

CroSeed: pipeline bioinformatica per l'individuazione di miRNA con attività nutraceutica in specie e varietà vegetali tipiche della dieta mediterranea.

Domenico Catalano

CNR – ITB

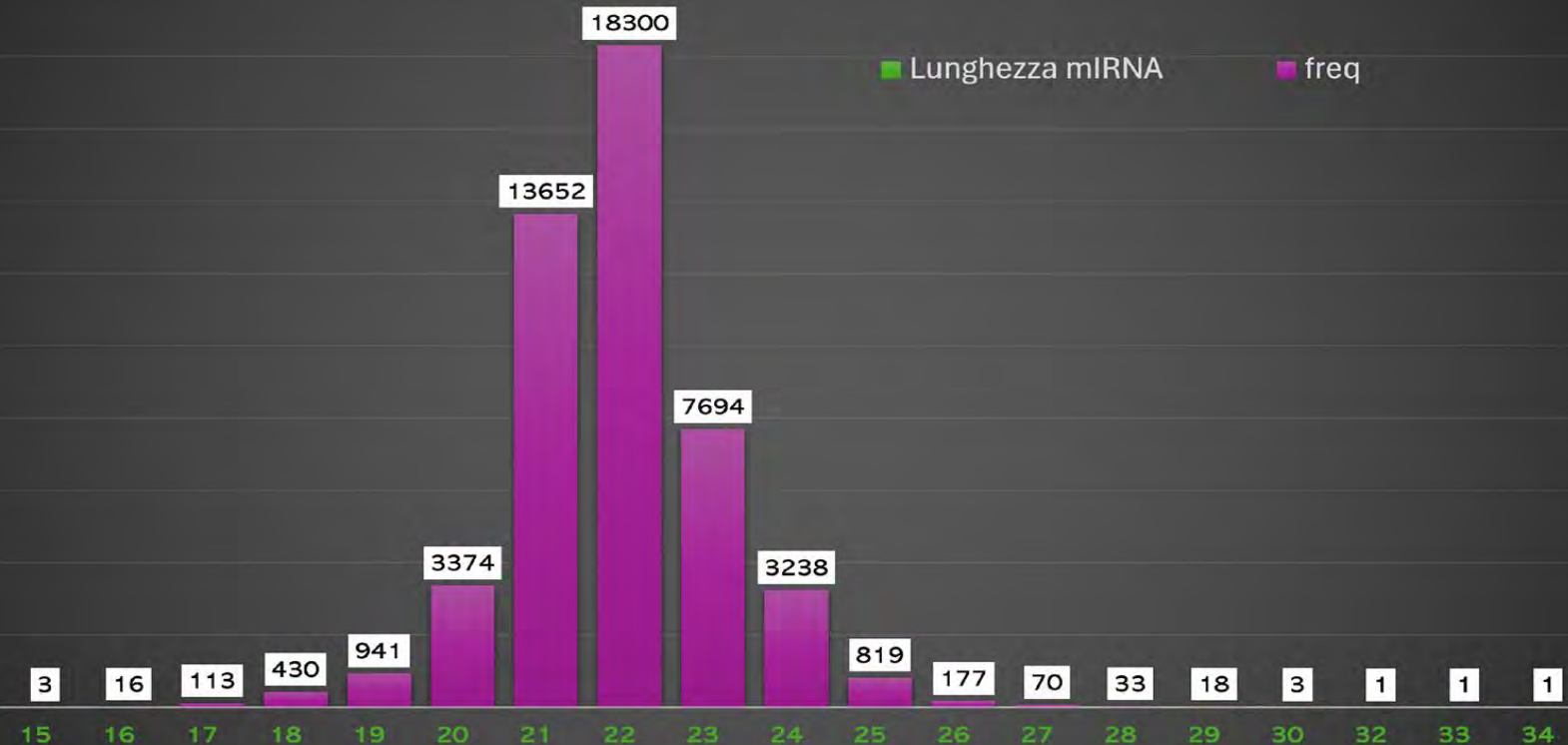
Istituto di Tecnologie Biomediche - Bari



microRNA caratteristiche : lunghezza dei geni e prodotti maturi

(mirbase release 22.1 analisi aprile 2024)

Lunghezza miRNA maturi (aprile 2024)

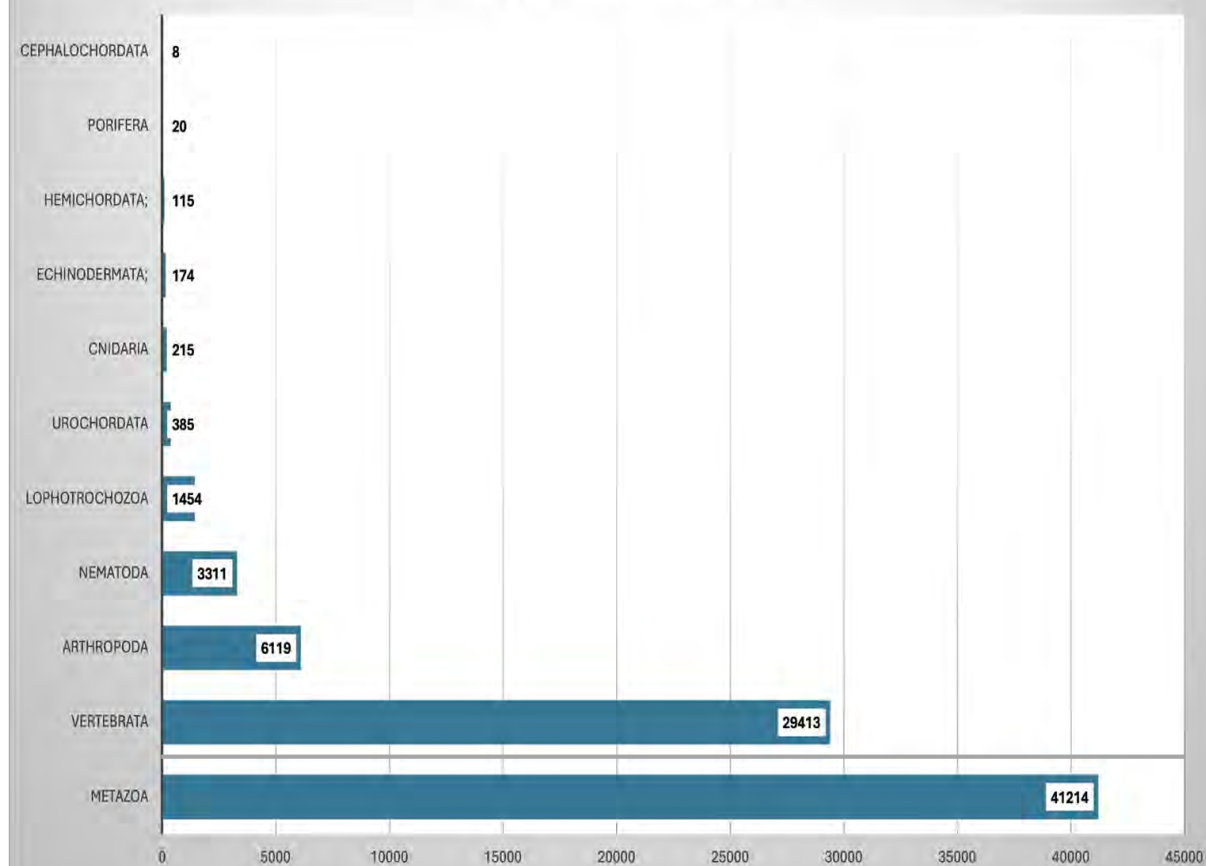


- I miRNA sono trascritti a partire da geni non codificanti per proteine dalle Polimerasi II e III
- Ubiquitari e conosciuti in quasi tutti gli organismi compresi i virus, con la sola eccezione dei batteri.
- I geni sono evolutivamente conservati nelle diverse specie e organizzati in famiglie
- Nei Metazoi la lunghezza del gene si attesta intorno alle 200bp mentre nelle piante essa può superare le 2000 bp
- Il miRNA maturo è una molecola di RNA a singolo filamento compresa 21-24 pb
- Nell'uomo si stima che più del 60% dei geni sono regolati da miRNA

