

*Establishment and verification of
miRNAs expression molecules for
breast cancer and its distant metastasis*

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□ 1999.08-2002.06 Academy of Medical Sciences, Master degree

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□ 2012.10-2013.10 The cancer institute of New Jersey , Rutgers University, visitor scholar

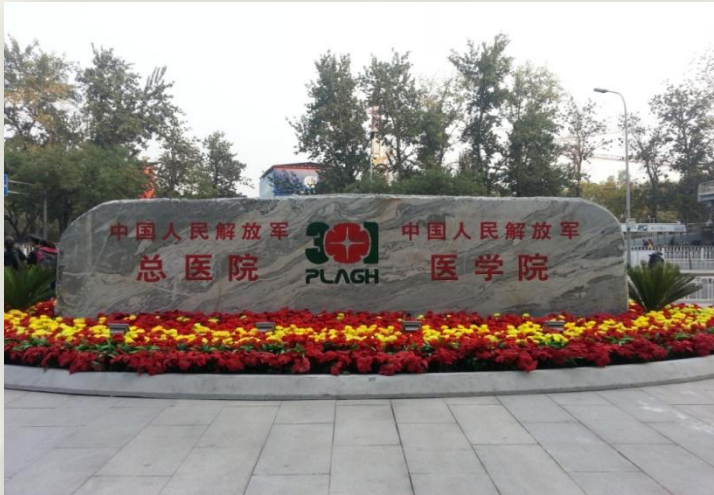


My Work

- *Information and automation management of Clinical Biochemistry ;
- *Explorating new tumor biomarkers for diagnoses and prognostic from blood by advanced technology methods



PLA General Hospital



PLA General Hospital



- ✓ 450000 square meters
- ✓ 15 floors in the ground
- ✓ 5 floors underground
- ✓ 50000 people



PLA General Hospital



Department of Clinical Biochemistry





Department of Clinical Biochemistry

1

Biochemistry Laboratory

2

Immunology Laboratory

3

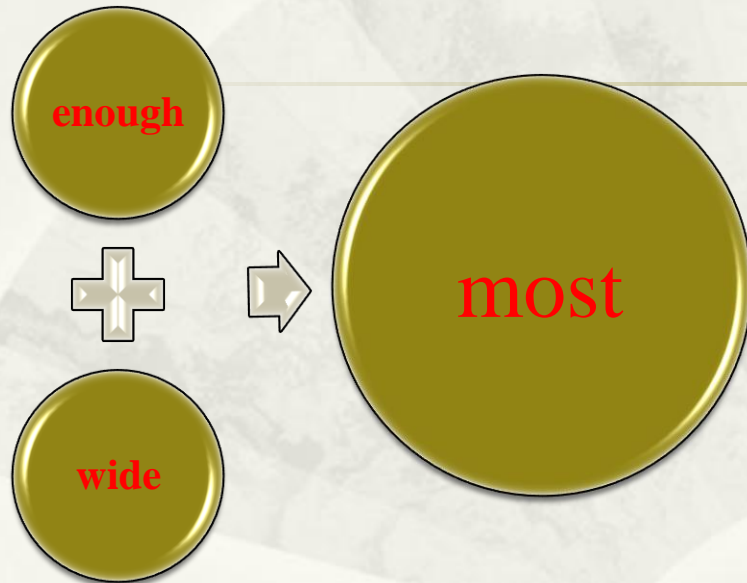
PCR Laboratory

4

Emergency Laboratory

Biochemical Test Items

112 kinds of biochemical items



Disease	Items number
Liver Function	12
Renal Function	4
Myocardial function	8
Pancreatic function	2
Lipid examination	12
Tumor marker	12
Diabetes mellitus	5
Bone metabolism test	4
Inorganic ion test	8
Nutritional index	8
Blood gas analysis	15
Other items	6
Drug concentration test	3
Molecular biology examination	2

Technology platform

- ✓ Fully automatic sample processing system
- ✓ Biochemical and Immunology analysis system



