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Editorial

Micro Rnas in Human Papillomavirus Mediated Cervical Cancer

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Editorial

Cervical cancer is the third most common cancer among women after breast and ovarian cancers. Almost 99% of cervical cancer samples contain Human Papillomavirus (HPV) DNA [1]. HPV is a non enveloped virus containing circular double stranded DNA as its genome. There are more than 100 types of HPV that have been identified till date. HPVs are classified into high risk types (HPV16, HPV18, and HPV31) or low risk types (HPV6, HPV11) depending on their ability to cause malignant tumor or benign warts/lesions respectively.

Micro RNAs (miR) are short single stranded RNA molecules of 20-24 nucleotides in length that are important molecules involved in epigenetic regulation of gene expression [2]. The inhibition of gene expression can be through transcriptional repression as well inhibition of translation by degradation of the corresponding messenger RNA. The genes encoding the miRs are found in the introns and intergenic sequences. Studies from different types of cancer samples using microarray expression analysis have clearly pointed to the role of miRs in cancer [3-6]. Mouse models having miRs overexpressed or ablated demonstrated the critical link between miRs and cancer progression.

Micro RNAs in Cervical Cancer

Since the discovery about the roles of miRs in influencing cancer phenotype, several studies have been done on the miRs that are aberrantly expressed in cervical cancer cells. The analysis of the expression profile analysis was reviewed recently by Sharma et al. [7]. The expression of miRs vary between different stages of Cervical Intraepithelial Neoplasia (CIN) i.e. CIN1, 2 and 3. Most miRs show a consistent up regulation or down regulation throughout the different CIN stages e.g. miR181, 191, 429, 214, 218, 143, 145, 497 etc. However, some miRs show an opposite trend while progressing from low grade (CIN1) to high grade (CIN3) cervical cancer e.g. miR 212, 132, 100 etc. The up regulation or down regulation of the respective miRs might be the cause of transition of the cancer from low to high grade. Thus miRs might be a useful marker for different stages of cervical cancer and to indicate the progression through different stages. Circulating miRs like miR-20a is one such biomarker for cervical cancer to found in lymph node [8].

Since miRs control the expression of several genes, studies have identified the cellular target genes that are affected by specific miRs. Some miRs like miR-214 have five validated cellular targets while others like miR-205, miR-34a and miR-133b have three validated cellular targets. The table below shows the miRs along with their respective validated cellular target genes in cervical cancer.

Micro RNA	Validated cellular target genes
miR10a	HOX [9], CHL1 [10]
miR17	TP53INP1 [11]
miR19a, miR19b	CUL5 [12]
miR20a	TNKS2 [13]
miR21	PDCD4 [14,15], CCL20 [16]
miR23b	Urokinase type Plasminogen Activator (uPA) [17]
miR29a	YY1, CDK6 [18]
miR34a	Notch 1, Jagged 1 [19], p18Ink4c [20]
miR100	PLK1 [21]
miR125b	PIK3CD [22]
miR133b	MST2, CDC42 , RHOA [23]
miR143	Bcl2 [24]
miR145	IRS1 [25]
miR155	SMAD2, CCND1 [26]
miR182	FOXO1 [27]
miR196a	HOX [9]
miR205	SHIP2 [28], CYR61, CTGF [29]
miR 214	MEK3, JNK1, plexinB1, GALNT7, Bcl2l2 [30-33]
miR218	LAMB3 [34-36]
miR223	FOXO1 [37]
miR302-367	CYCLIND1 [38]
miR372	CDK2, CYCLINA1 [39]
miR375	SP1 [40]
miR424	Chk1 [41]
miR497	IGF-1R [42]
miR886-5p	Bax [43]

There are about 246 miRNAs in cervical cancer that are deregulated and the cellular targets for these miRNAs have been experimentally validated. These deregulated miRNAs affect a host of cellular processes like apoptosis, cell cycle regulation, metastasis, angiogenesis etc. The complex interplay of hundreds of miRNAs ensures the development of cancerous phenotype and ultimately progression from CIN1 to CIN3 stage.

The miRNA mediated gene regulation is fast becoming a hot topic for cervical cancer research. Their ability to post transcriptionally affect diverse cellular pathways makes them good candidates for targeting

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in cancer therapy. MiRNAs are also being studied for their ability to act as biomarkers for different stages of cervical cancer. Expression profile analysis for miRNAs from a patient sample can give a lot of information about the disease prognosis. More studies will reveal the detailed mechanisms by which the miRNAs gets deregulated in cervical cancer. It is important to determine the suitable miRNAs for therapeutic purpose.

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