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Research article

Evidences for big roles of miRNAs from *Pristionchus pacificus to* human targeted genes via bioinformatics approaches

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Abstract

Micro RNA regulates gene expression & miRNAs are well conserved in both plants and animals, and are thought to be a vital and evolutionarily ancient component of genetic regulation. Extensive studies have revealed critical roles for miRNAs in human genomics. In this study we are using nematode worm (*Pristionchus pacificus*) with a view to enhancing our understanding of genomics via this approach identified the genes these gene have been associated with basal cell nevus syndrome, esophageal squamous cell carcinoma, trichoepitheliomas, transitional cell carcinomas of the bladder, as well as holoprosencephaly. In present study this concept reveals that use of *Pristionchus pacificus* as an model to investigate targeted genes via Pristionchus *pacificus* miRNAs in human model with help of bioinformatics . Identified genes code several genomics functionality. *Pristionchus pacificus* miRNA targeted 65 genes in human via two selected high confident miRNAs.

Keywords: *Pristionchus pacifics* , miRNAs, Nematode, Gene expression

Introduction

Mature microRNAs (miRNAs) are a class of naturally occurring small non-coding RNA molecules; about 21 to 25 nucleotides in length. MicroRNAs are partially complementary to one or more messenger RNA (mRNA) molecules, and their main function is to down- regulate gene expression in a variety of manners, including translational repression, mRNA cleavage and deadenylation.(Vijay Laxmi Saxena & Alka Dwivedi., 2003). These important regulatory mechanisms mediate much biological process such as development, cell proliferation and differentiations (Alka Dubey *et al*., 2013). Micro RNA are the noncoding class of RNA which plays major role post transcriptional regulation of genes endogenous in nature (Alka Dubey *et al*., 2013). *Pristionchus pacificus*, which have diverged up to 400 million years ago, to establish the repertoire and evolutionary dynamics of miRNAs in these species. In addition to previously known miRNA genes from *C. elegans* and *C. briggsae* we demonstrate expression of many of their homologs in *C. remanei* and *P. pacificus*, and identified in total more than 100 novel expressed miRNA genes, the majority of which belong to *P. pacificus*. Interestingly, more than half of all identified miRNA genes are conserved at the seed level in all four nematode species, whereas only a few miRNAs appear to be species specific. In our compendium of miRNAs we observed evidence for known mechanisms of miRNA evolution including antisense transcription and arm switching, as well as miRNA family expansion through gene duplication. In addition, we identified a novel mode of miRNA evolution, termed "hairpin shifting," in which an alternative hairpin is formed with up- or downstream sequences, leading to shifting of the hairpin and creation of novel miRNA* species. Finally, we identified 21U-RNAs in all four nematodes, including*P. pacificus*, where the upstream 21U-RNA motif is more diverged. The identification and systematic analysis of small RNA repertoire in four nematode species described here provides a valuable resource for understanding the evolutionary dynamics of miRNA-mediated gene regulation.(http://genome.cshlp.org/content/19/11/2064.short)

Most miRNA genes are transcribed by RNA polymerase II as long primary transcripts, or primary (pri)-miRNAs (Kim VN et al ., 2009). (Cai X et al ., 2004) , but some miRNAs can be also transcribed by RNA polymerase III (Lee Y *et al*., 2004). The pri-miRNA transcripts fold into stem-loop structures that are recognized and cleaved in the nucleus by RNase III-type nuclease Drosha (Borchert GM *et al*.,2006).(Lee Y *et al* ., 2002)to release precursor miRNA hairpins (pre-miRNAs). Drosha functions together with the Pasha-DGCR8 cofactor, which recognizes the RNA substrate (Lee Y *et al* ., 2003) (Denli AM *et al* ., 2004) the Drosha-containing protein complex is called a Microprocessor. Recently, it has been shown that the Microprocessor is not only involved in miRNA biogenesis but can also directly regulate the stability of mRNAs by processing mRNA-embedded hairpins (Gregory RI *et al., 2004)* The pre-miRNAs hairpins produced by the Microprocessor are exported from the nucleus by exportin 5 (Han J *et al* ., 2009 - Bohnsack MT *et al* ., 2004) and further processed by another RNase III-type nuclease Dicer (Lund E *et al.,2004* - Abbott AL *et al* ., 2005 *)*. The strand with less stable basepairing at its 5' end in the resulting ~22 nt RNA duplex is loaded into Argonaute protein within RNA-induced silencing complex (RISC) and becomes mature miRNA, whereas the other strand, miRNA*, is degraded (Khvorova A *et al* ., 2003) (Schwarz DS *et al* ., 2003)

Materials and Method

For this study we used as research materials is software's and database all prediction based on bioinformatics approaches. The micro RNAs (miRNA) sequences of ***Pristionchus pacificus*** were retrieved from miRBase (mirbase@manchester.ac.uk) (Ambros V et al , 2003) . Then we select potential miRNA on behalf of precursor thermodynamics ratings and miRBase high-confidence sequences of ***Pristionchus pacificus*** then we select high confidence miRNAs after that submitted to Diana Tv3.0 and results were analyzed for targeted genes of human.

Results and Discussion

Identified genes in human via *Pristionchus pacificus* miRNA this process done by DIANA - microT 3.0 novel miRNA target prediction

***Table 1: Pristionchus pacificus* high confidence miRNA with accession number**

S.No.	Stem loop sequence with accession number	Mature sequence (miRNA)with accession number
1.	>ppc-let-7 MI0011149 GCGACCGAGCUCCUGCUGAGGUAGUAGGUUGUAUAGUUCG GAAUAAUACCAACUGUAUCAAUUGGUGAAACUGUACAACC UGUCUAGCUUGCCAGGCAUCGCCCAGUUGCG	>ppc-let-7 MIMAT0011657 UGAGGUAGUAGGUUGUAUAGUU **(Nema_1 >ppc-let-7 MIMAT0011657)**
2.	>ppc-mir-2272 MI0011234 GCAGUACCCUGCUCGCUGAGCCGUCUAGGGUACACCCAUA CUGAGCCGACGAGAGUGCAUGAAGCGAUCGGCUUUAUGGC GCGUACCCUAUGCGGCGAGGCAUGAGCGGGGAUACUGU	>ppc-miR-2272 MIMAT0011729 UAGGGUACACCCAUACUGAGCCG **(Nema_2>ppc-miR-2272 MIMAT0011729)**

Table 1 Explains: These are high confidence sequences in miRBase that's why we selected these sequence as potential candidate for this analysis .