RSA Pro



Cobas 8000 702/701、e602

✓ Emergency automatic sample processing analysis system



✓ PCR analysis system



COBAS® AmpliPrep



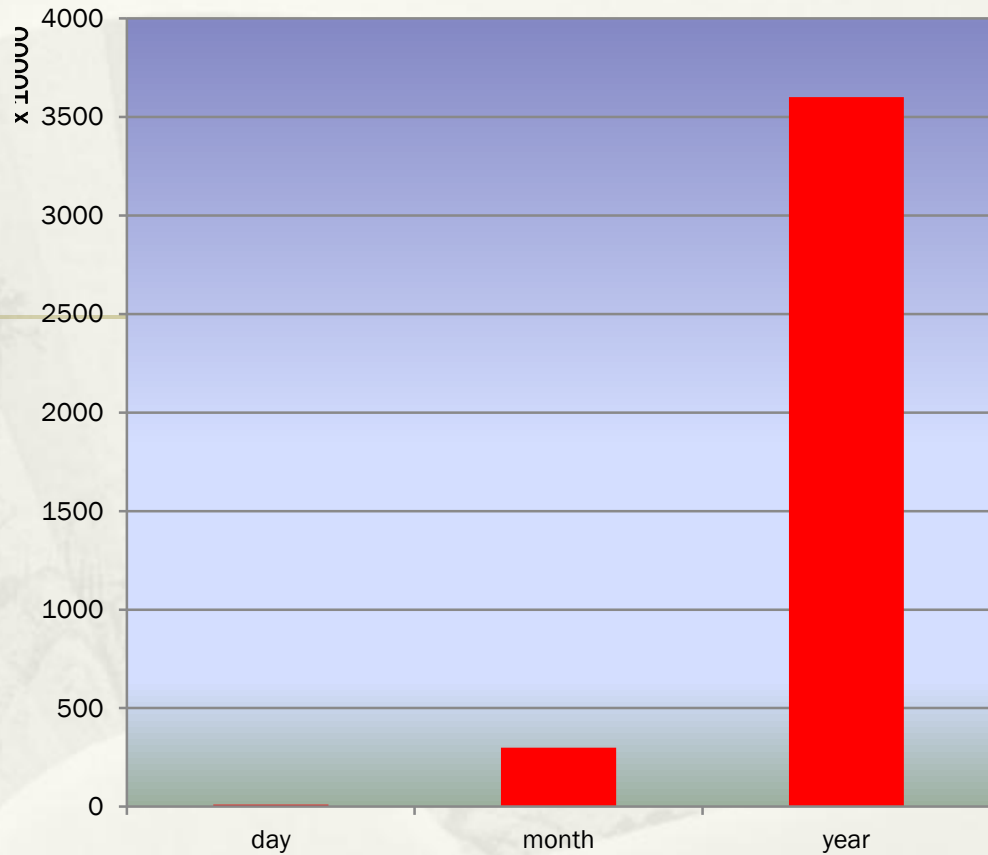
COBAS® TaqMan 48 PCR

Biochemical Test Data

Every Day : 10,000

Every Month : 300,000

Every Year : 3600,000





What is big data?

How many types of data in medicine ?

How to deal with big data?

The background of the slide is a light beige color with a large, semi-circular fan graphic in the center. The fan is open and features a traditional Chinese landscape painting in a muted, greyish-green tone. The painting depicts a mountainous landscape with a river or path winding through it, and several small figures or structures scattered across the scene. The overall aesthetic is classic and scholarly.

Establishment and verification of miRNAs
expression molecules for breast cancer and
its distant metastasis

