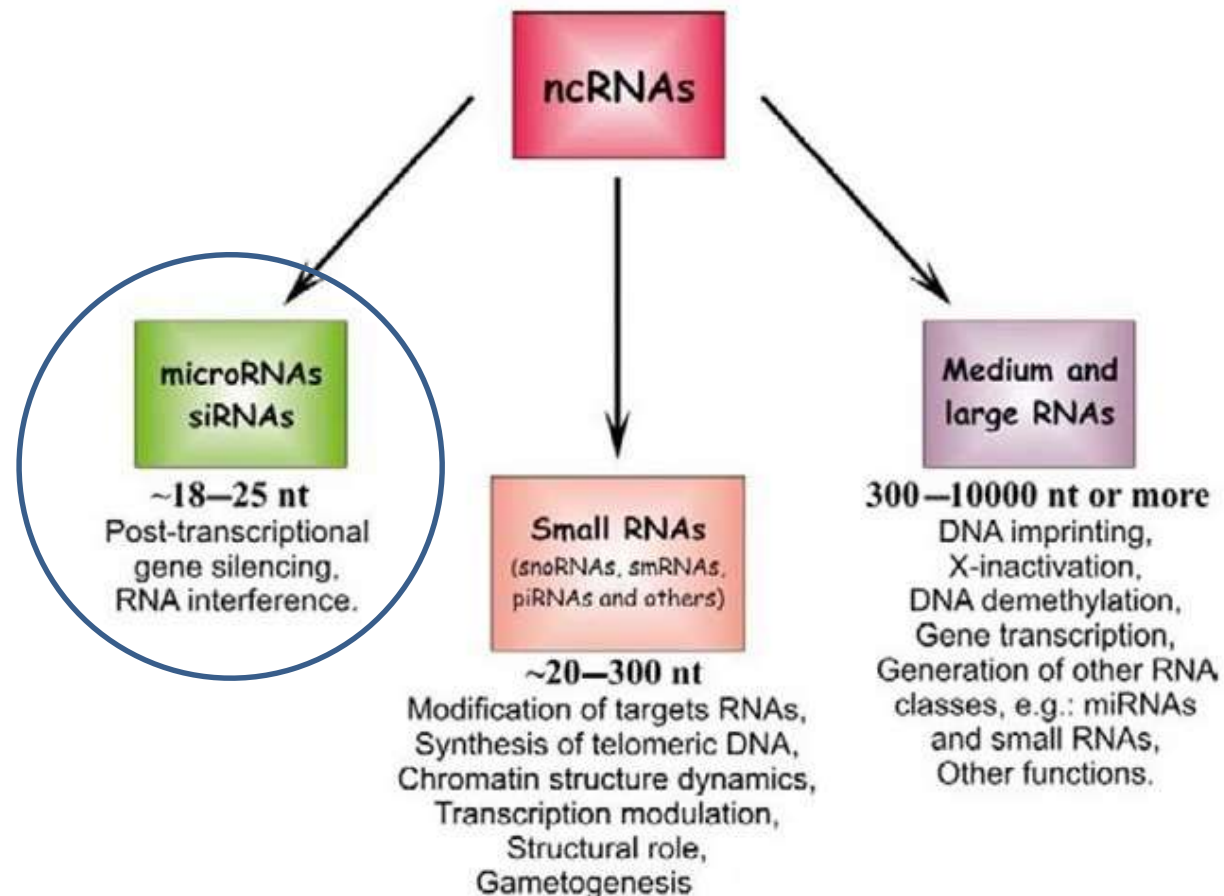


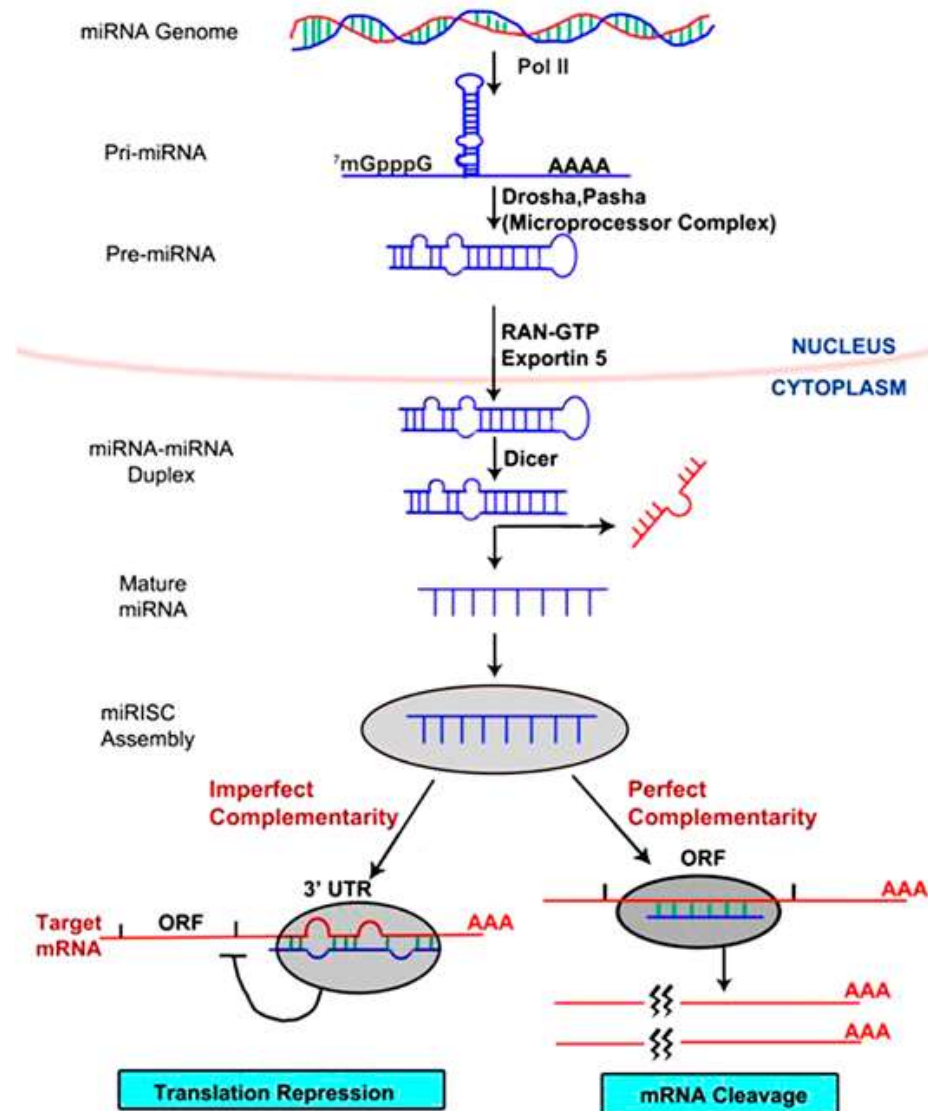
Pharmacoepigeneretics:
an element of personalized
therapy?

RNA non codificante

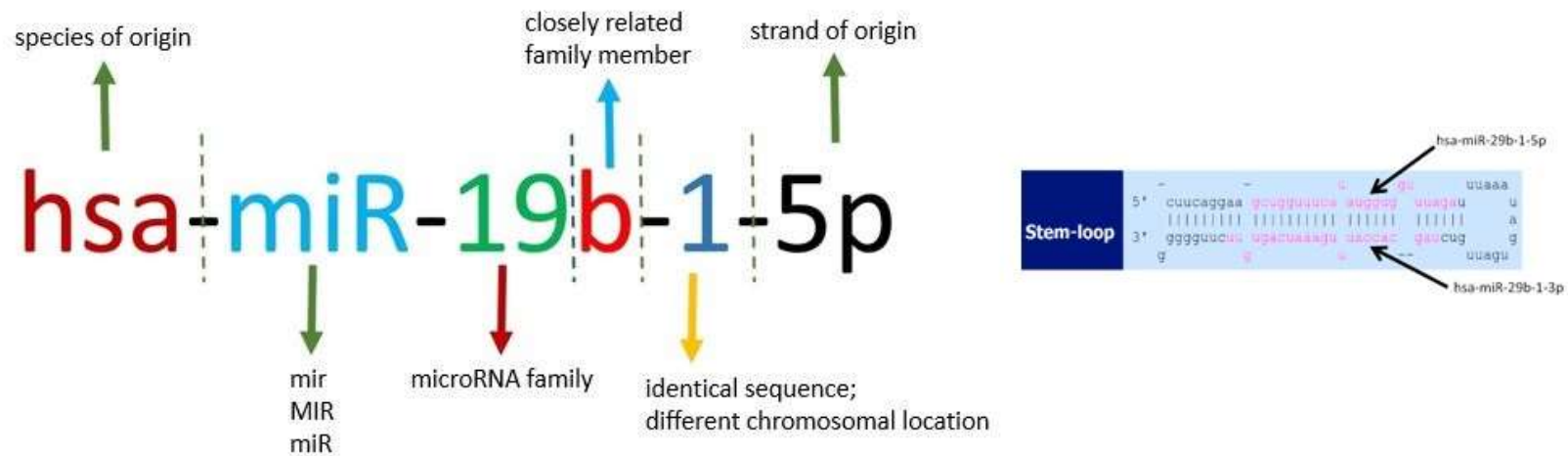
Non-coding RNA is an RNA that functions without being translated to a protein.



micro-RNA

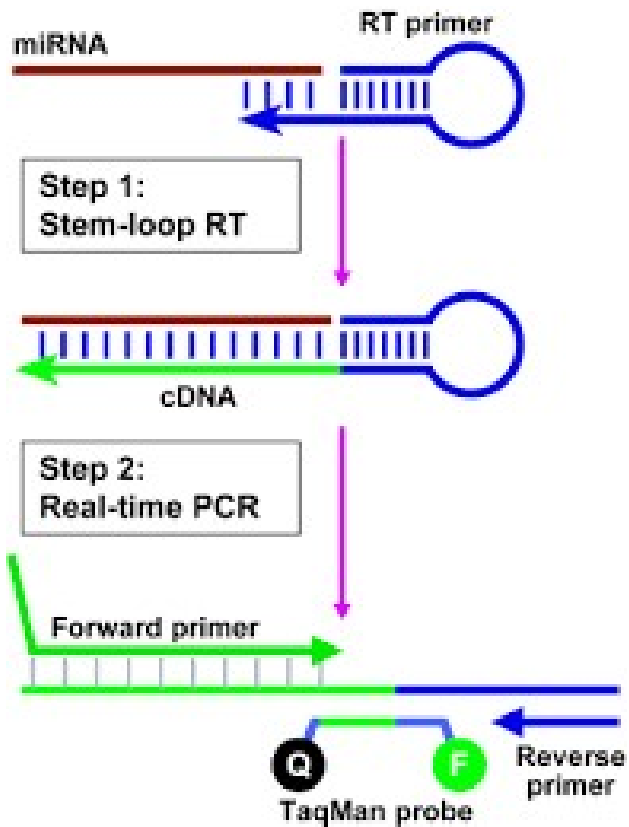


Nomenclature of microRNA



- According to standard nomenclature system, name of any MicroRNA is written as mir-123.
- miR = MicroRNA (mature form).
- mir = Precursor MicroRNA.
- Number indicates order of discovery.
- Annotated with an additional lower case letter e.g.- miR-123a & miR-123b, if deference in only one or two nucleotides.

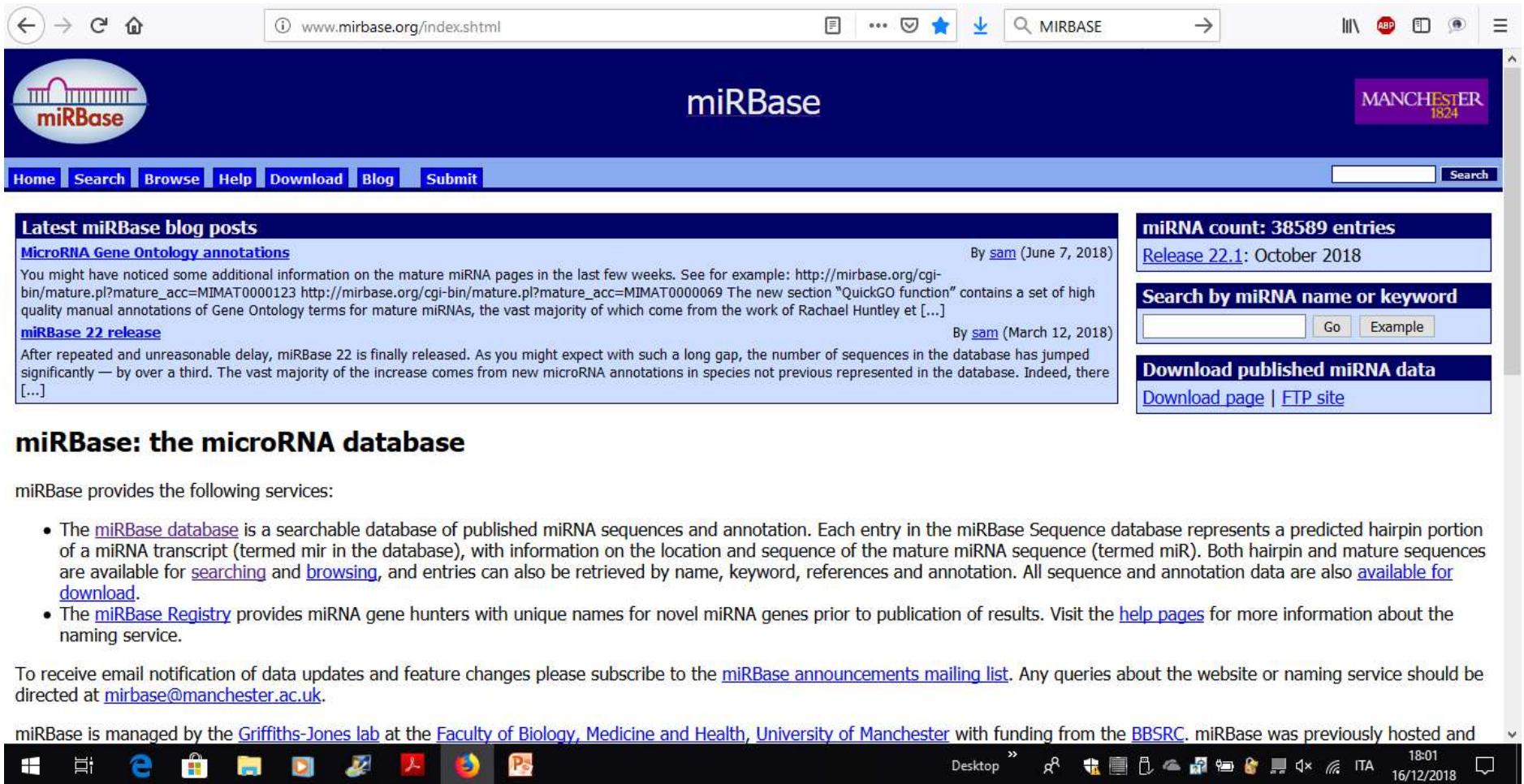
microRNA detection methods



- qRT-PCR;
- TaqMan miRNA array;
- Microarray;
- NGS.

microRNA database

<http://www.mirbase.org/>



miRBase

MANCHESTER 1824

Home Search Browse Help Download Blog Submit

Search

Latest miRBase blog posts

MicroRNA Gene Ontology annotations By [sam](#) (June 7, 2018)
You might have noticed some additional information on the mature miRNA pages in the last few weeks. See for example: http://mirbase.org/cgi-bin/mature.pl?mature_acc=MIMAT0000123 http://mirbase.org/cgi-bin/mature.pl?mature_acc=MIMAT0000069 The new section "QuickGO function" contains a set of high quality manual annotations of Gene Ontology terms for mature miRNAs, the vast majority of which come from the work of Rachael Huntley et [...]

miRBase 22 release By [sam](#) (March 12, 2018)
After repeated and unreasonable delay, miRBase 22 is finally released. As you might expect with such a long gap, the number of sequences in the database has jumped significantly — by over a third. The vast majority of the increase comes from new microRNA annotations in species not previous represented in the database. Indeed, there [...]

miRNA count: 38589 entries
Release 22.1: October 2018

Search by miRNA name or keyword

Download published miRNA data
[Download page](#) | [FTP site](#)

miRBase: the microRNA database

miRBase provides the following services:

- The [miRBase database](#) is a searchable database of published miRNA sequences and annotation. Each entry in the miRBase Sequence database represents a predicted hairpin portion of a miRNA transcript (termed mir in the database), with information on the location and sequence of the mature miRNA sequence (termed miR). Both hairpin and mature sequences are available for [searching](#) and [browsing](#), and entries can also be retrieved by name, keyword, references and annotation. All sequence and annotation data are also [available for download](#).
- The [miRBase Registry](#) provides miRNA gene hunters with unique names for novel miRNA genes prior to publication of results. Visit the [help pages](#) for more information about the naming service.

To receive email notification of data updates and feature changes please subscribe to the [miRBase announcements mailing list](#). Any queries about the website or naming service should be directed at mirbase@manchester.ac.uk.

miRBase is managed by the [Griffiths-Jones lab](#) at the [Faculty of Biology, Medicine and Health, University of Manchester](#) with funding from the [BBSRC](#). miRBase was previously hosted and

microRNA database

<http://www.mirbase.org/>



miRBase

MANCHESTER
1824

Home Search Browse Help Download Blog Submit **Search results** Search

Search Results

We found 1 unique result for your query ("*hsa-miR-331-3p*"), in 1 section of the database.

Section	Description	Number of hits
miRNA name	match the accession or ID of a hairpin precursor entry	0
Previous ID	match the previous ID of a hairpin precursor entry	0
Mature name	match the accession or ID of a mature miRNA sequence	1
Previous Mature ID	match the previous mature ID of a mature entry	0
Dead entry	match the accession or ID of a dead entry	0
Dead entry previous ID	match the accession or ID of a dead entry	0
Gene symbol	find miRNA entries based on gene symbols	0
Description	search miRNA entry description	0
Comments	search miRNA entry comments	0
PubMed ID	find miRNA entries based on literature reference PubMed ID	0
Literature reference	search title and authors of associated literature references	0

The above key shows a brief description of each of the database sections, along with the number of hits found in each one. Only unique miRNA entries are shown in the results table below. Click the column headings to sort the results table, or [restore to the original order](#).