Table 2: Analysis of stem loop sequence & structure

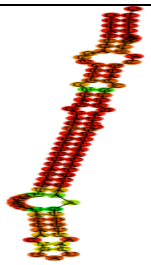
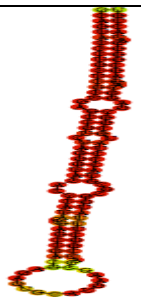
S.No.	Stem loop with accession num	Minimum free energy	MFE secondary structure
1.	>ppc-let-7 MI0011149 GCGACCGAGCUCCUGCUGAGGUAGUAGGU UGUAUAGUUCGGAAUAAUACCAACUGUAU CAAUUGGUGAAACUGUACAACCUGUCUAG CUUGCCAGGCAUCGCCCAGUUGCG	-41.70 kcal/mol	
2.	>ppc-mir-2272 MI0011234 GCAGUACCCUGCUCGCUGAGCCGUCUAGG GUACACCCAUACUGAGCCGACGAGAGUGC AUGAAGCGAUCGGCUUUAUGGCGCGUACC CUAUGCGGCGAGGCAUGAGCGGGGAUACU GU	-66.10 kcal/mol	

Table 2: Explains the thermodynamic structure with Minimum free energy for selection of potential miRNA for identification of targeted genes in humans

Table 3: (Nema_1 >ppc-let-7 MIMAT0011657) (*Pristionchus pacificus*)

S.No.	Name of gene	Position of chromosome	3 UTR	Conserved Information of gene
1	**FIGN**	164169404 – 164169432	4875 - 4903	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		164169302 – 164169330	4977 - 5005	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2,

				xenTro1, tetNig1
		164172899 – 164172927	1380 - 1408	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		164173652 – 164173680	627 - 655	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		164173565 – 164173593	714 - 742	mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		164167395 – 164167423	6884 - 6912	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galG
2	**IGF2BP1**	44483416 – 44483444	1610 - 1638	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
		44483434 – 44483462	1628 - 1656	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, tetNig1
		44486707 – 44486735	4901 - 4929	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, monDom4
		44487352 – 44487380	5546 - 5574	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4
		44486053 – 44486081	4247 - 4275	bosTau2, canFam2, monDom4
3	**LIN28B**	105633374 – 105633402	22 - 50	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		105635801 – 105635829	2449 - 2477	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, monDom4, galGal2, xenTro1, tetNig1
		105637422 – 105637450	4070 - 4098	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, galGal2, xenTro1
		105635983 – 105636011	2631 - 2659	oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, galGal2, xenTro1
		105637606 – 105637634	4254 - 4282	mm8, oryCun1, canFam2, dasNov1, loxAfr1, galGal2
4	**NR6A1**	126324410 – 126324438	366 - 394	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		126320048 – 126320076	4728 - 4756	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		126323439 – 126323467	1337 - 1365	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1
		126319516 – 126319544	5260 - 5288	rn4, mm8, oryCun1, bosTau2, canFam2, echTel1
		126323411 - 126323439	1365 - 1393	loxAfr1
5	**ONECUT2**	53302465 - 53302493	7511 - 7539	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		53304484 - 53304512	9530 - 9558	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, tetNig1
		53304729 - 53304757	9775 - 9803	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		53303045 - 53303073	8091 - 8119	echTel1
		53306945 - 53306973	11991 - 12019	dasNov1
		53299106 - 53299134	4152 - 4180	Not Conserved
6	**ARID3B**	72676079 - 72676107	910 - 938	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
		72675214 - 72675242	45 - 73	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1,
		72676800 - 72676828	1631 - 1659	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, galGal2
		72677398 - 72677426	2229 - 2257	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
		72677489 - 72677517	2320 - 2348	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
7	**FBN1**	46490532 - 46490560	1342 - 1370	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		46490649 - 46490677	1225 - 1253	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1

		46500206 - 46500234	571 - 599	rn4, mm8
8	**BACH1**	29639285 - 29639313	2259 - 2287	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
		29638985 - 29639013	1959 - 1987	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
9	**CLCN5**	49750357 - 49750385	6740 - 6768	mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1
		49746089 - 49746117	2472 - 2500	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1
		49748808 - 49748836	5191 - 5219	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1
		49745429 - 49745457	1812 - 1840	rn4, mm8, bosTau2, loxAfr1, echTel1
		49746393 - 49746421	2776 - 2804	rn4, mm8, dasNov1
		49749379 - 49749407	5762 - 5790	rn4, mm
10	**YOD1**	205288952 - 205288980	7 - 35	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2, xenTro1
		205287597 - 205287625	1362 - 1390	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
11	**HIC2**	20135165 - 20135193	4132 - 4160	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1
		20132169 - 20132197	1136 - 1164	rn4, mm8, oryCun1, bosTau2, canFam2, echTel1, galGal2, xenTro1
		20131554 - 20131582	521 - 549	rn4, mm8, oryCun1, bosTau2, canFam2, echTel1
		20131222 - 20131250	189 - 217	rn4, mm8, oryCun1, canFam2, echTel1
12	**IGF1R**	97320792 - 97320820	2597 - 2625	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		97318271 - 97318299	76 - 104	mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		97324834 - 97324862	6639 - 6667	Not Conserved
13	**FOXP2**	114119190 - 114119218	1972 - 2000	rn4, mm8, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		114119530 - 114119558	2312 - 2340	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		114120282 - 114120310	3064 - 3092	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2, xenTro1
14	**PBX3**	127768916 - 127768944	1027 - 1055	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		127768848 - 127768876	959 - 987	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2, xenTro1
15	**TRIM71**	32908458 - 32908486	150 - 178	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		32908538 - 32908566	230 - 258	bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2, xenTro1
16	**CCND2**	4281397 - 4281425	1960 - 1988	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		4281464 - 4281492	2027 - 2055	rn4, mm8, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2, xenTro1
		4284327 - 4284355	4890 - 4918	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, monDom4, galGal2
17	**PKN2**	89071604 - 89071632	1354 - 1382	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, xenTro1, tetNig1
		89072937 - 89072965	2687 - 2715	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		89073186 – 89073214	2936 - 2964	rn4, mm8, bosTau2, dasNov1, loxAfr1, echTel1, monDom4
18	**MAP4K3**	39330200 - 39330228	1034 - 1062	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4,

