

Serous ovarian cancer microRNA profiling

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SEROUS OVARIAN CANCER

FIGO grading (The International Federation of Gynecology and Obstetrics)

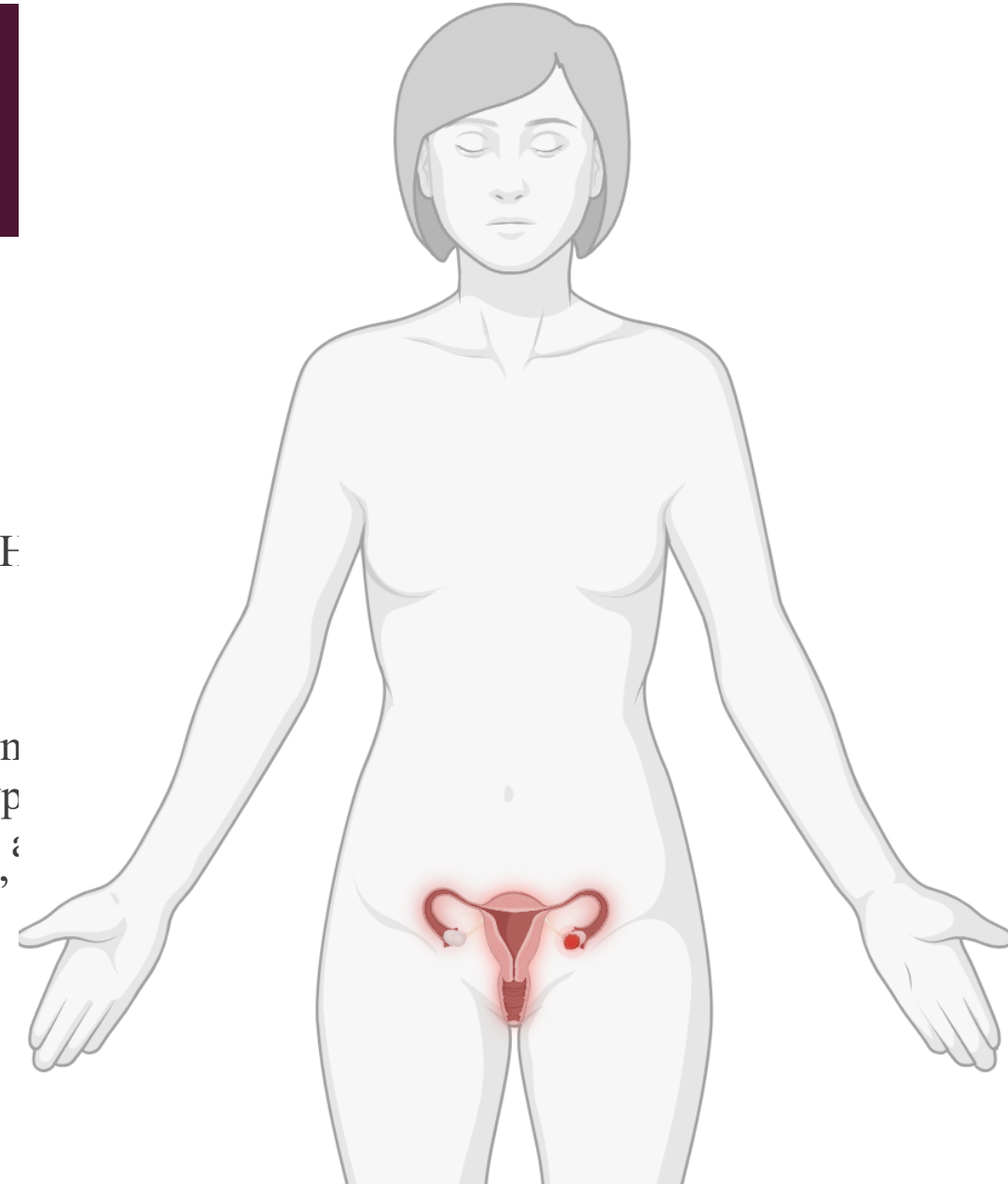
Low-grade serous carcinoma (LGSC)
FIGO I-II grade

ascites may be present

“Essential diagnostic criteria: invasive serous tumor with small nests, glands, papillae or micropapillae, frequently free-floating within unlined clear spaces, low-grade cytological atypia, and low mitotic activity.” WHO

High-grade serous carcinoma (HGSC)
FIGO III-IV grade

“Serous tumor with solid, papillary, glandular, or cribriform architecture; large, markedly atypical nuclei; WT1 immunoreactivity; and mutation-type p53 expression.”



