

## *Supplementary Material*

### **In silico identification and clinical validation of a Novel Long non-coding RNA/mRNA/ miRNA Molecular network as Potential biomarker for discriminating SARS COV-2 infection severity**

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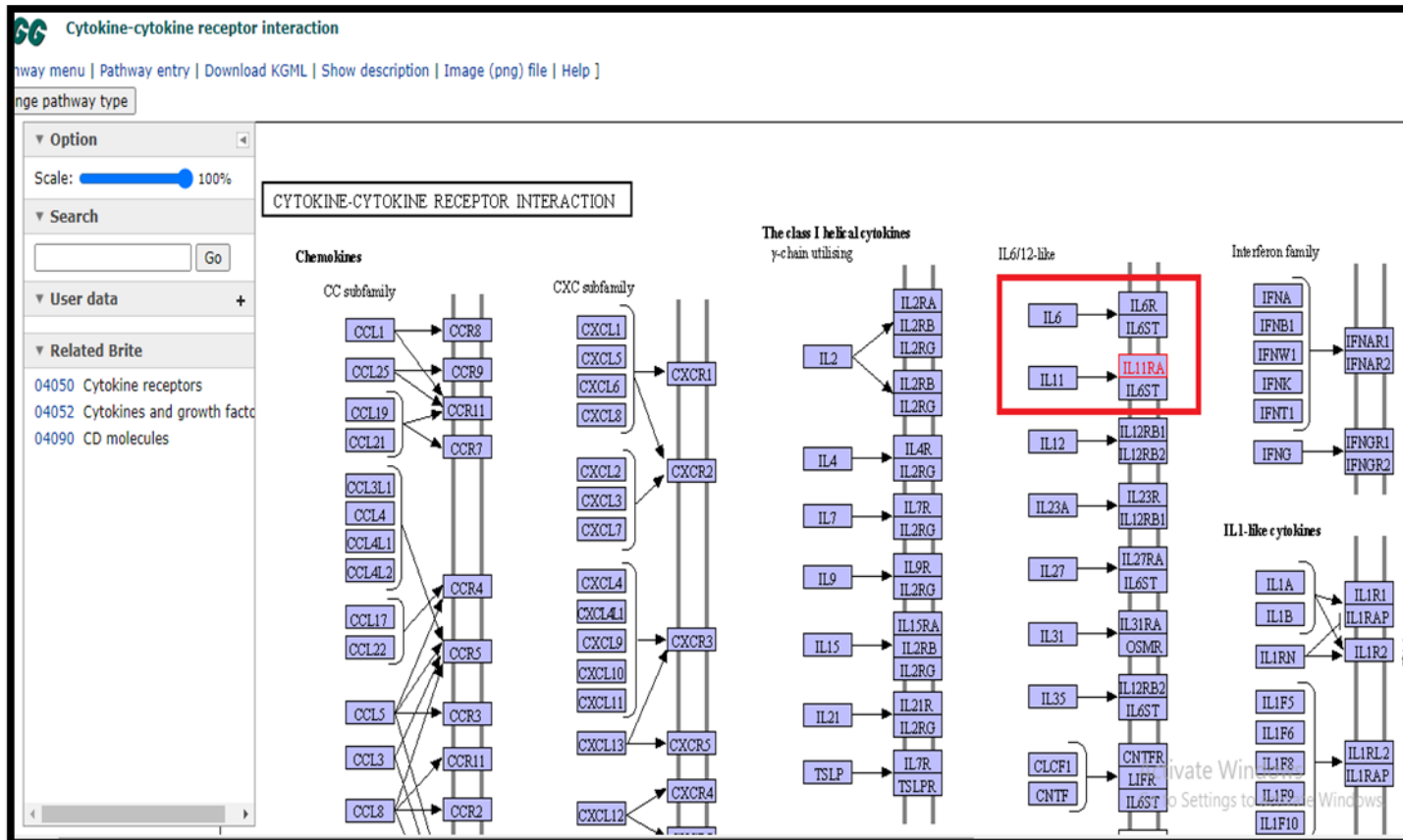
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**Supplementary Table S1: Correlation between IL11RA-molecular network,  
ferritin, procalcitonin and IL11RA protein:**