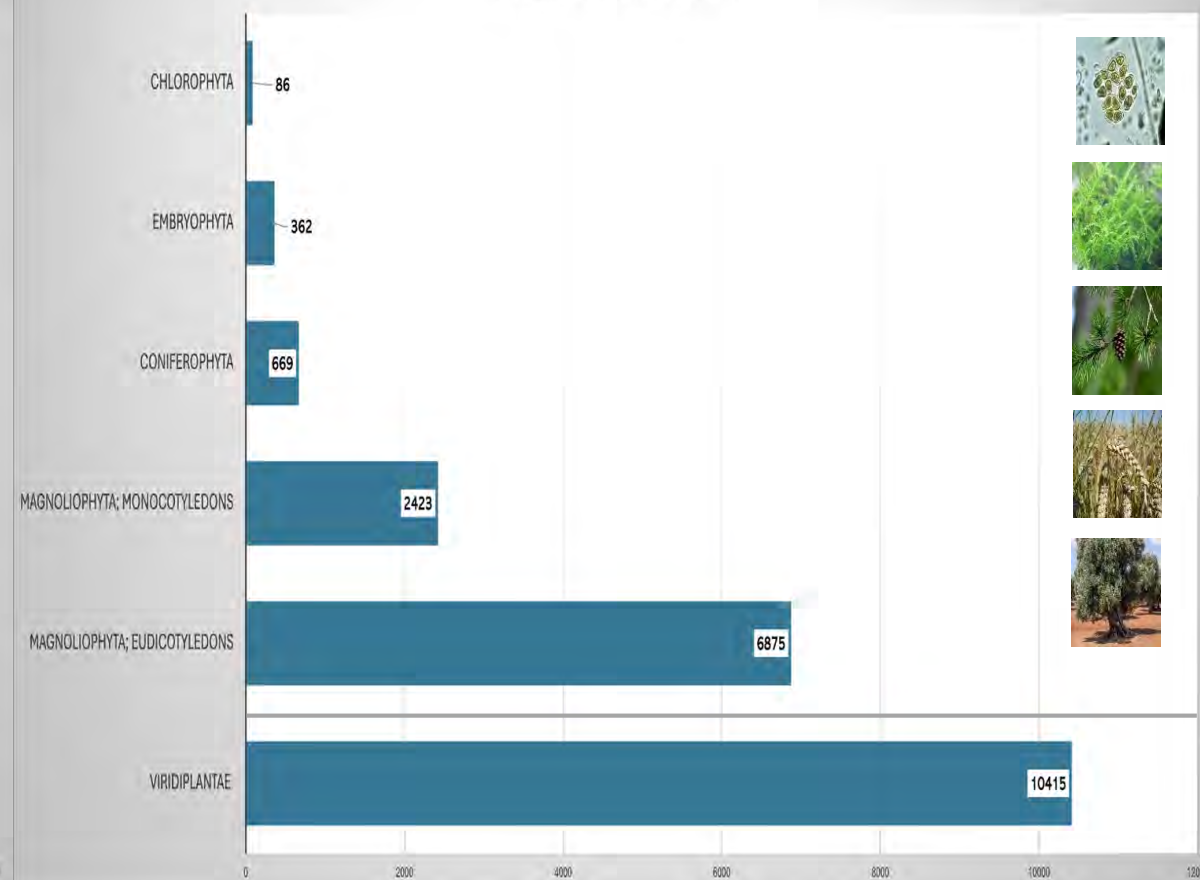


microRNA caratteristiche: distribuzione fra i regni

miRNA distribuzione: metazoi



miRNA distribuzione: viridiplantae



La regolazione genica cross-kingdom è un fatto o finzione ?



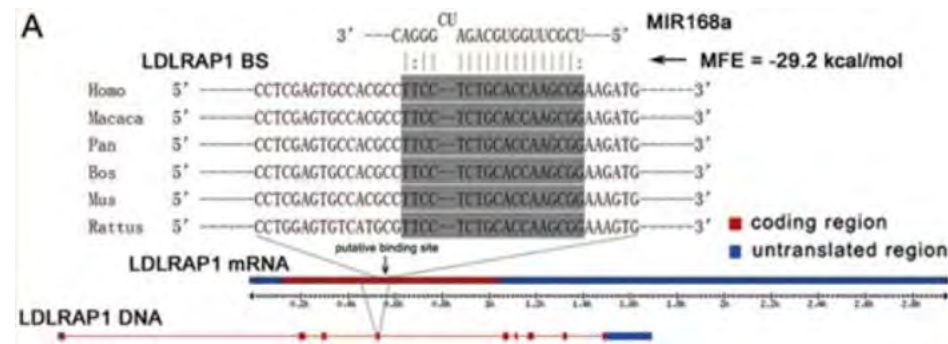
Cell Research (2012) 22:107-126.
 © 2012 IBCB, SIBS, CAS All rights reserved 1001-0602/12 \$ 32.00
www.nature.com/cr



ORIGINAL ARTICLE

Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA

Lin Zhang^{1*}, Dongxia Hou^{1*}, Xi Chen^{1*}, Donghai Li^{1*}, Lingyun Zhu^{1,2}, Yujing Zhang¹, Jing Li¹, Zhen Bian¹, Xiangying Liang¹, Xing Cai¹, Yuan Yin¹, Cheng Wang¹, Tianfu Zhang¹, Dihan Zhu¹, Dianmu Zhang¹, Jie Xu¹, Qun Chen¹, Yi Bai³, Jing Liu¹, Qiang Wang¹, Jianqun Chen¹, Jin Wang¹, Meng Wang¹, Qipeng Zhang¹, Junfeng Zhang¹, Ke Zen¹, Chen-Yu Zhang¹



Il mir-168a di Oriza sativa riconosce un sito target sull'esone 4 del gene LDLRAP1 (Recettore per le lipoproteine a bassa intensità) di mammifero.



Evidence for plant-derived xenomiRs based on a large-scale analysis of public small RNA sequencing data from human samples

Qi Zhao, Yuanling Liu, Ning Zhang, Menghan Hu, Hao Zhang, Trupti Joshi, Dong Xu

Published: June 27, 2018 • <https://doi.org/10.1371/journal.pone.0187519>

Home > Plant Foods for Human Nutrition > Article

Looking for Plant microRNAs in Human Blood Samples: Bioinformatics Evidence and Perspectives

Research | Open access | Published: 31 May 2023

Volume 78, pages 399–406, (2023) [Cite this article](#)



Article

Human Breast Milk microRNAs, Potential Players in the Regulation of Nervous System

Luis Freiria-Martínez^{1,2}, Marta Iglesias-Martínez-Almeida^{1,2}, Cynthia Rodríguez-Jamardo^{1,2}, Tania Rivera-Baltanás¹, María Comis-Tuche^{1,2}, Daniela Rodríguez-Amorim^{1,3}, Patricia Fernández-Palleiro¹, María Blanco-Formoso⁴, Yolanda Diz-Chaves⁵, Natalia González-Freiria⁶, María Suárez-Albo⁶, Montserrat Martín-Forero-Maestre⁷, Cristina Durán Fernández-Feijoo⁸, José Ramón Fernández-Lorenzo⁶, Ana Concheiro Guisán⁶, José Manuel Olivares^{1,9} and Carlos Spuch^{1,9,*}



The American Journal of Clinical Nutrition

Volume 117, Issue 6, June 2023, Pages 1195-1210



Original Research Article

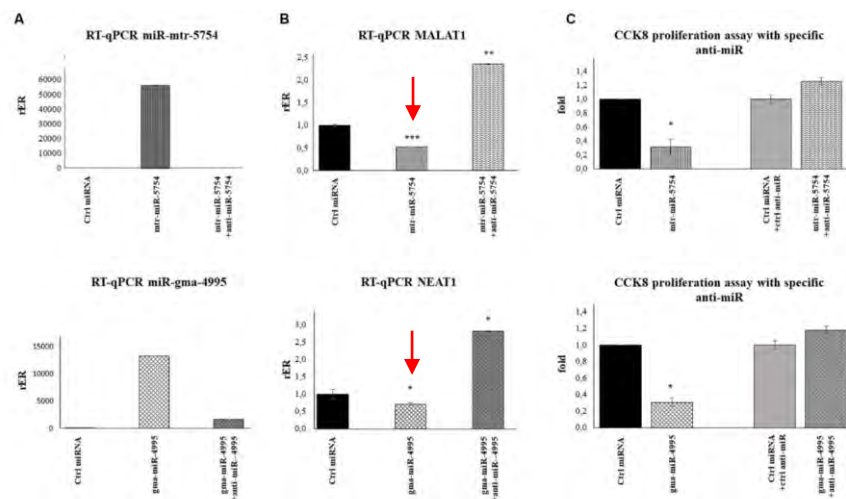
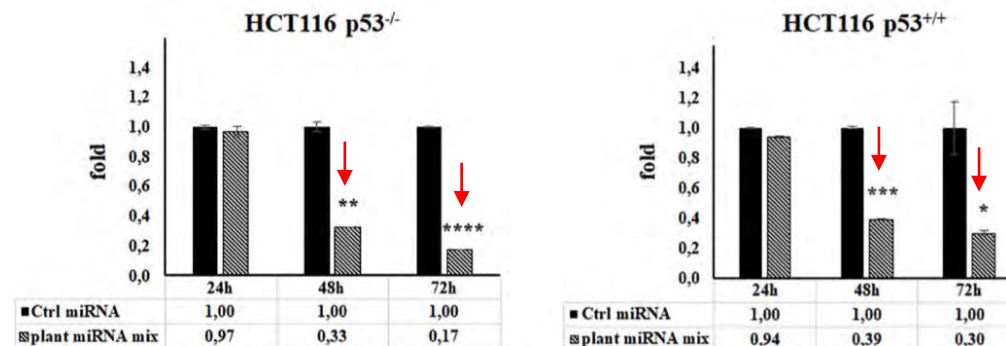
Uncovering the gastrointestinal passage, intestinal epithelial cellular uptake, and AGO2 loading of milk miRNAs in neonates using xenomiRs as tracers

La regolazione genica cross-kingdom è un fatto o finzione ?

> [Front Genet.](https://doi.org/10.3389/fgene.2020.552490) 2020 Sep 18;11:552490. doi: 10.3389/fgene.2020.552490. eCollection 2020.

