about the novel piRNA and their role in diseases propagation.

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