MicroRNA

- 19-25 nucleotide
- Well regulated biogenesis
- Function: development, embryogenesis, metabolism, cell-cell communication.
- In cancer: resistance to therapy, biomarker, therapeutic target
 - Oncogene
 - Tumorsupressor
- Functions:

Disease	Example	MicroRNA
Tumors	Ovarian cancer	miR-200c; overexpressed
Reproduction organ disease	PCOS	miR-222; overexpressed
Cardiovascular disease	Coronary artery disease	miR-221; overexpressed
Endocrine disease	Diabetes mellitus type 2	mir-9; overexpressed
Infections	Sars-Cov-2	miR-146; overexpressed

Aims

1

Find specific **serous ovarian cancer** biomarkers (cell-free nucleic acids) from liquid biopsy samples.

2

Find ovarian cancer specific housekeeping microRNA.

3

Find specific **grade** marker microRNAs.

Housekeeping microRNA problem

Microarray: elevated expression of

- hsa-miR-93-3p (possible FIGO III grade marker)
- hsa-miR-103-5p

Solution: hsa-miR-4463

- Low expression level
- Stable
- no FIGO grade correlation

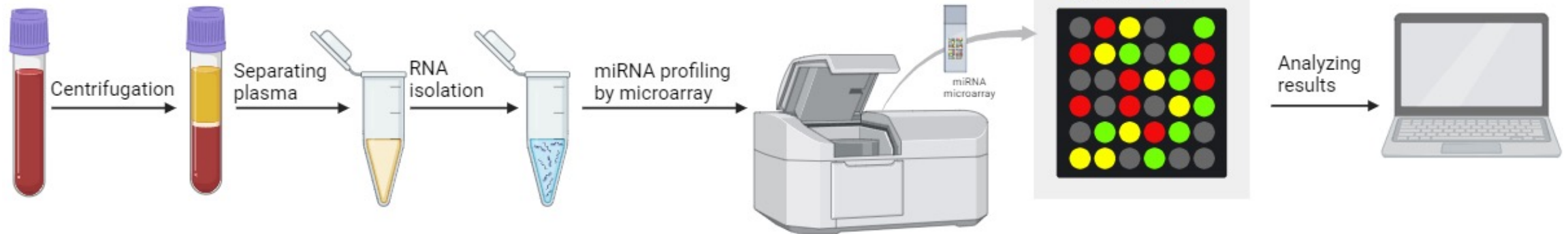
	hsa_miR-4463	hsa_miR-103-5p
control 1	35,51	30,31
control 2	35,965	30,895
control 3	36,475	29,52
control 4	36,275	32,53
sample 1	36,885	30,62
sample 2	35,76	26,725
sample 3	35,66	32,49
sample 4	36,55	26,615
sample 5	36,385	28,8
sample 6	35,65	28,925
sample 7	35,91	31,01
sample 8	33,49	31,1
sample 9	36,675	29,24
sample 10	36,06	31,8
sample 11	36,035	29,63
sample 12	35,235	29,295
sample 13	35,315	31,675
sample 14	35,99	14,79
sample 15	36,66	29,865
sample 16	35,25	29,315
sample 17	35,8	29,125
sample 18	36,485	30,855
sample 19	36,03	31,925

Microarray

- G3 Human microarray chip
Agilent v.21 8x60K

Samples:

- 10 control plasma sample
- 18 Ovarian cancer plasma sample
(FIGO grade III-IV)