Accession <small>Sort</small>	ID <small>Sort</small>	Mature name <small>Sort</small>
MIMAT0000760	hsa-miR-331-3p	✓

microRNA database

<http://www.mirbase.org/>



miRBase MANCHESTER 1834

Home Search Browse Help Download Blog Submit Search

Mature sequence hsa-miR-331-3p

Accession number	MIMAT0000760				
ID	hsa-miR-331-3p				
Previous IDs	hsa-miR-331				
Stem-Loop	hsa-mir-331				
Sequence	<p>gcccugggcccuaucuuagaa</p> <p>Get sequence</p>				
Deep sequencing	118219 reads, 152 experiments				
Database links	RNAcentral: URS00003DDE27_9606				
Predicted targets	TargetMiner: hsa-miR-331-3p TargetScanVert: hsa-miR-331-3p miRDB: hsa-miR-331-3p microrna.org: hsa-miR-331-3p				
QuickGO function	<i>Qualifier</i>	<i>GO term</i>	<i>Evidence</i>	<i>Notes</i>	<i>Reference</i>
	part_of	GO:0005615 extracellular space	ECO:0007005 high throughput direct assay evidence used in manual assertion	undefined UBERON:0001969	PMID:26646931

[Records 1-1 of 1] [\[QuickGO full record\]](#)

References

- PMID: [14691248](#)
"Identification of many microRNAs that copurify with polyribosomes in mammalian neurons"
Kim J, Krichevsky A, Grad Y, Hayes GD, Kosik KS, Church GM, Ruvkun G
Proc Natl Acad Sci U S A. 101:360-365(2004).
- PMID: [15634332](#)
"New human and mouse microRNA genes found by homology search"
Weber MJ

microRNA database

<http://mirdb.org/>



[Target Search](#)

[Target Mining](#)

[Custom Prediction](#)

[FuncMir Collection](#)

[Data Download](#)

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[Comments](#)

[Citation | Policy](#)

Choose one of the following search options:

Search by miRNA name

Human

Search by gene target

Human Gene Symbol

miRDB is an online database for miRNA target prediction and functional annotations. All the targets in miRDB were predicted by a bioinformatics tool, MirTarget, which was developed by analyzing thousands of miRNA-target interactions from high-throughput sequencing experiments. Common features associated with miRNA target binding have been identified and used to predict miRNA targets with machine learning methods. miRDB hosts predicted miRNA targets in five species: human, mouse, rat, dog and chicken. As a recent update, users may provide their own sequences for customized target prediction. In addition, through combined computational analyses and literature mining, functionally active miRNAs in humans and mice were identified. These miRNAs, as well as associated functional annotations, are presented in the FuncMir Collection in miRDB.

References:

- Nathan Wong and Xiaowei Wang (2015) miRDB: an online resource for microRNA target prediction and functional annotations. *Nucleic Acids Research*. [43\(D1\):D146-152](#).
- Xiaowei Wang (2016) Improving microRNA target prediction by modeling with unambiguously identified microRNA-target pairs from CLIP-Ligation studies. *Bioinformatics*. [32\(9\):1316-1322](#).

microRNA database

<http://mirdb.org/>



There are 411 predicted targets for hsa-miR-331-3p in miRDB.

Target Detail	Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
Details	1	99	hsa-miR-331-3p	NRP2	neuropilin 2
Details	2	96	hsa-miR-331-3p	PTPN2	protein tyrosine phosphatase, non-receptor type 2
Details	3	96	hsa-miR-331-3p	ZBTB2	zinc finger and BTB domain containing 2
Details	4	96	hsa-miR-331-3p	PHLPP1	PH domain and leucine rich repeat protein phosphatase 1
Details	5	94	hsa-miR-331-3p	CPSF2	cleavage and polyadenylation specific factor 2
Details	6	94	hsa-miR-331-3p	ZNF652	zinc finger protein 652
Details	7	93	hsa-miR-331-3p	DCLRE1B	DNA cross-link repair 1B
Details	8	93	hsa-miR-331-3p	TSPAN18	tetraspanin 18
Details	9	92	hsa-miR-331-3p	SLAMF9	SLAM family member 9
Details	10	92	hsa-miR-331-3p	SEMA7A	semaphorin 7A (John Milton Hagen blood group)
Details	11	92	hsa-miR-331-3p	BAIAP2	BAI1 associated protein 2
Details	12	91	hsa-miR-331-3p	CNTNAP4	contactin associated protein like 4
Details	13	90	hsa-miR-331-3p	FBLN7	fibulin 7
Details	14	90	hsa-miR-331-3p	CDC42EP4	CDC42 effector protein 4
Details	15	90	hsa-miR-331-3p	ARHGEF37	Rho guanine nucleotide exchange factor 37
Details	16	90	hsa-miR-331-3p	XPO7	exportin 7
Details	17	88	hsa-miR-331-3p	DUSP5	dual specificity phosphatase 5
Details	18	88	hsa-miR-331-3p	APBA1	amyloid beta precursor protein binding family A member 1
Details	19	88	hsa-miR-331-3p	UBL3	ubiquitin like 3
Details	20	87	hsa-miR-331-3p	TGFBR1	transforming growth factor beta receptor 1
Details	21	87	hsa-miR-331-3p	ZMYM4	zinc finger MYM-type containing 4
Details	22	87	hsa-miR-331-3p	SARM1	sterile alpha and TIR motif containing 1

microRNA database

<http://mirtarbase.mbc.nctu.edu.tw/php/index.php>

Search... Search Example

miRTarBase

Home Search Browse Statistics Help Download Contact Us

miRTarBase: the experimentally validated microRNA-target interactions database

As a database, miRTarBase has accumulated more than three hundred and sixty thousand miRNA-target interactions (MTIs), which are collected by manually surveying pertinent literature after NLP of the text systematically to filter research articles related to functional studies of miRNAs. Generally, the collected MTIs are validated experimentally by reporter assay, western blot, microarray and next-generation sequencing experiments. While containing the largest amount of validated MTIs, the miRTarBase provides the most updated collection by comparing with other similar, previously developed databases.

Major improvements

Features	miRTarBase 6.0	miRTarBase 7.0
Release date	2015/09/15	2017/09/15
Known miRNA entry	miRBase v20	miRBase v21
Known Gene entry	Entrez 2015	Entrez 2017
Species	18	23
Curated articles	4,966	8,510
miRNAs	3,786	4,076
Target genes	22,563	23,054
CLIP-seq datasets	138	231
Curated miRNA-target interactions	366,181	422,517
Text-mining technique to prescreen literature	NLP	Enhanced NLP

Current curation

Release 7.0: Sept. 15, 2017

Number of articles: 8,510

Number of species: 23

Number of target genes: 23,054

Number of miRNAs: 4,076

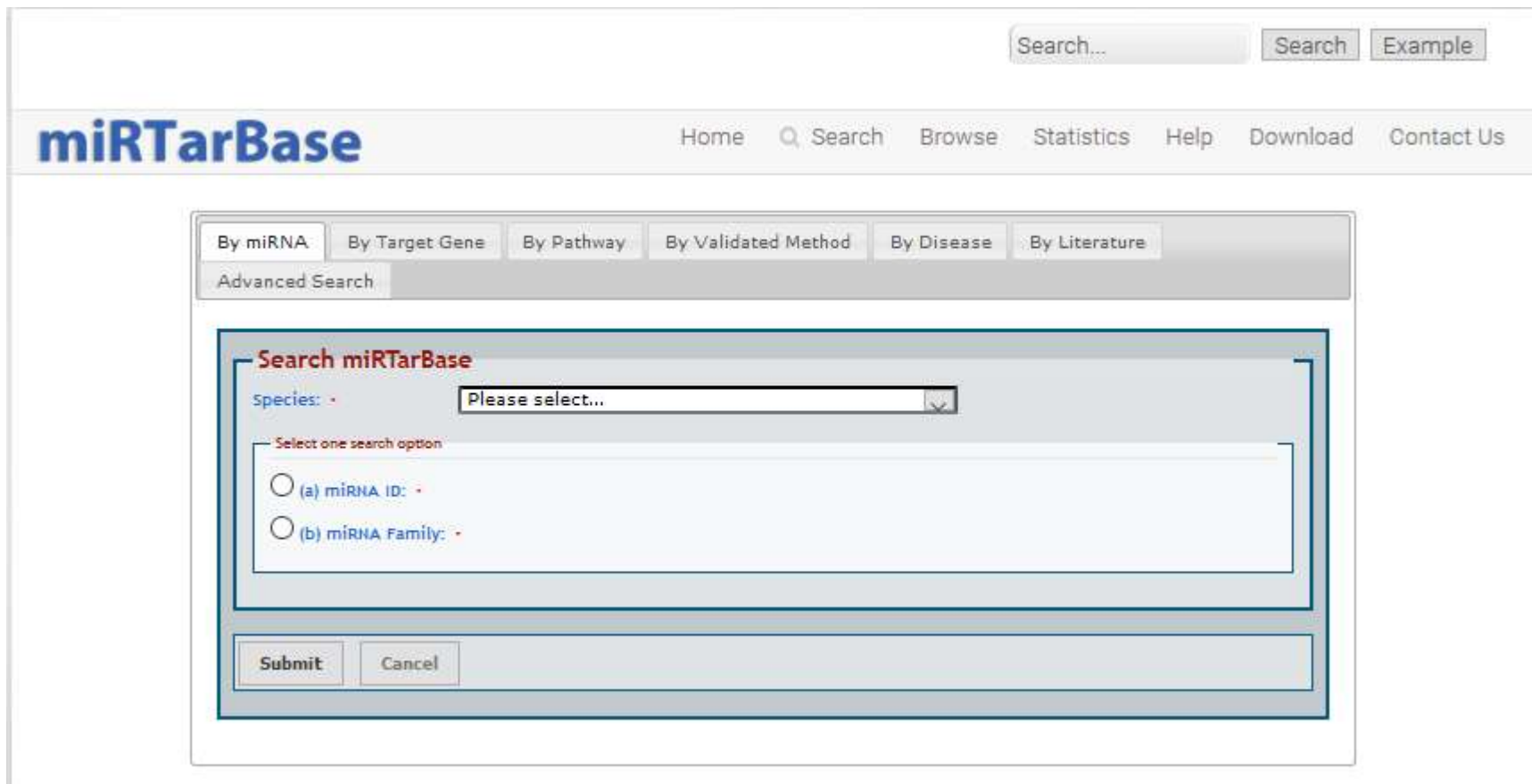
Number of miRNA-target interactions: 422,517

MicroRNA resources from ISBLAB

miRTar - An integrated web server for identifying miRNA target interactions

microRNA database

<http://mirtarbase.mbc.nctu.edu.tw/php/index.php>



The screenshot displays the miRTarBase search interface. At the top right, there is a search bar with a "Search..." input field, a "Search" button, and an "Example" button. Below this is a navigation menu with the "miRTarBase" logo and links for "Home", "Search", "Browse", "Statistics", "Help", "Download", and "Contact Us". The main search area features a tabbed interface with options: "By miRNA", "By Target Gene", "By Pathway", "By Validated Method", "By Disease", and "By Literature". The "Advanced Search" tab is currently selected. Within this tab, the "Search miRTarBase" section includes a "species:" dropdown menu set to "Please select...", a "Select one search option" label, and two radio button options: "(a) miRNA ID:" and "(b) miRNA Family:". At the bottom of the search form are "Submit" and "Cancel" buttons.

microRNA database

<http://mirtarbase.mbc.nctu.edu.tw/php/index.php>

miRTarBase

Home Search Browse Statistics Help Download Contact Us

Page of 15 < Prev 1 2 ... 15 Next >

Pulsed stable isotope labeling by amino acids in cell culture (pSILAC)

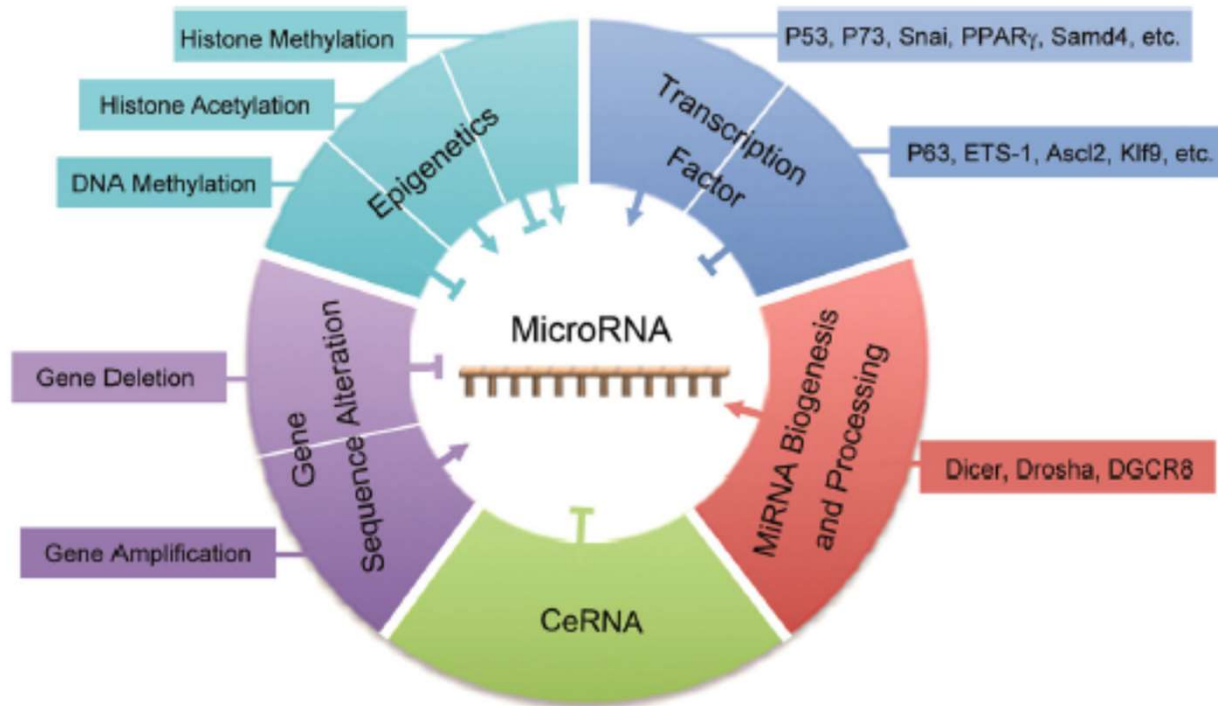
ID	Species (miRNA)	Species (Target)	miRNA	Target	Validation methods								Sum	# of papers
					Strong evidence			Less strong evidence						
					Reporter assay	Western blot	qPCR	Microarray	NGS	pSILAC	Other			
MIRT002222	Rattus norvegicus	Rattus norvegicus	no-miR-331-3p	Fgf16				✓			✓	2	1	
MIRT005805	Homo sapiens	Homo sapiens	hsa-miR-331-3p	ERBB2	✓	✓	✓	✓			✓	5	5	
MIRT006364	Homo sapiens	Homo sapiens	hsa-miR-331-3p	FHIT	✓							1	1	
MIRT006506	Homo sapiens	Homo sapiens	hsa-miR-331-3p	E2F1	✓	✓						2	1	
MIRT006887	Homo sapiens	Homo sapiens	hsa-miR-331-3p	DOHH	✓	✓	✓		✓			4	2	
MIRT019230	Homo sapiens	Homo sapiens	hsa-miR-331-3p	WDR60					✓			1	1	
MIRT019231	Homo sapiens	Homo sapiens	hsa-miR-331-3p	RNF7					✓			1	1	
MIRT019232	Homo sapiens	Homo sapiens	hsa-miR-331-3p	ARLBA					✓			1	1	

MicroRNAs in the Control of Drug Metabolism and Transport

Some P450 drug-metabolizing enzymes and ABC transporters shown to be targeted by noncoding miRNAs

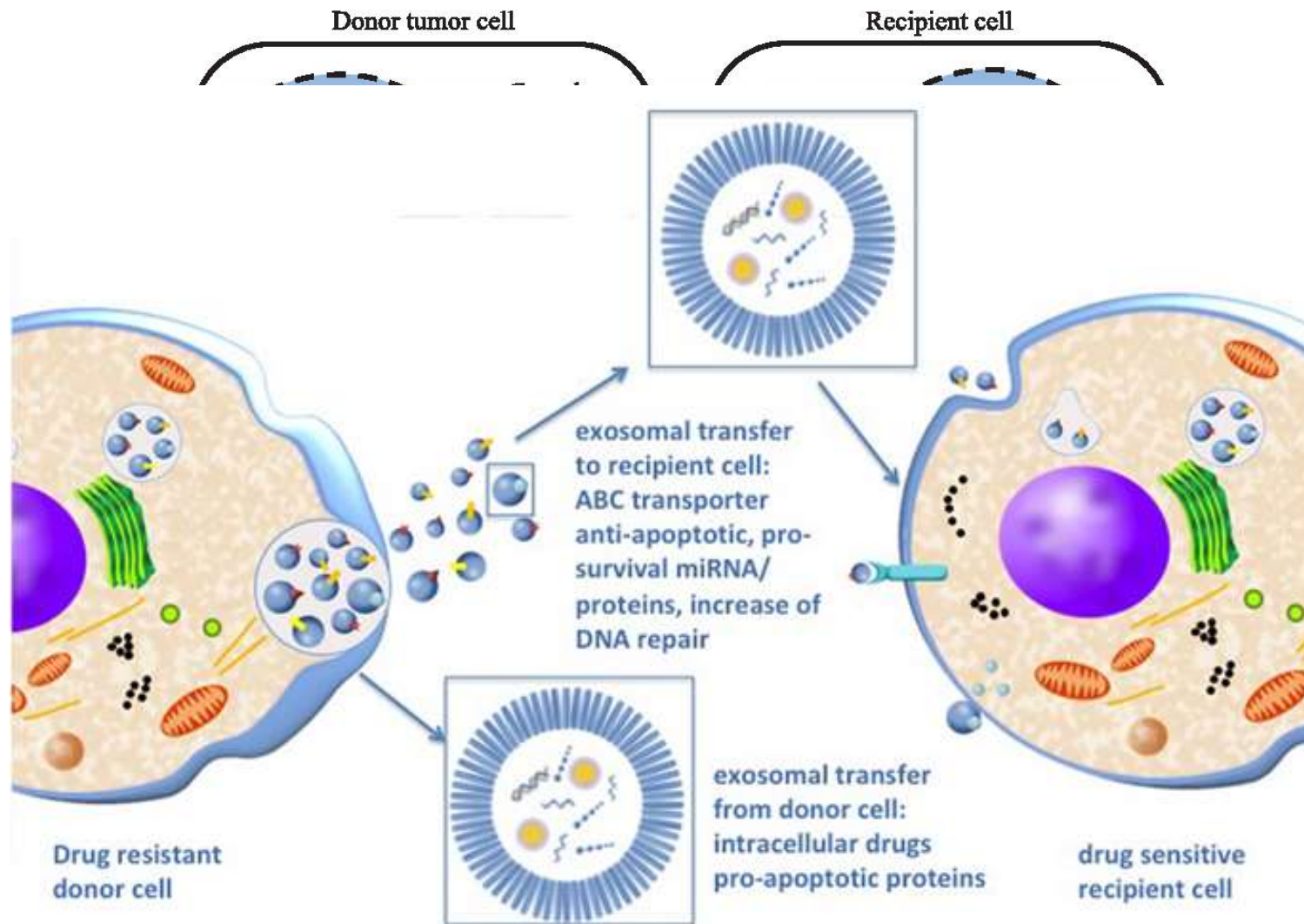
		MicroRNA	Reference
Enzymes	CYP1B1	miR-27b	Tsuchiya et al., 2006
	CYP2E1	miR-378	Mohri et al., 2010
	CYP3A4	miR-27b, mmu-miR-298	Pan et al., 2009a
Transporters	ABCB1	miR-451	Kovalchuk et al., 2008
		miR-27a	Zhu et al., 2008
	ABCG2	miR-520h	Liao et al., 2008; Wang et al., 2010; Li et al., 2011
		miR-519c	To et al., 2008; To et al., 2009; Li et al., 2011
		miR-328	Pan et al., 2009b; Li et al., 2011
	ABCC1	miR-134	Guo et al., 2010
		miR-326	Liang et al., 2010
		miR-199a, miR-199b, miR-296	Borel et al., 2012
		miR-1291	Pan et al., 2013
	ABCC2	miR-379	Haenisch et al., 2011
	ABCC3	miR-9-3p	Jeon et al., 2011
	ABCC4	miR-125a, miR-125b	Borel et al., 2012
	ABCC5	miR-101, miR-125a, Let-7a	Borel et al., 2012
miR-128		Zhu et al., 2011	
ABCC6	miR-9-3p	Jeon et al., 2011	