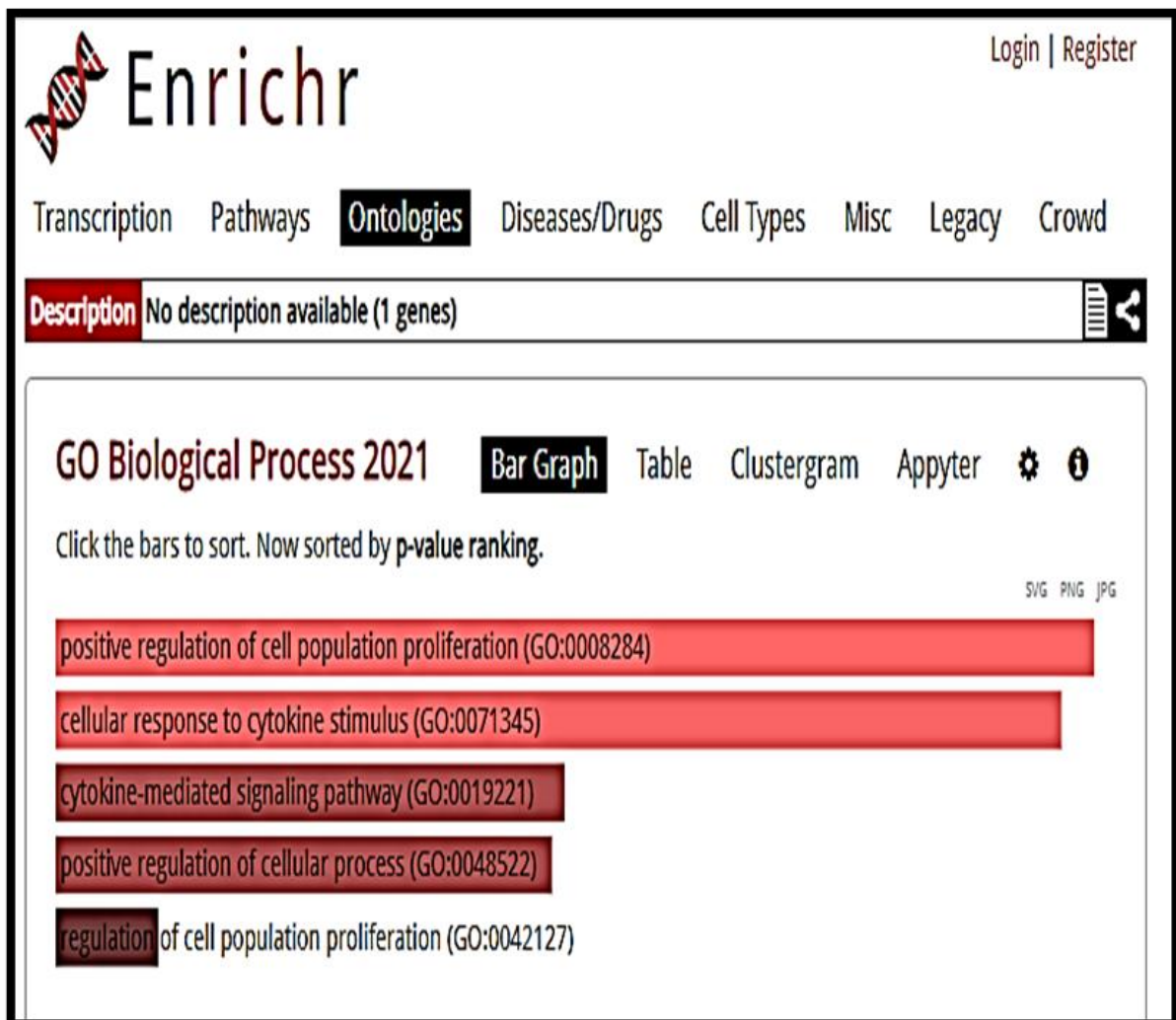
			lncRNA RP11- 773H22. 4	HSA-MIR- 4257	IL11RA mRNA	IL11RA protein (pg/mL)	Procalciton in protein (pg/mL )	Ferritin (ng/ml)
Spearman's Rho	Relative quantity of lncRNA RP11- 773H22.4	Correlation Coefficient	1.000	-.475**	.530**	.497**	.210**	.389**
		Sig. (2-tailed)	.	.000	.000	.000	.003	.000
	Relative quantity of HSA-MIR- 4257	Correlation Coefficient	-.475**	1.000	-.664**	-.607**	-.327**	-.538**
		Sig. (2-tailed)	.000	.	.000	.000	.000	.000
	Relative quantity of IL11RA mRNA	Correlation Coefficient	.530**	-.664**	1.000	.838**	.449**	.511**
		Sig. (2-tailed)	.000	.000	.	.000	.000	.000
	IL11RA protein(pg/mL)	Correlation Coefficient	.497**	-.607**	.838**	1.000	.482**	.544**
		Sig. (2-tailed)	.000	.000	.000	.	.000	.000
	Procalcitonin protein(pg/mL)	Correlation Coefficient	.210**	-.327**	.449**	.482**	1.000	.264**
		Sig. (2-tailed)	.003	.000	.000	.000	.	.000
	Ferritin(ng/ml)	Correlation Coefficient	.389**	-.538**	.511**	.544**	.264**	1.000
		Sig. (2-tailed)	.000	.000	.000	.000	.000	.