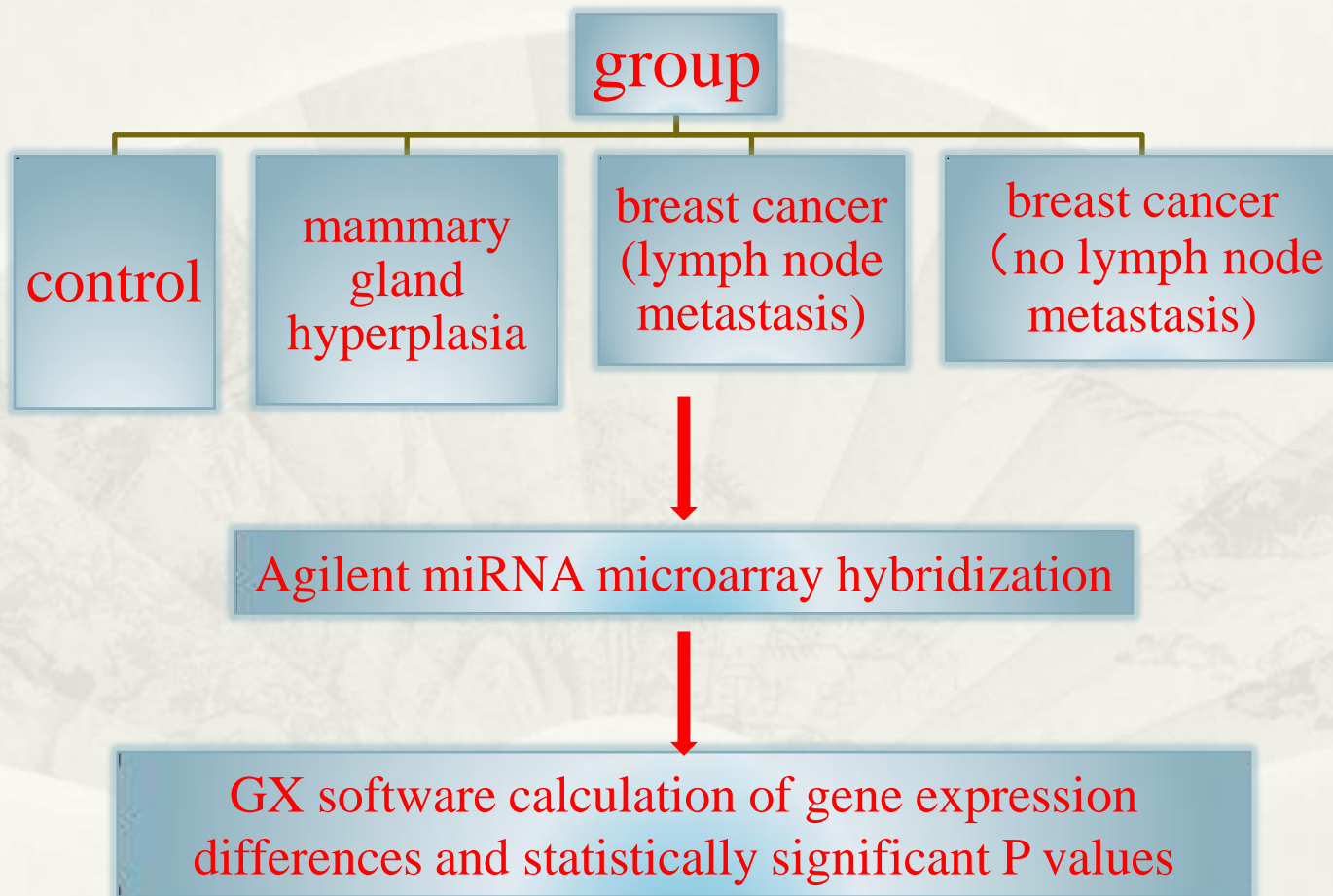
Breast cancer

- Breast cancer is one of malignant tumors in women
- Distant metastasis is the main death cause for breast cancer patients
- The early detection of laboratory is the key for prevention and therapy breast cancer

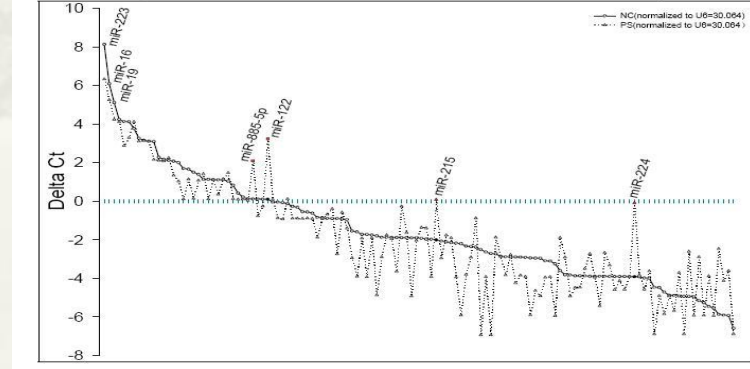
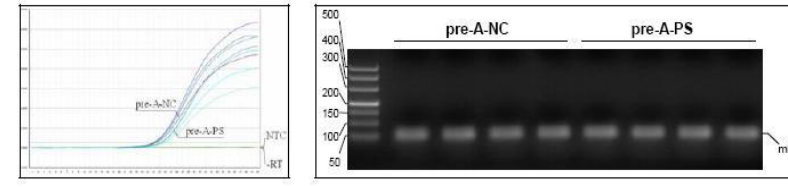
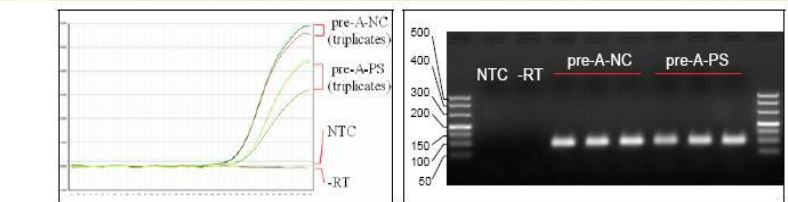
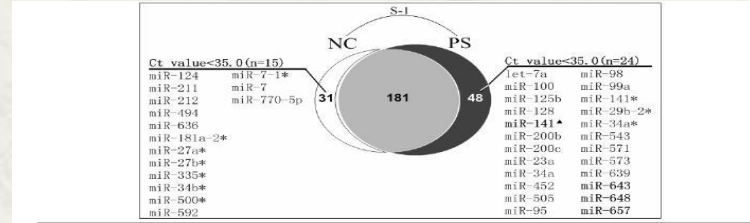
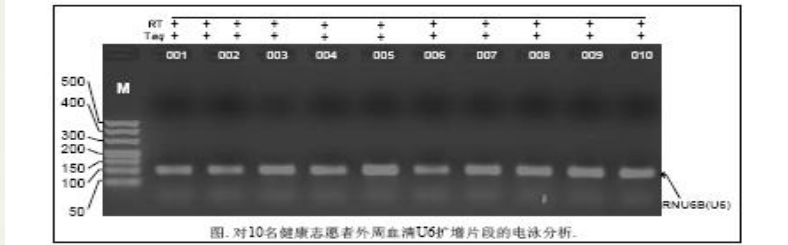
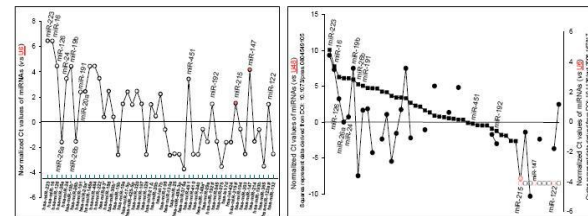
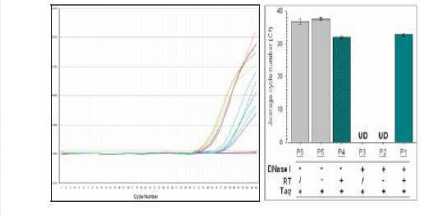
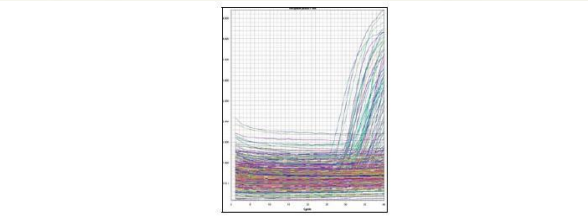
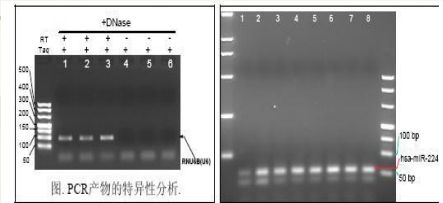
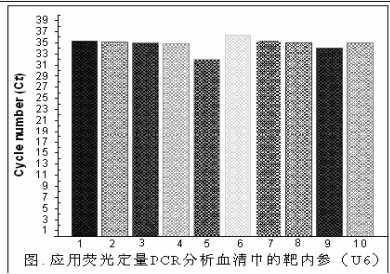
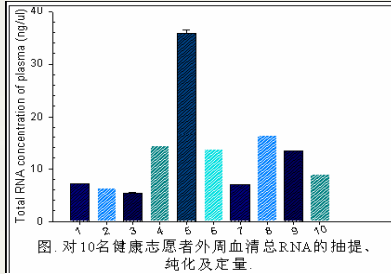
- MicroRNAs (miRNAs) are a major class of small endogenous RNA molecules that post-transcriptionally regulate gene expression.
- Recent researches demonstrated that miRNAs are closely associated with breast cancer the loss of several tumor suppressor
- miRNAs and the overexpression of certain oncogenic miRNAs have been observed in breast cancers
- miRNA can be found in the plasma and serum, and it has some advantages over other diseases, and has been shown to be unique in the diagnosis and prognosis of breast cancer, liver cancer, and other diseases.