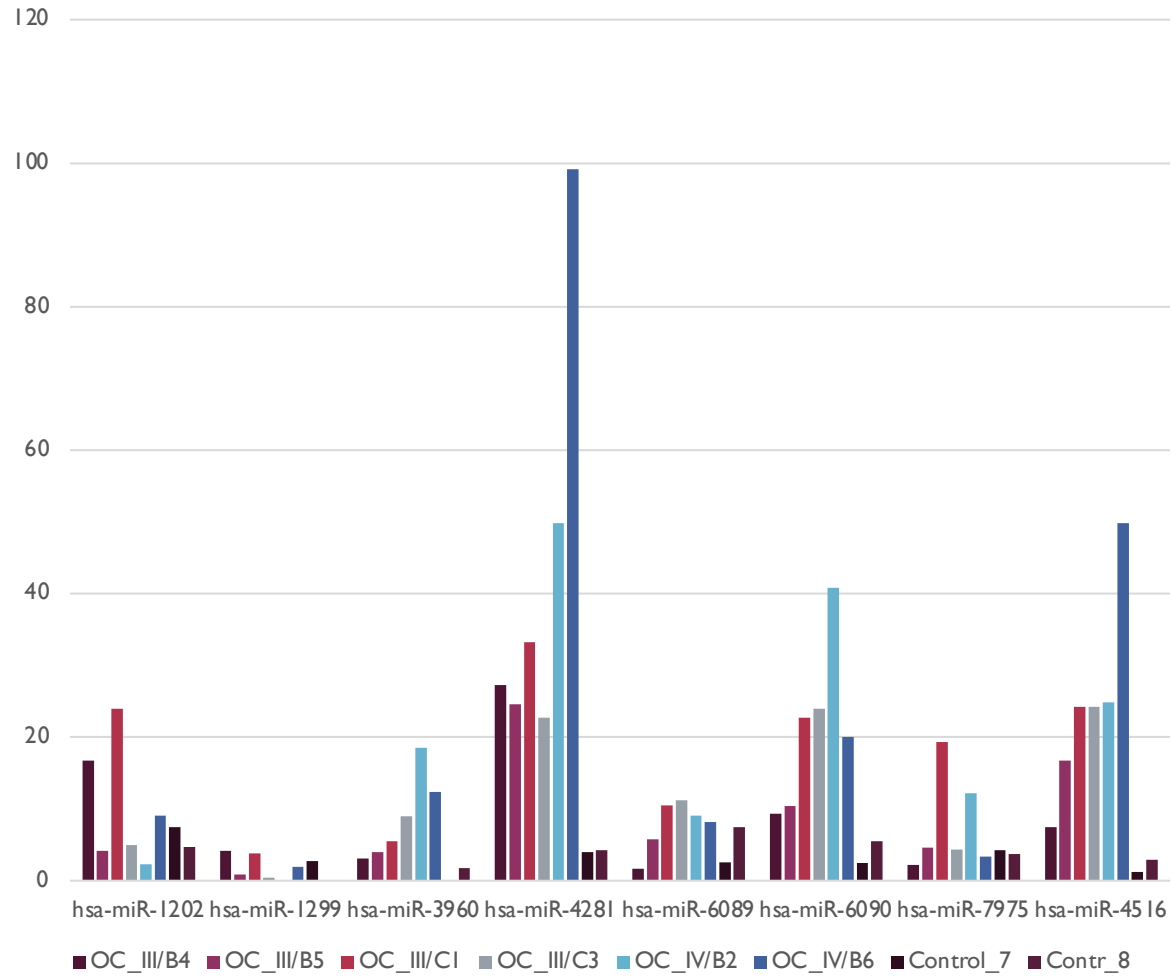


- MiRNeasy
Serum
plasma kit

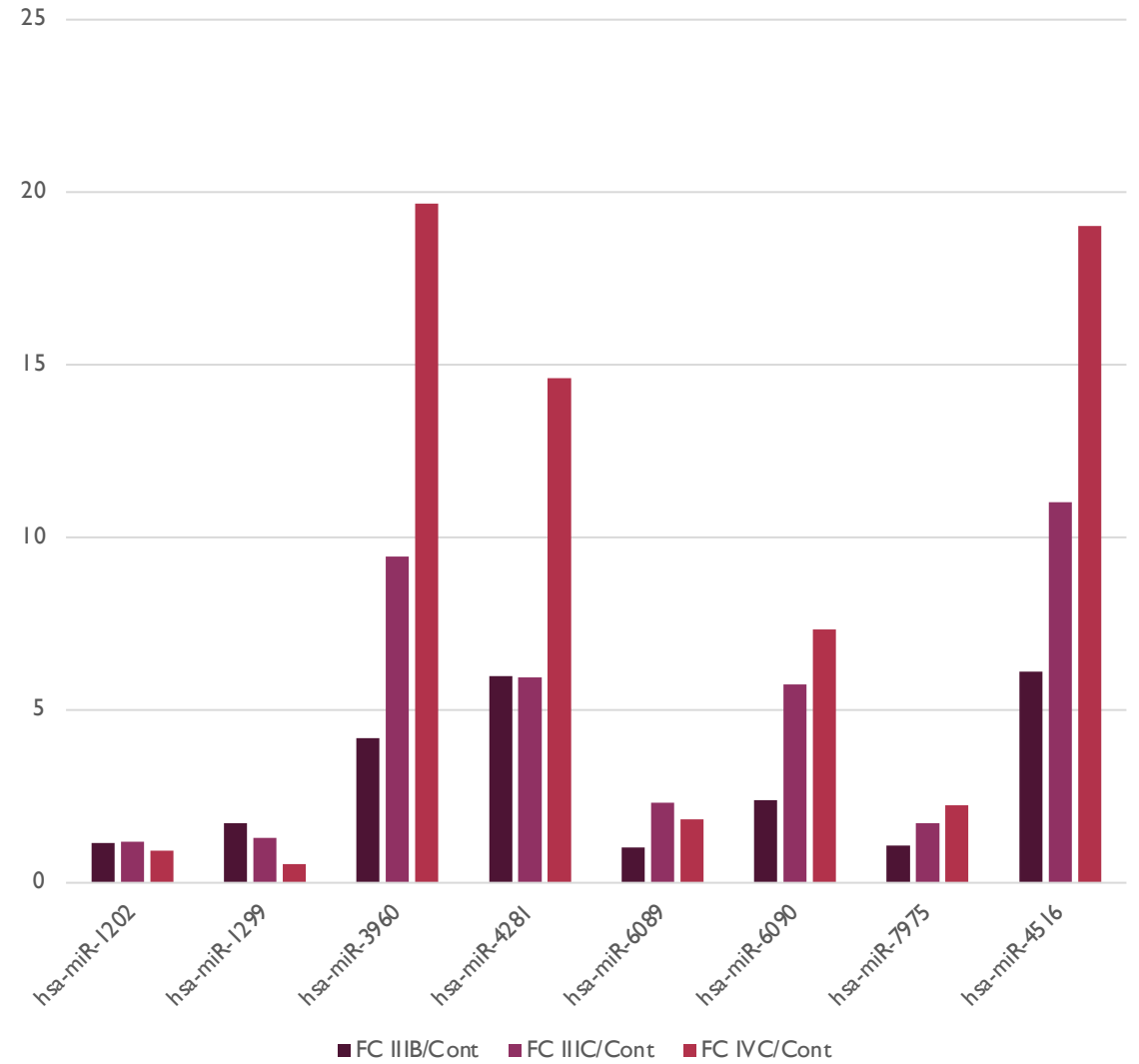
- iDEP
- miRNET
(express analyst)



Normalised



Fold changes



“The expression levels of **miR-1202** and miR-195 in the cervical cancer patients are different in different stages.”

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6396133/>

“**MiR-1202** is downregulated in ovarian cancer and clear cell papillary renal cell carcinoma.”

<https://pubmed.ncbi.nlm.nih.gov/30867774/>