Plant miRNAs Reduce Cancer Cell Proliferation by Targeting MALAT1 and NEAT1: A Beneficial Cross-Kingdom Interaction

Flaviana Marzano ¹, Mariano Francesco Caratozzolo ¹, Arianna Consiglio ², Flavio Licciulli ², Sabino Liuni ², Elisabetta Sbisà ², Domenica D'Elia ², Apollonia Tullo ¹, Domenico Catalano ²



miRNAs sono:

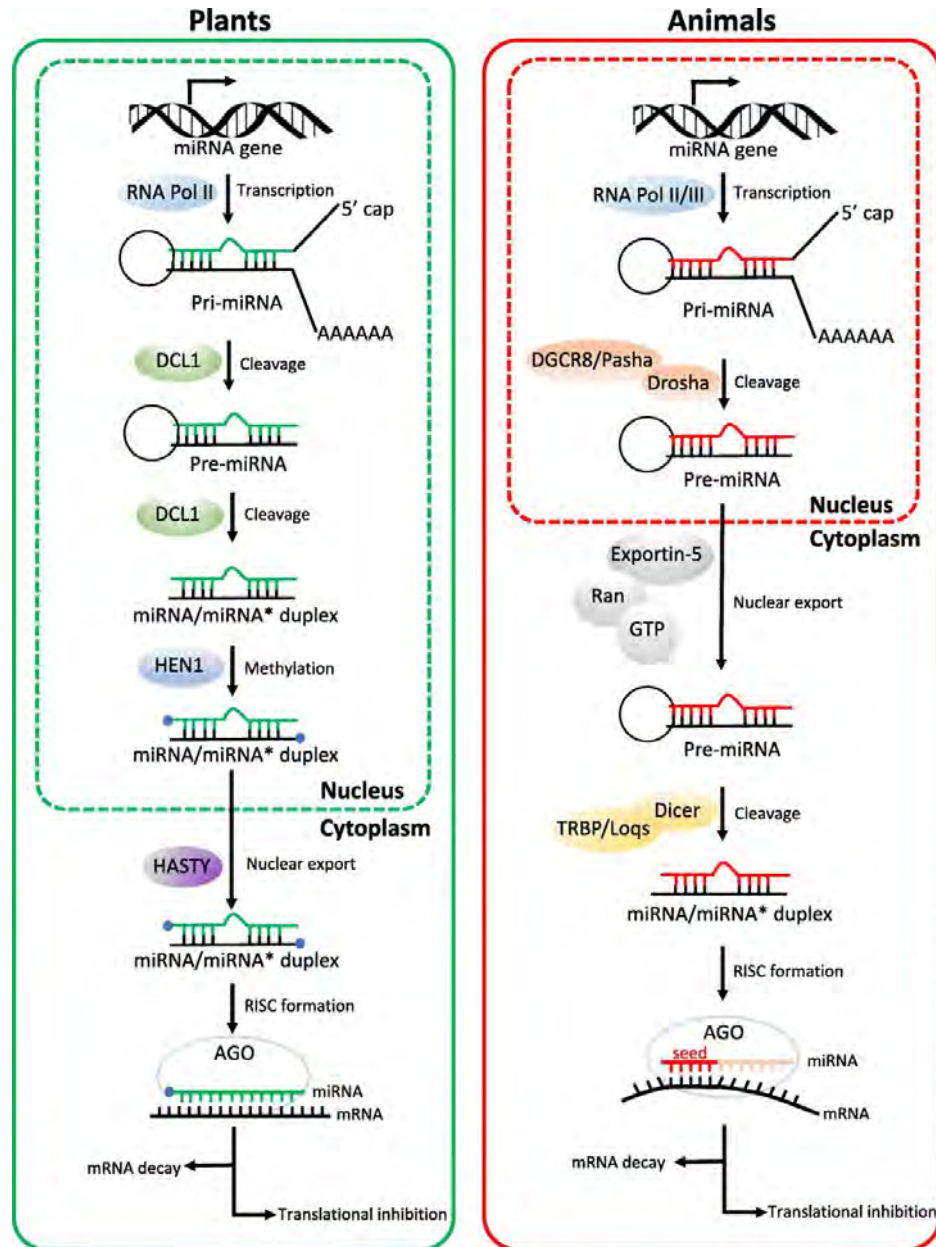
- ✓ Sono resistenti alla digestione nel tratto GI
- ✓ Sono ritrovati come molecole stabili nel siero umano
- ✓ Mostrano attività regolatoria dell'espressione genica di tipo cross-kingdom nell'uomo e in altri modelli animali
- ✓ Sono veicolati dalle micro vescicole
- ✓ Transfettati in linee cellulari di cancro al colon sono in grado di rallentare la proliferazione legando gli oncogeni NEAT1 e MALAT1 determinandone la down-regolazione



Biogenesi dei miRNA

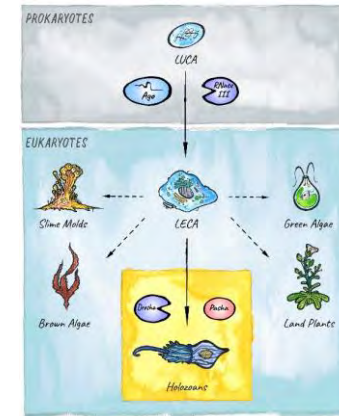
1. DCL1 = dicer like-1 (Ribonucleasi)
2. DCL1 = dicer like-1 (Ribonucleasi)

HEN1=Small RNA 2'-O-methyltransferase



DGCR8 = Microprocessor Complex Subunit + **Drosha**
Ribonucleasi III

DICER1 =
Ribonucleasi III



Philipp J. Dexheimer and Luisa Cochella
Front. Cell Dev. Biol., 03 June 2020 Sec. Stem Cell Research
Volume 8 - 2020

Li et al. Nutrition & Metabolism (2018) 15:68



“Differenze”

I miRNA **vegetali** possiedono un gruppo metile aggiunto al ribosio del primo nucleotide alla esermità 3'.

Tale modifica risulta essenziale per la resistenza alla degradazione nel tratto GI (Bin Yu 2010)

Artificially introduced 2-O-methyl groups in small interfering RNAs (siRNAs) can stabilize siRNAs in serum without affecting their activities in RNA interference in mammalian cells (Bin Yu,* et al. 11 FEBRUARY 2005 VOL 307 SCIENCE)

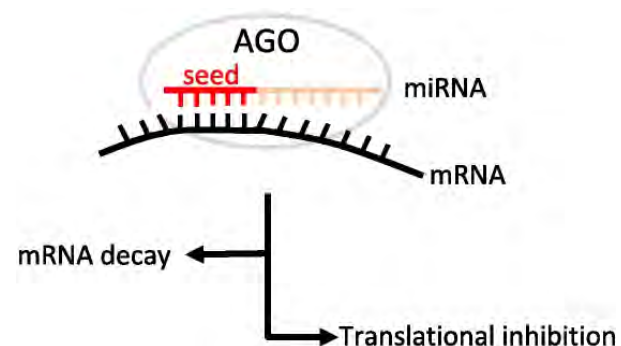
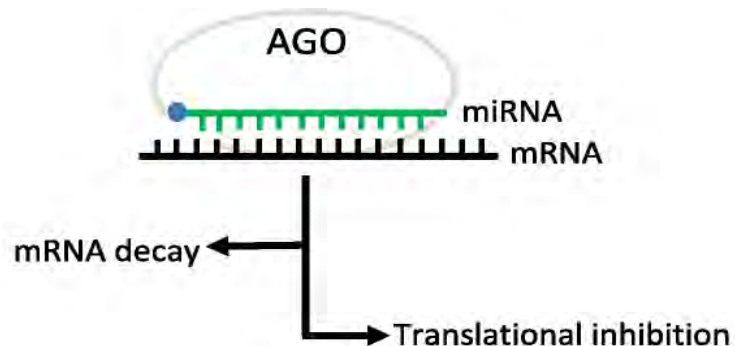
7mer-m8 site position 2-8 Brennecke et al 2005;

7mer-A1 site position 2-7 an A opposite position 1. Lewis et al 2005

6mer site position 2-7. Lewis et al 2005

Offset-6mers site position 3-8. Friedman et al 2009.

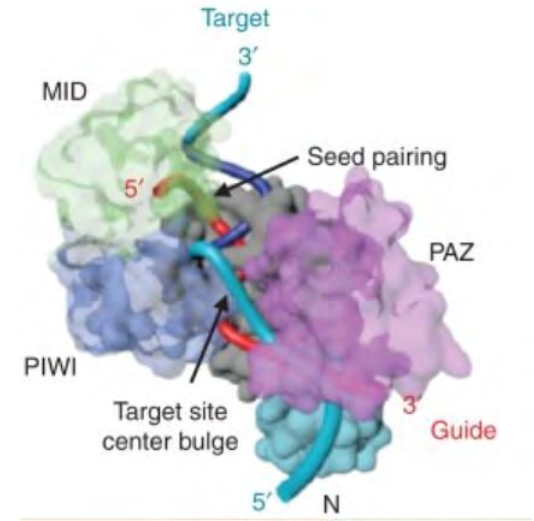
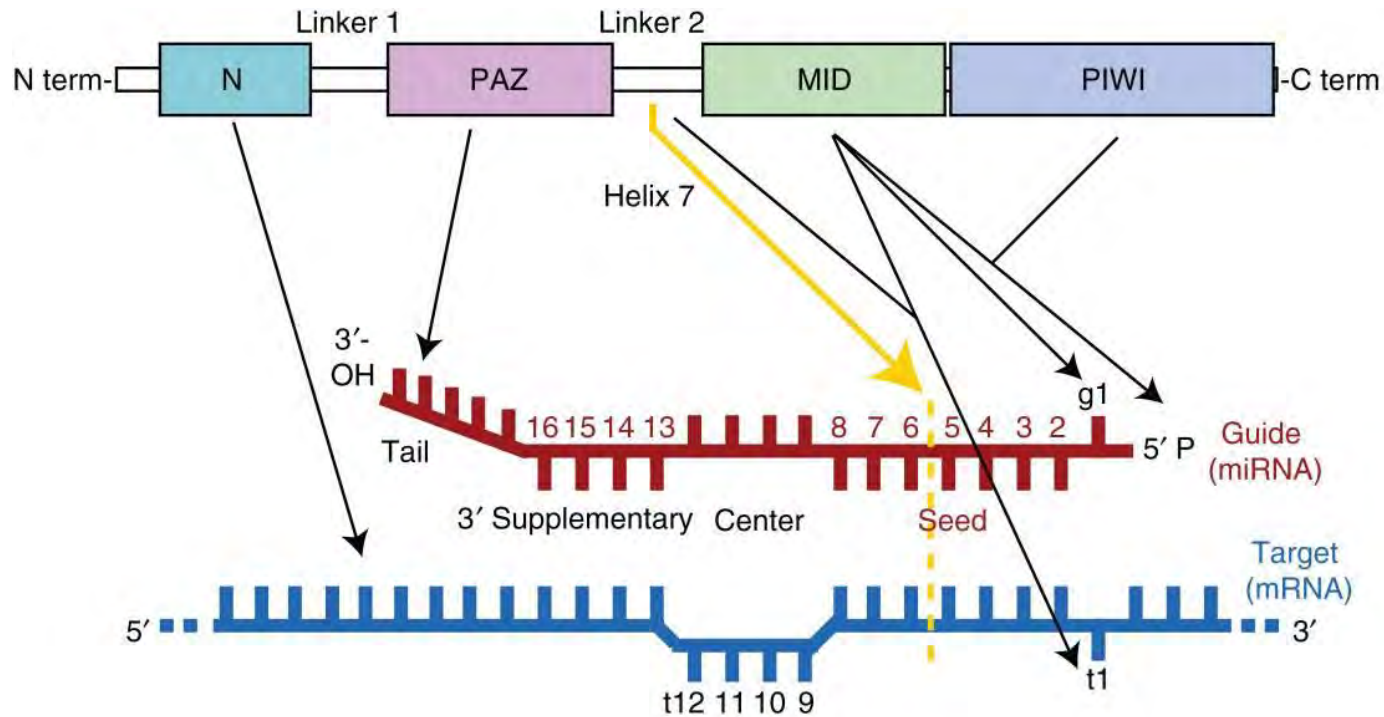
I miRNA **vegetali** legano i messaggeri riconoscendo siti target caratterizzati da match di complementarità perfetti o quasi perfetti.(Bin Yu 2010)