-
- When breast cancer and distant metastasis occur, it may be that the main (is) the release of endogenous miRNAs into the peripheral blood circulation.
 - It is very important to explore the breast cancer and its distant metastasis specific miRNAs for screening, diagnosis and prognosis assessment of breast cancer.

Methods

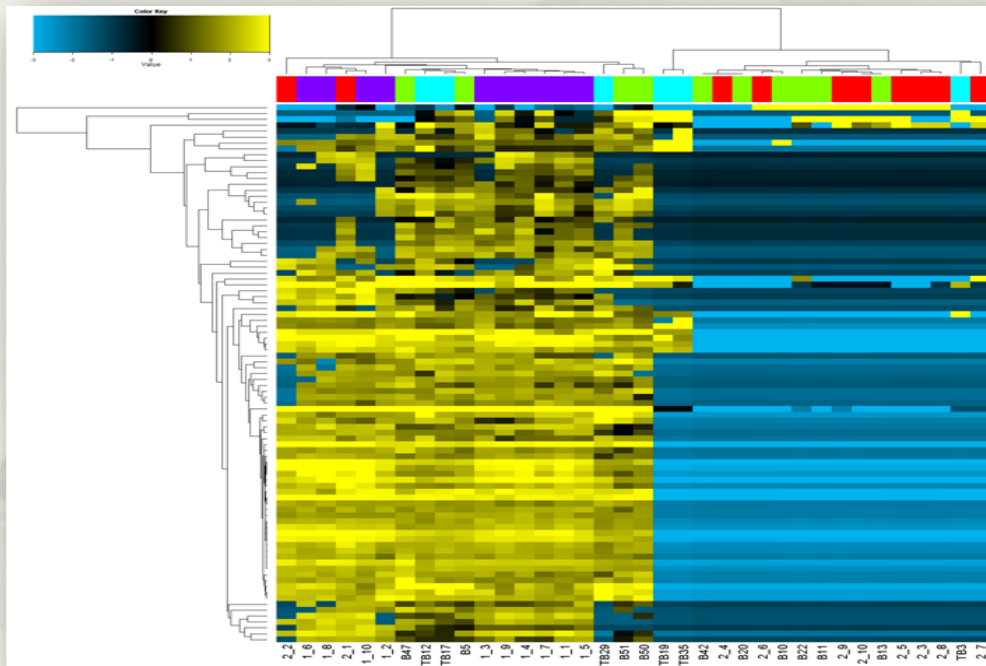


Research Work



Results

MiRNAs molecules of the normal group was up-regulated, while miRNAs for group B1, B2 and B3 were down-regulated.