\*\* . Correlation is significant at the 0.01 level (2-tailed)

## Supplementary figures



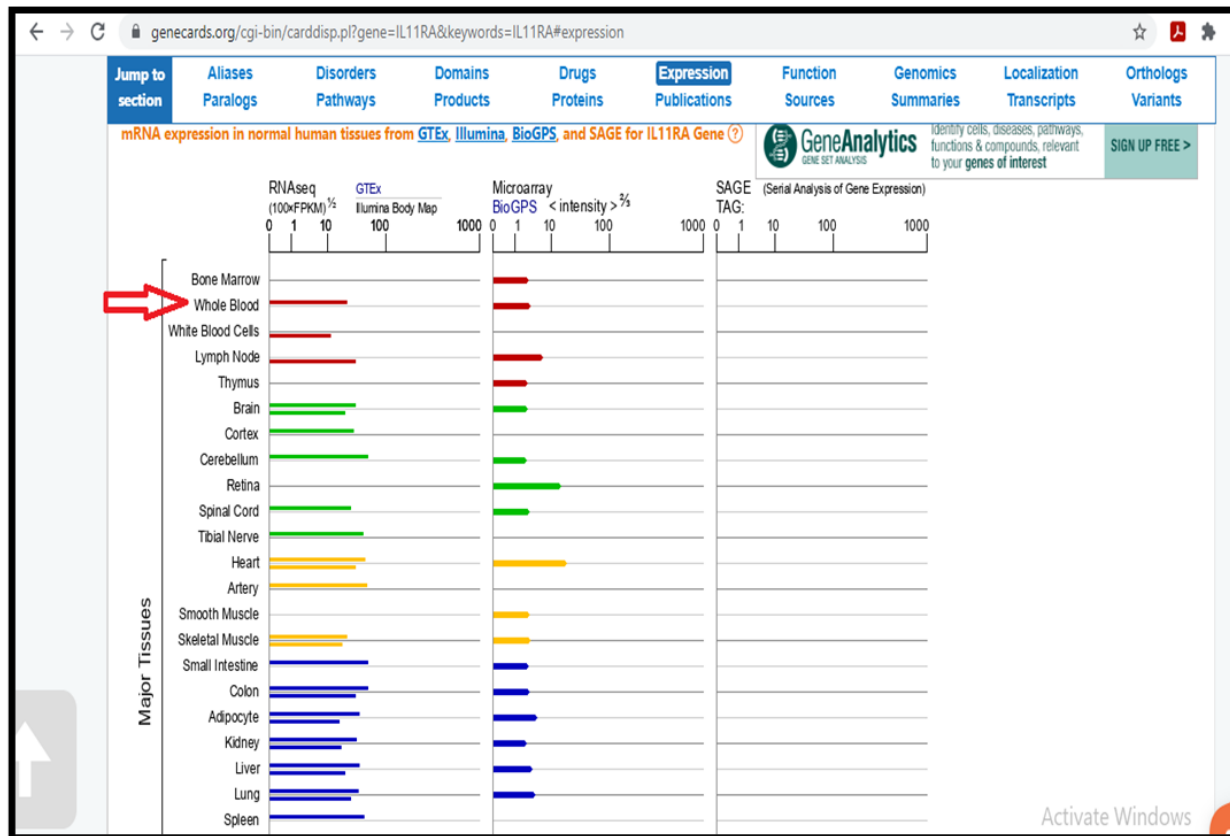
**Supplementary figure S1:** KEGG ontology pathway database revealed that IL11RA interacts with IL6ST in cytokine signaling and cytokine-cytokine interaction pathway including IL11RA gene interacting with IL6ST. Available at (<https://www.genome.jp/kegg/pathway.html>)



