**Entomology and Applied Science Letters**
**Volume 4, Issue 4, Page No: 4-6**

Available Online at: www.easletters.com

**ISSN No: 2349-2864**

# Bioinformatic Evaluation of the MiR-5011 Effect on the Crutial Genes That Involved in Colorectal Cancer

**Zahra Bayat[1], Bahram Mohamad Soltani[2]**

*[1]Master of Genetics, Department of Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran*
*[2]Associate Professor of Genetics, Department of Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran*

**ABSTRACT**

*Introduction: The microarray technique has been established as the reference method for studying the genes that are in the control of miRNAs. However, the high cost of this method has hampered its use in most research centers. On the other hand, the improvement of the bioinformatical algorithms and computer modeling systems has led to the development of the bioinformatical softwares that can predict mRNA targets for miRNAs. Therefore, the aim of this theoretical study was bioinformatically evaluation of the effect of miR-5011 on genes that can be involved in colorectal cancer, by using various specific softwares.*
*Methods/Materials: By Using different algorithms in TargetScan, DIANA and miRWalk databases, the potential gene targets of miR-5011 were identified. Then, a score table from the candidate genes was prepared based on the affinity of the seed region of miR-5011 and the number of MRE in the 3`-UTR region of genes. Finally, genes with highest scores were chosen as the candidates for practical analysis.*
*Results: The results of bioinformatical analysis showed that SMAD6 and SMAD7 genes in TGFB signaling pathway and WNT3A and LRP6 genes in WNT signaling pathway are the most potential genes that might be affected by miR-5011 in colorectal cancer.*
*Discussion: It seems that WNT3A, LRP6, SMAD6 and SMAD7 suppressed by miR-5011 and this microRNA maybe act as a tumor suppressor and downregulated in colorectal cancer Therefore, this microRNA and its target genes can be considered as a suitable new candidate for experimental evaluation.*

**Keywords:** Bioinformatics, MicroRNA, Colorectal Cancer, MiR-5011

**HOW TO CITE THIS ARTICLE:** Zahra Bayat, Bahram Mohamad Soltani, Bioinformatic evaluation of the miR-5011 effect on the crutial genes that involved in colorectal cancer, Entomol Appl Sci Lett, 2017, 4 (4), pp:4-6.

**Corresponding author**: Zahra Bayat
**e-mail**✉ Zahra.bayat2@yahoo.com
**Received:** 11/05/2017
**Accepted:** 24/09/2017

## INTRODUCTION

In recent years, a new network of regulatory cycles at the level of mRNA has been considered Among them can be a class of RNAs Non-coding agent called microRNAs. In 1993, the first microRNA, called 4-lin, was discovered [1]. The miRNA is referred to as small RNAs that they originated from the stem-loop structure and interfered with the regulation of the expression of the genes by targeting the mRNAs and degradation or by inhibiting the expression of their genes [2]. About seven nucleotides from the 5′end of the mature miRNA molecules is called seed region, and this region binds to The 3`-UTR from its complementary mRNA [3]. The miRNA sequence identifies the target mRNA molecule. If miRNA completely binds to the target mRNA, it completely degradate mRNA, and if the binding to the target mRNA is incomplete, miRNA prevents the translation of the mRNA [4]. MiRNAs are involved in some biological processes including cell proliferation, differentiation, angiogenesis, apoptosis and tumorigenesis through targeting mRNAs [5].

Colorectal cancer (CRC) is one of the most common life-threatening malignancies that its symptoms shows up so late. recent study indicated that expression of various miRNAs are altered in CRC [6]. Almost all colorectal cancers (CRC) demonstrate hyperactivation of the WNT pathway and disregulation of the transforming growth factor beta (TGF-β) signaling pathway, which in many cases is believed to be the initiating and driving events. MiRNAs are one of the key regulators of thease pathways [7,8]

Today, with the help of techniques such as Northern blot, Microarray (hybridization in situ) and Real -time- PCR can be found the presence

of mi-RNA in the Specific tissues or the association of any mi-RNA with diseases. Multiple computer programs with Different algorithms to predict the mi-RNA targets exists [9].