Normal control group (C group): purple;
mammary gland hyperplasia group(group B1): red;
breast lymph node metastasis (group B2): green;
breast lymph node metastasis group (group B3): blue.
horizontal coordinates: different colors on behalf of different groups.
Vertical coordinates: representing the miRNA molecule.

Figure 1. MiRNA Agilent microarray in normal control group, breast hyperplasia group and breast cancer group (yellow shows expressed up, blue shows down regulated).

B2 vs C Result

systematic	p (Corr)	p	FC (abs)	Regulation	B10:gTotal	B11:gTotal	B13:gTotal	B20:gTotal	B22:gTotal	B42:gTotal	B47:gTotal	B5:gTotal
hsa-miR-4	0.017252	0.010822	13.62833	up	7.7928	14.0879	7.41923	0.1	10.0489	0.1	14.9427	16.5205
hsa-miR-1	0.007408	0.003926	4.796492	down	0.1	0.1	0.1	0.1	0.1	0.1	79.0043	35.1783
hsa-miR-1	0.004002	0.001641	6.43993	down	0.1	0.1	0.1	0.1	0.1	0.1	144.6712	79.6578
hsa-miR-1	0.000956	0.000152	6.611596	down	0.1	0.1	0.1	0.1	0.1	0.1	24.0463	19.71815
hsa-miR-1	0.000956	0.000131	6.183637	down	0.1	0.1	0.1	0.1	0.1	0.1	47.4756	12.9018
hsa-miR-1	0.002333	0.000747	10.31755	down	0.1	0.1	0.1	0.1	0.1	0.1	469.758	101.3764
hsa-miR-1	0.011572	0.006596	6.294055	down	0.1	0.1	0.1	0.1	0.1	0.1	168.1858	144.7519
hsa-miR-1	0.000253	1.52E-05	4.746404	down	0.1	0.1	0.1	0.1	0.1	0.1	31.953	6.70616
hsa-miR-1	0.004025	0.001774	3.200518	down	0.1	0.1	0.1	0.1	0.1	0.1	17.8155	9.71535
hsa-miR-1	0.001711	0.000391	8.509321	down	0.1	0.1	0.1	0.1	0.1	0.1	83.0411	68.5585
hsa-miR-1	0.016072	0.009482	4.438121	down	0.1	0.1	0.1	0.1	0.1	0.1	244.442	33.1442
hsa-miR-2	0.001893	0.000454	14.1815	down	0.1	0.1	0.1	0.1	0.1	0.1	298.7388	205.5406
hsa-miR-3	0.013091	0.007593	4.05793	down	0.1	0.1	0.1	0.1	0.1	0.1	48.6381	42.6363
hsa-miR-3	0.004644	0.002183	4.819182	down	0.1	0.1	0.1	0.1	0.1	0.1	58.7436	30.2987
hsa-miR-3	0.000184	7.86E-06	4.540431	down	0.1	0.1	0.1	0.1	0.1	0.1	11.305	5.48684
hsa-miR-3	0.00346	0.001246	4.173489	down	0.1	0.1	0.1	0.1	0.1	0.1	49.9385	17.098
hsa-miR-3	0.001711	0.000394	12.25385	down	0.1	0.1	0.1	0.1	0.1	0.1	214.4448	156.743
hsa-miR-3	0.009025	0.004873	6.648063	down	0.1	0.1	0.1	0.1	0.1	0.1	231.504	103.9133
hsa-miR-3	0.003995	0.001581	14.23455	down	0.1	0.1	0.1	0.1	0.1	0.1	576.401	375.0161
hsa-miR-3	0.000138	4.15E-06	8.479019	down	0.1	0.1	0.1	0.1	0.1	0.1	31.1353	21.41802
hsa-miR-3	0.002059	0.000618	6.924864	down	0.1	0.1	0.1	0.1	0.1	0.1	79.4381	39.3588
hsa-miR-3	0.033138	0.022534	2.501641	down	0.1	0.1	0.1	0.1	0.1	0.1	11.9122	7.69866
hsa-miR-3	0.000548	5.48E-05	65.51481	down	0.1	0.1	0.1	0.1	0.1	0.1	1404.801	623.201
hsa-miR-4	0.005541	0.002881	4.019872	down	0.1	0.1	0.1	0.1	0.1	0.1	57.3831	15.79635
hsa-miR-4	0.033317	0.023322	13.43571	down	0.1	0.1	0.1	0.1	0.1	0.1	2347.79	987.655