Nella maggior parte dei **metazoi**, il riconoscimento del target avviene attraverso una breve regione di 6-8 pb posta all'estremità 5' indicata come seed. E' emerso da dati strutturali, recentemente pubblicati, che appaiamenti in regioni site a valle dei seed, influenzano l'efficacia del legame dei miRNA al sito target.



Argonaute protein domain



- (g1) 5' anchor;
- (g2–g8 or shorter) 5' anchor;
- (g9–g12) the center;
- the 3' supplementary (g14–g16),
- and tail sequences (the 3'-most nucleotides)

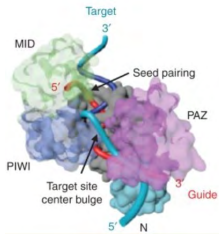
Cold Spring Harb Perspect Biol. 2019 Mar; 11(3): a032771. Thomas F. Duchaine



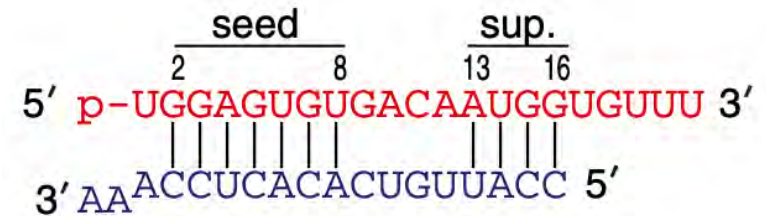
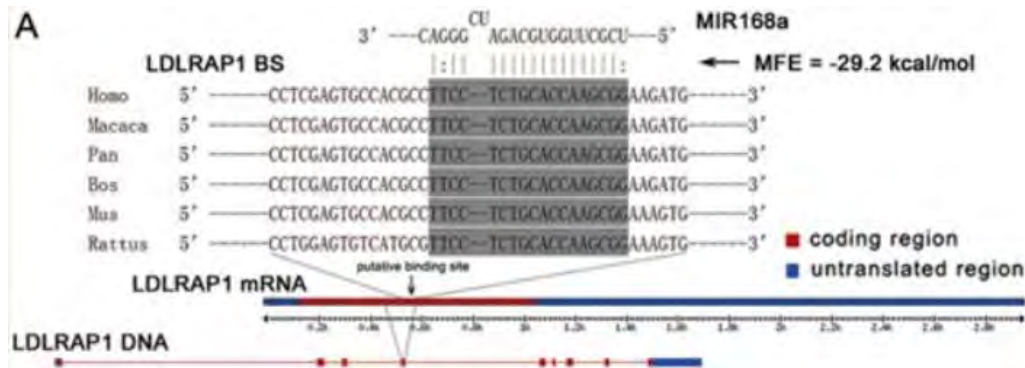


Ipotesi degli analoghi funzionali

E' possibile che i miRNA vegetali una volta entrati nelle cellule di mammifero vengano riconosciuti dal complesso RISC ed entrino in competizione legando gli stessi siti target riconosciuti dai miRNA endogeni ?

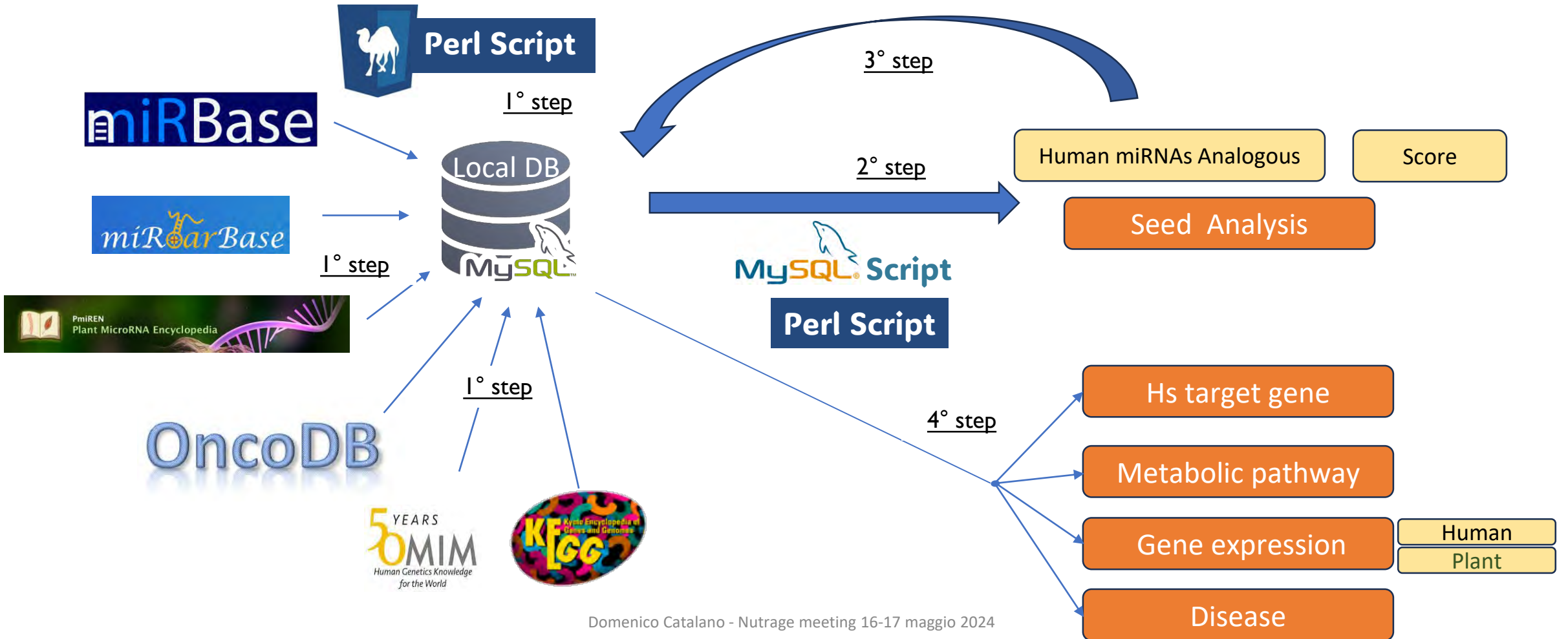
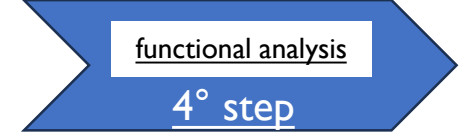
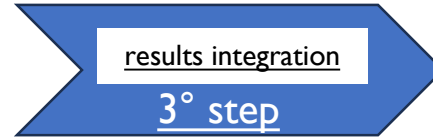
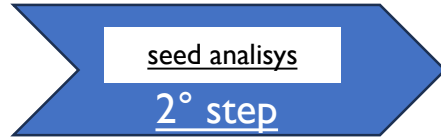


Thomas F. Duchaine (2019)





Architettura della Pipeline





E' un database che raccoglie le sequenze e annotazioni dei pre-mRNA e miRNA in tutte le specie studiate

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



E' un database di miRNA e dei rispettivi geni e sequenze target validati sperimentalmente.

<https://mirtarbase.cuhk.edu.cn/>



Contiene dati di espressione in diversi 8 differenti tessuti relativi a miRNA appartenenti a piante di interesse agricolo

<https://pmiren.com/>



OncoDB è un database che contiene dati di espressione che esplora pattern di espressione anormali correlati a caratteristiche cliniche di 37 tipi di Cancro