				galGal2, xenTro1
19	**CDV3**	134789890 - 134789918	309 - 337	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
20	**COL1A2**	93897998 - 93898026	356 - 384	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, galGal2, xenTro1, tetNig1
21	**IGF2BP3**	23317939 – 23317967	538 - 566	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
22	**PAPPA**	118202028 - 118202056	3311 - 3339	rn4, mm8, oryCun1, bosTau2, canFam2, echTel1, monDom4, galGal2
		118204015 - 118204043	5298 - 5326	mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		118203018 - 118203046	4301 - 4329	rn4, mm8, bosTau2, canFam2, dasNov1, echTel1
23	**CPEB2**	14679243 - 14679271	2140 - 2168	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		14677612 - 14677640	509 - 537	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		14679601 - 14679629	2498 - 2526	rn4, mm8, bosTau2, canFam2
24	**NAP1L1**	74727268 - 74727296	1179 - 1207	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1
		74726857 - 74726885	1590 - 1618	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
25	**C14orf28**	44446090 - 44446118	1586 - 1614	oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4
		44446172 - 44446200	1668 - 1696	rn4, mm8, oryCun1, bosTau2, canFam2
		44444919 - 44444947	415 - 443	oryCun1, bosTau2, canFam2
		44444757 - 44444785	253 - 281	rn4, mm8, oryCun1
26	**PPP1R15B**	202640403 - 202640431	1411 - 1439	rn4, mm8, bosTau2, canFam2, loxAfr1, echTel1, monDom4
		202641804 - 202641832	10 - 38	bosTau2, loxAfr1, echTel1, monDom4
27	**PTPRD**	8305600 - 8305628	2245 - 2273	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		8307614 - 8307642	231 - 259	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
28	**RAPGEF6,FNIP1**	131007060 - 131007088	1188 - 1216	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
29	**GALNT1**	31543755 - 31543783	22 - 50	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
		31544310 - 31544338	577 - 605	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
30	**SOCS4**	54582657 - 54582685	1821 - 1849	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1
		54583633 - 54583661	2797 - 2825	rn4, oryCun1
		54584482 - 54584510	3646 - 3674	Not Conserved
31	**DUSP16**	12520430 - 12520458	1977 - 2005	rn4, mm8, oryCun1, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
		12521991 - 12522019	416 - 444	oryCun1, canFam2, dasNov1, loxAfr1, monDom4, galGal2
		12520167 - 12520195	2240 - 2268	oryCun1, canFam2, loxAfr1
32	**TGFBR1**	100951462 - 100951490	53 - 81	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2
		100955275 - 100955303	3866 - 3894	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4
33	**HOXA1**	27100608 - 27100636	338 - 366	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, monDom4

		27100590 - 27100618	356 - 384	rn4, mm8, canFam2, dasNov1, loxAfr1, monDom4
34	**ARHGAP28**	6904931 - 6904959	2777 - 2805	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4
35	**MAP3K1**	56227395 - 56227423	2130 - 2158	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2
36	**LRIG2**	113468280 - 113468308	33 - 61	mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2, xenTro1
37	**UHRF2**	6496437 - 6496465	257 - 285	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
38	**LRIG3**	57552581 - 57552609	11 - 39	rn4, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
39	**Not found**	38976186 – 38976214	1948 - 1976	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, galGal2
40	**BPTF**	63386366 - 63386394	740 - 768	oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
41	**GAS7**	9760630 – 9760658	611 - 639	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, monDom4
		9757695 – 9757723	3546 - 3574	rn4, mm8, oryCun1
42	**CCNJ**	97809939 - 97809967	1950 - 1978	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1
		97809827 - 97809855	1838 - 1866	bosTau2, canFam2, dasNov1
43	**B3GNT7**	231972496 - 231972524	615 - 643	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1
		231972964 - 231972992	1083 - 1111	echTel1
44	**ABL2**	177343349 - 177343377	98 - 126	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, galGal2, tetNig1
		177339970 - 177339998	3477 - 3505	bosTau2, canFam2, loxAfr1, echTel1
45	**CPEB3**	93799752 - 93799780	2168 - 2196	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		93801362 - 93801390	558 - 586	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
46	**ACVR2A**	148401880 - 148401908	566 - 594	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		148404542 - 148404570	3228 - 3256	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
47	**ABCC5**	185120635 - 185120663	2724 - 2752	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, galGal2
		185127911;185129229 - 185127925;185129243	1213 - 1241	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, monDom4
48	**BCAT1**	24855778 – 24855806	6402 - 6430	mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2
49	**RANBP2**	108767468 – 108767496	678 - 706	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4
50	**PCDH19**	99435984 - 99436012	1918 - 1946	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1
51	**GAN**	79969820 - 79969848	1117 - 1145	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4
52	**MAPK8**	49316656 - 49316684	3577 - 3605	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4
53	**COL3A1**	189585132 – 189585160	386 - 414	rn4, mm8, bosTau2, canFam2, echTel1, monDom4, galGal2, xenTro1
54	**PPARGC1B**	149207324 - 149207352	9 - 37	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		149207316 - 149207344	1 - 29	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
55	**BZW1**	201395376 - 201395404	229 - 257	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		201395209 - 201395237	62 - 90	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2