Therefore, the aim of this theoretical study was bioinformatically evaluation of the effect of miR-5011 on genes that can be involved in colorectal cancer wia WNT and TGF-β signaling pathway, by using various specific softwares.

## 2. MATERIALS AND METHODS

### 2.1. Getting the miR-5011 sequence

The sequence of miR-5011 was captured from Entrez ( http://www.ncbi.nlm.nih. gov/Entrez/) and miRBase (**www.mirbase.org/**).

### 2.2. Bioinformatic analysis of miR-5011 target mRNAs

By Using different algorithms in TargetScan, DIANA and miRWalk databases, the potential gene targets of miR-5011 were identified. Then, an score table from the candidate genes was prepared based on the affinity of the seed region of miR-5011 and the number of MRE in the 3`-UTR region of genes. Finally, genes with highest scores were chosen as the candidates for practical analysis.

## 3. RESULTS

### 3.1. Analysis of miR-5011 at Targetscan database

Target Scan Software (http://www.targetscan.org/) is one of the case programs that use to predict mammalian mi-RNA targets. This software identifies seven or eight nucleotides of mRNA That is complementary to mi-RNA and it also examines thermodynamic stability (examination of secondary structures and intermolecular interactions of a nucleic acid). Pct Indicates that miRNA binding to the target area is Not based on chance, and the amount of this factor is between 0 to 1. The closer Pct to 1 indicated exclusively specific binding of miRNA to its target mRNA [10].

Based on the results of this study the genes listed in table 1 have the highest score as the target of miR-5011.

**Table 1.** The studied genes in Target scan software

| Target gene | Conservity region | Poor conservity region | Aggregate Pct |
|---|---|---|---|
| SMAD6 | 3 | 1 | 0.97 |
| SMAD7 | 2 | 0 | 0.99 |
| LRP6 | 2 | 1 | 0.91 |
| WNT3A | 1 | 0 | 0.97 |

### 3.2. Analysis of miR-5011 at DIANA database

This algorithm identifies mRNA targets Based on several parameters calculated for each miRNA Separately. Then scores protected regions and unprotected combined and a general score of that Suggests changes in the expression of the target mRNA. Specifically, indicators for each program's forecast are the signal-to-background ratio and the accuracy score (this parameter is between 0 and 1, indicating the likelihood of being real mRNA is the target for any miRNA). Which serves as an indicator for detecting false positives is considered. Another parameters examined at this base Information, overall miTG score (this is in fact the final score Prophecy) and the Threshold score (Threshold). Higher values of the miTG suggests a near-expected reality [11].

Thus, the most highly rated genes in the algorithms of this software have been determined and specified which can play a role in the CRC are summarized in Table 2, respectively.

**Table 2.** The studied genes in DIANA software

| Target gene | miTG score | Accuracy score | Threshold score | The signal-to-background ratio |
|---|---|---|---|---|
| SMAD6 | 10.9 | 0.7 | 4.65 | 7.2 |
| SMAD7 | 29.7 | 0.86 | 6.6 | 7.2 |
| WNT3A | 23.7 | 0.79 | 6.76 | 7.2 |
| LRP6 | 11.56 | 0.5 | 4.67 | .2 |

### 3.3. Analysis of miR-5011 at miRwalk database

This database is based on the programming method Perl is written based on the complementary relationship between the region the core of miRNA with the target mRNA and according to complementarity the bases are based on Watson and Creek's law. In this software heptemer core sequence based on Watson's and Carrick's law. other databases are searched and when the region seven nucleotide were complemented by a target extends from both ends and this will go as long as one mis - mach goes on. After reaching mismach extensions stops and eventually results analyzed, then the complementary seven nucleotide regions their ability to connect to the UTR-3 genes in the results list is shown. Also, the probability of distributing a pair of bundles Accidental sequences analyzed by Poisson distribution. The results are reported as p value [12].

Based on the results obtained from this software also genes are likely to be involved in CRC wia TGFB and WNT signaling pthway that are

SMAD6 (p value= 0.022), SMAD7 (p value= 0.013), LRP6 (p value= 0.050) and (p value= 0.030).