“**miR-1299**/NOTCH3/TUG1 feedback loop contributes to the malignant proliferation of ovarian cancer.”

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7958896/>

“**hsa-miR-4516** was significantly upregulated in patients with Premature ovarian insufficiency.”

<https://pubmed.ncbi.nlm.nih.gov/36139370/>

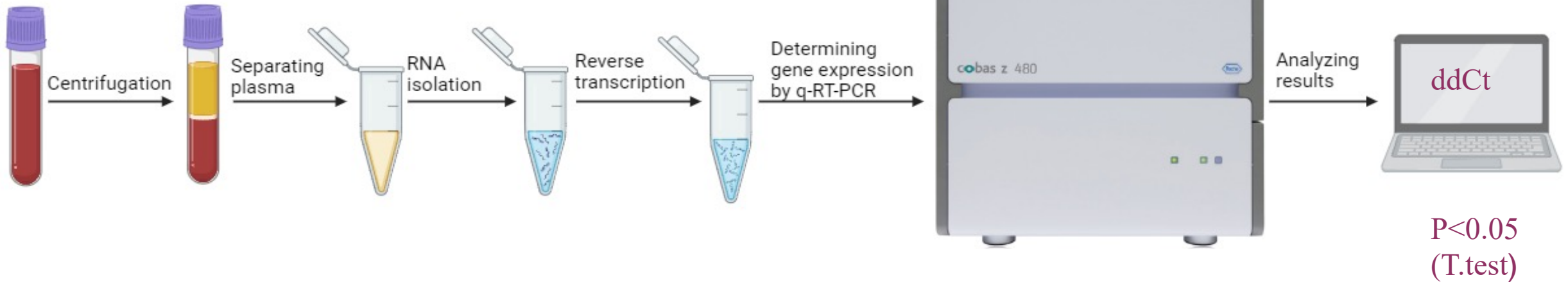
“**MiR-6089** serves as a tumor-suppressive miRNA, and miR-6089/MYH9/ β -catenin/c-Jun negative feedback loop inhibits ovarian cancer carcinogenesis and progression.”