56	**POU2F1**	165660357 - 165660385	8685 - 8713	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		165657547 - 165657575	5875 - 5903	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2
57	**CPEB4**	173317941 - 173317969	2194 - 2222	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		173316744 - 173316772	997 - 1025	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4, galGal2
58	**FNDC3A**	48681512 - 48681540	1979 - 2007	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		48679976 - 48680004	443 - 471	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, monDom4, galGal2, xenTro1
59	**HDX**	83459642 – 83459670	3882 - 3910	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, echTel1, monDom4
		83462616 - 83462644	908 - 936	rn4, mm8, oryCun1, canFam2, loxAfr1, echTel1
60	**DLC1**	12985974 – 12986002	1688 - 1716	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, galGal2, xenTro1
		12985948 – 12985976	1714 - 1742	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
61	**NAT12**	56946454 – 56946482	466 - 494	rn4, mm8, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2, xenTro1
		56947461 – 56947489	1473 - 1501	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, echTel1, monDom4, galGal2
62	**IDE**	94224643 – 94224671	1217 - 1245	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1, tetNig1
		94220053 – 94220081	1311 - 1339	rn4, mm8, bosTau2, canFam2, loxAfr1, echTel1, monDom4
63	**ZNF512B**	62061179 – 62061207	477 - 505	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1
		62061080 – 62061108	576 - 604	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1
		62059091 – 62059119	2565 - 2593	rn4, mm8, bosTau2, canFam2
64	**IGF2BP2**	186844687 - 186844715	1297 - 1325	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, loxAfr1, monDom4
		186844702 – 186844730	1282 - 1310	rn4, mm8, oryCun1, bosTau2, canFam2, loxAfr1
65	**PTCH1**	97260355 – 97260383	1931 - 1959	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1, echTel1, monDom4, galGal2, xenTro1, tetNig1
		97270944 – 97270972	1166 - 1194	mm8, oryCun1, dasNov1

Table 3: This table explains that name of 65-targeted genes in humans that genes identified via miRNA of *Pristionchus pacificus* (>ppc-let-7 MIMAT0011657) with conserved information.

Table 4: (Nema_2>ppc-miR-2272 MIMAT0011729) (*Pristionchus pacificus*)

S.No.	Name of gene	Position of chromosome	3 UTR	Conserved information of genes
1	Gene name not found	125783257 - 12578328	57 – 85	Not Conserved
		125783306 - 125783334	106 – 134	rn4, mm8, oryCun1, bosTau2, canFam2, dasNov1
		125783355 - 125783383	155 – 183	Not Conserved
2	GSG1	13128337 - 13128365	983 – 1011	Not Conserved
		13127767 - 13127795	1553 - 1581	Not Conserved

Table 4: This table explains that name of 1 targeted genes in humans that genes identified via miRNA of *Pristionchus pacificus* (**>ppc-miR-2272 MIMAT0011729**) with conserved information.

Conclusion

Finally, in this study with two potential miRNAs of *Pristionchus pacificus* and these potential miRNAs target 65 genes in human. These genes are shown in Table no. 4 . These genes play an important role in the regulation of gene expression with their genomic participation. That shown in Table no. 5. In conclusion, we can say that if we control malfunction of protein at transcriptional level via identification of genomics expression with single targeted genes with potential analysis .

Table: 5 Identified human targeted genes from *Pristionchus pacificus* miRNAs via bioinformatics approaches

S.No.	Name of genes	Function involved in humans
1	**FIGN**	ATP-dependent microtubule severing protein. Severs microtubules along their length and depolymerizes their ends, primarily the minus-end, that may lead to the suppression of microtubule growth from and attachment to centrosomes. Microtubule severing may promote rapid reorganization of cellular microtubule arrays and the release of microtubules from the centrosome following nucleation. Microtubule release from the mitotic spindle poles may allow depolymerization of the microtubule end proximal to the spindle pole, leading to poleward microtubule flux and poleward motion of chromosome
2	**IGF2BP1**	This gene encodes a member of the insulin-like growth factor 2 mRNA-binding protein family. The protein encoded by this gene contains four K homology domains and two RNA recognition motifs. It functions by binding to the mRNAs of certain genes, including insulin-like growth factor 2, beta-actin and beta transduction repeat-containing protein, and regulating their translation. Two transcript variants encoding different isoforms have been found for this gene.
3	**LIN28B**	The protein encoded by this gene belongs to the lin-28 family, which is characterized by the presence of a cold-shock domain and a pair of CCHC zinc finger domains. This gene is highly expressed in testis, fetal liver, placenta, and in primary human tumors and cancer cell lines. It is negatively regulated by microRNAs that target sites in the 3' UTR, and over expression of this gene in primary tumors is linked to the repression of let-7 family of microRNAs and derepression of let-7 targets, which facilitates cellular transformation.
4	**NR6A1**	This gene encodes an orphan nuclear receptor which is a member of the nuclear hormone receptor family. Its expression pattern suggests that it may be involved in neurogenesis and germ cell development. The protein can homodimerize and bind DNA, but in vivo targets have not been identified. Alternate splicing results in multiple transcript variants.
5	**ONECUT2**	This gene encodes a member of the onecut family of transcription factors, which are characterized by a cut domain and an atypical homeodomain. The protein binds to specific DNA sequences and stimulates expression of target genes, including genes involved in melanocyte and hepatocyte differentiation.
6	**ARID3B**	This gene encodes a member of the ARID (AT-rich interaction domain) family of DNA-binding proteins. The encoded protein is homologous with two proteins that bind to the retinoblastoma gene product, and also with the mouse Bright and Drosophila dead ringer proteins. A pseudogene on chromosome 1p31 exists for this gene. Members of the ARID family have roles in embryonic patterning, cell lineage gene regulation, cell cycle control, transcriptional regulation and possibly in chromatin structure modification.
7	**FBN1**	This gene encodes a member of the fibrillin family. The encoded protein is a large, extracellular matrix glycoprotein that serve as a structural component of 10-12 nm calcium-binding microfibrils. These microfibrils provide force bearing structural support in elastic and nonelastic connective tissue throughout the body. Mutations in this gene are associated with Marfan syndrome, isolated ectopia lentis, autosomal dominant Weill-Marchesani syndrome, MASS syndrome, and Shprintzen-Goldberg craniosynostosis syndrome.
8	**BACH1**	This gene encodes a transcription factor that belongs to the cap'n'collar type of basic region leucine zipper factor family (CNC-bZip). The encoded protein contains broad complex, tramtrack, bric-a-brac/poxvirus and zinc finger (BTB/POZ) domains, which is atypical of CNC-bZip family members. These BTB/POZ domains facilitate protein-protein interactions and formation of homo- and/or hetero-oligomers. When this encoded protein forms a heterodimer with MafK, it functions as a repressor of Maf recognition element (MARE) and transcription is repressed. Multiple alternatively spliced transcript variants have been identified for this gene.
9	**CLCN5**	This gene encodes a member of the ClC family of chloride ion channels and ion transporters. The encoded protein is primarily localized to endosomal membranes and may function to facilitate albumin uptake by the renal proximal tubule. Mutations in this gene have been found in Dent disease and renal tubular disorders complicated by nephrolithiasis. Alternatively spliced transcript variants have been found for this gene.
10	**YOD1**	Protein ubiquitination controls many intracellular processes, including cell cycle progression, transcriptional activation, and signal transduction. This dynamic process, involving ubiquitin conjugating enzymes and deubiquitinating enzymes, adds and removes ubiquitin. Deubiquitinating enzymes are cysteine proteases that specifically cleave ubiquitin from ubiquitin-conjugated protein substrates. The protein encoded by this gene belongs to a DUB subfamily characterized by an ovarian tumor (OTU) domain. Alternative splicing results in multiple transcript variants.