Deregulated expression of microRNAs



The mechanisms of deregulated expression of microRNAs. Different mechanisms can promote or/and inhibit the expression of miRNA

Exosomes-derived microRNA and drug resistance



 miR-binding Protein



Circulating microRNA

cerebrospinal fluid
 PCNSL miR-19, miR-21, miR-92a [33]
 Glioblastoma miR-21 [34]

pleural effusion
 Lung cancer miR-198 [35]
 Lung cancer miR-22, miR-134, miR-185 [36]
 Malignant pleural mesothelioma let-7a, miR-125a-5p, miR-320, miR-484 [37]

ascites
 Ovarian cancer miR-21, miR-23b, miR-29a [38]
 Serosa-invasive gastric cancer miR-21, miR-1225-5p [39]

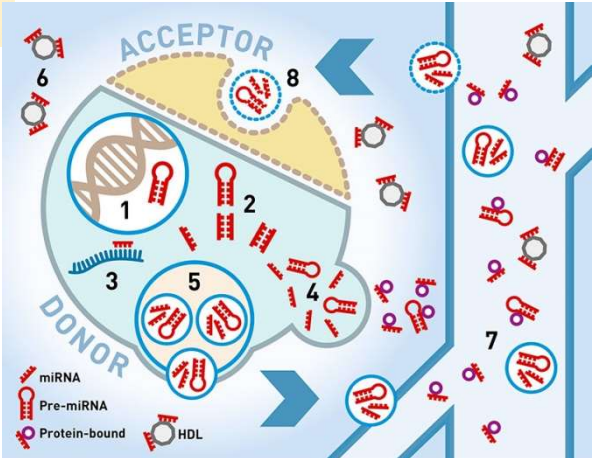
vaginal discharge
 Cervical cancer miR-21, miR-146a [40]

urine
 Ovarian cancer miR-30-5p [41]
 Bladder cancer miR-106b [42]
 Bladder cancer miR-99a, miR-125b [43]
 Bladder cancer miR-155, miR-21, miR-125b, miR-451 [44]
 Prostate cancer miR-484, miR-1825 [45]

saliva
 Oral cancer miR-125a, miR-200a [46]
 Esophageal cancer miR-10b-3p, miR-21, miR-144, miR-451 [47]
 Pancreatic cancer miR-940, miR-3679-5p [48]

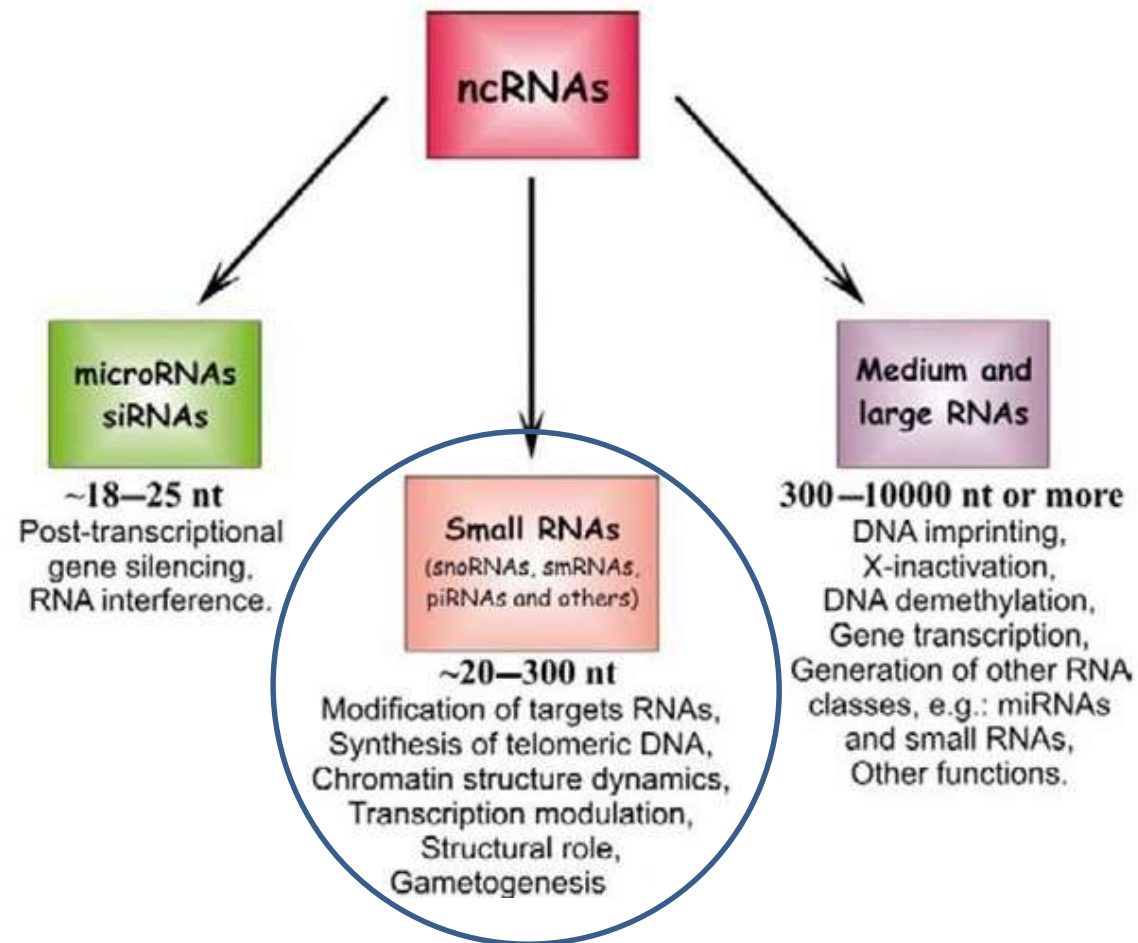
breast milk
 miR-335-3p, miR-26a-2-3p, miR-181d [49]

blood (serum/plasma)
 Ovarian cancer miR-21, miR-141, miR-200a, miR-200b, miR-200c, miR-203, miR-205, miR-214 [50]
 Gastric cancer miR-1, miR-20a, miR-27a, miR-34, miR-423-5p [51]
 Malignant melanoma miR-221 [52]
 Cervical cancer miR-218 [53]
 Thyroid cancer let-7e, miR-151-5p, and miR-222 [54]
 Renal cell cancer miR-378, miR-451 [55]
 Colorectal cancer miR-7, miR-93, miR-409-3p [56]
 Breast cancer miR-148-3p, miR-652-3p [57]
 NSCLC miR-21, miR-148a, miR-148b, miR-152 [58]



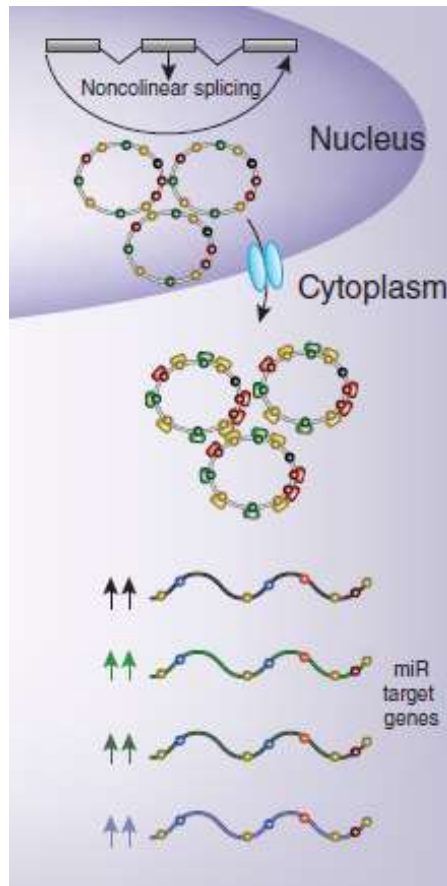
RNA non codificante

Non-coding RNA is an RNA that functions without being translated to a protein.

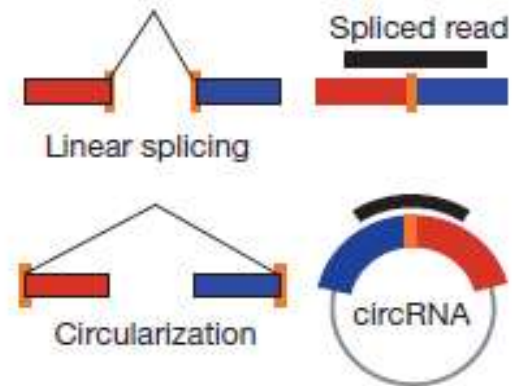


circRNAs

- Covalently circularized RNA loops
- Stable in cells and long in half-lives
- Multiple miRNA binding sites as miRNA sponges



Nature Structural & Molecular Biology (2013), 20:5, 541-3

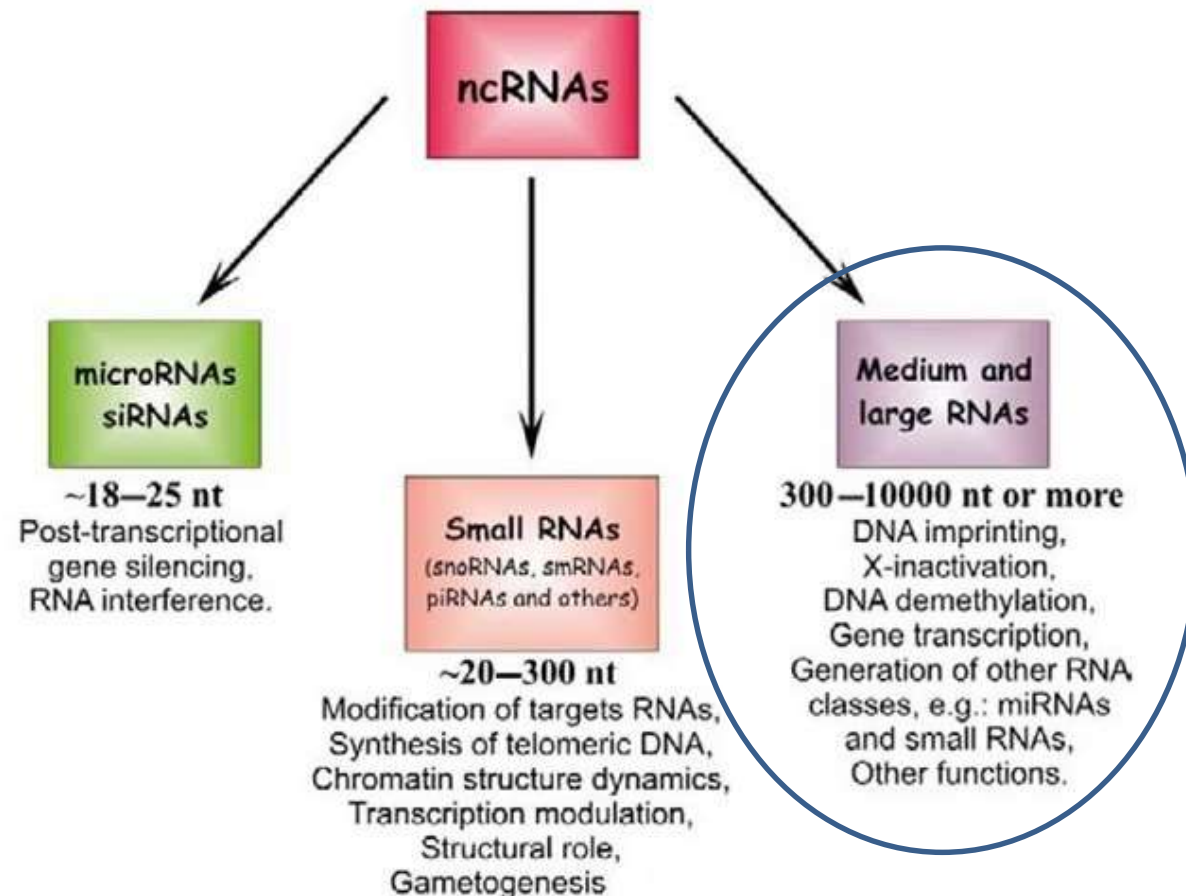


Nature (2013) 495, 333-343



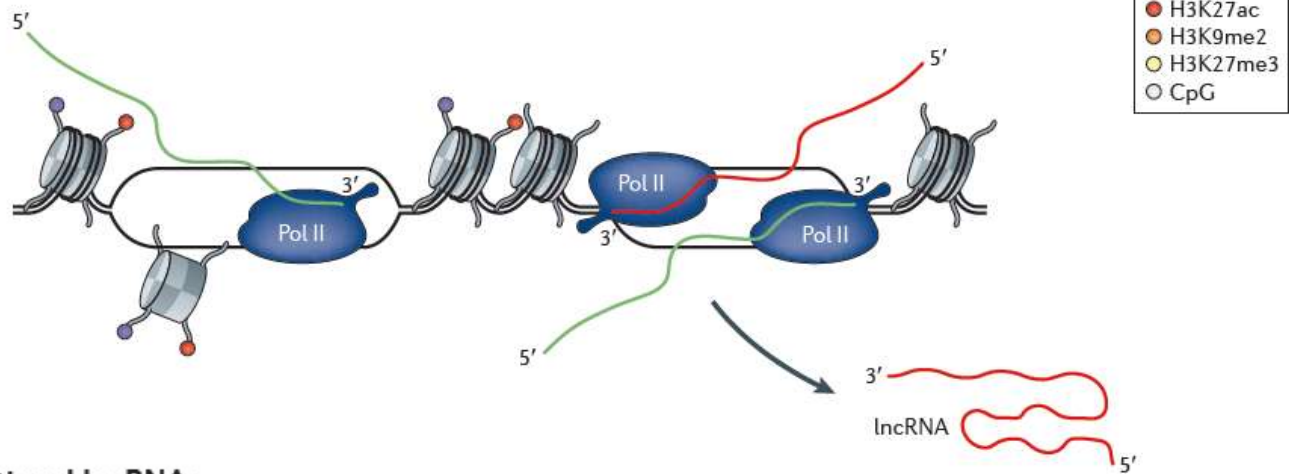
What is non-coding RNA ?

Non-coding RNA is an RNA that functions without being translated to a protein.