<https://oncodb.org/>



Database di geni e pathway metabolici

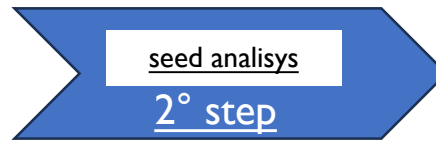
<https://www.kegg.jp/>



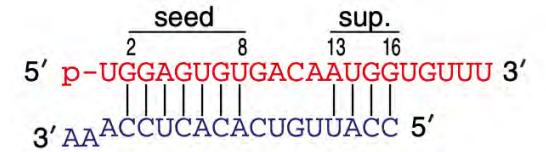
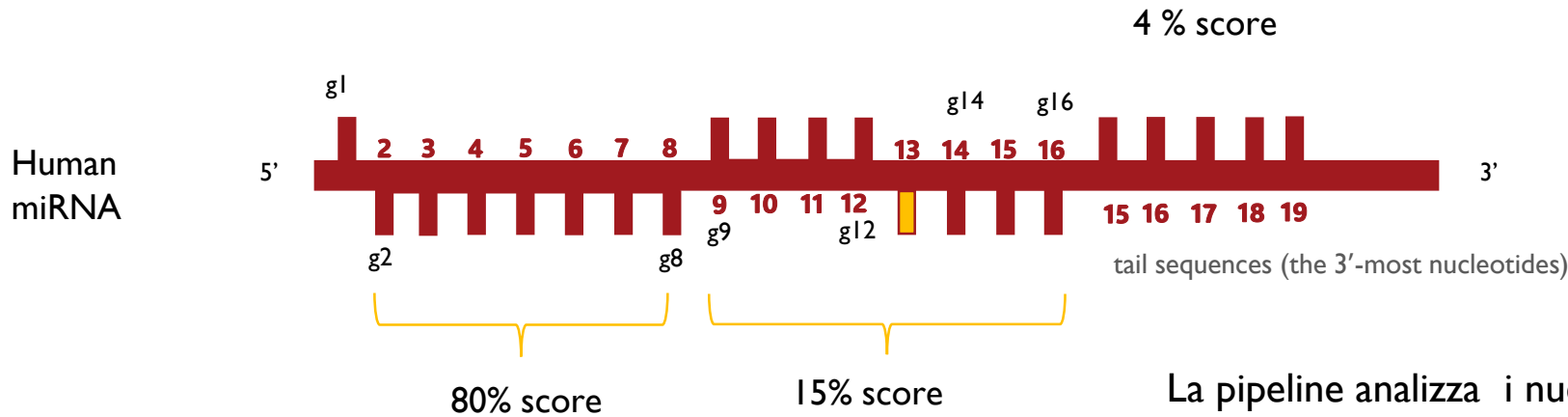
Database di geni e disturbi genetici e malattie ad eredità Mendeliana

<https://www.omim.org/>



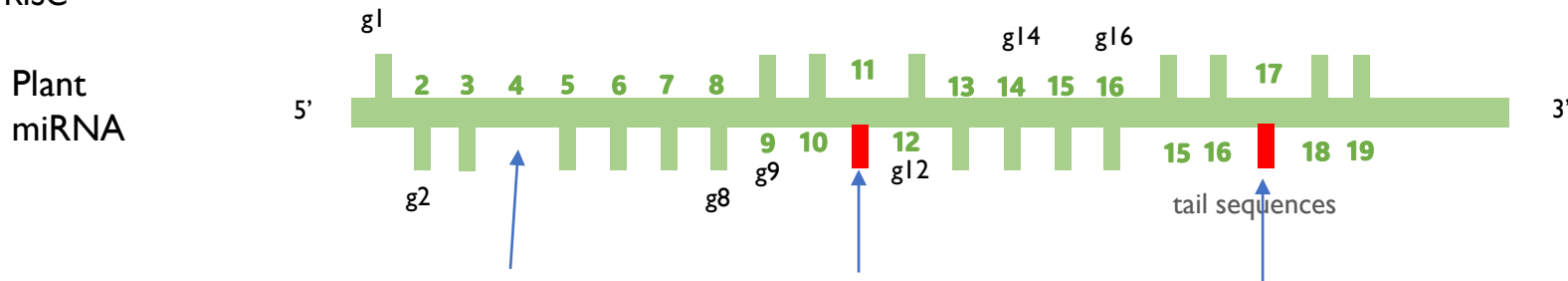


Individuazione degli analoghi



Match di sequenze fra miRNA e messaggero nelle posizioni g9-g12 sfavoriscono il legame al sito target. Match di sequenza nelle posizioni g13-g16 favoriscono la formazione del complesso RISC e posso compensare dei mismatch nella regione del seed. Lunghie code non appaiate al 3' sono preferite nella formazione del complesso RISC

La pipeline analizza i nucleotidi considerando le singole posizione e per ognuna restituisce uno score calcolato in base a quanto descritto in Thomas F. Duchaine et al 2019



Esempio di applicazione «Progetto Nutrage» specie: *Brassica rapa*



B. Rapa sono conosciuti 157 miRNA



la pipeline CroSeed ricerca gli analoghi funzionali nell'uomo (e topo/ratto) e fornisce uno score che è indicativo della analogia di sequenza

2879 miRNA



Homo sapiens

88 miRNA (score > 65) di Brassica Rapa potrebbero comportarsi come analoghi funzionali in uomo e....

...e per 39 miRNA è stato possibile ottenere i valori di espressione nei diversi tessuti

miRNA Brassica	Human_miRNA	Total_score	Seed_score	bridge_score	suppl Region score	Seed (pos 2-8)	Suppl. Match (pos 13-16)
bra-miR164a	hsa-miR-4516	83.7	80.0	0.0	2.3	GGAGAAG	G:::::
bra-miR9558-5p	hsa-miR-143-3p	76	68.6	0.0	4.8	GAGAUG:	CU:::::
bn-miR390a	hsa-miR-24-3p	74.7	68.6	0.0	4.7	:GCUCAG	G::G:::
bra-miR390-5p	hsa-miR-24-3p	74.7	68.6	0.0	4.7	:GCUCAG	G::G:::
bn-miR167a	hsa-miR-320c	73.5	68.6	0.0	3.7	:AAGCUG	:A:::::
bn-miR167a	hsa-miR-320b	72.3	68.6	0.0	2.5	:AAGCUG	:A:::::
bn-miR167a	hsa-miR-320d	72.3	68.6	0.0	2.5	:AAGCUG	:A:::::
bra-miR162-5p	hsa-miR-485-5p	70.6	57.2	0.0	9.7	GAGGC:G	U:AU::A
bra-miR156c-3p	hsa-miR-106b-3p	70.6	57.2	0.0	6.2	C:CACUG	::CU::C
bra-miR162-5p	hsa-let-7a-5p	65.8	57.2	1.2	6.0	GAGG:AG	U::U::A
bra-miR162-5p	hsa-let-7e-5p	65.8	57.2	1.2	6.0	GAGG:AG	U::U::A
bra-miR162-5p	hsa-let-7f-5p	65.8	57.2	1.2	6.0	GAGG:AG	U::U::A
bra-miR162-5p	hsa-let-7g-5p	65.8	57.2	2.4	6.0	GAGG:AG	U::U::A
bra-miR162-5p	hsa-miR-124-3p	65.8	57.2	1.2	6.0	:AGGCA:	U:A::G:



RPM= reads X milion

miRNA	Leaf	Inflorescence	Ovule	Endosperm	Embryo	Petal	Pollen	Seeding	mature_seq
Bra-MIR390a	246.245225844052	27.764075731532	93.2184055792227	81.3975413936762	126.841270937144	1630.96323170515	22.2178849265473	13.8043185813639	AAGCUCAGGAGGGGAUAGCGCC
Bra-MIR156c	80.9719525957431	1944.44383744793	18.3649327471587	1498.29778698085	2729.59820023548	72.805273091249	175.753752607689	1719.30964011185	UGACAGAAGAGAGUGAGCAC
Bra-MIR164a	57.2075111261265	7.04731643638707	9.82763072469925	1.64356714658525	1.18612162397608	136.88136183552	1.73781710063275	121.206356136103	UGGAGAAGCAGGCCACGUGCA
Bra-MIR167a	19.2477658212013	184.515814141569	480.852649492716	107.339323295036	110.597805088841	61.6399870480734	95.7437226823105	126.323782997305	UGAAGCUGCCAGCAUGAUCUA
Bra-MIR162c*	6.27692970750017	4.44291242275848	0.448899138107042	2.13484723305029	2.39346435370175	12.2930919965304	0.236796241570054	2.23247753776802	GGAGGCAGCGGUUCAUCGAUC
Bra-MIR162b*	0.196841249107325	2.53788691310094	0	0	0.136950056505593	0.184111984736081	0	0.398419933007351	GGAGGCAGCGGUUCAUCGAUC
Bra-MIR9558*	0.196841249107325	1.13193984230379	1.53932963551811	2.41923918189803	3.10994988881119	0.610817954670177	0.236796241570054	0	UGCAAGCCAGACAUUCCUUU
Bra-MIR156c*	0	4.02896498920026	0	3.11615272269038	9.70838159244011	2.22047814562479	2.27437722284674	1.36503108903571	CUCACUGCUCUAUCUGUCAGA



functional analysis

4° step

Individuazione dei geni target



NUTRAGE
Consiglio Nazionale delle Ricerche

Croseed individua 181
geni, **potenziali target** oggetto della
regolazione di tipo
cross-Kingdom,
effettuata dai miRNA
espressi nelle parti
edibili di Brassica
rapa