11	**HIC2**	Transcriptional repressor
12	**IGF1R**	This receptor binds insulin-like growth factor with a high affinity. It has tyrosine kinase activity. The insulin-like growth factor I receptor plays a critical role in transformation events. Cleavage of the precursor generates alpha and beta subunits. It is highly overexpressed in most malignant tissues where it functions as an anti-apoptotic agent by enhancing cell survival. Alternatively spliced transcript variants encoding distinct isoforms have been found for this gene.
13	**FOXP2**	This gene encodes a member of the forkhead/winged-helix (FOX) family of transcription factors. It is expressed in fetal and adult brain as well as in several other organs such as the lung and gut. The protein product contains a FOX DNA-binding domain and a large polyglutamine tract and is an evolutionarily conserved transcription factor, which may bind directly to approximately 300 to 400 gene promoters in the human genome to regulate the expression of a variety of genes. This gene is required for proper development of speech and language regions of the brain during embryogenesis, and may be involved in a variety of biological pathways and cascades that may ultimately influence language development. Mutations in this gene cause speech-language disorder 1 (SPCH1), also known as autosomal dominant speech and language disorder with orofacial dyspraxia. Multiple alternative transcripts encoding different isoforms have been identified in this gene.
14	**PBX3**	pre-B-cell leukemia homeobox 3) is a protein-coding gene. GO annotations related to this gene include *sequence-specific DNA binding* and*sequence-specific DNA binding transcription factor activity*.
15	**TRIM71**	TRIM71 (tripartite motif containing 71, E3 ubiquitin protein ligase) is a protein-coding gene. GO annotations related to this gene include *ubiquitin-protein ligase activity* and *miRNA binding*. An important paralog of this gene is TRIM3.
16	**CCND2**	The protein encoded by this gene belongs to the highly conserved cyclin family, whose members are characterized by a dramatic periodicity in protein abundance through the cell cycle. Cyclins function as regulators of CDK kinases. Different cyclins exhibit distinct expression and degradation patterns which contribute to the temporal coordination of each mitotic event. This cyclin forms a complex with CDK4 or CDK6 and functions as a regulatory subunit of the complex, whose activity is required for cell cycle G1/S transition. This protein has been shown to interact with and be involved in the phosphorylation of tumor suppressor protein Rb. Knockout studies of the homologous gene in mouse suggest the essential roles of this gene in ovarian granulosa and germ cell proliferation. High level expression of this gene was observed in ovarian and testicular tumors. Mutations in this gene are associated with megalencephaly-polymicrogyria-polydactyly-hydrocephalus syndrome 3 (MPPH3).
17	**PKN2**	**Function**: PKC-related serine/threonine-protein kinase and Rho/Rac effector protein that participates in specificsignal transduction responses in the cell. Plays a role in the regulation of cell cycle progression, actincytoskeleton assembly, cell migration, cell adhesion, tumor cell invasion and transcription activation signalingprocesses. Phosphorylates CTTN in hyaluronan-induced astrocytes and hence decreases CTTN ability to associate with filamentous actin. Phosphorylates HDAC5, therefore lead to impair HDAC5 import. Direct RhoA target required for the regulation of the maturation of primordial junctions into apical junction formation in bronchial epithelial cells. Required for G2/M phases of the cell cycle progression and abscission during cytokinesis in aECT2-dependent manner. Stimulates FYN kinase activity that is required for establishment of skin cell-celladhesion during keratinocytes differentiation. Regulates epithelial bladder cells speed and direction of movementduring cell migration and tumor cell invasion. Inhibits Akt pro-survival-induced kinase activity. Mediates Rhoprotein-induced transcriptional activation via the c-fos serum response factor (SRF). Phosphorylates HCV NS5Bleading to stimulation of HCV RNA replication
18	**MAP4K3**	This gene encodes a member of the mitogen-activated protein kinase kinase kinase kinase family. The encoded protein activates key effectors in cell signalling, among them c-Jun. Alternatively spliced transcripts encoding multiple isoforms have been observed for this gene.
19	**CDV3**	Not identified
20	**COL1A2**	This gene encodes the pro-alpha2 chain of type I collagen whose triple helix comprises two alpha1 chains and one alpha2 chain. Type I is a fibril-forming collagen found in most connective tissues and is abundant in bone, cornea, dermis and tendon. Mutations in this gene are associated with osteogenesis imperfecta types I-IV, Ehlers-Danlos syndrome type VIIB, recessive Ehlers-Danlos syndrome Classical type, idiopathic osteoporosis, and atypical Marfan syndrome. Symptoms associated with mutations in this gene, however, tend to be less severe than mutations in the gene for the alpha1 chain of type I collagen (COL1A1) reflecting the different role of alpha2 chains in matrix integrity. Three transcripts, resulting from the use of alternate polyadenylation signals, have been identified for this gene.
21	**IGF2BP3**	The protein encoded by this gene is primarily found in the nucleolus, where it can bind to the 5' UTR of the insulin-like growth factor II leader 3 mRNA and may repress translation of insulin-like growth factor II during late development. The encoded protein contains several KH domains, which are important in RNA binding and are known to be involved in RNA synthesis and metabolism. A pseudogene exists on chromosome 7, and there are putative pseudogenes on other chromosomes.
22	**PAPPA**	This gene encodes a secreted metalloproteinase which cleaves insulin-like growth factor binding proteins (IGFBPs). It is thought to be involved in local proliferative processes such as wound healing and bone remodeling. Low plasma level of this protein has been suggested as a biochemical marker for pregnancies with aneuploid fetuses.
23	**CPEB2**	The protein encoded by this gene is highly similar to cytoplasmic polyadenylation element binding protein (CPEB), an mRNA-binding protein that regulates cytoplasmic polyadenylation of mRNA as a trans factor in oogenesis and spermatogenesis. Studies of the similar gene in mice suggested a possible role of this protein in transcriptionally inactive haploid spermatids. Alternatively spliced transcript variants encoding distinct isoforms have been described.
24	**NAP1L1**	This gene encodes a member of the nucleosome assembly protein (NAP) family. This protein participates in DNA replication and may play a role in modulating chromatin formation and contribute to the regulation of cell proliferation. Alternative splicing results in multiple transcript variants encoding different isoforms; however, not all have been fully described.
25	**C14orf28**	Protein-coding gene.
26	**PPP1R15B**	PPP1R15B promotes dephosphorylation of the transcription initiation factor EIF2-alpha (EIF2S1; MIM 603907) through recruitment of protein phosphatase-1 (PP1) catalytic subunits (see MIM 176875) (Harding et al., 2009
27	**PTPRD**	The protein encoded by this gene is a member of the protein tyrosine phosphatase (PTP) family. PTPs are known to be signaling

		molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle, and oncogenic transformation. This PTP contains an extracellular region, a single transmembrane segment and two tandem intracytoplasmic catalytic domains, and thus represents a receptor-type PTP. The extracellular region of this protein is composed of three Ig-like and eight fibronectin type III-like domains. Studies of the similar genes in chicken and fly suggest the role of this PTP is in promoting neurite growth, and regulating neurons axon guidance. Multiple alternatively spliced transcript variants of this gene have been reported. A related pseudogene has been identified on chromosome 5.
28	**RAPGEF6,FNIP1**	May be involved in energy and/or nutrient sensing through the AMPK and mTOR signaling pathways. Mayregulate phosphorylation of RPS6KB1
29	**GALNT1**	This gene encodes a member of the UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase (GalNAc-T) family of enzymes. GalNAc-Ts initiate mucin-type O-linked glycosylation in the Golgi apparatus by catalyzing the transfer of GalNAc to serine and threonine residues on target proteins. They are characterized by an N-terminal transmembrane domain, a stem region, a lumenal catalytic domain containing a GT1 motif and Gal/GalNAc transferase motif, and a C-terminal ricin/lectin-like domain. GalNAc-Ts have different, but overlapping, substrate specificities and patterns of expression. Transcript variants derived from this gene that utilize alternative polyA signals have been described in the literature.
30	**SOCS4**	The protein encoded by this gene contains a SH2 domain and a SOCS BOX domain. The protein thus belongs to the suppressor of cytokine signaling (SOCS), also known as STAT-induced STAT inhibitor (SSI), protein family. SOCS family members are known to be cytokine-inducible negative regulators of cytokine signaling. Two alternatively spliced transcript variants encoding the same protein have been found for this gene.
31	**DUSP16**	This gene encodes a mitogen-activated protein kinase phosphatase that is a member of the dual specificity protein phosphatase subfamily. These phosphatases inactivate their target kinases by dephosphorylating both the phosphoserine/threonine and phosphotyrosine residues. The encoded protein specifically regulates the c-Jun amino-terminal kinase (JNK) and extracellular signal-regulated kinase (ERK) pathways.
32	**TGFBR1**	The protein encoded by this gene forms a heteromeric complex with type II TGF-beta receptors when bound to TGF-beta, transducing the TGF-beta signal from the cell surface to the cytoplasm. The encoded protein is a serine/threonine protein kinase. Mutations in this gene have been associated with Loeys-Dietz aortic aneurysm syndrome (LDAS). Multiple transcript variants encoding different isoforms have been found for this gene.
33	**HOXA1**	In vertebrates, the genes encoding the class of transcription factors called homeobox genes are found in clusters named A, B, C, and D on four separate chromosomes. Expression of these proteins is spatially and temporally regulated during embryonic development. This gene is part of the A cluster on chromosome 7 and encodes a DNA-binding transcription factor which may regulate gene expression, morphogenesis, and differentiation. The encoded protein may be involved in the placement of hindbrain segments in the proper location along the anterior-posterior axis during development. Two transcript variants encoding two different isoforms have been found for this gene, with only one of the isoforms containing the homeodomain region.
34	**ARHGAP28**	--
35	**MAP3K1**	The protein encoded by this gene is a serine/threonine kinase and is part of some signal transduction cascades, including the ERK and JNK kinase pathways as well as the NF-kappa-B pathway. The encoded protein is activated by autophosphorylation and requires magnesium as a cofactor in phosphorylating other proteins. This protein has E3 ligase activity conferred by a plant homeodomain (PHD) in its N-terminus and phospho-kinase activity conferred by a kinase domain in its C-terminus.
36	**LRIG2**	(leucine-rich repeats and immunoglobulin-like domains 2) is a protein-coding gene. Diseases associated with LRIG2 include *urofacial syndrome 2*, and *lrig2-related urofacial syndrome*.
37	**UHRF2**	This gene encodes a nuclear protein which is involved in cell-cycle regulation. The encoded protein is a ubiquitin-ligase capable of ubiquinating PCNP (PEST-containing nuclear protein), and together they may play a role in tumorigenesis. The encoded protein contains an NIRF_N domain, a PHD finger, a set- and ring-associated (SRA) domain, and a RING finger domain and several of these domains have been shown to be essential for the regulation of cell proliferation. This protein may also have a role in intranuclear degradation of polyglutamine aggregates. Alternative splicing results in multiple transcript variants some of which are non-protein coding.
38	**LRIG3**	May play a role in craniofacial and inner ear morphogenesis during embryonic development. May act within the optic vesicle epithelium to control formation of the lateral semicircular canal in the inner ear, possibly byrestricting the expression of NTN1
39	**Not found**	
40	**BPTF**	This gene was identified by the reactivity of its encoded protein to a monoclonal antibody prepared against brain homogenates from patients with Alzheimer's disease. Analysis of the original protein (fetal Alz-50 reactive clone 1, or FAC1), identified as an 810 aa protein containing a DNA-binding domain and a zinc finger motif, suggested it might play a role in the regulation of transcription. High levels of FAC1 were detected in fetal brain and in patients with neurodegenerative diseases. The protein encoded by this gene is actually much larger than originally thought, and it also contains a C-terminal bromodomain characteristic of proteins that regulate transcription during proliferation. The encoded protein is highly similar to the largest subunit of the Drosophila NURF (nucleosome remodeling factor) complex. In Drosophila, the NURF complex, which catalyzes nucleosome sliding on DNA and interacts with sequence-specific transcription factors, is necessary for the chromatin remodeling required for transcription. Two alternative transcripts encoding different isoforms have been described completely. [provided by RefSeq, Jul 2008]
41	**GAS7**	Growth arrest-specific 7 is expressed primarily in terminally differentiated brain cells and predominantly in mature cerebellar Purkinje neurons. GAS7 plays a putative role in neuronal development. Several transcript variants encoding proteins which vary in the N-terminus have been described.
42	**CCNJ**	CCNJ (cyclin J) is a protein-coding gene.
43	**B3GNT7**	May be involved in keratane sulfate biosynthesis. Transfers N-acetylgalactosamine on to keratansulfate-related glycans. May play a role in preventing cells from migrating out of the original tissues and invading surrounding tissues
44	**ABL2**	This gene encodes a member of the Abelson family of nonreceptor tyrosine protein kinases. The protein is highly similar to the c-