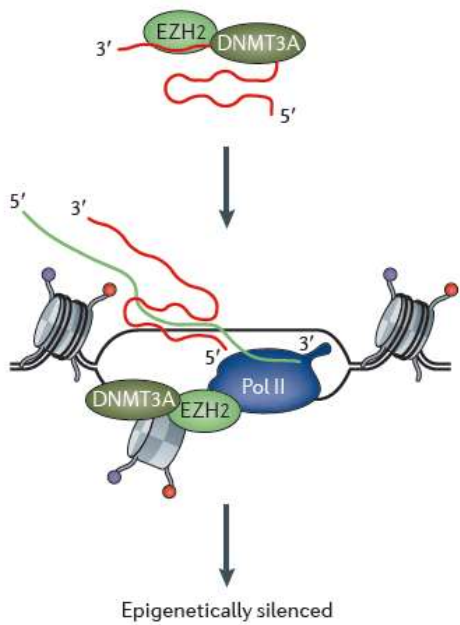


lncRNA

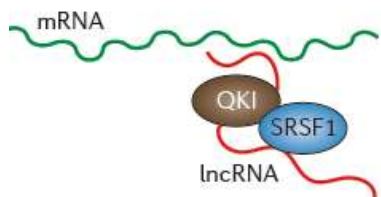
Transcription of lncRNAs



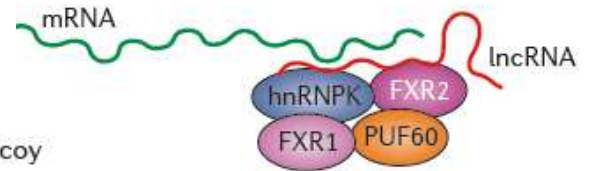
Nuclear and cytoplasmic functional lncRNAs



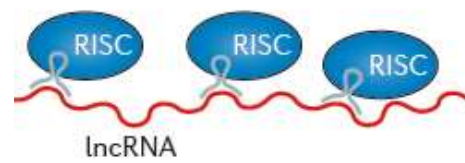
lncRNA as splicing regulator



lncRNA as translational regulator



lncRNA as miRNA decoy



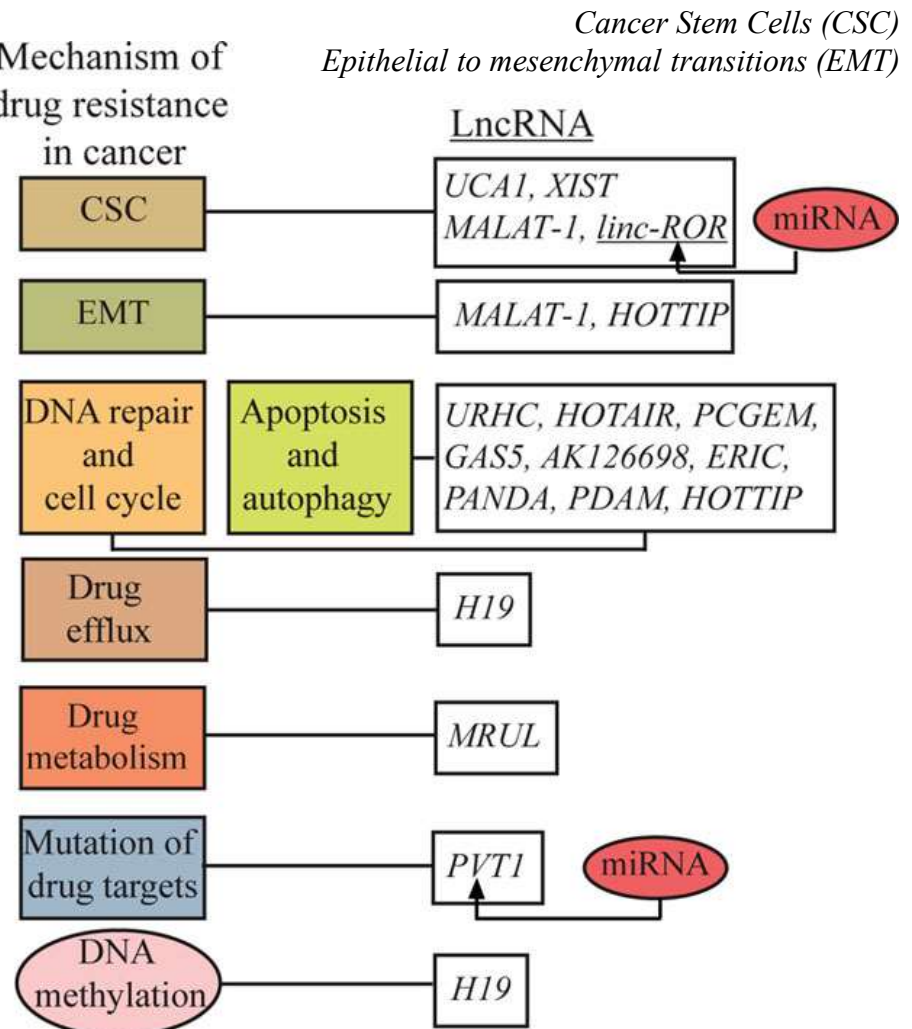
lncRNA

LncRNAs and drugs affecting their expression in cancers

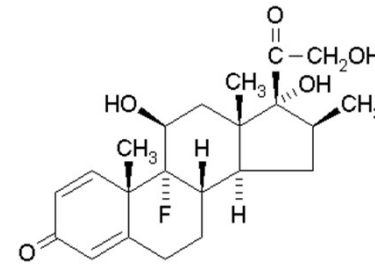
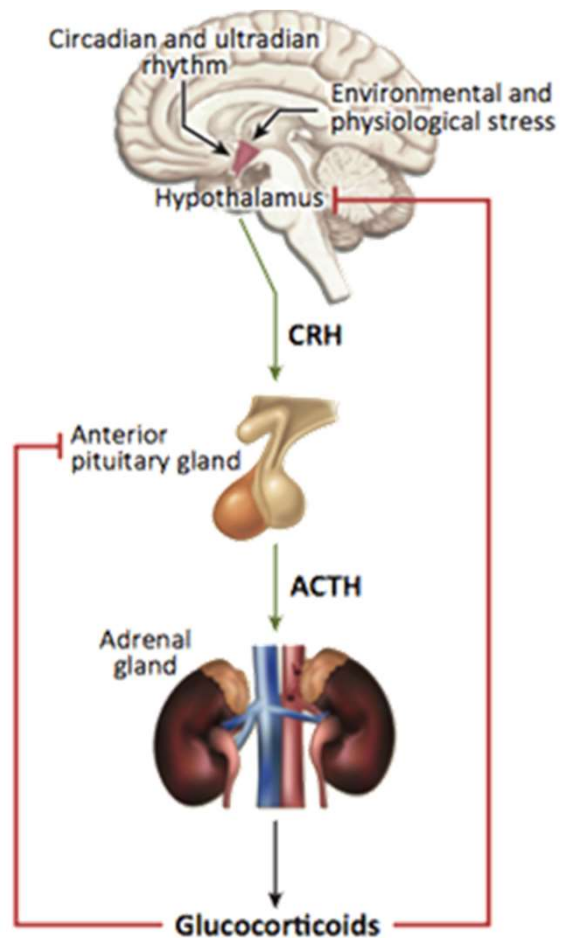
LncRNA	Cancer	Drug
<i>UCA1</i>	Bladder	?
<i>Linc-ROR</i>	Hepatocellular carcinoma	Sorafenib and doxorubicin
<i>XIST</i>	Ovarian, breast	Cisplatin, abexinostat
<i>MALAT-1</i>	Pancreas	Gemcitabine
<i>URHC</i>	Hepatocellular carcinoma	PD98059
<i>HOTAIR</i>	Lung	Cisplatin
<i>PCGEM1</i>	Prostate	Doxorubicin
<i>GAS5</i>	Lung	Gefitinib
<i>AK126698</i>	Lung	Cisplatin
<i>ERIC</i>	Bone osteosarcoma	Etoposide
<i>PANDA</i>	Breast	Doxorubicin
<i>PDAM</i>	Oligodendroglial	Cisplatin
<i>HOTTIP</i>	Pancreas	Gemcitabine
<i>rRNA</i>		Mitoxantrone
<i>H19</i>	Hepatocellular carcinoma cells	Paclitaxel, doxorubicin, etoposide, and vincristine
<i>MRUL</i>	Gastric	Doxorubicin and vincristine
<i>ARA</i>	Breast, hepatocellular carcinoma cells	Doxorubicin
<i>PVT1</i>	Pancreas, gastric cancer	Gemcitabine, paclitaxel
<i>BCAR4</i>	Breast	Tamoxifen

Urothelial Carcinoma-Associated 1 (UCA1)
Metastasis-Associated Lung Adenocarcinoma Transcript 1 (MALAT-1)

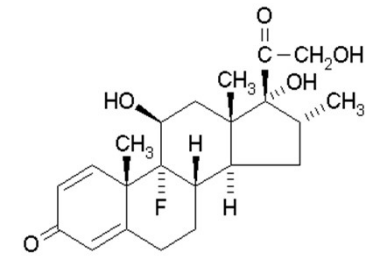
Mechanism of drug resistance in cancer



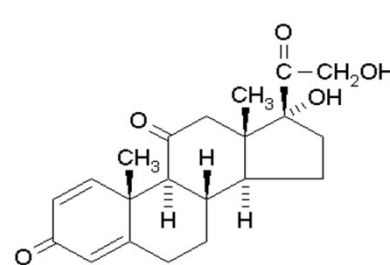
Pharmacogenetics of Glucocorticoids



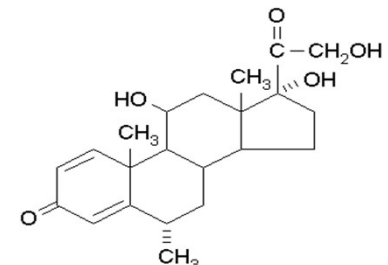
BETAMETHASONE



DEXAMETHASONE

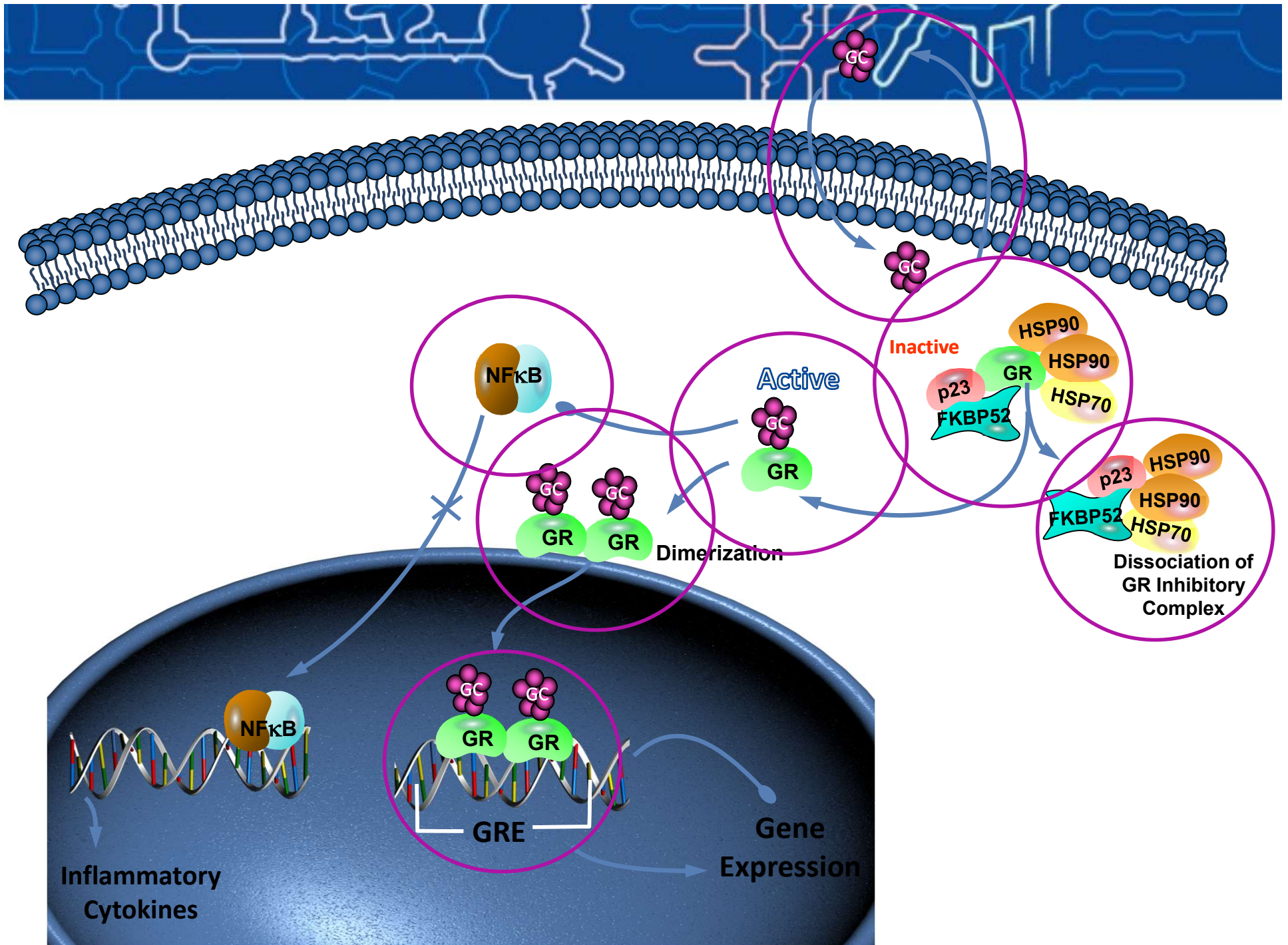


PREDNISONE

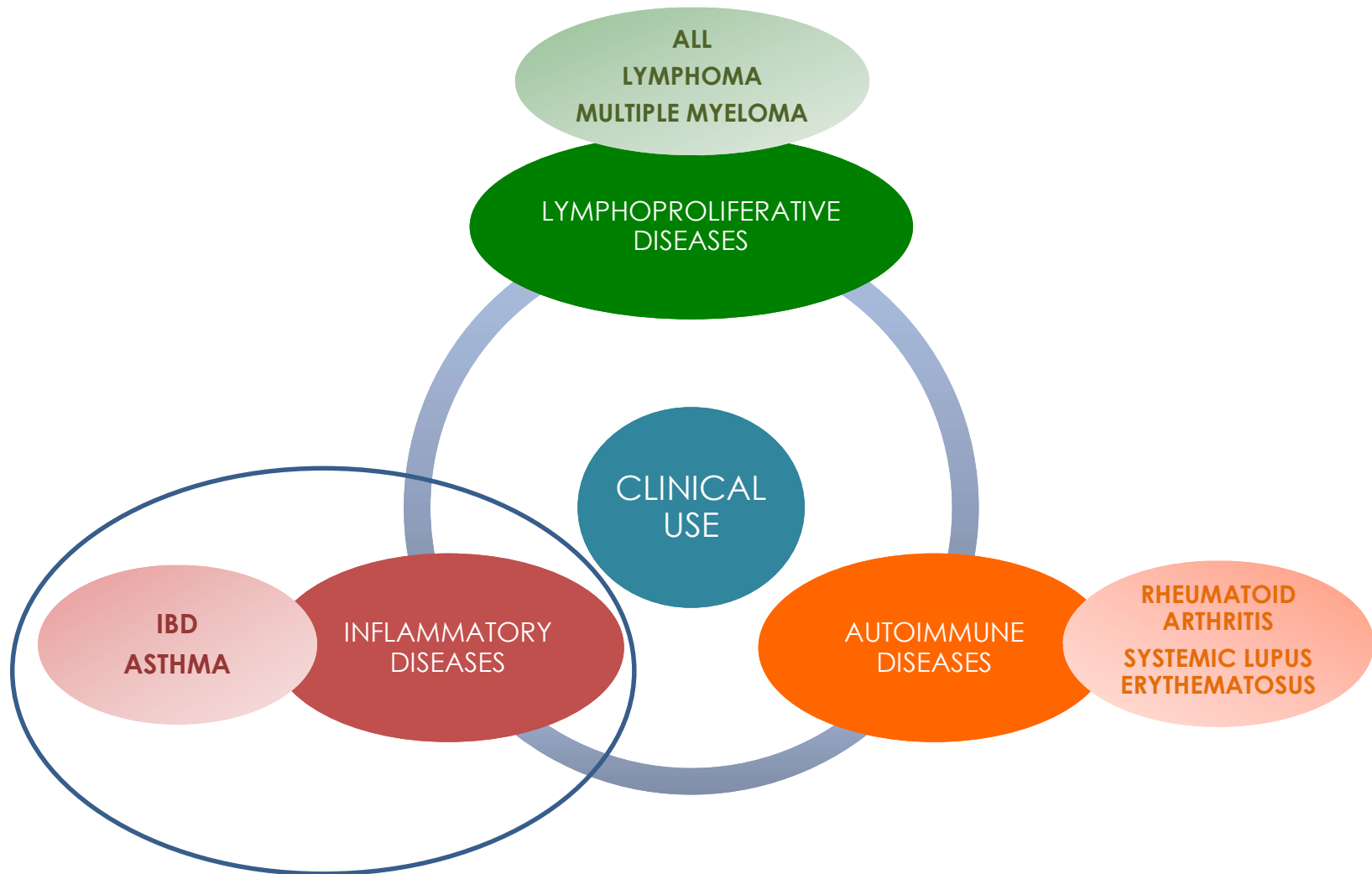


METHYLPREDNISOLONE

(Kadmiel & Cidlowski, 2013)

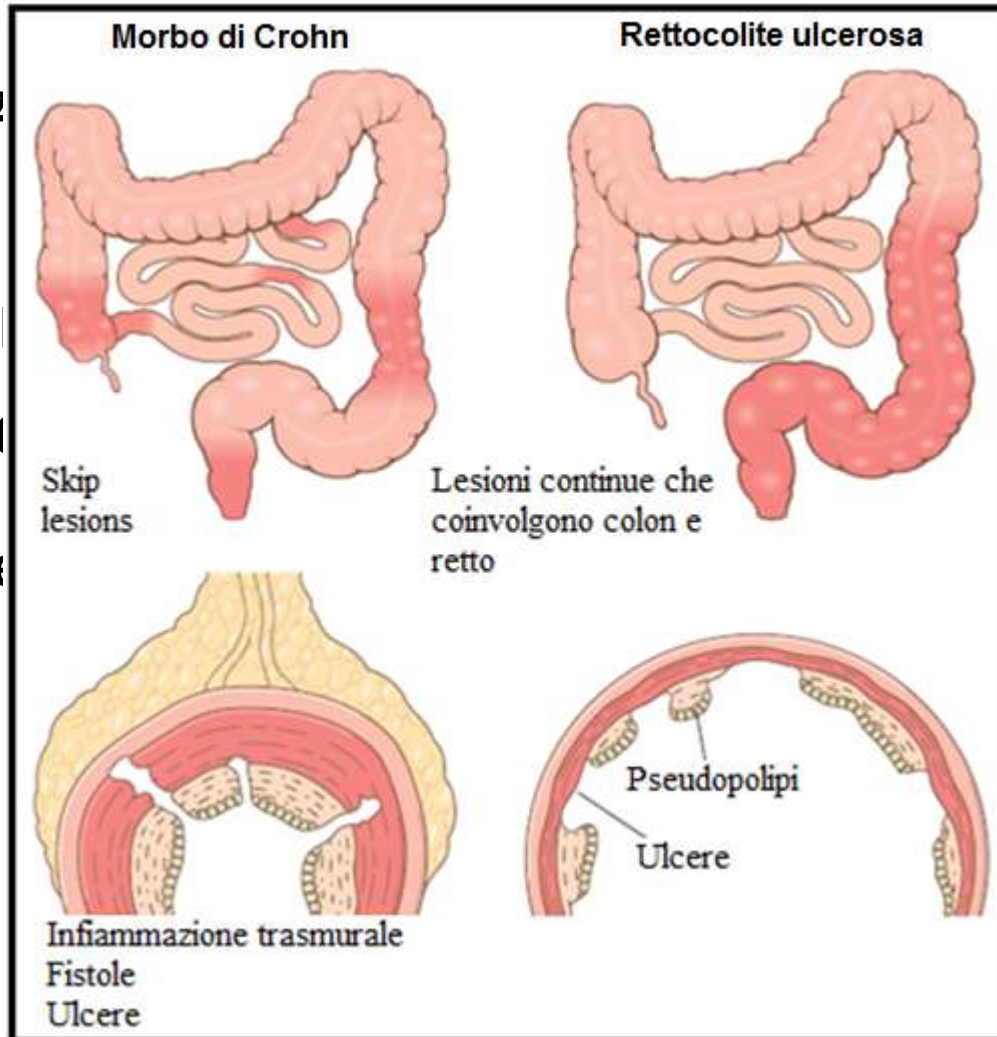
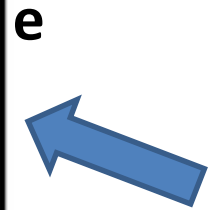


GLUCOCORTICOIDS



IBD

- **Infiammaz**
- **Due princ**
- **Morbo di C**
- **Rettocolite**



e

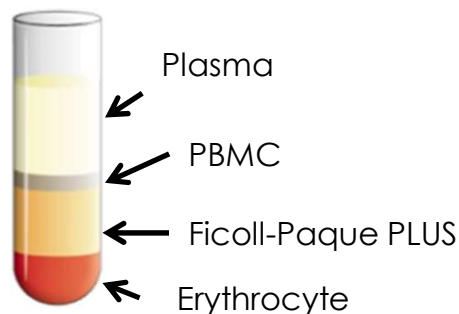
EPIGENETIC PREDICTORS OF GLUCOCORTICOID RESPONSE IN CHILDREN WITH IBD

The research project was supported by Italian Ministry of Health, No. 44/GR-2010-2300447








Correlation
between miRNAs expression and the clinical response to GC therapy

CANDIDATE PREDICTORS OF GLUCOCORTICOID RESPONSE IN CHILDREN WITH IBD



Article

High-Throughput Sequencing of microRNAs in Glucocorticoid Sensitive Paediatric Inflammatory Bowel Disease Patients

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T4 vs T0

Table 1. Differentially expressed miRNAs.