Brassica miRNA	human miRNA	TargetGene	Target_site	Experiment	Experiment
VARCHAR	VARCHAR	VARCHAR	LONGTEXT	VARCHAR	LONGTEXT
bra-miR9558-5p	hsa-miR-143-3p	FNDC3B	ACCCAAAAACCATAATCATCTCT	19472311	Luciferase reporter assay//qRT-PCR//Western blot
bra-miR162-5p	hsa-let-7a-5p	TRIM71	GAAGTGATAATTTCTATCTACCTCA	17890240	Luciferase reporter assay
bna-miR390a	hsa-miR-24-3p	ACVR1B	CTCTCACAGGCAGCTCTGAGCCG	17906079	Western blot//Luciferase reporter assay
bra-miR390-5p	hsa-miR-24-3p	ACVR1B	CTCTCACAGGCAGCTCTGAGCCG	17906079	Western blot//Luciferase reporter assay
bra-miR162-5p	hsa-let-7g-5p	HMGA2	CCAACGTTCCGATTCTACCTCA	17600087	Luciferase reporter assay//Western blot//qRT-PCR
bra-miR162-5p	hsa-let-7a-5p	PRDM1	TGTCAACAACAGTTACCTCA	18583325	Luciferase reporter assay
bra-miR162-5p	hsa-let-7a-5p	PRDM1	TGTTCAACAACAGTTACCTCA	20651244	Immunohistochemistry//Luciferase reporter assay//qRT-PCR//Western blot
bna-miR390a	hsa-miR-24-3p	MAPK14	CTGCTGAAGTTCTGAGCC	15131085	Luciferase reporter assay
bra-miR390-5p	hsa-miR-24-3p	MAPK14	CTGCTGAAGTTCTGAGCC	15131085	Luciferase reporter assay
bra-miR162-5p	hsa-miR-124-3p	RELA	GTGCCT	15685193	Luciferase reporter assay//Microarray
bra-miR162-5p	hsa-miR-124-3p	CDK6	TTTCATACCATCTCTGCCTTAT	17308079	Immunohistochemistry//Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bra-miR162-5p	hsa-miR-124-3p	CDK6	ATTTCCATACCATCTCTGCCTTAT	18607543	Luciferase reporter assay//Western blot
bra-miR162-5p	hsa-miR-124-3p	SLC16A1	TAAAGATTATAATATGTCCTTAAG	19427019	Luciferase reporter assay//Western blot
bra-miR9558-5p	hsa-miR-143-3p	MAPK7	TGGATTATTCTGCAGGTTCACTCA	19464056	Luciferase reporter assay
bra-miR9558-5p	hsa-miR-143-3p	MAPK7	ATTATTCTGCAGGTTCACTCAGA	19855844	Luciferase reporter assay//Western blot
bra-miR9558-5p	hsa-miR-143-3p	MAPK7	AGTTACTCTGCAGGTTCACTCA	22374674	Luciferase reporter assay//qRT-PCR//Western blot
bra-miR162-5p	hsa-let-7a-5p	DICER1	TGCACTGTAATAATAACCTCT	18700235	Luciferase reporter assay//Western blot//Northern blot
bra-miR9558-5p	hsa-miR-143-3p	DNMT3A	GGGCTTTGCCTTGCAGAAAGGGTTGGACATCATCTC	19638978	qRT-PCR//Luciferase reporter assay//Western blot
bra-miR162-5p	hsa-let-7e-5p	SMC1A	CAACCTTCCCCTACCTC	15131085	Luciferase reporter assay
bra-miR9558-5p	hsa-miR-143-3p	KRAS	TGTTAAAGAAGTCATCTCAA	19137007	qRT-PCR//Luciferase reporter assay//Microarray
bra-miR162-5p	hsa-let-7g-5p	BCL2L1	AGCCCCAGGGTCTCCCTACCTCA	20347499	Luciferase reporter assay//qRT-PCR//Western blot
bra-miR162-5p	hsa-let-7a-5p	NKIRAS2	TCCTCTGGCCCTCCTTCTTACCTCAGA	20351193	ELISA//qRT-PCR//Luciferase reporter assay//Western blot
bra-miR162-5p	hsa-miR-124-3p	ELK3	AACCAGTTGTGCCTTC	20144220	Luciferase reporter assay
bra-miR162-5p	hsa-let-7a-5p	AGO4	GATGCACTGGACTGAATTTTACCTCAA	20144220	Luciferase reporter assay
bna-miR390a	hsa-miR-24-3p	HNF4A	CCTGTCAATGTTCCAGACAGAGCCCT	20018894	Luciferase reporter assay//qRT-PCR//Western blot
bra-miR390-5p	hsa-miR-24-3p	HNF4A	CCTGTCAATGTTCCAGACAGAGCCCT	20018894	Luciferase reporter assay//qRT-PCR//Western blot
bra-miR162-5p	hsa-let-7a-5p	LIN28A	GAGTGCACAGCCATATTGAACCTACCTCA	16495412	B-globin reporter assay//Luciferase reporter assay//Microarray
bra-miR162-5p	hsa-let-7e-5p	HMGA2	ACGTTCCGATTCTACCTCA	17437991	Luciferase reporter assay//qRT-PCR
bna-miR390a	hsa-miR-24-3p	MYC	TGTTTCTCTGTAATATTGCCA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bra-miR390-5p	hsa-miR-24-3p	MYC	TGTTTCTCTGTAATATTGCCA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bna-miR390a	hsa-miR-24-3p	MYC	TGGCAAATATATCATTGAGCCAA	26159387	Immunohistochemistry//In situ hybridization//Luciferase reporter assay//qRT-PCR//Western blot
bra-miR390-5p	hsa-miR-24-3p	MYC	TGGCAAATATATCATTGAGCCAA	26159387	Immunohistochemistry//In situ hybridization//Luciferase reporter assay//qRT-PCR//Western blot
bna-miR390a	hsa-miR-24-3p	E2F2	GTGGGTGCTCTGGGCTGAACCA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bra-miR390-5p	hsa-miR-24-3p	E2F2	GTGGGTGCTCTGGGCTGAACCA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bna-miR390a	hsa-miR-24-3p	AURKB	CGTGTGTTTGTATGTCTGTGTA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bra-miR390-5p	hsa-miR-24-3p	AURKB	CGTGTGTTTGTATGTCTGTGTA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bna-miR390a	hsa-miR-24-3p	BRCA1	AGGTGGAGTTGCAGTGAGCCA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot
bra-miR390-5p	hsa-miR-24-3p	BRCA1	AGGTGGAGTTGCAGTGAGCCA	19748357	Luciferase reporter assay//Microarray//qRT-PCR//Western blot

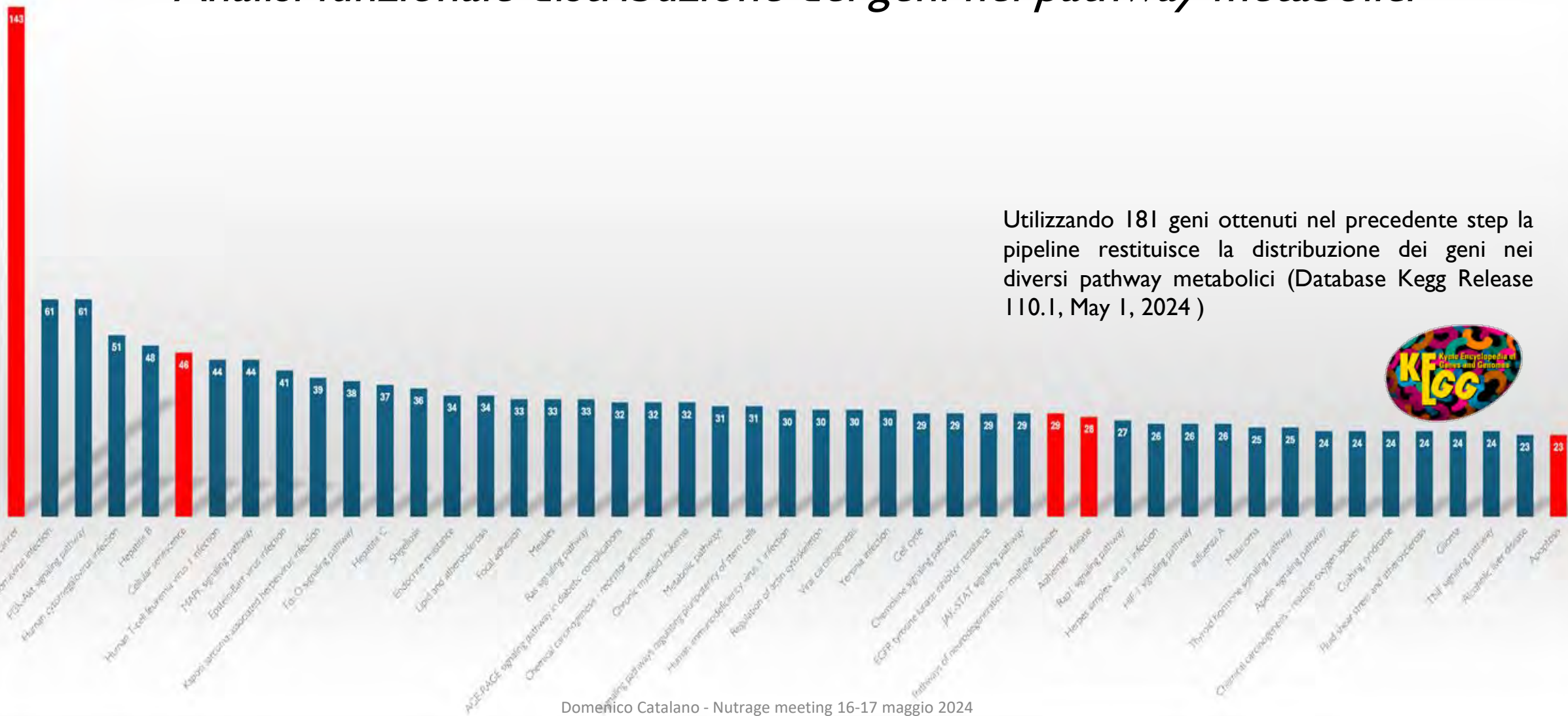
miRearBase

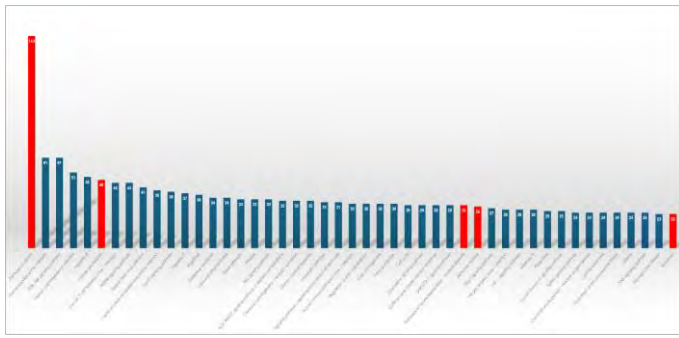




Analisi funzionale distribuzione dei geni nei pathway metabolici

Utilizzando 181 geni ottenuti nel precedente step la pipeline restituisce la distribuzione dei geni nei diversi pathway metabolici (Database Kegg Release 110.1, May 1, 2024)





functional analysis
4° step



Selezione dei Geni Up Regolati

Interrogando il database OncoDb si ottengono 116 geni risultati up regolati in diversi forme di cancro e quindi potenziali target per la validazione in sistemi in vitro o in vivo