<https://www.sciencedirect.com/science/article/pii/S075333222030055X?via%3>

Q-RT-PCR

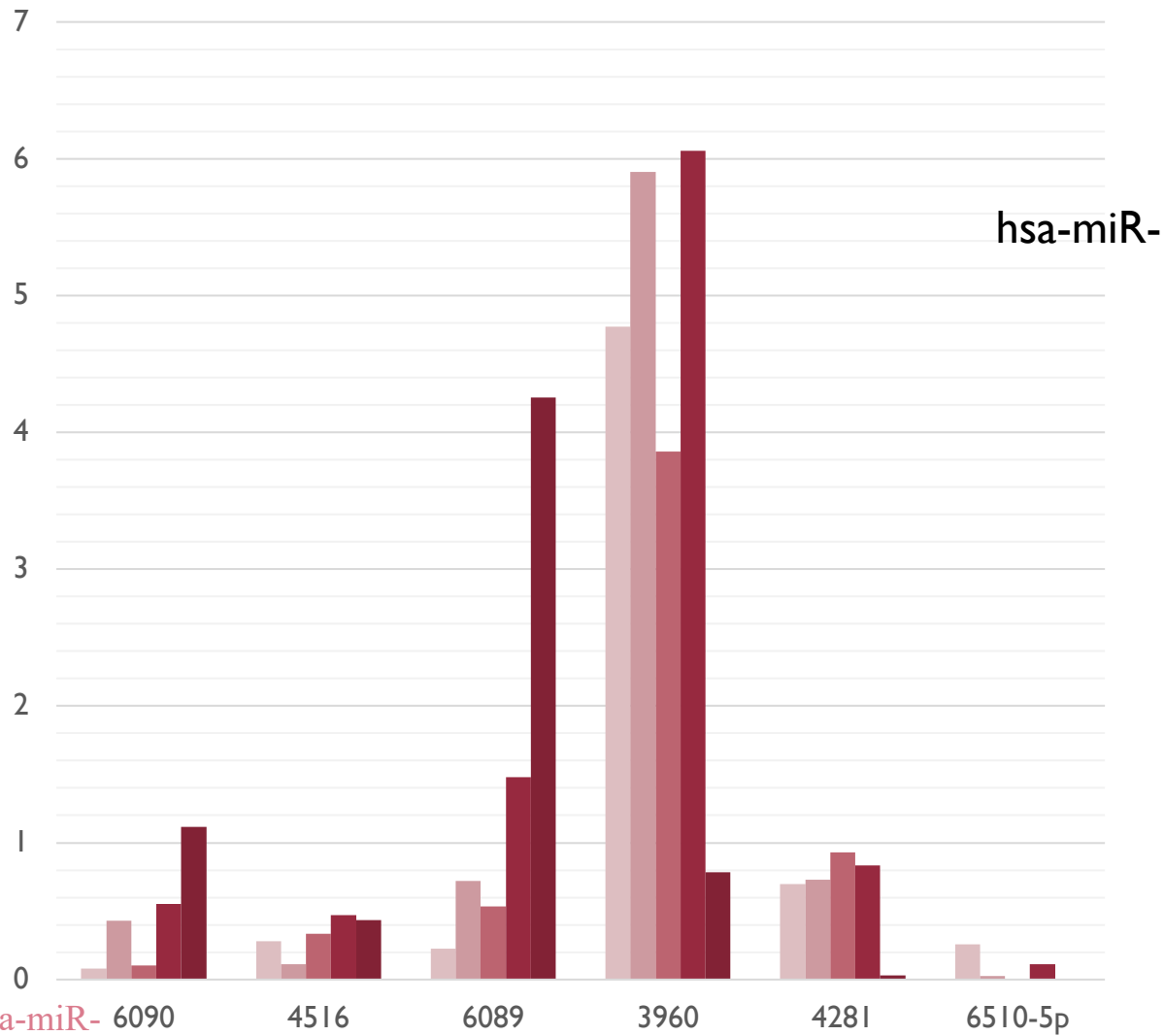
Samples:
4 control plasma sample
23 ovarian cancer plasma samples
(FIGO grade I, III,IV)