Upregulated miRNAs	FC	FDR Corrected P-Value	Downregulated miRNAs	FC	FDR Corrected p-Value
hsa-miR-451a * [13]	4.16	1.66×10^{-6}			
hsa-miR-144-3p * [14,15]	4.44	1.04×10^{-5}			
hsa-miR-96-5p * [13,14]	2.96	6.38×10^{-3}			
hsa-miR-29b-3p * [13]	2.89	0.026			
hsa-miR-142-3p * [14]	2.21	0.026			
hsa-miR-873-5p	3.36	0.026			
hsa-miR-29c-3p * [16,17]	3.37	0.037			
hsa-miR-29a-3p * [13]	2.72	0.041	hsa-miR-7109-3p	-4.62	0.044
hsa-miR-363-3p	2.31	0.041	hsa-miR-654-5p	-2.27	0.049
hsa-miR-141-3p	2.59	0.041			
hsa-miR-548ak	3.11	0.042			
hsa-let-7g-3p* [18]	2.44	0.042			
hsa-miR-4772-5p	2.70	0.047			
hsa-miR-106a-3p	3.52	0.047			
hsa-miR-31-3p	3.36	0.049			
hsa-miR-146b-5p * [19]	2.27	0.049			

Fold changes (FC) for each miRNA regulated by glucocorticoids (GCs); * Linked to GC regulation in the literature. FDR, False Discovery Rate.

EPIGENETIC PREDICTORS OF GLUCOCORTICOID RESPONSE IN CHILDREN WITH IBD

Validation of Selected Differentially Expressed miRNAs by qRT-PCR

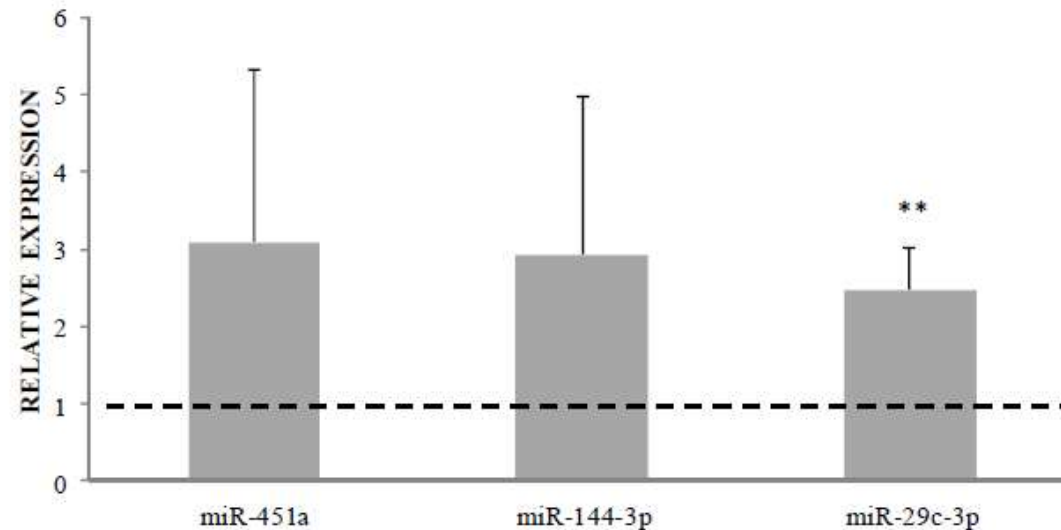


Figure 2. Relative expression of miR-451a, miR-144-3p, and miR-29c-3p (calculated as $2^{-\Delta\Delta C_t}$ T4 vs. T0). Values > 1 (dotted line) indicate upregulation, values < 1 indicate downregulation. Parametric *t*-test ΔC_t T0 vs. T4, ** $p < 0.01$.

Table 2. Glucocorticoid responsive element (GRE) sites predicted on miRNA promoter regions.

miRNA	pGRE	Start	End	Strand	Chrom	Expression
hsa-miR-363	GTGATAATGTGTGCTT	133303695	133303710	-	chrX	Up
hsa-miR-96	AGGACAAAGAGTCCTC	129416083	129416098	-	chr7	Up
hsa-miR-142	CTCACCTTCAGTTCTG	58331606	58331621	+	Chr17	Up
hsa-miR-142	CTGTCACTCTGTCTC	58332656	58332671	-	Chr17	Up

GC-sensitive miRNAs presenting positive GREs (pGRE).

CANDIDATE PREDICTORS OF GLUCOCORTICOID RESPONSE IN CHILDREN WITH IBD

T0 PRvsPS			
UP	FC	DOWN	FC
hsa-miR-1180-3p	7,96	hsa-miR-100-5p	43,95
hsa-miR-3591-3p	11,2	hsa-miR-1227-5p	2093,27
		hsa-miR-1255a	45,07
		hsa-miR-1271-5p	17,98
		hsa-miR-24-2-5p	15
		hsa-miR-25-5p	19,44
		hsa-miR-3065-5p	22,25
		hsa-miR-31-3p	25,65
		hsa-miR-3196	38,62
		hsa-miR-3656	19,63
		hsa-miR-3960	150,33
		hsa-miR-4443	47,81
		hsa-miR-4772-3p	20,55
		hsa-miR-5586-3p	17,04
		hsa-miR-6075	4465,59
		hsa-miR-6087	25,93
		hsa-miR-618	26,38
		hsa-miR-876-5p	19,32



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MiR-1180 promotes apoptotic resistance to human hepatocellular carcinoma via activation of NF- κ B signaling pathway

Received: 00 July 2015
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Guosheng Tan^{1,2}, Linwei Wu^{2,3}, Jinfu Tan², Bing Zhang⁴, William Chi-shing Tai^{5,6}, Shiqiu Xiong⁷, Wei Chen¹, Jianyong Yang¹ & Heping Li^{1,8}

T4 PRvsPS			
UP	FC	DOWN	FC
hsa-miR-1180-3p	6,48	hsa-miR-1197	10,19
hsa-miR-4732-5p	5	hsa-miR-1227-5p	434,07
		hsa-miR-154-3p	10,26
		hsa-miR-4443	64,78
		hsa-miR-4523	11,82
		hsa-miR-6075	1561,21
		hsa-miR-6087	20,31
		hsa-miR-876-5p	25,93

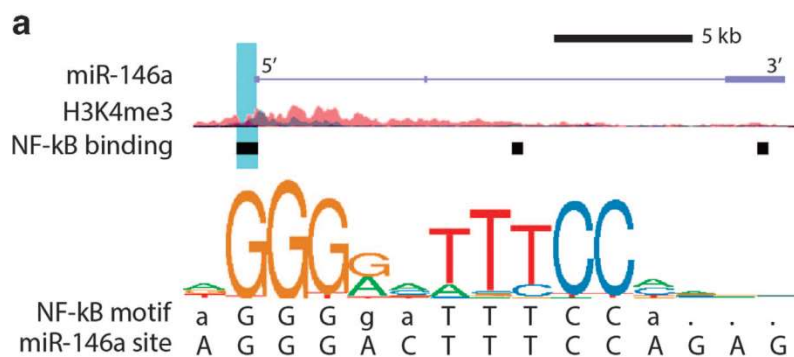
CANDIDATE PREDICTORS OF GLUCOCORTICOID RESPONSE IN CHILDREN WITH IBD

Clin Transl Gastroenterol. 2016 Sep 15;7(9):e192. doi: 10.1038/ctg.2016.49.

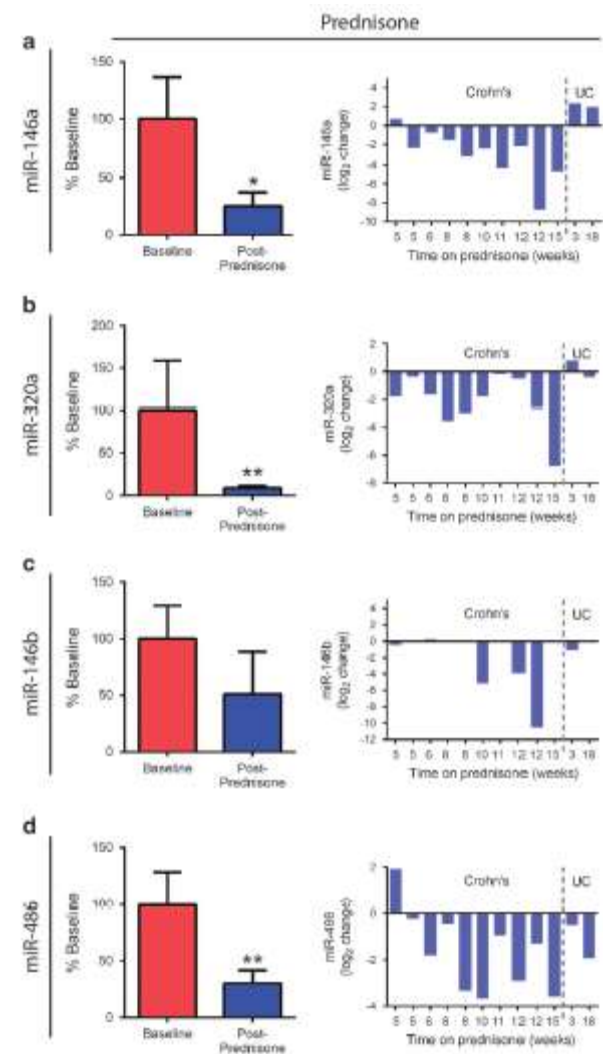
Identification of Pathway-Specific Serum Biomarkers of Response to Glucocorticoid and Infliximab Treatment in Children with Inflammatory Bowel Disease.

Heier CR¹, Fiorillo AA¹, Chaisson E², Gordish-Dressman H^{1,3}, Hathout Y^{1,3}, Damsker JM^{1,4}, Hoffman EP^{1,3,4}, Conklin LS^{1,2}.

Bioinformatic analysis of gene regulation pathways



Molecular marker	Expression Regulated by	Source	Drug changed	Up or Down
miR-146a	NF-kB	Wang 2012	Both	Down
miR-146b	NF-kB	Wang 2012	Both	Down
miR-320a	NF-kB and GR	Wang 2012	Both	Down
miR-486	GR	Wang 2012	Prednisone	Down



DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE

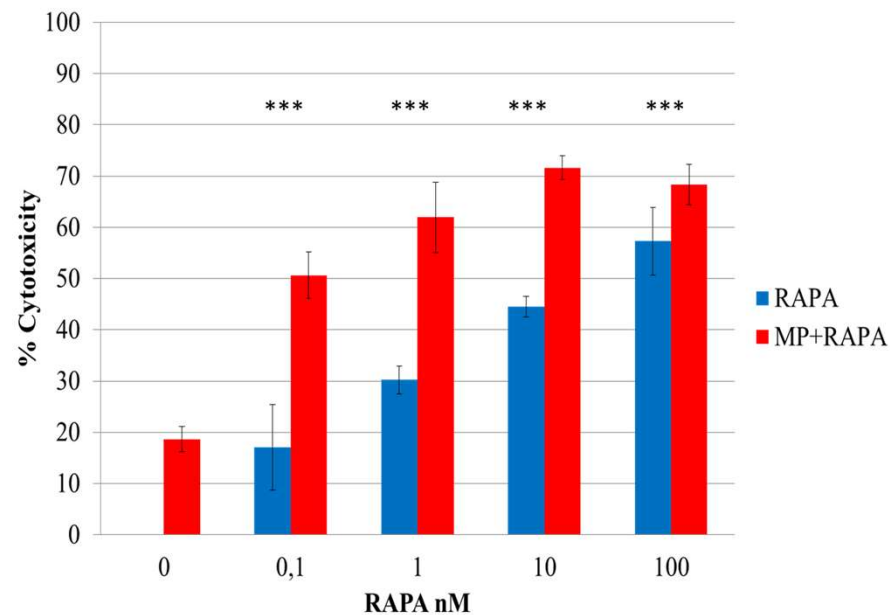


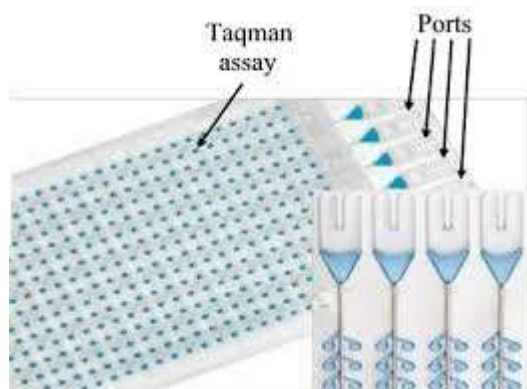
Fig. 1 Cells were exposed for 72 h to MP at 20 $\mu\text{g}/\text{ml}$ and/or different concentrations of RAPA, and cell proliferation was evaluated by MTT assay. Two-way ANOVA ($P < 0.0001$) and Bonferroni post-test *** $p\text{-value} < 0.001$.

miR-331-3p is involved in glucocorticoid resistance reversion by rapamycin through suppression of the MAPK signaling pathway

DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE

Differentially expressed miRNAs.

The expression analysis identified 70, 99 and 96 miRNAs that were differentially expressed after treatment with MP, RAPA and MP+RAPA, respectively.



TaqMan® Array MicroRNA Cards

miRNA up e downregolati selettivamente dai diversi trattamenti farmacologici

	UP	DOWN
MP	hsa-miR-200b-3p	hsa-miR-181c-5p hsa-miR-192-5p hsa-miR-324-3p hsa-miR-361-5p hsa-miR-455-5p hsa-miR-576-3p
RAPA	hsa-miR-140-3p hsa-miR-26b-5p hsa-miR-28-5p hsa-miR-324-5p hsa-miR-454-3p	hsa-miR-142-5p hsa-miR-365a-3p hsa-miR-455-3p hsa-miR-501-5p
MP+RAPA	hsa-miR-30b-5p hsa-miR-30c-5p hsa-miR-331-3p hsa-miR-345-5p hsa-miR-744-5p	hsa-miR-19a-3p hsa-miR-886-3p hsa-miR-886-5p

DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE

DIANA miRPath v.2.0: investigating the combinatorial effect of microRNAs in pathways

<http://snf-515788.vm.oceanos.gnet.gr/>

The screenshot shows a web browser window displaying the DIANA miRPath v.3 interface. The browser's address bar shows the URL snf-515788.vm.oceanos.gnet.gr. The page features a red header with the text "DIANA TOOLS" and logos for the University of Thessaly, IMIS Athens IC, and BSRC AL Fleming. Below the header, there are navigation buttons for "HOME" and "SOFTWARE". A blue box contains a citation: "Please cite: Vlachos, Ioannis S., Konstantinos Zagganas, Maria D. Paraskevopoulou, Georgios Georgakilas, Dimitra Karagkouni, Thanasis Vergoulis, Theodore Dalamagas, and Artemis G. Hatzigeorgiou. "DIANA-miRPath v3. 0: deciphering microRNA function with experimental support." Nucleic acids research (2015): gkv403." The main content area is titled "mirPath v.3" and includes a "New search" section with tabs for "KEGG analysis" and "GO analysis". The "KEGG analysis" tab is active, showing a "Species" dropdown set to "Human", a "Gene filter" set to "determine genes (optional)", and an "Add miRNAs" input field. There are also buttons for "Reverse Search" and "Run example". A paragraph of text describes the tool: "DIANA-miRPath is a miRNA pathway analysis web-server, providing accurate statistics, while being able to accommodate advanced pipelines. mirPath can utilize predicted miRNA targets (in CDS or 3'-UTR regions) provided by the DIANA-microT-CDS algorithm or even experimentally validated miRNA interactions derived from DIANA-TarBase. These interactions (predicted and/or validated) can be subsequently combined with sophisticated merging and meta-analysis algorithms." The browser's taskbar at the bottom shows the time as 13:33 on 12/12/2017.