Cancer	Gene	FDR_adjusted_pvalue	log2_fod_change	pvalue
Colon adenocarcinoma	TP53	0.00000000000000000666	0.7370679340120960000000	0.00000000000000005913
Glioblastoma multiforme	TP53	0.0000000000000010163000	2.5262468392470000000000	0.0000000000000214981473
Kidney renal papillary cell carcinoma	TP53	0.00000000000009958700000	0.7786401435017190000000	0.0000000000082630611744
Liver hepatocellular carcinoma	TP53	0.000000000000026967000	0.5335685594118400000000	0.000000000000077468978
Lung adenocarcinoma	TP53	0.000000000000000000100	0.57993491944496020000000	0.000000000000000000549
Lung squamous cell carcinoma	TP53	0.000000000000000000100	0.6791824072041750000000	0.000000000000000000481
Rectum adenocarcinoma	TP53	0.0000078520000000000000	0.7912535571198390000000	0.0000535831410588671000
Uterine Corpus Endometrial Carcinoma	TP53	0.0000000010902000000000	0.5349135630431890000000	0.000000007657285106383
Bladder Urothelial Carcinoma	TP63	0.0006165500000000000000	1.6535627756699800000000	0.0023346479253472200000
Head and Neck squamous cell carcinoma	TP63	0.0000000010902000000000	1.2395238197649700000000	0.000000000000000000939
Lung squamous cell carcinoma	TP63	0.000000000000000000100	5.6383900523567400000000	0.000000000000000000481
Cholangiocarcinoma	VEGFA	0.0000084355000000000000	1.6479042488363400000000	0.0000186564493319144000
Colon adenocarcinoma	VEGFA	0.000000000000000000100	1.4557941892750700000000	0.000000000000000000946
Glioblastoma multiforme	VEGFA	0.0000000000000000009603	2.6678425656294500000000	0.000000000000000270255
Head and Neck squamous cell carcinoma	VEGFA	0.000000000000000000100	1.1614158220823000000000	0.000000000000000000939
Kidney Chromophobe	VEGFA	0.0000000740990000000000	0.8198918579336070000000	0.000000000000000000000
Kidney renal clear cell carcinoma	VEGFA	0.000000000000000000100	3.3092107120761500000000	0.000000000000000000000
Liver hepatocellular carcinoma	VEGFA	0.0000000000000012148000	0.6256735847205250000000	0.000000000000000000000
Rectum adenocarcinoma	VEGFA	0.000000000007172600000	1.7636693069642900000000	0.000000000000000000000

La pipeline fornisce informazioni anche sulla metilazione all'interno della regione genica e del promotore (OncoDb release 1.0 August, 2021)

'FDR_adjusted_pValue' < 0.05 and 'log2_fod_change' > 0.5 and pValue < 0.05

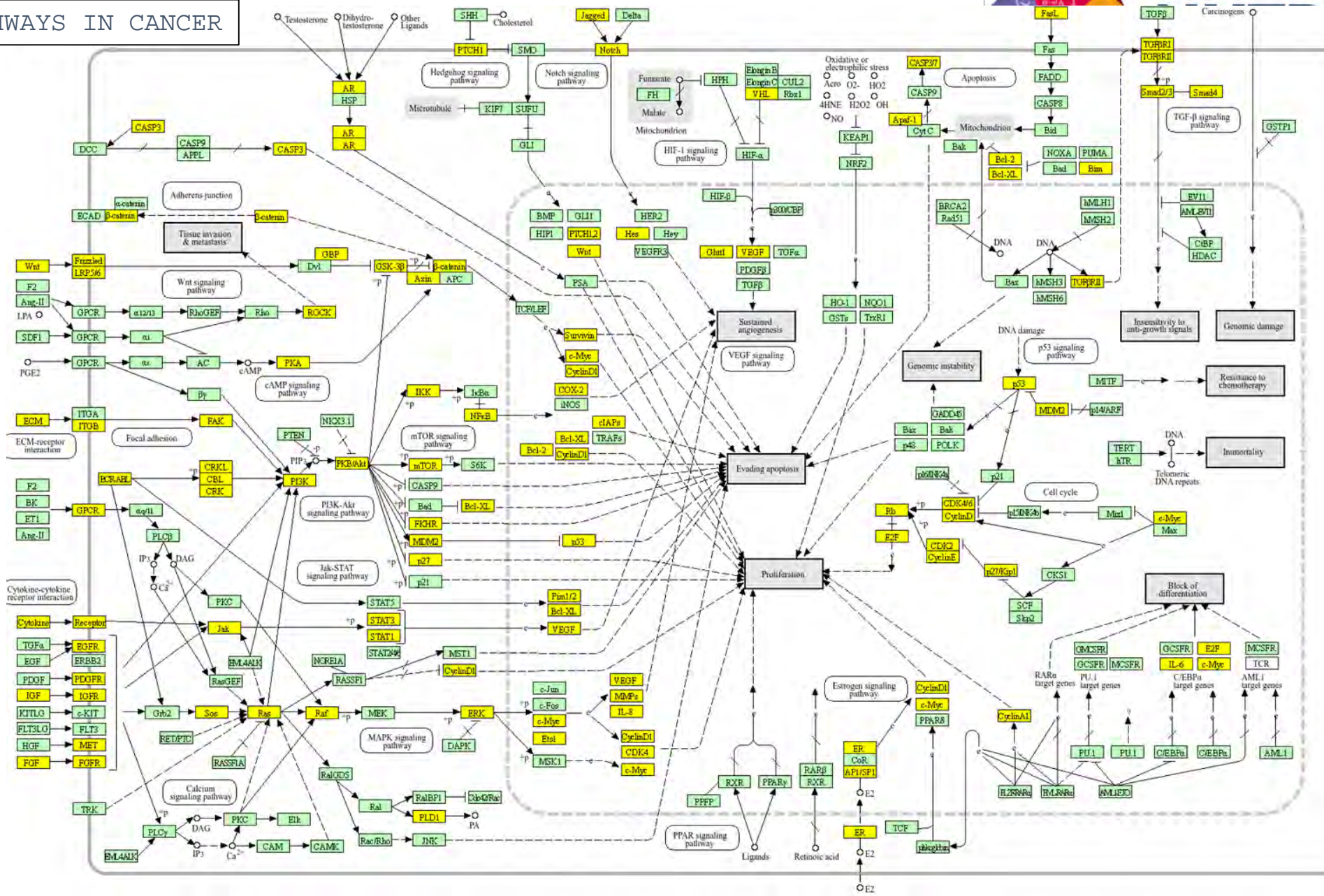
Gene	FDR_adjusted_pvalue	pVALUE	Beta_Differenca_value	Cancer_Sample_Median	Normal_Sample_Median
TP53	0.0000462770000000000000	0.000112546250713154000	0.0750000000000000000000	0.2250000000000000000000	0.1500000000000000000000
TP53	0.0075940000000000000000	0.0148917638286201010000	0.0550000000000000000000	0.2280000000000000000000	0.1730000000000000000000
TP53	0.0000000004032900000000	0.000000000794737822960	0.1290000000000000000000	0.2180000000000000000000	0.0890000000000000000000
TP53	0.0002598800000000000000	0.0010559890617829000000	0.0230000000000000000000	0.2090000000000000000000	0.2320000000000000000000
TP53	0.0000000251420000000000	0.0000000726667813871817	0.0860000000000000000000	0.1660000000000000000000	0.0800000000000000000000
TP53	0.0000000000004150400000	0.000000000000652983785	0.1270000000000000000000	0.1650000000000000000000	0.0380000000000000000000
TP53	0.0076390000000000000000	0.0200129554986339000000	0.0370000000000000000000	0.2360000000000000000000	0.1990000000000000000000
TP53	0.0000000020242000000000	0.0000000064074614686469	0.1270000000000000000000	0.2270000000000000000000	0.1000000000000000000000
TP53	0.0000000897740000000000	0.000002446150220170450	0.1220000000000000000000	0.2320000000000000000000	0.1100000000000000000000
TP53	0.0000106270000000000000	0.0000157192464336204000	0.0380000000000000000000	0.1870000000000000000000	0.2250000000000000000000
TP53	0.0019604000000000000000	0.0051285882032049100000	0.0370000000000000000000	0.2400000000000000000000	0.2030000000000000000000
TP63	0.000000000000000000100	0.0000000000000000002835	0.3410000000000000000000	0.5510000000000000000000	0.8920000000000000000000
TP63	0.0000000167690000000000	0.000000055620405043228	0.4510000000000000000000	0.8050000000000000000000	0.3540000000000000000000
TP63	0.0000585710000000000000	0.000072264879080238000	0.3590000000000000000000	0.7610000000000000000000	0.4020000000000000000000
TP63	0.0000249890000000000000	0.0000414665886080507000	0.2270000000000000000000	0.5150000000000000000000	0.2880000000000000000000
TP63	0.0000000182540000000000	0.000000052061569322265	0.1890000000000000000000	0.6440000000000000000000	0.8330000000000000000000
TP63	0.0047890000000000000000	0.0116387450401010000000	0.2130000000000000000000	0.8320000000000000000000	0.6190000000000000000000
TP63	0.0000000218400000000000	0.0000031692721460573500	0.2970000000000000000000	0.8420000000000000000000	0.5450000000000000000000
TP63	0.0000000004623700000000	0.00000000000879683860650	0.3940000000000000000000	0.6680000000000000000000	0.2740000000000000000000
TP63	0.0011616000000000000000	0.0047062957233368500000	0.1410000000000000000000	0.8850000000000000000000	0.7440000000000000000000
TP63	0.0026103000000000000000	0.0219453965303141000000	0.0399999999999999999999	0.7940000000000000000000	0.8340000000000000000000
TP63	0.0000000000000227870000	0.0000000000000386510908	0.4320000000000000000000	0.5580000000000000000000	0.1260000000000000000000
VEGFA	0.00000000000000036221000	0.00000000000000087178084	0.2410000000000000000000	0.3080000000000000000000	0.0670000000000000000000
VEGFA	0.0202070000000000000000	0.1897002173735730000000	0.1010000000000000000000	0.4040000000000000000000	0.3030000000000000000000
VEGFA	0.0025280000000000000000	0.0100852368083261000000	0.0710000000000000000000	0.4050000000000000000000	0.3340000000000000000000





