Human PIWI Protein Orthologues and their Effects on Cancer

Çağrı ÖNER

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Abstract:

PIWI proteins are a subclass of Argonout proteins which have an important role on PIWI interacting RNA (piRNA) mechanisms. piRNAs are the novel class of small non-coding RNAs which regulate genetic and epigenetic regulations via transposon silencing. However, first studies about PIWI proteins and piRNAs focused on the development of germline stem cells; the similarities between stem cells and cancer cells caused cancer researchers to observe the relationship between PIWI protein/piRNA complex and cancer cells. This letter indicates researches which were identified the potential of PIWI proteins in various cancers.

Researches about PIWI Proteins and Cancer:

While PIWI family members are normally expressed in germline stem cells, their expression

changes during normal development. HIWI (human PIWIL1 orthologues) was found to be aberrantly expressed in various cancers, and its expression correlates with a poor clinical prognosis [1]. PIWIL1 (HIWI), PIWIL2 (HILI), PIWIL3 and PIWIL4 (HIWI2) expression was determined in breast cancer cell lines according to the oestrogen dependence compared with MCF10A healthy breast cells [2]. HILI and HIWI2 were found to be expressed in all cell lines, analysed with the latter present at a very high level in SKBR3 cells, while HIWI and PIWIL3 were undetectable [2]. In a study concerning the relationship between HIWI and glioma, the researchers suggested that HIWI protein is overexpressed in glioma and determined that HIWI protein expression increases according to the tumour grade [3]. A growing number studies has found that HIWI and HILI were over-expressed in various human cancers [3-5], including cancers originating from the germline (testicular seminomas) [6] and those originating from mesenchymal stem cells (sarcomas) [7]. In gastric cancer, the HIWI expression pattern was determined to be almost identical to Ki-67, a marker of cell proliferation. Moreover, HIWI inhibition in gastric cancer cells caused the induction of cell growth at the G2/M phase [8]. Furthermore, HILI expression is high and thought to be an oncogene in various cancer types [9]. Overexpression of HILI results in decreased LINE 1 transposon expression and decreased expression of piRNAs that are derived from LINE 1 sequences in the HeLa cell line. Nevertheless, several piRNAs did not change signi cantly when HILI was expressed. Lu et al. suggested that piRNA populations may be modulated in response to the expression of PIWI proteins in HeLa cells [10]. Lee et al. determined that PIWIL2 inhibits apoptosis and regulates proliferation via Stat3/Bcl-XL activation and increment of the Stat3/cyclin D1 signalling cascade. Furthermore, inhibition of signalling pathways by inhibiting PIWIL2 expression can inhibit tumour cell growth both in vitro and in vivo [9]. In another study concerning the potential effect of the piRNA/PIWI cascade in classical Hodgkin Lymphoma (cHL), it was determined that PIWIL1 and PIWIL2 were expressed in Hodgkin/Reed Sternberg (HRS) cells, indicating that the piRNA/PIWI cascade is active in cHL [11]. Knockdown of PIWIL2 in colon cancer increased the motility and invasion properties of tumour cells via activation of matrix metalloproteinase 9 (MMP-9) in vitro and upregulated the cell growth in vivo [12]. Greither et al. identified a significant association between PIWIL2 and PIWIL4 expressions with gender related tumour-specific survival of soft tissue sarcoma (STS) patients [13].

Conclusion:

piRNAs and PIWI proteins are novel small non-coding molecules in scientific literature. Their impacts on cancer cases have not clearly known yet. Although more studies are needed on piRNAs and PIWI proteins in the future, their effects on cancer development should be determined genetically and epigenetically.

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Name: Çagrı ÖNER

Afiliation: Maltepe University, Turkey Email: cagri.oner@maltepe.edu.tr