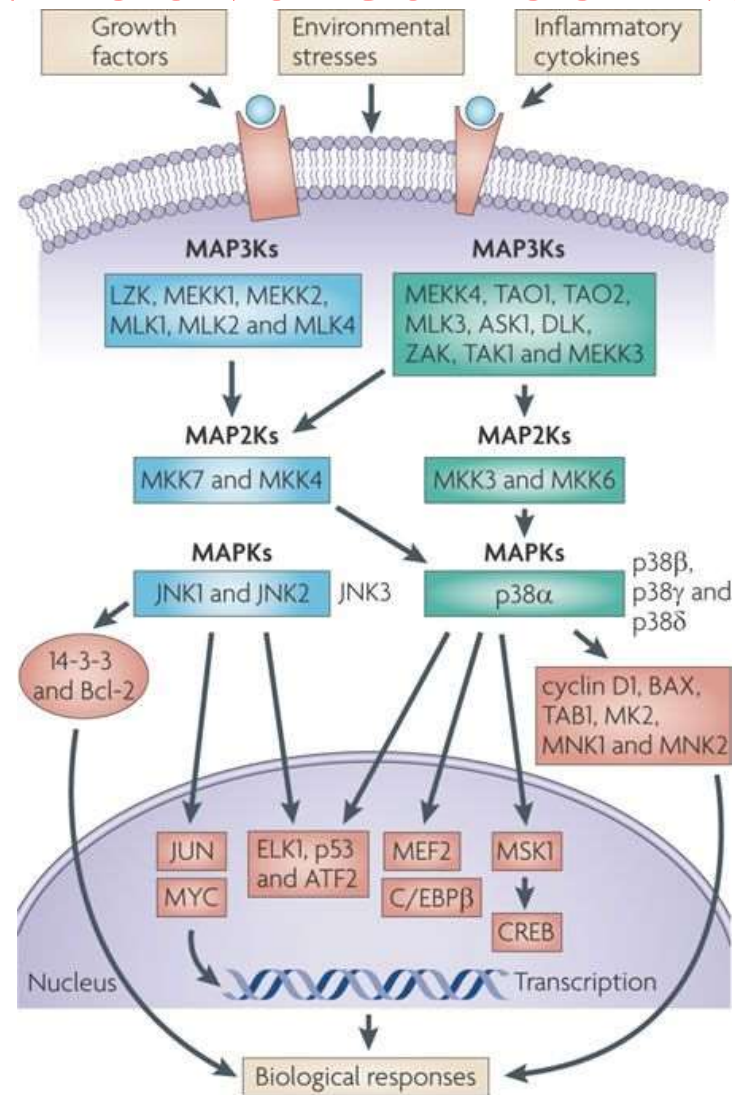
DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE

Pathways	UPREGULATED miRNAs								
	MP			RAPA			MP+RAPA		
	p-Value	Gene	miRNA	p-Value	Gene	miRNA	p-Value	Gene	miRNA
ECM-receptor interaction	5.067 e-27	26	14	1.611 e-27	30	20	1.674 e-21	36	21
Biotin metabolism	7.131 e-5	2	2	0.0009	2	3	0.002	2	3
Vitamin B6 metabolism	0.00057	4	4	0.0294	3	3	0.0416	3	4
PI3K-Akt signaling pathway	0.00687	96	29	0.0009	124	44	0.0025	130	48
p53 signaling pathway	0.0086	24	18	0.0071	30	27	0.00271	33	31
Protein digestion and absorption	0.02	31	15	-	-	-	-	-	-
Ras signaling pathway	0.0201	64	26	0.003	85	39	0.027	83	42
Glycosaminoglycan biosynthesis	0.025	6	5	-	-	-	0.0065	11	11
Tight junction	0.028	41	21	-	-	-	-	-	-
Estrogen signaling pathway	0.0291	29	16	-	-	-	-	-	-
Neurotrophin signaling pathway	0.042	36	22	0.0294	47	31	0.0053	53	34
Fatty acid biosynthesis	-	-	-	1.898 e-13	4	4	3.734 e-12	4	5
Prion diseases	-	-	-	5.169	9	12	-	-	-
Bacterial invasion of epithelial cells	-	-	-	0.0052	34	28	-	-	-
Ubiquitin mediated proteolysis	-	-	-	0.0071	55	33	0.0146	57	37
MAPK signaling pathway	-	-	-	-	-	-	0.00576	98	41
Proteoglycans in cancer	0.019	74	39	-	-	-	-	-	-

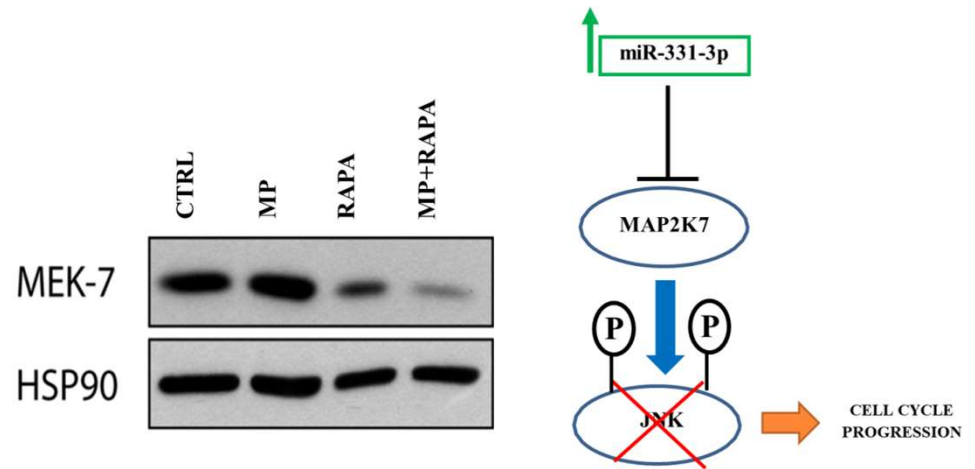
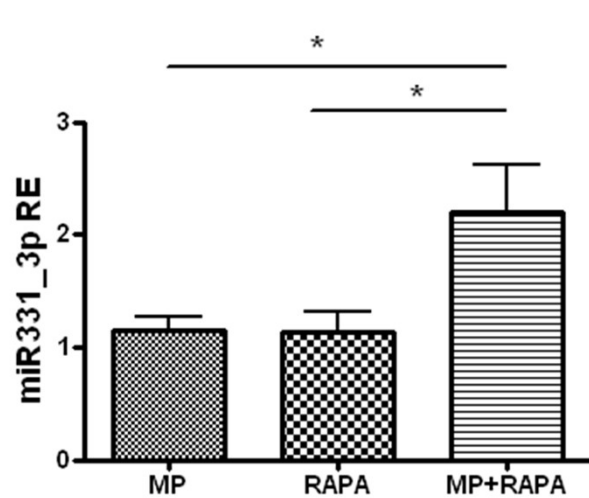
Pathways	DOWNREGULATED miRNAs								
	MP			RAPA			MP+RAPA		
	p-Value	Gene	miRNA	p-Value	Gene	miRNA	p-Value	Gene	miRNA
Fatty acid biosynthesis	3.31 e-26	4	3	1.123 e-23	3	2	7.532 e-21	3	1
Fatty acid metabolism	2.069 e-8	11	9	0.00064	9	8	0.007	9	6
Proteoglycans in cancer	3.569 e-5	40	16	0.00074	37	20	0.0019	35	15
Thyroid hormone signaling pathway	0.0015	20	15	-	-	-	-	-	-
Path regulat pluripot of stem cells	0.005	30	15	0.03099	30	20	-	-	-
Thyroid hormone synthesis	0.0075	12	8	-	-	-	-	-	-
Glycosphingolipid biosynthesis	0.0106	5	3	0.0248	6	7	-	-	-
N-Glycan biosynthesis	0.0314	10	9	0.0248	12	9	0.03	10	8
PI3K-Akt signaling pathway	-	-	-	0.0248	67	22	-	-	-
Acute myeloid leukemia	-	-	-	0.0309	15	14	-	-	-
ErbB signaling pathway	-	-	-	-	-	-	0.014	22	14

miR-331-3p

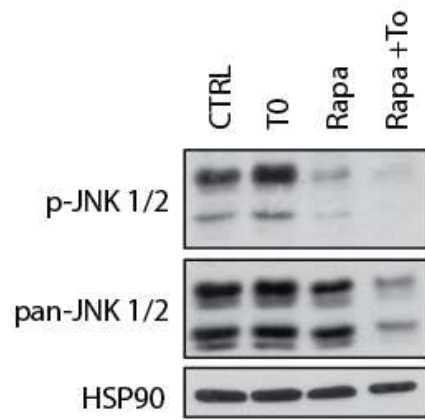
DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE



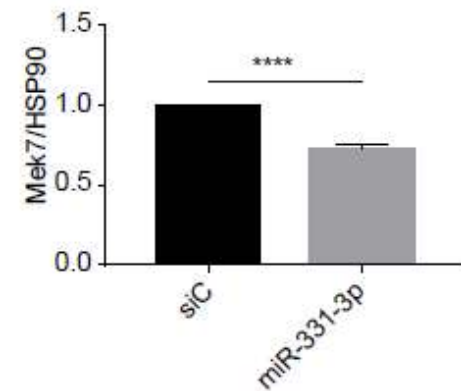
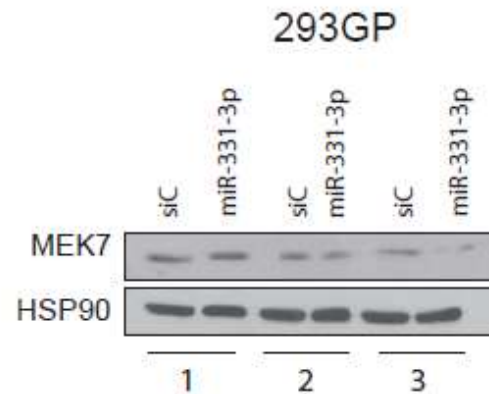
DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE



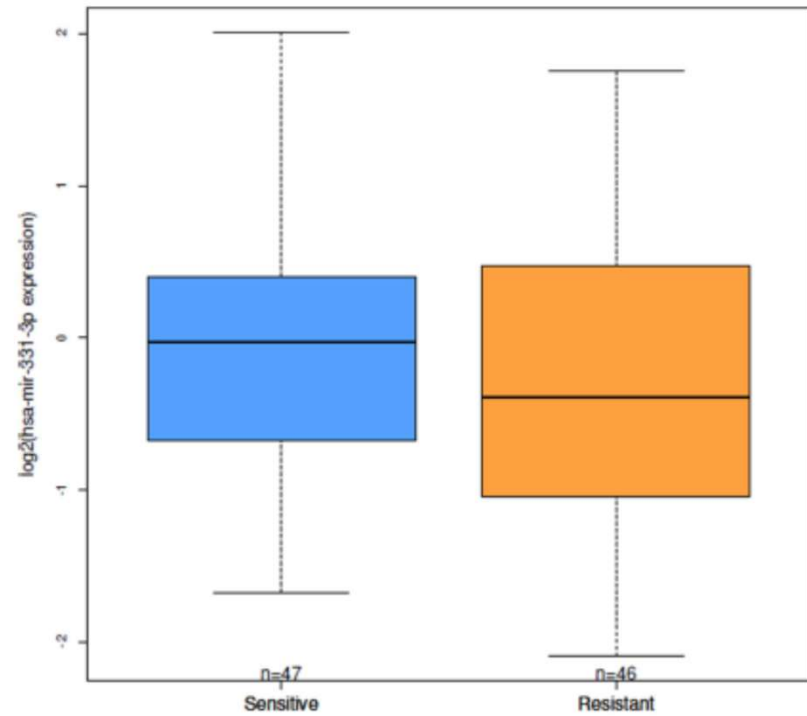
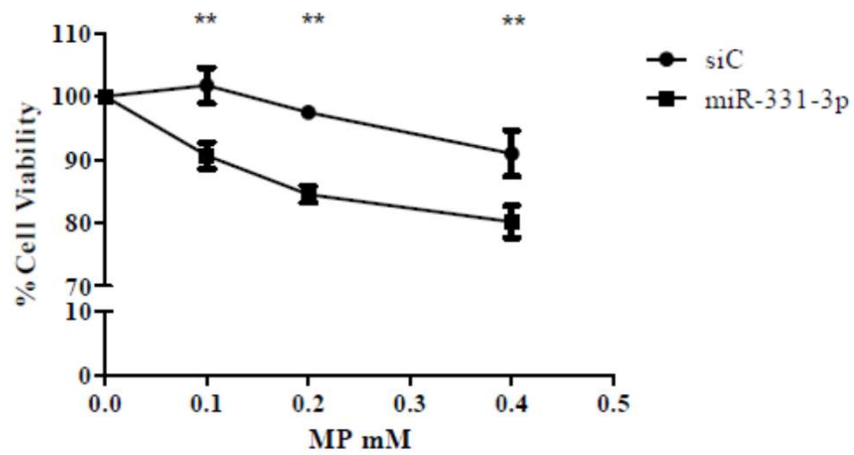
Validation of MAP2K7 as a target of miR-331-3p



GC resistance reversion by RAPA through suppression of the JNK protein

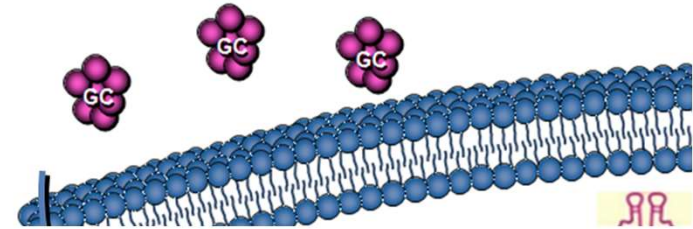
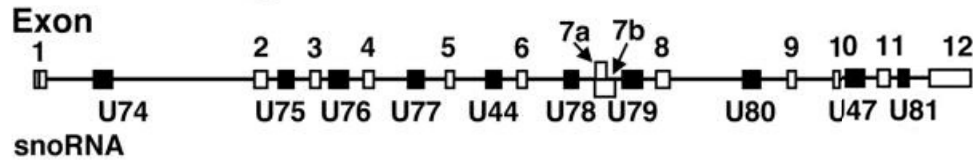


DIFFERENTIAL EXPRESSION OF miRNAs IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE

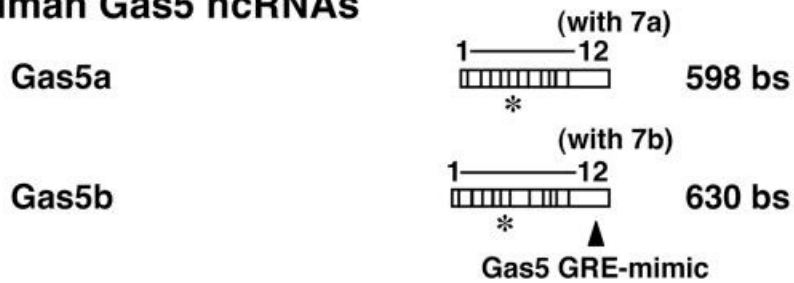


Growth arrest-specific 5 (GAS5)

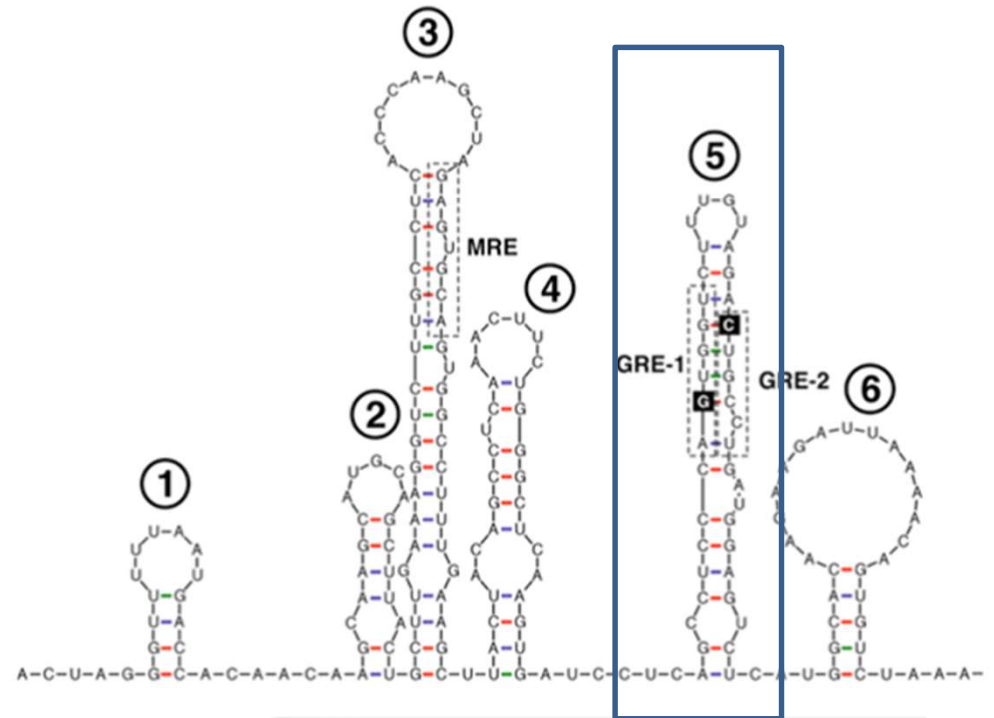
Human Gas5 gene



Human Gas5 ncRNAs

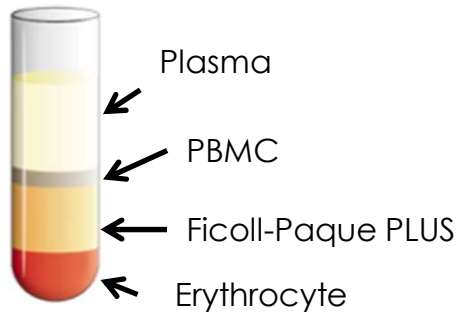


(Kino et al., *Sci Signal.* 2010)

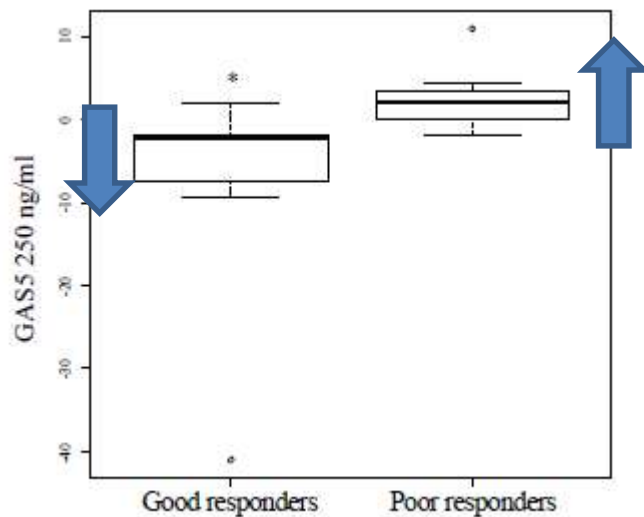
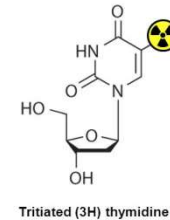


ROLE OF GAS5 IN GC RESPONSE

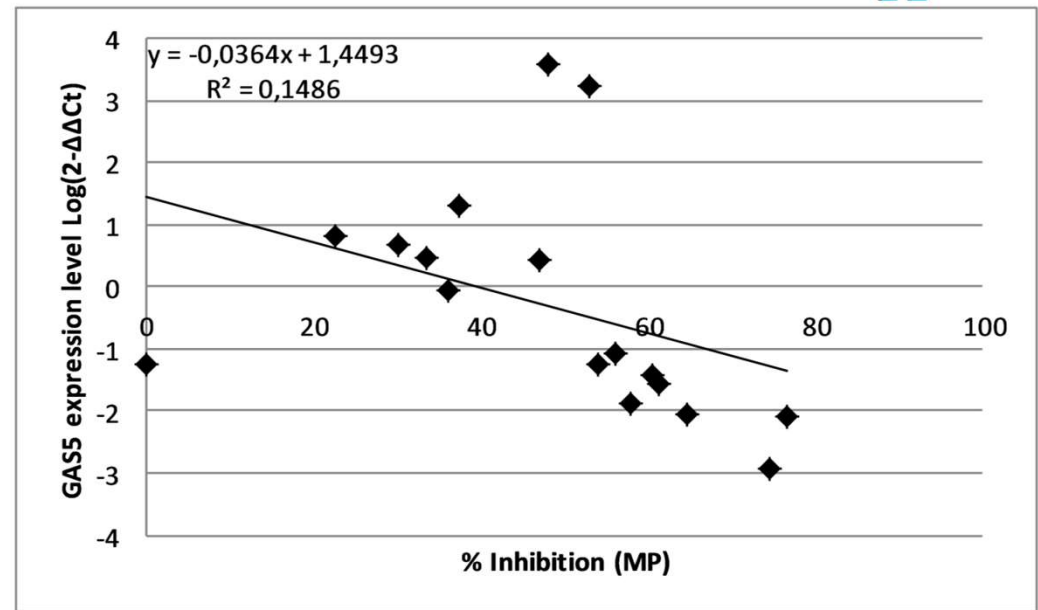
Samples from blood donors



Pharmacodynamic test: inhibition of in vitro proliferation by the test of incorporation of [³H]-thymidine.