		abl oncogene 1 protein, including the tyrosine kinase, SH2 and SH3 domains, and it plays a role in cytoskeletal rearrangements through its C-terminal F-actin- and microtubule-binding sequences. This gene is expressed in both normal and tumor cells, and is involved in translocation with the ets variant 6 gene in leukemia. Multiple alternatively spliced transcript variants encoding different protein isoforms have been found for this gene.
45	**CPEB3**	CPEB3 (cytoplasmic polyadenylation element binding protein 3) is a protein-coding gene. GO annotations related to this gene include *RNA binding*and *nucleotide binding*.
46	**ACVR2A**	This gene encodes a receptor that mediates the functions of activins, which are members of the transforming growth factor-beta (TGF-beta) superfamily involved in diverse biological processes. The encoded protein is a transmembrane serine-threonine kinase receptor which mediates signaling by forming heterodimeric complexes with various combinations of type I and type II receptors and ligands in a cell-specific manner. The encoded type II receptor is primarily involved in ligand-binding and includes an extracellular ligand-binding domain, a transmembrane domain and a cytoplasmic serine-threonine kinase domain. This gene may be associated with susceptibility to preeclampsia, a pregnancy-related disease which can result in maternal and fetal morbidity and mortality. Alternative splicing results in multiple transcript variants of this gene.
47	**ABCC5**	The protein encoded by this gene is a member of the superfamily of ATP-binding cassette (ABC) transporters. ABC proteins transport various molecules across extra- and intra-cellular membranes. ABC genes are divided into seven distinct subfamilies (ABC1, MDR/TAP, MRP, ALD, OABP, GCN20, White). This protein is a member of the MRP subfamily which is involved in multi-drug resistance. This protein functions in the cellular export of its substrate, cyclic nucleotides. This export contributes to the degradation of phosphodiesterases and possibly an elimination pathway for cyclic nucleotides. Studies show that this protein provides resistance to thiopurine anticancer drugs, 6-mercatopurine and thioguanine, and the anti-HIV drug 9-(2-phosphonylmethoxyethyl)adenine. This protein may be involved in resistance to thiopurines in acute lymphoblastic leukemia and antiretroviral nucleoside analogs in HIV-infected patients. Alternative splicing of this gene has been detected; however, the complete sequence and translation initiation site is unclear.
48	**BCAT1**	This gene encodes the cytosolic form of the enzyme branched-chain amino acid transaminase. This enzyme catalyzes the reversible transamination of branched-chain alpha-keto acids to branched-chain L-amino acids essential for cell growth. Two different clinical disorders have been attributed to a defect of branched-chain amino acid transamination: hypervalinemia and hyperleucine-isoleucinemia. As there is also a gene encoding a mitochondrial form of this enzyme, mutations in either gene may contribute to these disorders. Alternatively spliced transcript variants have been described.
49	**RANBP2**	RAN is a small GTP-binding protein of the RAS superfamily that is associated with the nuclear membrane and is thought to control a variety of cellular functions through its interactions with other proteins. This gene encodes a very large RAN-binding protein that immunolocalizes to the nuclear pore complex. The protein is a giant scaffold and mosaic cyclophilin-related nucleoporin implicated in the Ran-GTPase cycle. The encoded protein directly interacts with the E2 enzyme UBC9 and strongly enhances SUMO1 transfer from UBC9 to the SUMO1 target SP100. These findings place sumoylation at the cytoplasmic filaments of the nuclear pore complex and suggest that, for some substrates, modification and nuclear import are linked events. This gene is partially duplicated in a gene cluster that lies in a hot spot for recombination on chromosome .
50	**PCDH19**	The protein encoded by this gene is a member of the delta-2 protocadherin subclass of the cadherin superfamily. The encoded protein is thought to be a calcium-dependent cell-adhesion protein that is primarily expressed in the brain. Defects in this gene are a cause of epilepsy female-restricted with mental retardation (EFMR). Three transcript variants encoding different isoforms have been found for this gene.
51	**GAN**	This gene encodes a member of the cytoskeletal BTB/kelch (Broad-Complex, Tramtrack and Bric a brac) repeat family. The encoded protein plays a role in neurofilament architecture and is involved in mediating the ubiquitination and degradation of some proteins. Defects in this gene are a cause of giant axonal neuropathy (GAN).
52	**MAPK8**	The protein encoded by this gene is a member of the MAP kinase family. MAP kinases act as an integration point for multiple biochemical signals, and are involved in a wide variety of cellular processes such as proliferation, differentiation, transcription regulation and development. This kinase is activated by various cell stimuli, and targets specific transcription factors, and thus mediates immediate-early gene expression in response to cell stimuli. The activation of this kinase by tumor-necrosis factor alpha (TNF-alpha) is found to be required for TNF-alpha induced apoptosis. This kinase is also involved in UV radiation induced apoptosis, which is thought to be related to cytochrom c-mediated cell death pathway. Studies of the mouse counterpart of this gene suggested that this kinase play a key role in T cell proliferation, apoptosis and differentiation. Five alternatively spliced transcript variants encoding distinct isoforms have been reported.
53	**COL3A1**	This gene encodes the pro-alpha1 chains of type III collagen, a fibrillar collagen that is found in extensible connective tissues such as skin, lung, uterus, intestine and the vascular system, frequently in association with type I collagen. Mutations in this gene are associated with Ehlers-Danlos syndrome types IV, and with aortic and arterial aneurysms. Two transcripts, resulting from the use of alternate polyadenylation signals, have been identified for this gene.
54	**PPARGC1B**	The protein encoded by this gene stimulates the activity of several transcription factors and nuclear receptors, including estrogen receptor alpha, nuclear respiratory factor 1, and glucocorticoid receptor. The encoded protein may be involved in fat oxidation, non-oxidative glucose metabolism, and the regulation of energy expenditure. This protein is downregulated in prediabetic and type 2 diabetes mellitus patients. Certain allelic variations in this gene increase the risk of the development of obesity. Three transcript variants encoding different isoforms have been found for this gene.
55	**BZW1**	--
56	**POU2F1**	The OCT1 transcription factor was among the first identified members of the POU transcription factor family (summarized by Sturm et al., 1993 [PubMed 8314572]). Members of this family contain the POU domain, a 160-amino acid region necessary for DNA binding to the octameric sequence ATGCAAAT.
57	**CPEB4**	CPEB4 (cytoplasmic polyadenylation element binding protein 4) is a protein-coding gene. GO annotations related to this gene include *RNA binding* and *nucleotide binding*.
58	**FNDC3A**	Mediates spermatid-Sertoli adhesion during spermatogenesis
59	**HDX**	HDX (highly divergent homeobox) is a protein-coding gene. GO annotations related to this gene include *sequence-specific DNA*