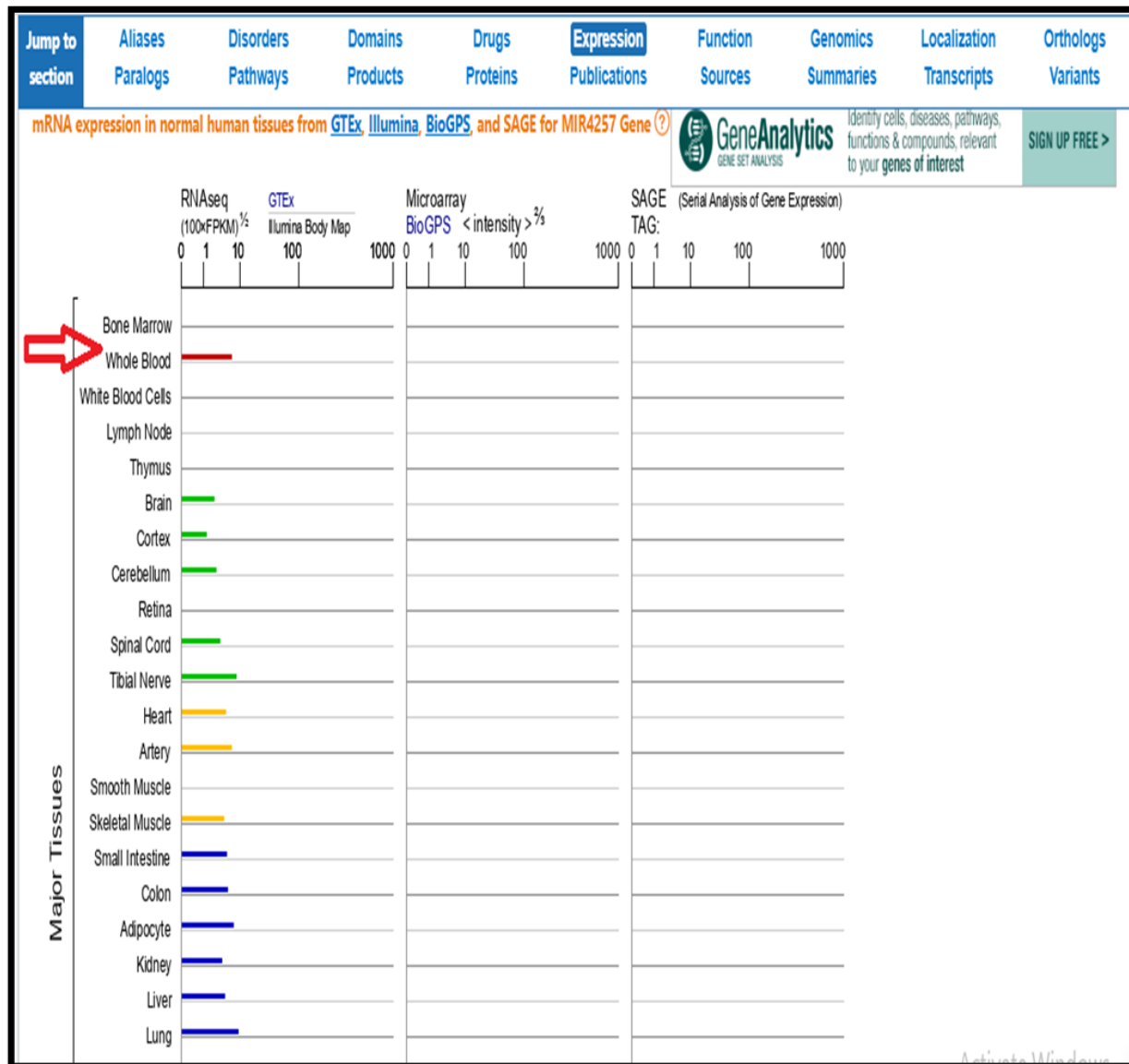
**Supplementary figure S2:** Showing gene ontology of IL11RA mRNA which is involved in cellular response to cytokine stimulus and involved in cytokine mediated signaling pathway that was retrieved from Enrichr tool.