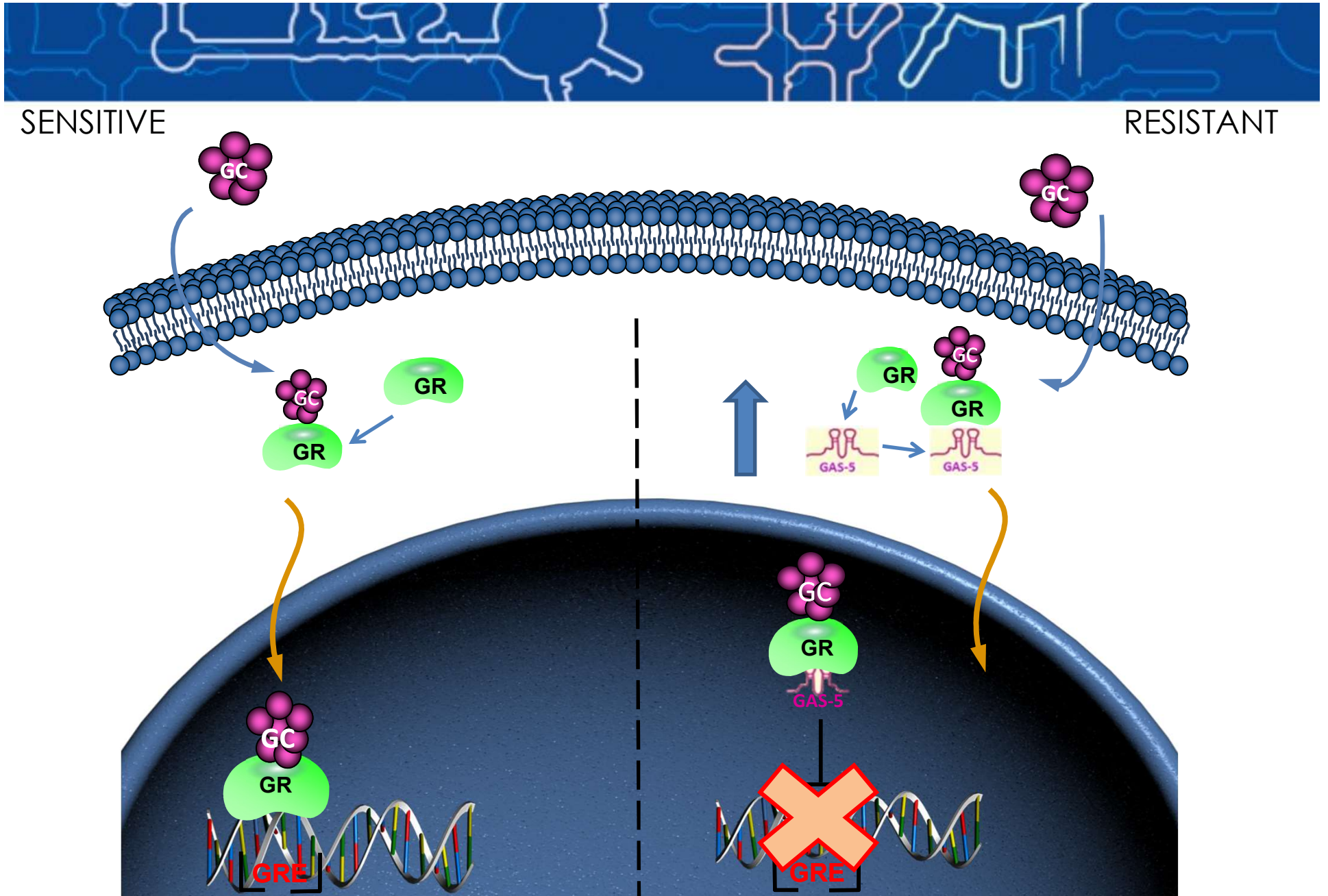


Lucafò M. et al., *Curr Mol Med* 2015

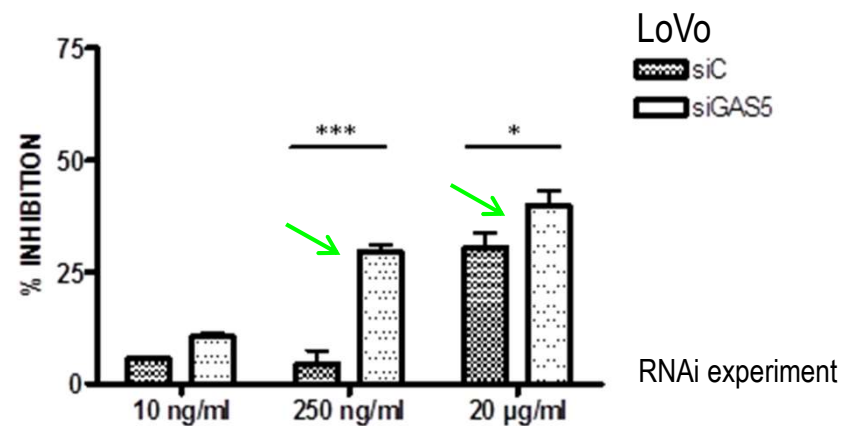
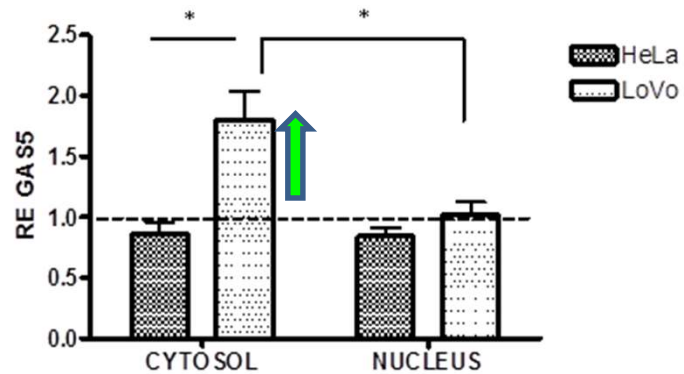
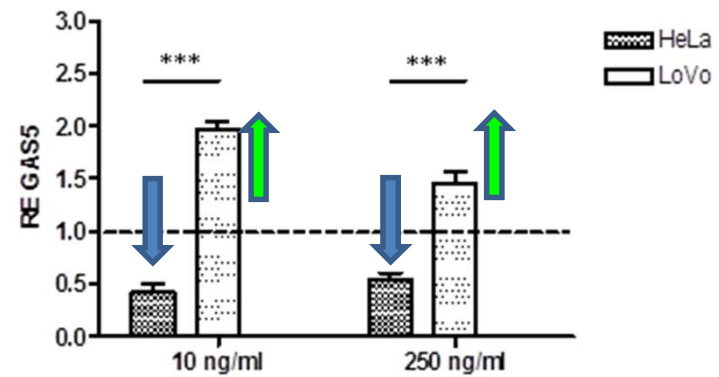
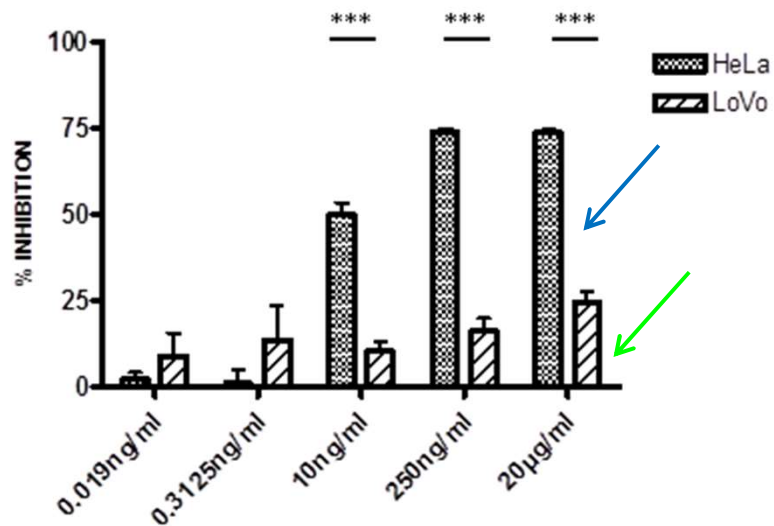


Spearman rho= -0,73; P value= 0.0009

Lucafò M. et al., *Clin and Exp Pharm and Phys* 2016

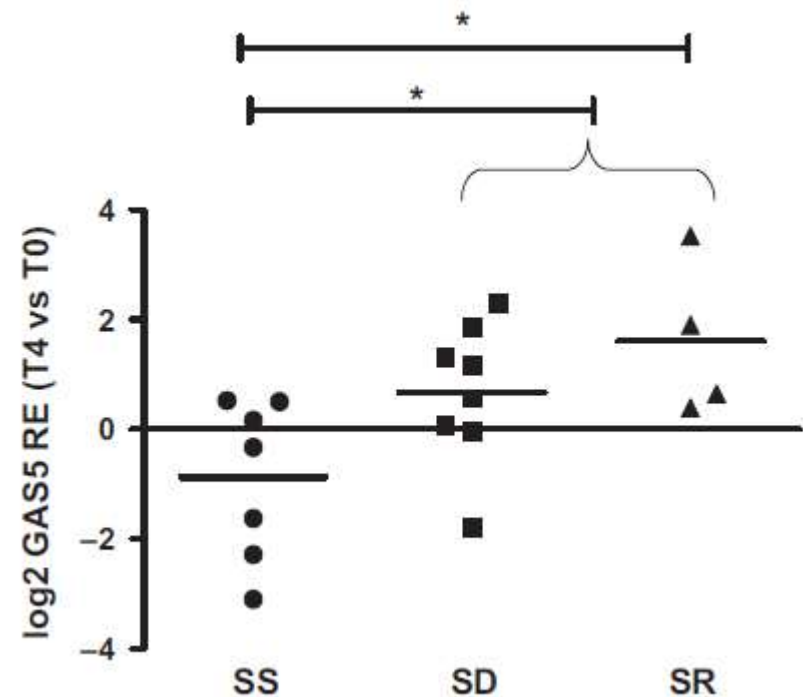
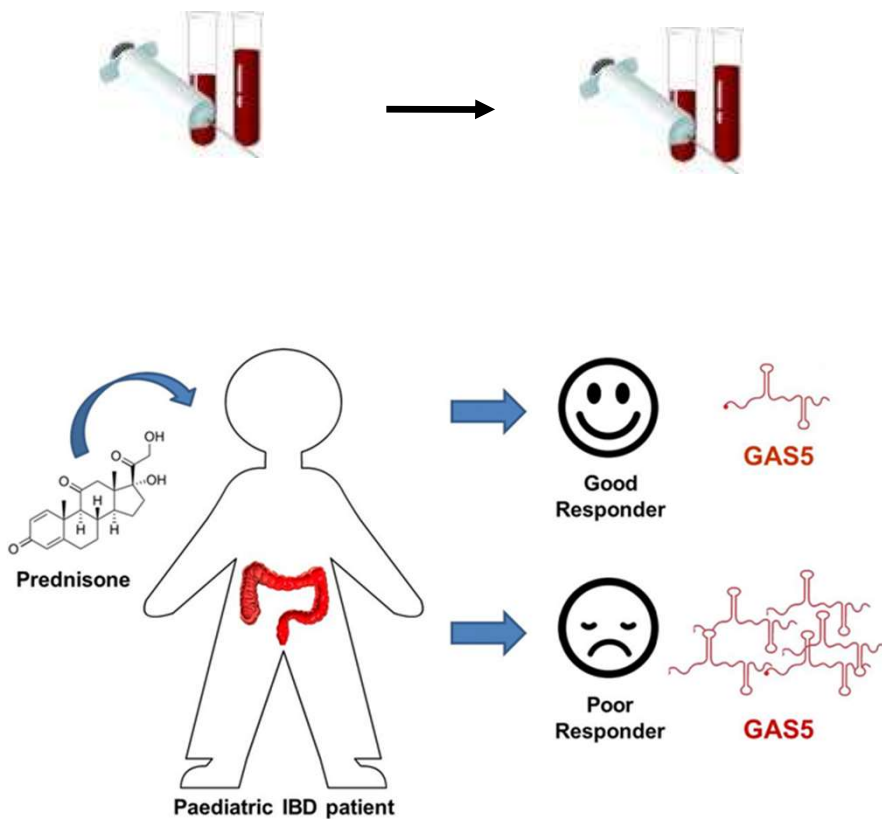


ROLE OF GAS5 IN GC RESPONSE

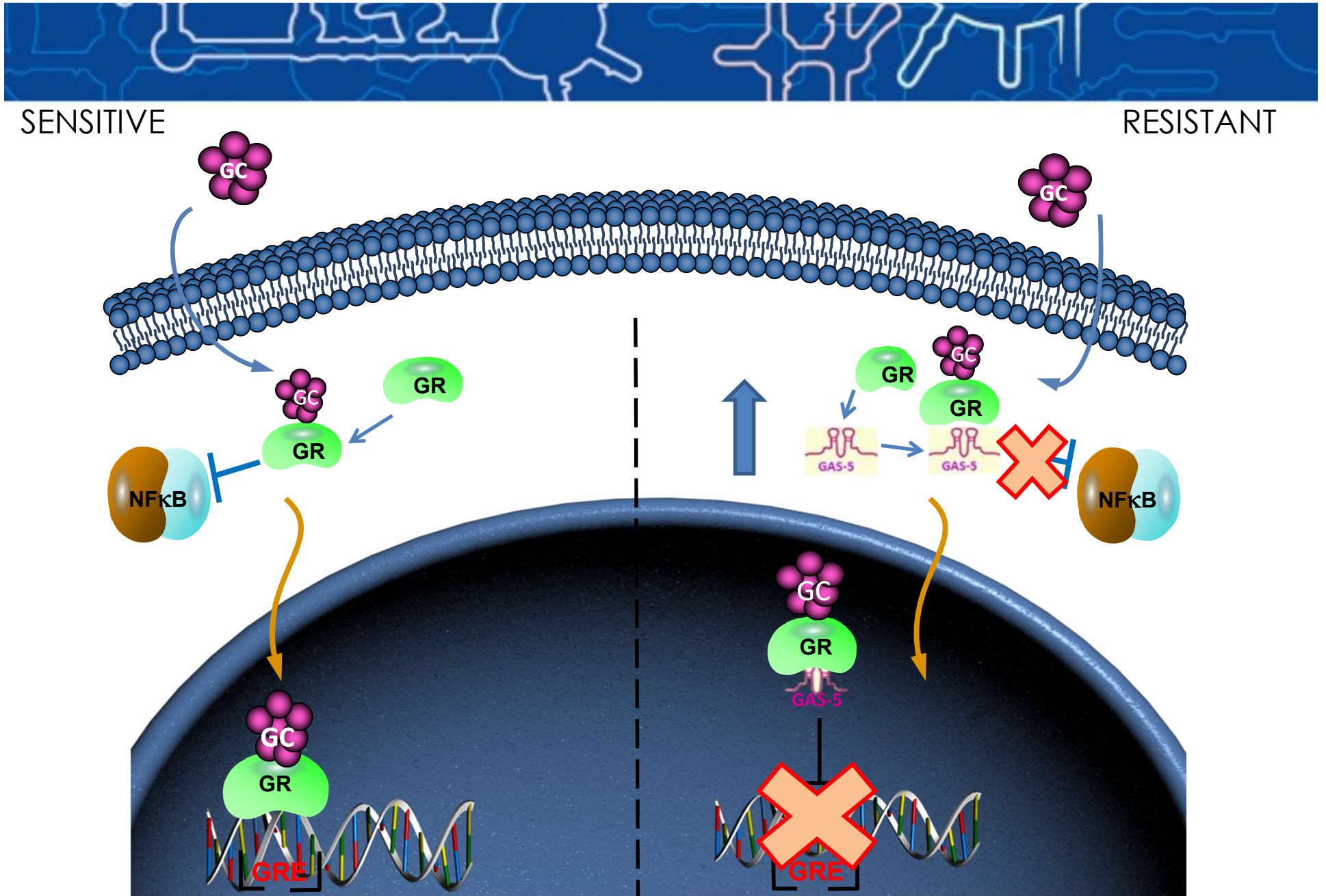


ROLE OF GAS5 IN GC RESPONSE IN CHILDREN WITH IBD

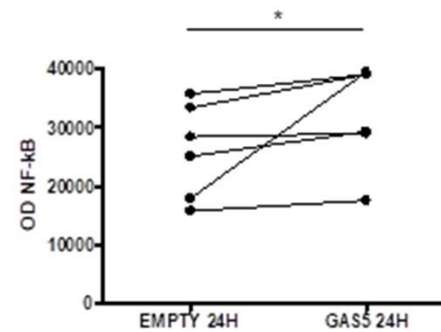
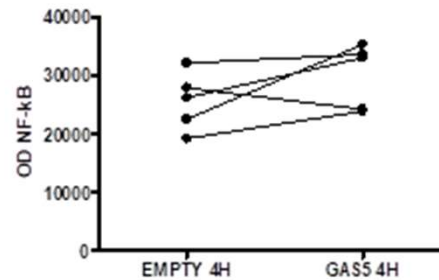
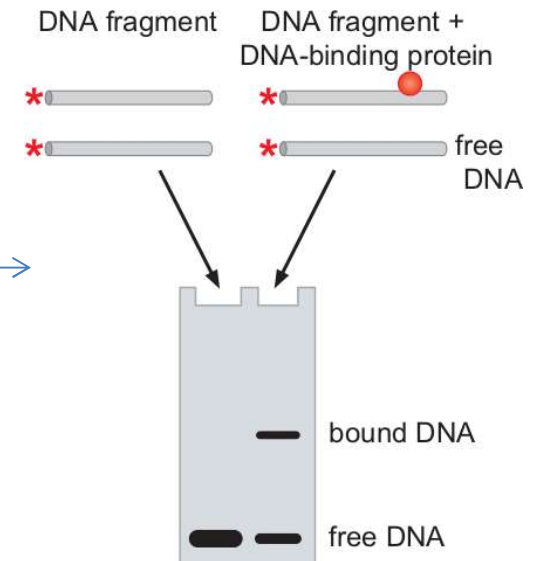
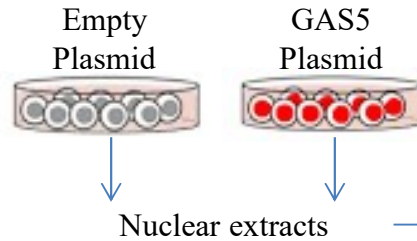
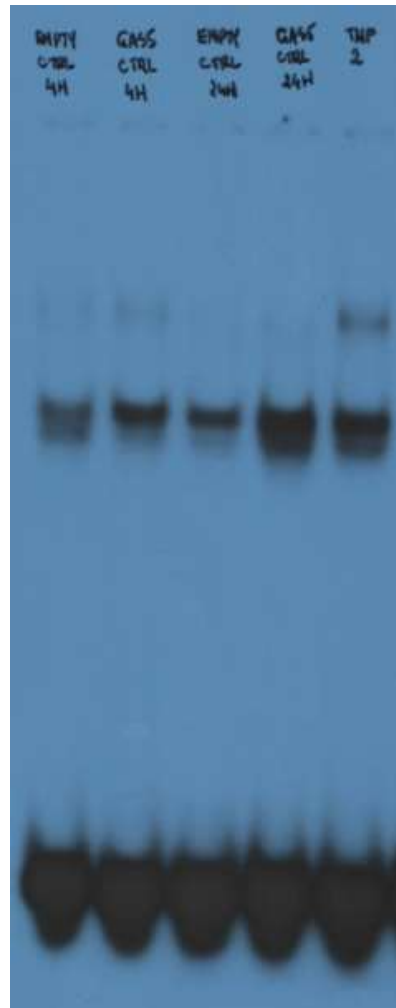
DIAGNOSIS (T0) → 30 DAYS OF TREATMENT WITH GC (T4)