		binding and*sequence-specific DNA binding transcription factor activity*.
60	**DLC1**	This gene encodes a GTPase-activating protein (GAP) that is a member of the rhoGAP family of proteins which play a role in the regulation of small GTP-binding proteins. GAP family proteins participate in signaling pathways that regulate cell processes involved in cytoskeletal changes. This gene functions as a tumor suppressor gene in a number of common cancers, including prostate, lung, colorectal, and breast cancers. Multiple transcript variants due to alternative promoters and alternative splicing have been found for this gene.
61	**NAT12**	Nucleobase- ascorbate transporter
62	**IDE**	This gene encodes a zinc metallopeptidase that degrades intracellular insulin, and thereby terminates insulins activity, as well as participating in intercellular peptide signalling by degrading diverse peptides such as glucagon, amylin, bradykinin, and kallidin. The preferential affinity of this enzyme for insulin results in insulin-mediated inhibition of the degradation of other peptides such as beta-amyloid. Deficiencies in this protein's function are associated with Alzheimer's disease and type 2 diabetes mellitus but mutations in this gene have not been shown to be causitive for these diseases. This protein localizes primarily to the cytoplasm but in some cell types localizes to the extracellular space, cell membrane, peroxisome, and mitochondrion. Alternative splicing results in multiple transcript variants encoding distinct isoforms. Additional transcript variants have been described but have not been experimentally verified.
63	**ZNF512B**	May be involved in transcriptional regulation
64	**IGF2BP2**	This gene encodes a member of the IGF-II mRNA-binding protein (IMP) family. The protein encoded by this gene contains four KH domains and two RRM domains. It functions by binding to the 5' UTR of the insulin-like growth factor 2 (IGF2) mRNA and regulating IGF2 translation. Alternative promoter usage and alternate splicing result in multiple variants encoding different isoforms
65	**PTCH1**	This gene encodes a member of the patched gene family. The encoded protein is the receptor for sonic hedgehog, a secreted molecule implicated in the formation of embryonic structures and in tumorigenesis, as well as the desert hedgehog and indian hedgehog proteins. This gene functions as a tumor suppressor. Mutations of this gene have been associated with basal cell nevus syndrome, esophageal squamous cell carcinoma, trichoepitheliomas, transitional cell carcinomas of the bladder, as well as holoprosencephaly. Alternative splicing results in multiple transcript variants encoding different isoforms. Additional splice variants have been described, but their full length sequences and biological validity cannot be determined currently.

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