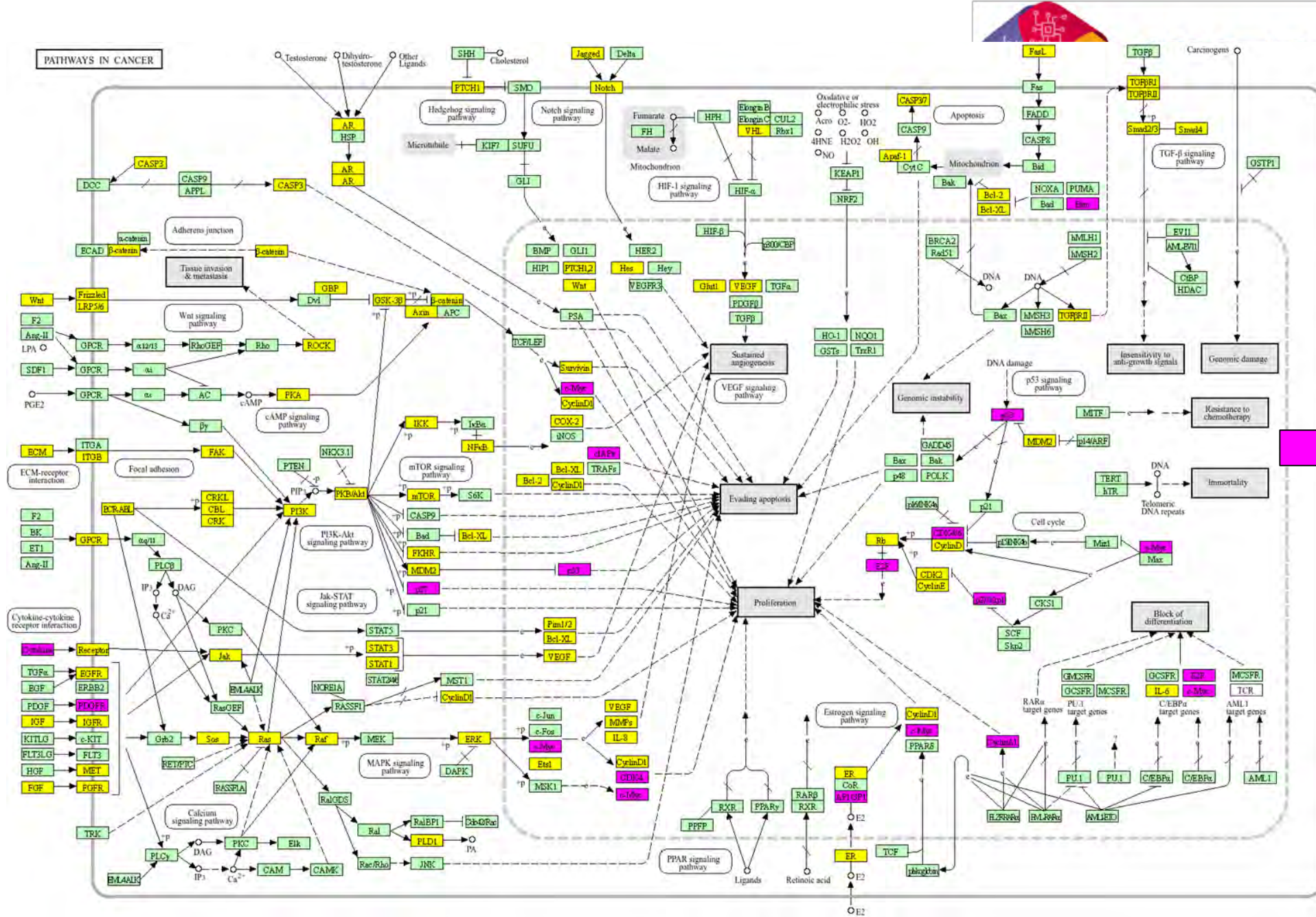
PATHWAYS IN CANCER

In giallo sono mostrati geni up regolati in diverse forme di cancro e potenziali target da parte dei miRNA di *Brassica rapa*





In magenta sono mostrati geni up regolati in diverse forme di cancro e potenziali target del mir390 di *Brassica rapa*



Bra-miR390

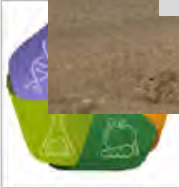
Conclusioni

- Croseed è una pipeline sviluppata per la ricerca in piante di interesse agronomico di miRNA vegetali con attività nutraceutica
- Croseed analizza nei miRNA vegetali caratteristiche di sequenza e conformazionali che le rendano compatibili ad essere riconosciute dal complesso RISC umano e quindi riconoscere le sequenze target presenti sui messaggeri umani.
- L'analisi svolta mediante la pipeline Croseed parte dal presupposto che i miRNA vegetali entrino in competizione con gli stessi siti target presenti sui messaggeri e riconosciuti dai miRNA endogeni
- *In Brassica rapa* la pipeline Croseed ci ha permesso di individuare **81 miRNA** analoghi funzionali
- Dall'analisi in miRTarbase risulta che i geni potenzialmente regolati dai miRNA di Brassica sono **181** coinvolti in stati patologici associati al cancro, senescenza o malattie neurodegenerative.
- Da un'analisi in OncoDB molti dei geni selezionati risultano **upregolati** in diverse forme tumorali.
- Appare chiaro che sarebbe interessante effettuare test in vitro e in vivo su alcuni miRNA di brassica (es miR390) che è risultato essere espresso nelle parti edibili della pianta e in grado di regolare importanti oncogeni come **TP53, TP63 e BCL2**





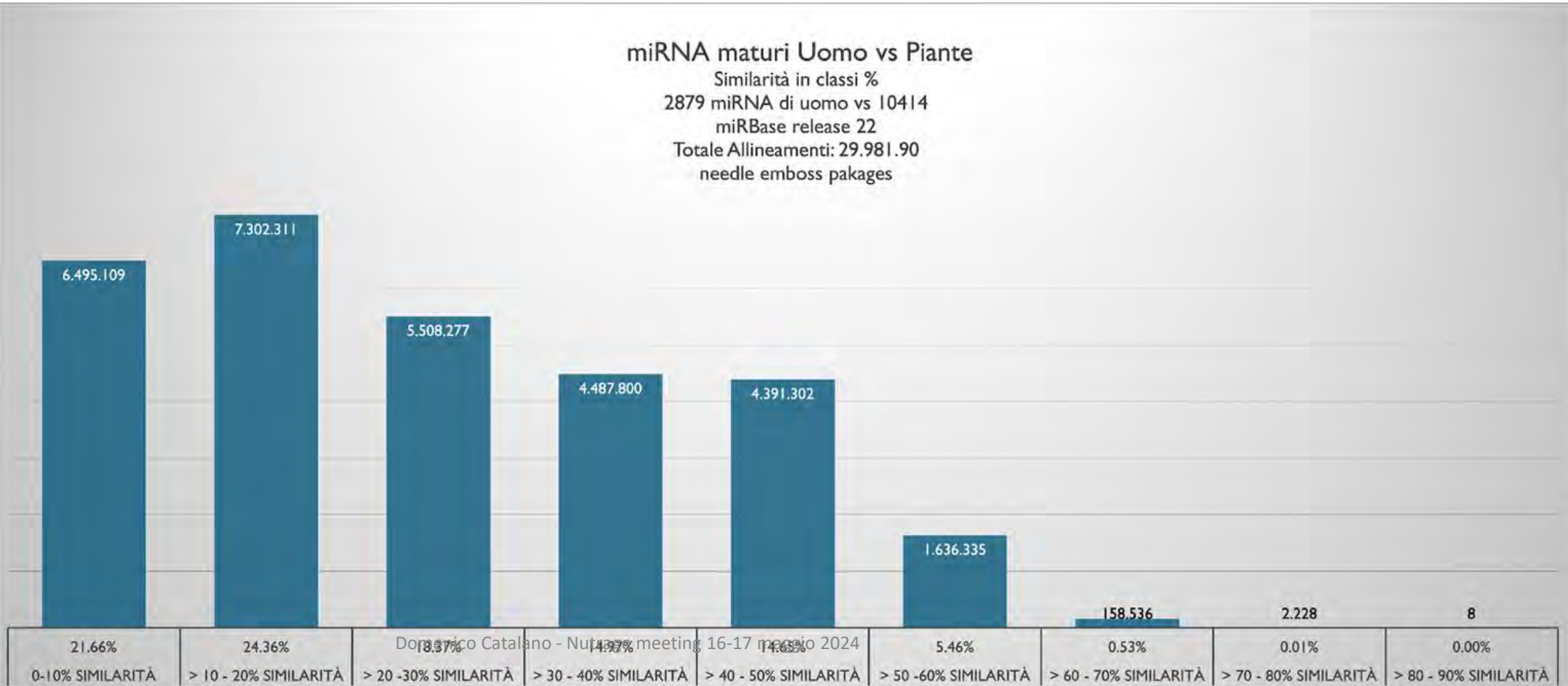
GRAZIE PER L'ATTENZIONE



Similarità di sequenza fra miRNA umani vs piante

miRNA maturi Uomo vs Piante

Similarità in classi %
 2879 miRNA di uomo vs 10414 miRBase release 22
 Totale Allineamenti: 29.981.90
 needle emboss packages



Dorcaso Catalano - Nutrasome meeting 16-17 maggio 2024