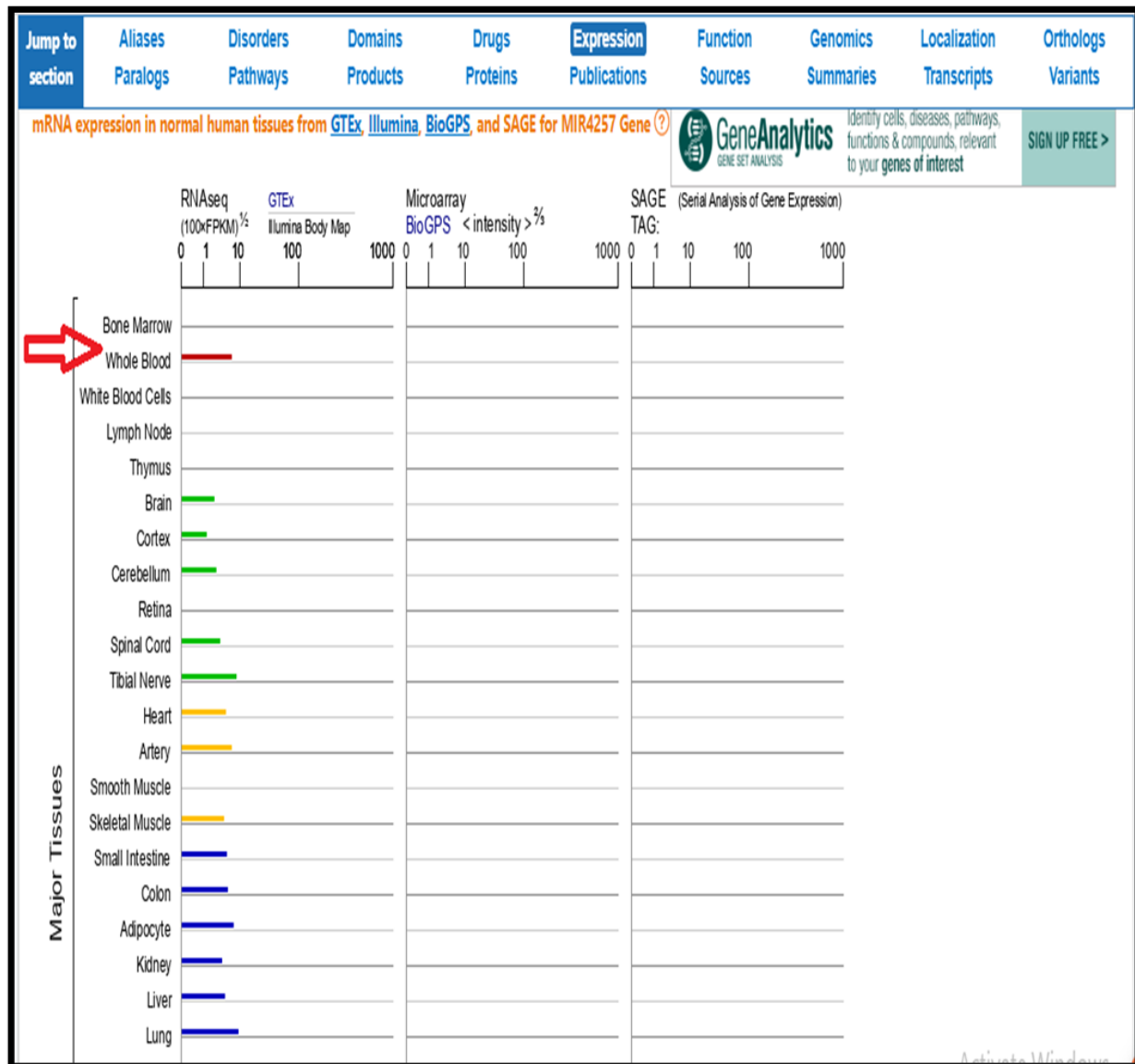
**Supplementary figure S3:** Showing the interaction between IL11RA mRNA, hsa-miR-4257 miRNA and lncRNA RP11-773H22.4 lncRNA that was retrieved from enricher tool