B3 vs C Result

systematic	p (Corr)	p	FC (abs)	Regulatio	TB19:gTo	TB3:gTota	TB35:gTo	TB29:gTo	TB12:gTo	TB17:gTo	1_1:gTota	1_2:gTota
hsa-miR-10	0.019946	0.005843	12.14919	up	6.91169	4.33997	27.21457	4.26795	4.22739	20.18547	6.15812	0.1
hsa-miR-4	0.01595	0.0029	30.29061	up	42.7637	25.9244	137.0537	23.37182	39.2149	121.6528	27.79633	0.1
hsa-miR-12	0.025393	0.010773	4.736928	down	0.1	0.1	0.1	13.653	46.8799	99.6409	88.9333	21.44074
hsa-miR-12	0.009868	0.000884	6.69974	down	0.1	0.1	0.1	0.1	9.85215	15.78086	46.7113	0.1
hsa-miR-12	0.019946	0.005123	4.765573	down	0.1	0.1	0.1	0.1	15.16847	16.59695	25.9361	0.1
hsa-miR-12	0.076811	0.041897	4.243626	down	0.1	0.1	0.1	62.93712	88.0993	212.566	88.78286	62.97969
hsa-miR-12	0.003645	0.000117	4.35054	down	0.1	0.1	0.1	0.1	8.08551	9.81403	11.8505	4.76069
hsa-miR-12	0.027798	0.012355	3.230964	down	0.1	0.1	0.1	0.1	10.7816	13.5745	15.7049	4.64138
hsa-miR-12	0.01595	0.00277	6.430509	down	0.1	0.1	0.1	12.5822	45.2451	74.9702	146.8405	31.204
hsa-miR-12	0.039872	0.019503	3.674612	down	0.1	0.1	0.1	13.077	42.0341	35.0842	40.486	19.19611
hsa-miR-21	0.01595	0.002709	10.14579	down	0.1	0.1	0.1	33.93522	114.4881	191.7858	531.0196	91.3131
hsa-miR-3	0.024507	0.009902	3.659262	down	0.1	0.1	0.1	4.59719	16.97233	50.3216	30.8952	4.83868
hsa-miR-3	0.036868	0.017503	3.595808	down	0.1	0.1	0.1	13.02498	30.2922	30.552	38.8802	13.04262
hsa-miR-3	0.028949	0.013159	2.970878	down	0.1	0.1	0.1	4.31563	6.36581	5.41472	7.39285	4.74524
hsa-miR-3	0.039872	0.019735	3.069135	down	0.1	0.1	0.1	6.18031	20.91097	23.05389	30.07172	6.8092
hsa-miR-30	0.016021	0.003168	8.614912	down	0.1	0.1	0.1	38.3901	93.3226	140.9644	413.082	69.3615
hsa-miR-30	0.047009	0.024692	4.733173	down	0.1	0.1	0.1	44.0788	88.7561	136.6941	103.7526	64.1256
hsa-miR-30	0.025393	0.010729	9.154843	down	0.1	0.1	0.1	103.266	263.3799	474.61	620.577	174.44
hsa-miR-30	0.009868	0.00092	5.070235	down	0.1	0.1	0.1	4.88026	11.5674	13.20428	26.4383	13.4884
hsa-miR-30	0.016021	0.003244	5.447403	down	0.1	0.1	0.1	9.32947	28.6139	54.3122	96.9247	21.83537
hsa-miR-30	0.068375	0.036605	2.781604	down	0.1	0.1	0.1	0.1	5.49121	7.42877	17.5855	0.1
hsa-miR-30	0.0231	0.008867	7.534578	down	22.33667	0.1	14.47875	163.341	496.347	744.035	1622.385	329.048
hsa-miR-4	0.042174	0.0213	3.522117	down	0.1	0.1	0.1	0.1	14.60298	24.6221	20.8641	4.53669
hsa-miR-4	0.019946	0.005193	3.710709	down	0.1	0.1	0.1	0.1	14.14277	24.47792	13.87402	5.30308
hsa-miR-4	0.003645	0.000147	7.175142	down	0.1	0.1	0.1	6.00936	12.98	21.51	98.12653	22.1532