MiRNeasy
Serum plasma kit



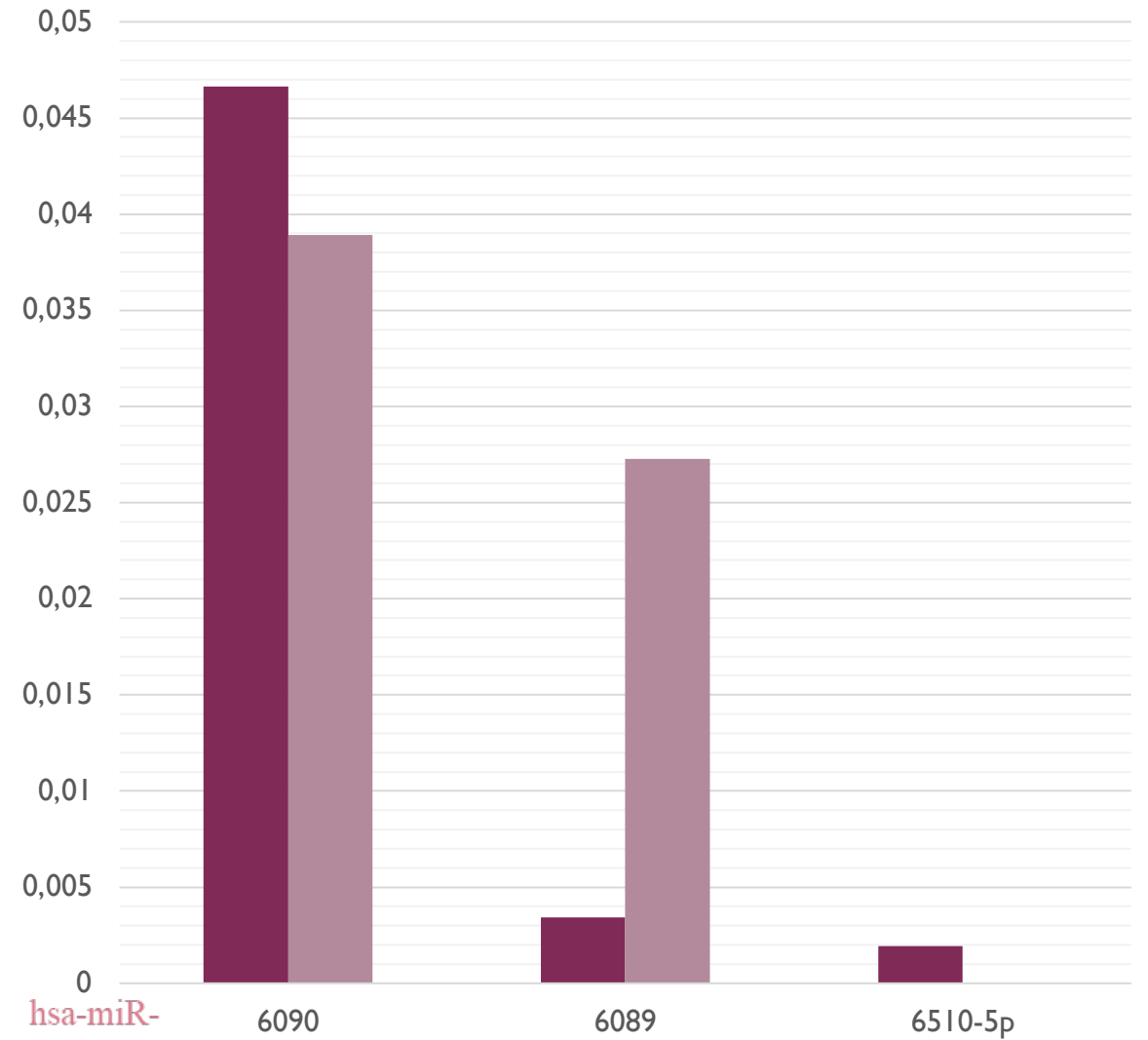
FIGO grades expression

Controls FIGO I FIGO 3/B FIGO 3/C FIGO IV



p-values

figo1 figo 3/c



FUTURE PLANS

1

Target more of these microRNAs (microarray)

2

Check target genes of these microRNAs

3

Possible pathway (microRNAs and their target genes)

4

Check the expressions of these microRNAs in exosomes.

ACKNOWLEDGMENT

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Nikolett Németh

Andrea Kapinová

Dana Dvorská

János Lukács

Zoárd Krasznai

Róbert Póka

Bálint Nagy

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THANK YOU