**Supplementary figure S4:** Showing gene expression of IL11RA mRNA which is expressed in the whole blood that was retrieved from Gene cards database Available at (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=IL11RA&keywords=IL11RA#expression>)



**Supplementary figure S5:** Showing gene expression of miR- 4257 which is expressed in the whole blood that was retrieved from gene card database (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=MIR4257&keywords=hsa%5C-miR%5C-4257> )



**Supplementary figure S6:** Showing gene expression of lncRNA RP11-773H22.4 which is expressed in the whole blood that was retrieved from gene cards database available at (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=ENSG00000266969&keywords=lnc%5C-PTPN2%5C-6#expression>)



**Gene '3590' is predicted to be targeted by 19 miRNAs in miRDB.**

Target Detail	Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
<a href="#">Details</a>	1	91	<a href="#">hsa-miR-4753-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	2	77	<a href="#">hsa-miR-6810-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	3	77	<a href="#">hsa-miR-6801-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	4	75	<a href="#">hsa-miR-4696</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	5	73	<a href="#">hsa-miR-4257</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	6	67	<a href="#">hsa-miR-1226-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	7	66	<a href="#">hsa-miR-4643</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	8	62	<a href="#">hsa-miR-6809-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	9	62	<a href="#">hsa-miR-603</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	10	60	<a href="#">hsa-miR-3941</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	11	60	<a href="#">hsa-miR-12123</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	12	59	<a href="#">hsa-miR-8485</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	13	59	<a href="#">hsa-miR-4717-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	14	58	<a href="#">hsa-miR-7155-5p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	15	56	<a href="#">hsa-miR-519d-5p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	16	56	<a href="#">hsa-miR-3678-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	17	56	<a href="#">hsa-miR-12114</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	18	54	<a href="#">hsa-miR-6747-3p</a>	IL11RA	interleukin 11 receptor subunit alpha
<a href="#">Details</a>	19	53	<a href="#">hsa-miR-5695</a>	IL11RA	interleukin 11 receptor subunit alpha

**Supplementary figure S7:** Showing that IL11RA mRNA is a direct target of miR- 4257 that was retrieved from miRDB database (<http://mirdb.org/>

	Predicted consequential pairing of target region (top) and miRNA (bottom)	Site type	Context++ score	Context++ score percentile	Weighted context++ score	Conserved branch length	P <sub>CT</sub>
Position 170-177 of IL11RA 3' UTR	5' ...CUGAAAGGUGCUUGUACCUCUGA...	8mer	-0.44	99	-0.44	0	N/A
hsa-miR-4257	3' GAGUCAGGGUGGAGACC						

**Supplementary figure S8:** Showing that IL11RA mRNA is a direct target of miR- 4257 that was retrieved from targetscan database available at ([http://www.targetscan.org/cgi-bin/targetscan/vert\\_72/view\\_gene.cgi?rs=ENST00000318041.9&taxid=9606&members=miR-4257&showcnc=0&showncf=0&showncf1=1&showncf2=1&subset=1](http://www.targetscan.org/cgi-bin/targetscan/vert_72/view_gene.cgi?rs=ENST00000318041.9&taxid=9606&members=miR-4257&showcnc=0&showncf=0&showncf1=1&showncf2=1&subset=1))

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EMBOSS_001	640 GGTGAACCCACTGGGTGCCAGCACACGCCTGCTGGATGTGAGCTTGCAGA		689
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EMBOSS_001	87 -----		86
EMBOSS_001	740 GGTTACCCCGACGCCTGCGAGCCAGCTGGACATACCCTGCCTCCTGGCC		789

**Supplementary figure S9:** Showing sequence alignment between IL11RA mRNA and miR-4257 that was performed using European bioinformatics institute database available at ([https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss\\_needle-I20210805-231255-0164-87398889-p1m](https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss_needle-I20210805-231255-0164-87398889-p1m))

[illegible]