B2 vs B1 Result

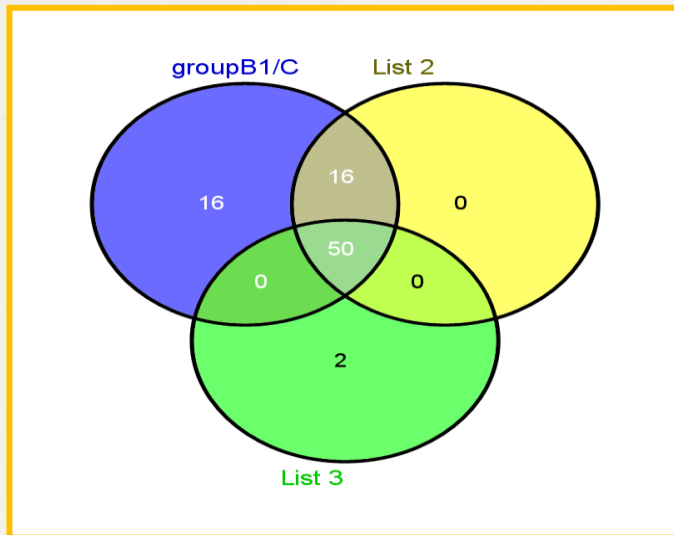
systematic	p (Corr)	p	FC (abs)	Regulatio	2_1:gTota	2_2:gTota	2_3:gTota	2_4:gTota	2_5:gTota	2_6:gTota	2_7:gTota	2_8:gTota
hsa-miR-4	0.785551	0.421068	2.975647	down	170.9063	63.1946	3.70549	0.1	12.8041	0.1	11.63904	3.63003
hsa-miR-4	0.785551	0.698268	1.68006	up	4.88473	0.1	0.1	0.1	10.74289	0.1	16.41067	0.1
hsa-miR-4	0.785551	0.623846	1.918535	down	6.68754	0.1	9.90835	0.1	5.04728	13.904	0.1	6.70042
hsa-miR-6	0.785551	0.465765	3.430115	up	1722.185	627.527	0.1	0.1	0.1	0.1	7.03332	2.55856

B3 vs B1

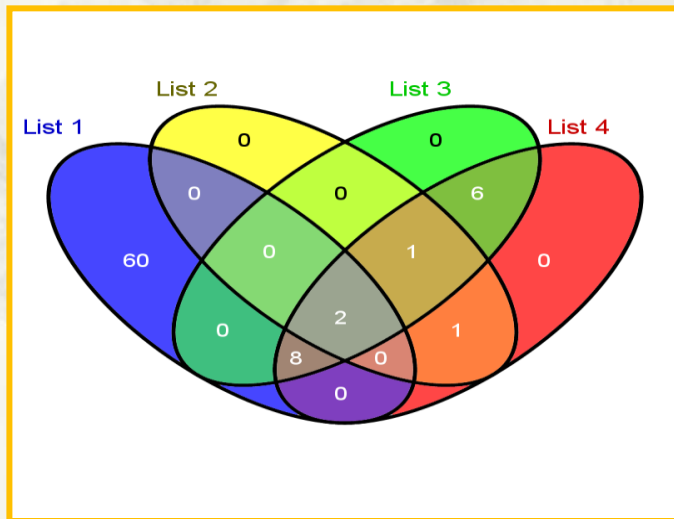
systematic	p (Corr)	p	FC (abs)	Regulatio	2_1:gTota	2_2:gTota	2_3:gTota	2_4:gTota	2_5:gTota	2_6:gTota	2_7:gTota	2_8:gTota
hsa-miR-141	0.029593	0.007398	8.160369	up	25.5646	9.7323	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-141	0.049617	0.03101	3.525788	up	15.4405	0.1	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-141	0.034955	0.017909	9.375454	up	174.1619	45.7324	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-141	0.001725	7.19E-05	26.85538	up	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-34a	0.069905	0.046603	16.03892	up	886.036	200.6418	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-429	0.03054	0.008958	40.99584	up	386.233	198.8679	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-429	0.017058	0.002132	44.34193	up	686.438	173.5183	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-429	0.03054	0.01018	3.808936	up	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-608	0.005291	0.000441	10.87901	up	8.62538	0.1	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-608	0.034955	0.018521	12.65836	up	377.956	91.9273	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-608	0.034955	0.018934	141.9156	up	3022.75	1347.944	0.1	0.1	0.1	0.1	4.22773	0.1
hsa-miR-608	0.034955	0.017904	56.43684	up	1722.185	627.527	0.1	0.1	0.1	0.1	7.03332	2.55856
hsa-miR-608	0.022721	0.004733	10.4385	up	30.2914	17.51701	0.1	0.1	0.1	0.1	0.1	0.1
hsa-miR-429	0.034955	0.01418	35.86911	down	6.68754	0.1	9.90835	0.1	5.04728	13.904	0.1	6.70042
hsa-miR-429	1	0.977396	1.040137	up	170.9063	63.1946	3.70549	0.1	12.8041	0.1	11.63904	3.63003
hsa-miR-429	0.074397	0.052698	17.36868	up	394.148	184.3179	0.1	0.1	0.1	0.1	12.53579	0.1
hsa-miR-429	0.150582	0.119211	11.59136	up	4.88473	0.1	0.1	0.1	10.74289	0.1	16.41067	0.1
hsa-miR-608	0.081947	0.06146	3.835599	up	18.13138	3.95915	0.1	0.1	0.1	0.1	0.1	0.1