Lucafò M. et al., *Basic & Clinical Pharmacology & Toxicology* 2017

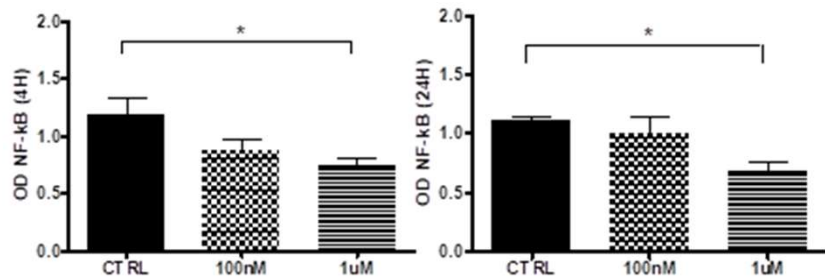


ROLE OF GAS5 on NF- κ B activity by EMSA

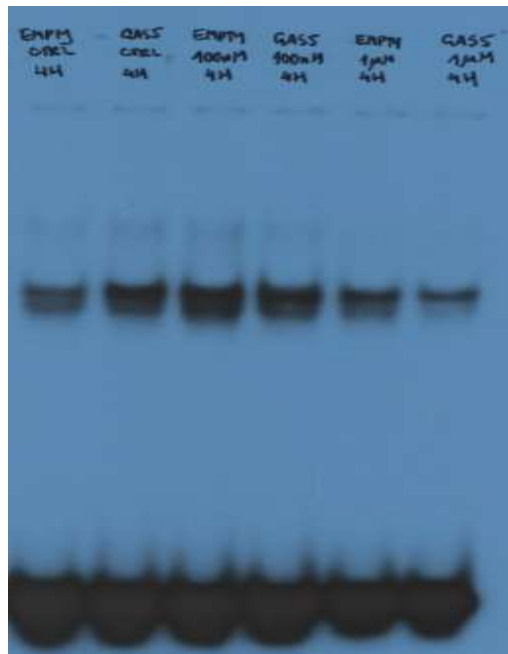


NF- κ B EMSA analyses in HeLa cells transfected with empty pcDNA3.1 (EMPTY CTRL) and pcDNA3.1_GAS5 (GAS5 CTRL), after 4 (lanes 1, 2) and 24 h (lanes 3, 4) from transfection or treated with TNF- α (lane 5).

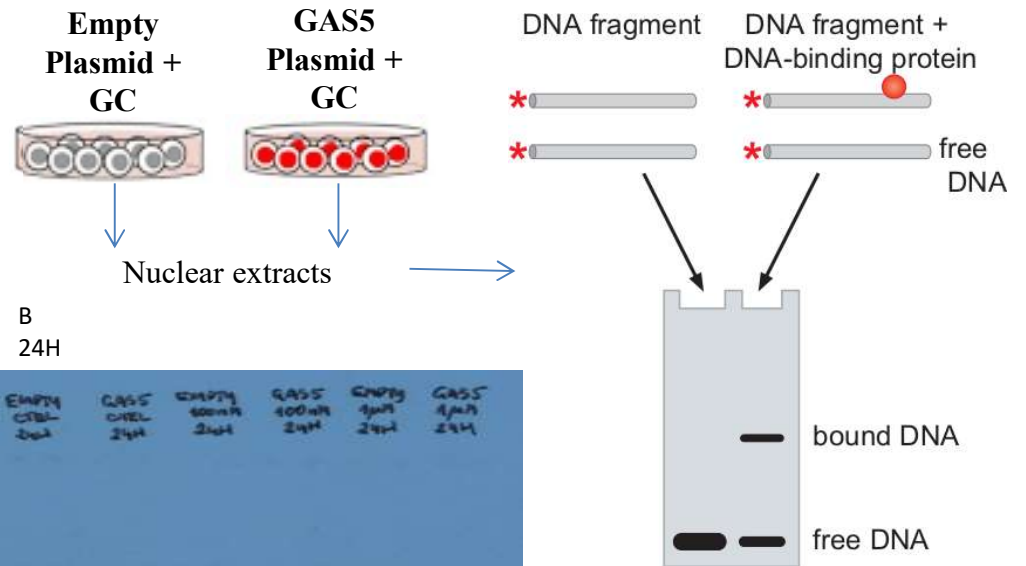
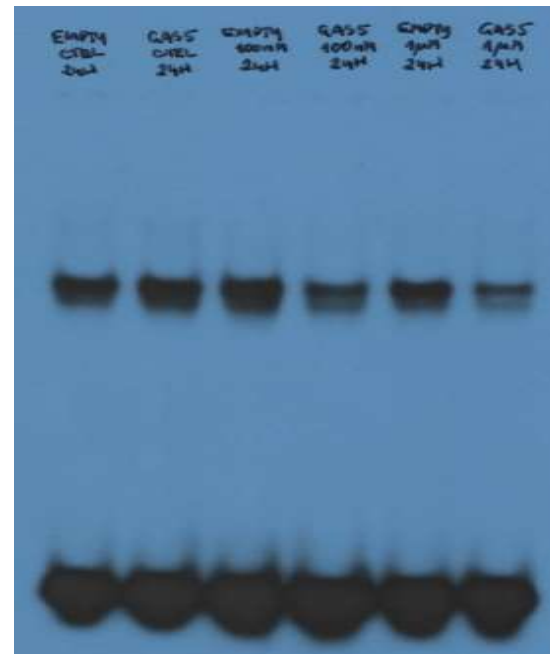
ROLE OF GAS5 on NF- κ B activity by EMSA



A
4H



B
24H

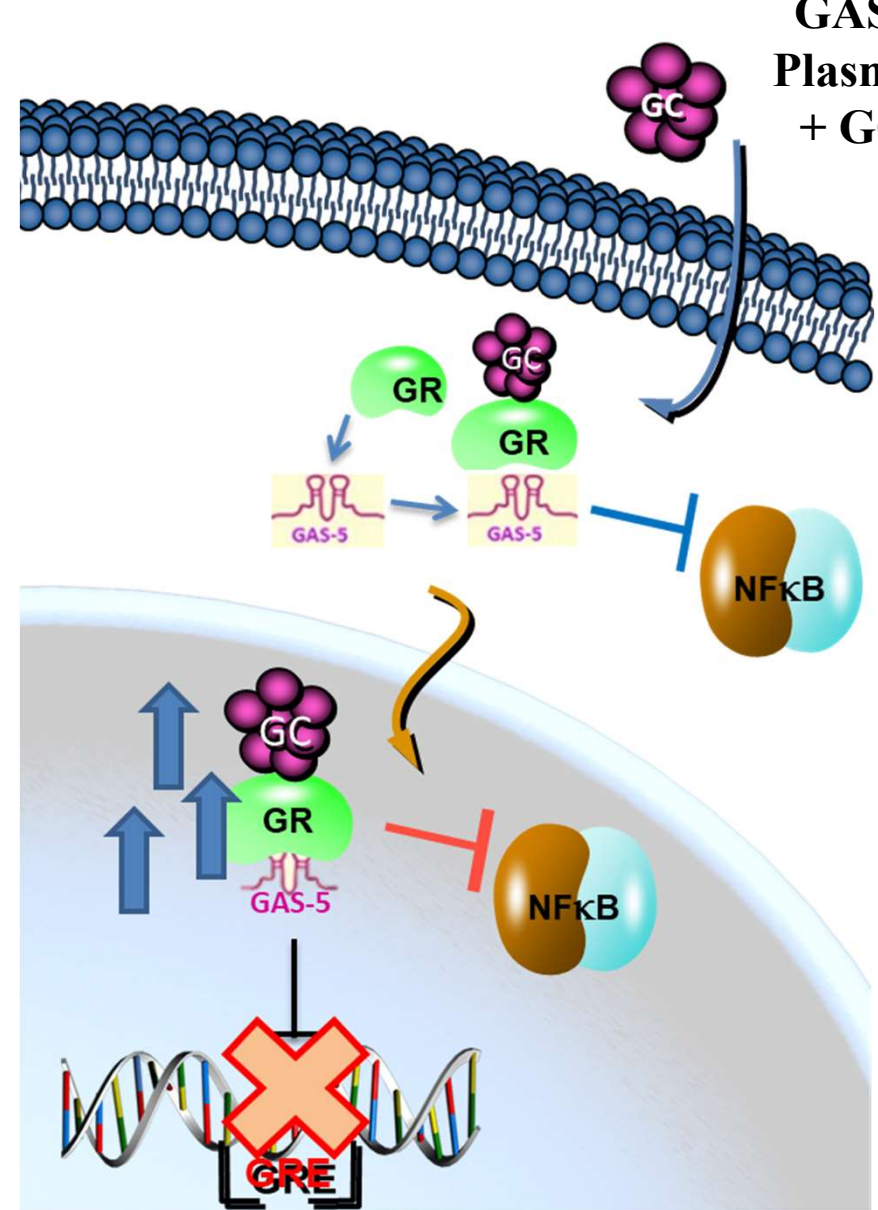
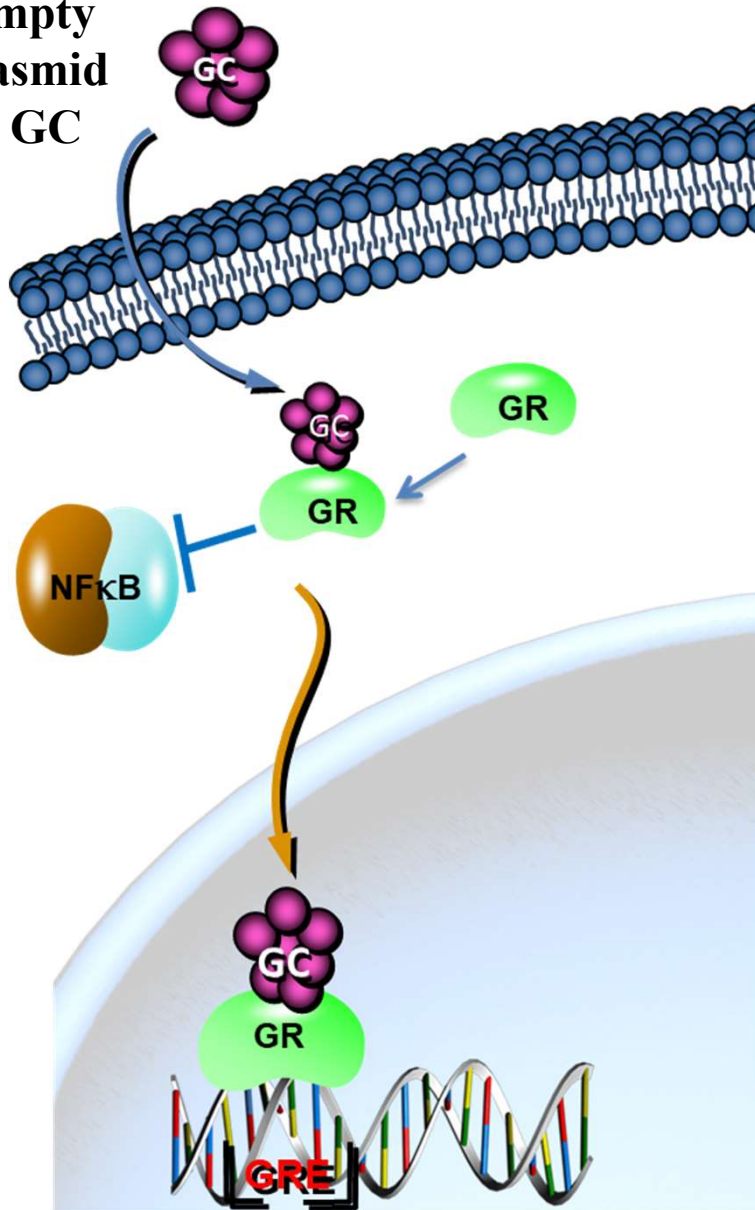


NF- κ B EMSA analyses in HeLa cells transfected with empty pcDNA3.1 (EMPTY) and pcDNA3.1_GAS5 (GAS5), treated with DEXA 100 nM (lanes A and B 3, 4) and 1 μ M (lanes A and B 5, 6) and untreated (CTRL; lanes A and B 1, 2) after 4 (A) or 24 h (B).

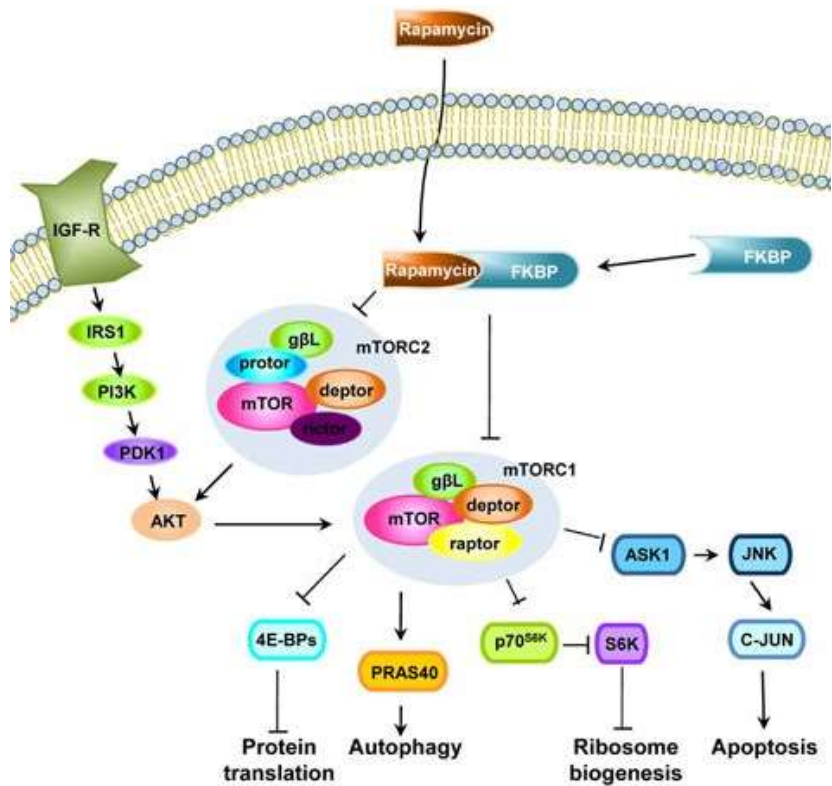


Empty
Plasmid
+ GC

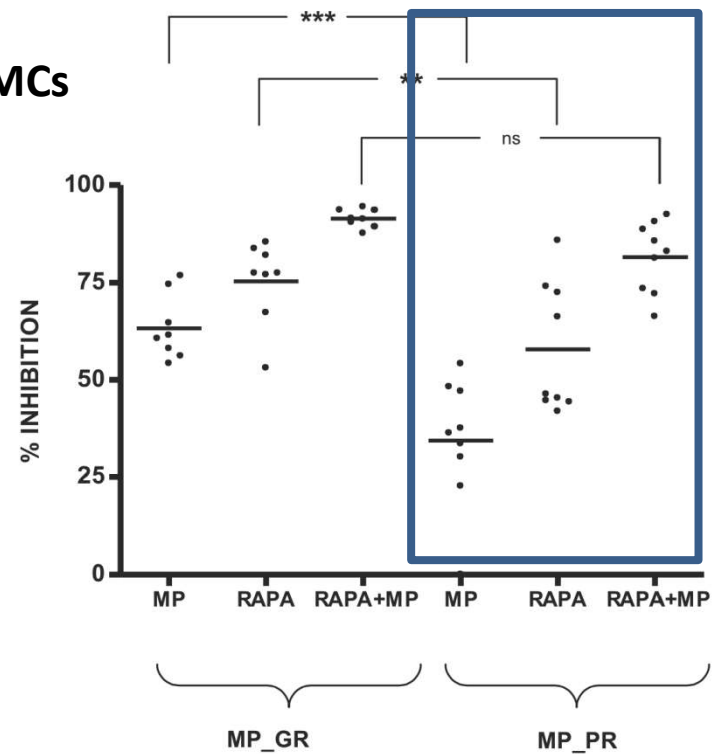
GAS5
Plasmid
+ GC



DIFFERENTIAL EXPRESSION OF GAS5 IN RAPAMYCIN-INDUCED REVERSION OF GC RESISTANCE



PBMCs



MPvsRAPA pvalue > 0.05
 MPvsRAPA+MP pvalue < 0.001
 RAPAvsRAPA+MP pvalue < 0.05

MPvsRAPA pvalue < 0.001
 MPvsRAPA+MP pvalue < 0.001
 RAPAvsRAPA+MP pvalue < 0.001

Lucafò M. et al., *Clin and Exp Pharm and Phys* 2016