## 4. DISCUSSION

SMAD6 and SMAD7 genes as I-SMADS inhibit the formation and activation of R-SMAD-CO-SMAD complexes in TGFB signaling pathway, therefore they will control and regulate TGFβ signaling pathway and involved in CRC [13,14,15]. LRP6 and WNT3A are the components of WNT signaling pathway and activate this pathway. Thease genes are mutated in many CRC cases and regulation of their expression is important [16,17].

According to the bioinformatics studies SMAD6, SMAD7, LRP6, WNTA3A is most likely to be affected by miR-5011 in CRC. Although The proteins are all as high targets the points are scored among all three above-mentioned bases They agree, however, to arrange the results in between different databases are slightly different than this more because of different algorithms and minor modifications of scoring pattern is among these bases. It should be noted that threshold is in default on Diana software set to 7.2 Though this is the minimum threshold and has a capacity of up to 19, meaning that Software only targets that score above this threshold they are showing. Therefore, by increasing the threshold to the maximum could be more rigorous judgment thus only mRNAs with a threshold of 19 or Are higher, will be shown. Therefore, only targetss their overall miTG score is higher than the specified threshold the software filter will be displayed. So, considering the way it works SMAD6, SMAD7, LRP6 and WNT3A interference in CRC in previous studies by researchers Identified, based on data from analyzes bioinformatics seems to be SMAD6, SMAD7, LRP6 and WNT3A as the targets of miR-5011 controlled factors in CRC and can be a new good candidate for practical reviews.

## 5. REFERENCES


1. Appasani K. MicroRNAs: from basic science to disease biology. Cambridge University Press. 2008;23(4) :123-87.
2. Bartel DP. MicroRNAs: genomics, biogenesis, mechanism, and function. Cell. 2004;116(2):128-90.
3. Shi M, Liu D, Duan H, Shen B, Guo N. Metastasis-related miRNAs, active players in breast cancer invasion, and metastasis. Cancer and Metastasis Reviews. 2010;29(4):785-99.
4. Shivdasani RA. MicroRNAs: regulators of gene expression and cell differentiation. Blood. 2006;108(12):3646-53.
5. Gao F-B. Context-dependent functions of specific microRNAs in neuronal development. Neural development. 2010;5(1):25-6.
6. Ren, Dong A, Tsoi H. Detection of miRNA as non-invasive biomarkers of colorectal cancer. International journal of molecular sciences. 2015;16(2):2810-2823.
7. Grady W. Transforming growth factor β signaling in colorectal cancer. Current Colorectal Cancer Reports. 2007;3(2):65-70.
8. Morin P , Sparks A, Barker N, Clevers H. Activation of β-catenin-Tcf signaling in colon cancer by mutations in β-catenin or APC. Science.1997; 275(2):1787-1790.
9. Quesne J, Caldas C. Micro-RNAs and breast cancer. Molecular oncology. 2010;4(3):230-41.
10. Friedman RC, Farh KK-H, Burge CB, Bartel DP. Most mammalian mRNAs are conserved targets of microRNAs. Genome research. 2009;19(1):92-105.
11. Maragkakis M, Reczko M, Simossis VA, Alexiou P, Papadopoulos GL, Dalamagas T, et al. DIANA-microT web server: elucidating microRNA functions through target prediction. Nucleic acids research. 2009;37(2): 273-6.
12. Dweep H, Sticht C, Pandey P, Gretz N. miRWalk–database: prediction of possible miRNA binding sites by "walking" the genes of three genomes. Journal of biomedical informatics. 2011;44(5):839-47.
13. Wrana J. Regulation of Smad activity. Cell. 2010;100(2):189-192.
14. Zhou S, Kinzler K, Vogelstein B. Going Mad with Smads. New England Journal of Medicine. 2010;341(15):1144-1146.
15. Li Q. Inhibitory SMADs: Potential Regulators of Ovarian Function. Biology of reproduction. 2015;92(2):111-117.
16. Edlund S, et al. Interaction between Smad7 and beta-catenin: importance for transforming growth factor beta-induced apoptosis.Mol, Cell Biol. 2007;25 (4):1475–1488.
17. Cheruku H. Mohamedali A, Cantor D. Transforming growth factor-β, MAPK and Wnt signaling interactions in colorectal cancer. EuPA Open Proteomics. 2015;8(98):104-115.