Query	Length_Query	Target	Length_Target	dG	ndG	Start_Position_Query	End_Position_Query	Start_Position_Target	End_Position_Target
RP11-773H22.4	474	hsa-mir-4257	86	-11.82	-0.1515	3	88	1	86

11

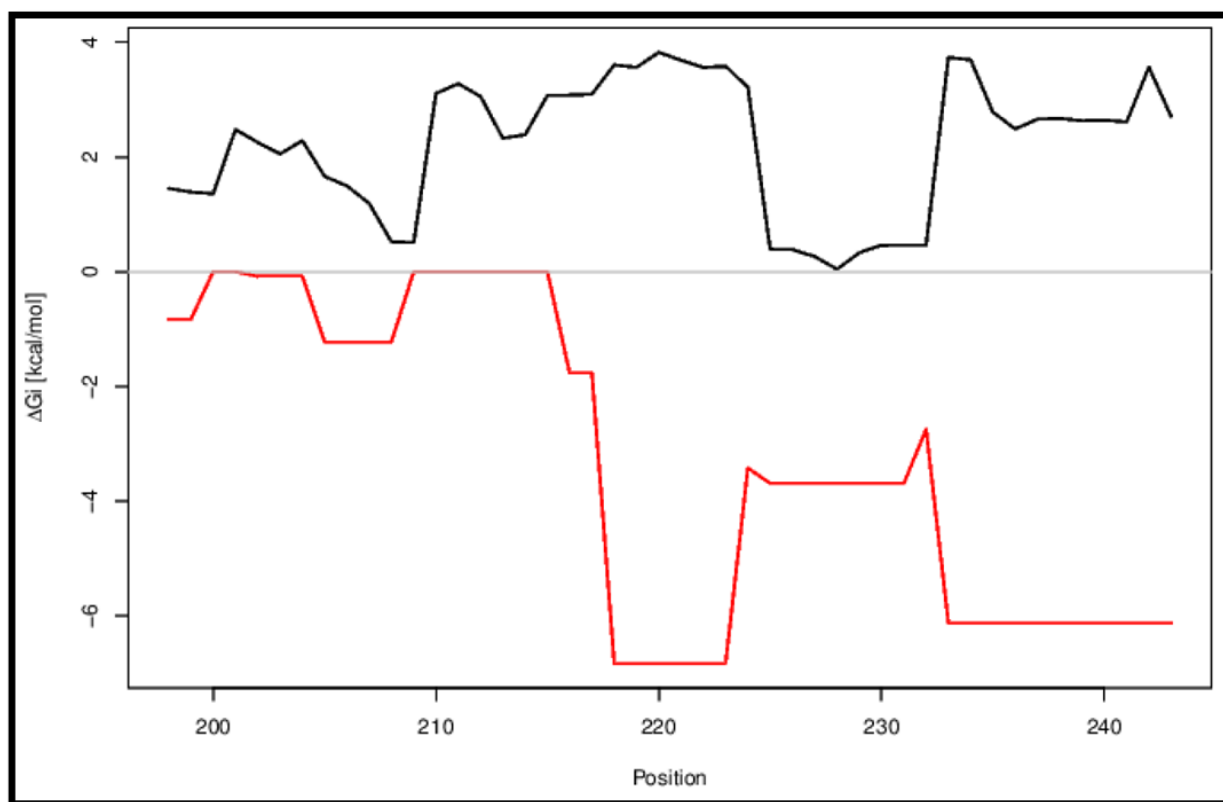


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EMBOSS_001	99 CAA-----GG-----TAAGGGATTAAGAG--GCCGAGA--		124
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EMBOSS_001	1200 C--CCTGGCACTGGGGCTCTGGCTGAGGCTGAGACGGGGTGGGAAGGATG		1247
EMBOSS_001	169 CAGCATCGAAGAGTGCTCTACCAGAGGAGGAGGAGGAGGAGGAAGGAG-		217
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EMBOSS_001	237 CT---CGATCCAGCCC-GTGGGGAATCCA-GAGGG-----GATAACA		273
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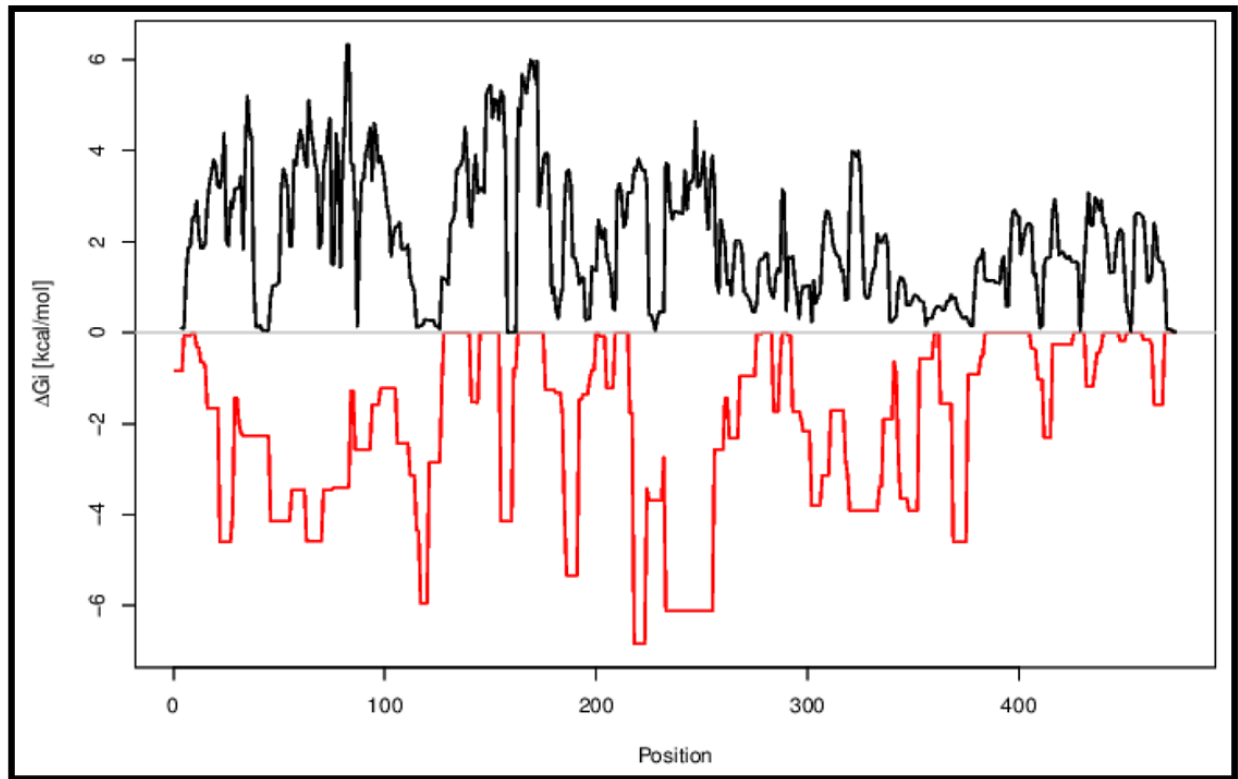
**Supplementary figure S11:** Showing sequence alignment between IL11RA mRNA and RP11-773H22.4 lncRNA that was performed using European bioinformatics institute database available at ([https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss\\_needle-l20210805-231838-0992-90221444-p2m](https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss_needle-l20210805-231838-0992-90221444-p2m) )

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**Supplementary figure S12:** Showing sequence alignment between miR- 4257 miRNA and RP11-773H22.4 lncRNA that was performed using European bioinformatics institute database available at ([https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss\\_needle-l20210805-232348-0040-53372138-p2m](https://www.ebi.ac.uk/Tools/services/web/toolresult.ebi?jobId=emboss_needle-l20210805-232348-0040-53372138-p2m))



**Supplementary figure S13:** Showing interaction between lncRNA RP11-773H22.4 and hsa-miR-4257 is thermodynamically favorable that was performed by The Vienna RNA Website. The plot below shows the interaction free energy (RED)  $G_i$  and the energy needed to open existing structures in the longer sequence (BLACK) for the target region (top) and the whole range (bottom).



**Supplementary figure S14:** Showing interaction between lncRNA RP11-773H22.4 and hsa-miR-4257 is thermodynamically favorable that was performed by The Vienna RNA Website. Results have been computed using RNAup 2.4.18.