B3 vs B2

systematic	p (Corr)	p	FC (abs)	Regulatio	B10:gTota	B11:gTota	B13:gTota	B20:gTota	B22:gTota	B42:gTota	B47:gTota	B5:gTotal
hsa-miR-101	0.142409	0.017089	10.46659	up	0.1	0.1	0.1	0.1	0.1	0.1	0.1	32.1095
hsa-miR-429	0.075617	0.006049	23.54545	up	0.1	0.1	0.1	0.1	0.1	0.1	1296.87	390.146
hsa-miR-608	0.142898	0.034074	5.043952	up	0.1	0.1	0.1	0.1	0.1	0.1	34.5324	17.25892
hsa-miR-409	0.142898	0.02505	18.69609	down	7.7928	14.0879	7.41923	0.1	10.0489	0.1	14.9427	16.5205
hsa-miR-151	0.23233	0.069544	4.530047	up	0.1	0.1	0.1	0.1	0.1	0.1	79.0043	35.1783
hsa-miR-151	0.474076	0.376139	1.810751	up	0.1	0.1	0.1	0.1	0.1	0.1	50.3633	15.5121
hsa-miR-151	0.23233	0.083242	5.177325	up	0.1	0.1	0.1	0.1	0.1	0.1	469.758	101.3764
hsa-miR-302	0.23233	0.091479	8.695217	up	0.1	0.1	0.1	0.1	0.1	0.1	1404.801	623.201
hsa-miR-429	0.290268	0.174161	9.46192	up	0.1	0.1	0.1	0.1	0.1	0.1	2347.79	987.655
hsa-miR-429	0.570031	0.478826	3.09508	up	0.1	0.1	3.01838	0.1	8.40435	0.1	650.215	985.928
hsa-miR-429	0.281614	0.155817	2.2946	up	0.1	0.1	0.1	0.1	0.1	0.1	4.51179	16.159
hsa-miR-429	0.4029	0.257856	5.630188	up	0.1	0.1	0.1	0.1	3.05451	0.1	2879.969	691.644
hsa-miR-429	0.281614	0.157704	6.899373	up	0.1	6.31799	2.32086	0.1	22.28651	0.1	8.44317	197.7143
hsa-miR-608	0.23233	0.100969	6.052623	up	0.1	0.1	0.1	0.1	0.1	0.1	549.115	332.047
hsa-miR-608	0.258928	0.124286	33.70969	up	0.1	0.1	0.1	0.1	5.48755	0.1	5845.16	4301.58
hsa-miR-608	0.23233	0.102225	16.45334	up	0.1	7.82411	5.11533	0.1	9.03554	0.1	4515.45	2483.53
hsa-miR-608	0.474076	0.346191	2.779317	up	8.347981	0.1	0.1	0.1	0.1	0.1	157.7886	60.2531
hsa-miR-608	0.404374	0.274974	2.301519	up	0.1	0.1	0.1	0.1	0.1	0.1	54.5557	28.5993



■ The common expression of difference miRNA molecules among the B1/C, B2/C, B3/C three groups were 50



■ Together with B3/B1, B3/B2, B2/B1, the common expression of the difference miRNA molecules is hsa-miR-6090, hsa-miR-451a

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- The common expression of miRNA molecules, which was obtained by using the appropriate tool software, was **hsa-miR-6090, hsa-miR-451a.**

<http://bioinfogp.cnb.csic.es/tools/venny/>

- hsa-miR-6090, hsa-miR-451a molecules in the normal control group, mammary gland hyperplasia, breast lymph node metastasis group, breast lymph node metastasis group were expressed.

miRNA	B1/C	B2/C	B3/C	B2/B1	B3/B1	B3/B2
hsa-miR-6090	up	down	down	up	up	up
hsa-miR-451a	up	up	up	up	up	up

Results

- ❑ The results indicated that the expression of hsa-miR-6090 was down regulated in the normal control group;
- ❑ The expression of hsa-miR-6090 in mammary gland hyperplasia group was lower than that in breast cancer;
- ❑ The expression of hsa-miR-6090 in breast cancer lymph node metastasis was lower than that in breast cancer.
- ❑ For hsa-miR-451a, the expression of hsa-miR-415a molecules in the other groups increased significantly compared with the normal control group.
- ❑ The expression of hsa-miR-451a in breast cancer tissues was up-regulated, and the expression of hsa-miR-451a in breast cancer lymph node metastasis was higher than that in breast cancer.

Conclusion

- Therefore, we speculate that hsa-miR-451a and hsa-miR-6090 play an important role in the development and metastasis of breast cancer
- The Further validation work will continue



THANK YOU!