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5th International Meeting on Aortic Diseases

New insights into an old problem CHU Liège, APF

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**Circulating miRNAs signature in
unstable abdominal aortic
aneurysms with positive
18FDG-PET**

Audrey Courtois





Disclosure of Interest

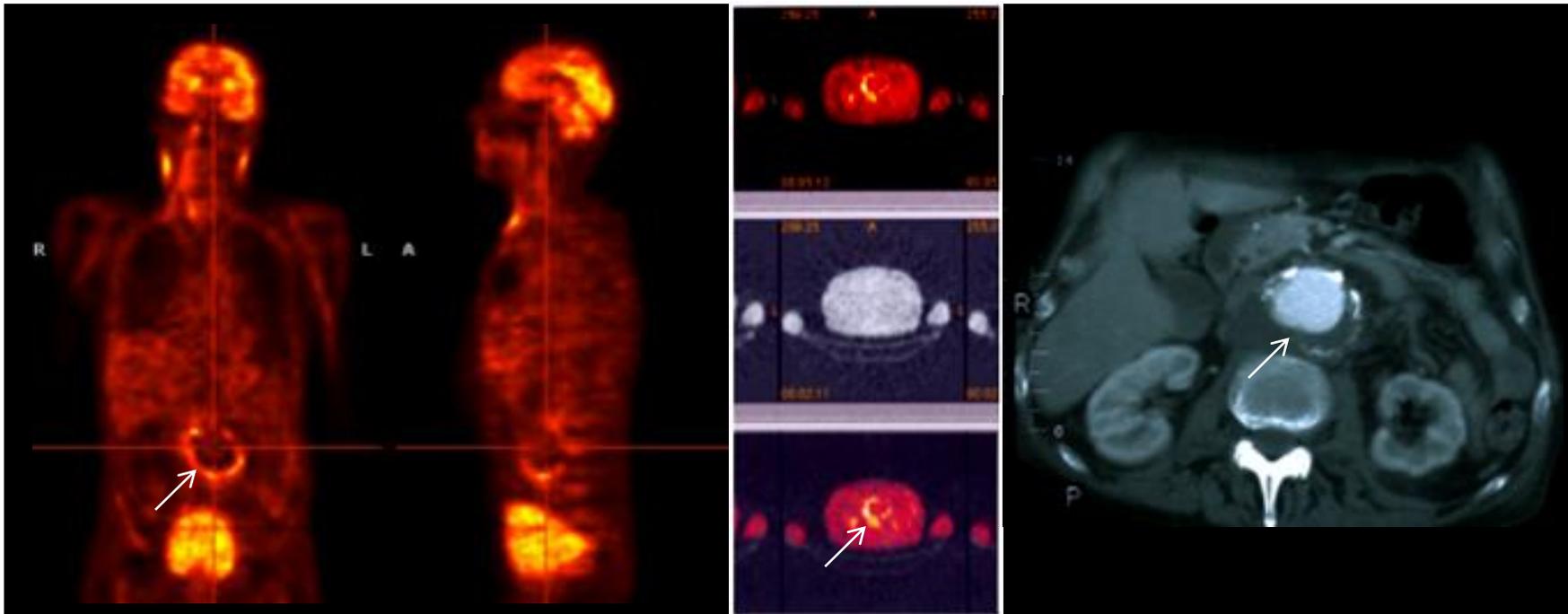
Speaker name: Courtois Audrey

- I have the following potential conflicts of interest to report:

*Grants from: FP7 European Program: "Fighting Aneurysmal Diseases"
n° 200647*

INTRODUCTION

- ❖ An uptake of FDG detected by PET/CT is observed in some AAA (*Sakalihan et al., EJVS, 2002*)
- ❖ In some cases, the FDG uptake site detected by PET/CT corresponds to the rupture site



- ❖ The FDG uptake site corresponds to the high peak wall stress site (*Xu et al., EJVS, 2010*)

AAA FDG-PET –
(A0)



« Stable » AAA

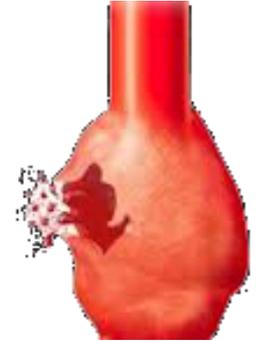
AAA FDG-PET +
(A+)



Instability of the wall



Rupture



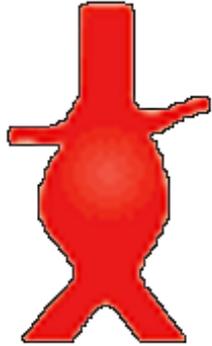
- Symptômes: accelerating growth, pain
- Inflammation: ↗ inflammatory cells in the wall,
↗ cytokines (CCL18)
- Matrix remodeling: ↗ MMP, ↗ collagen expression
- Smooth muscle cells loss: ↘ α-SMA positive cells

Courtois et al., Journal of Nuclear Medicine, 2013

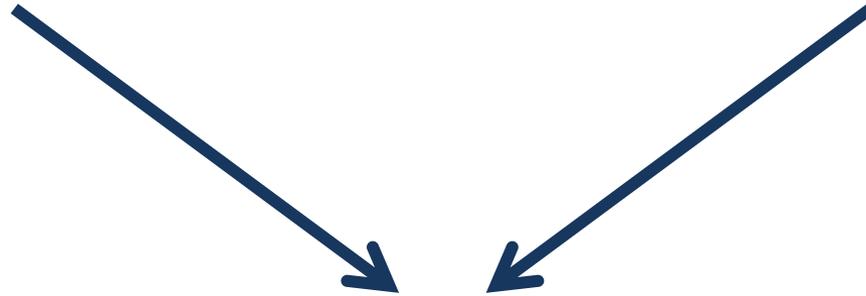
Courtois et al., Molecular Medicine, 2015

PURPOSE

AAA FDG-PET –
(A0)



AAA FDG-PET +
(A+)



Potential biomarkers ?



Circulating microRNA

- small non-coding RNA
- Stable in the blood
- Correlated with some diseases



Patient Characteristics	A0 (n=35)	A+ (n=22)
Age (y)	74 (68-79)	75 (68-81)
Gender distribution (M/F)	35/0	20/2
Aneurysm diameter (mm)	54 (50-62)	55 (51-59)
SUV	0.43 (0.35-0.62)	0.96 (0.87-1.09)***
Cardiovascular events	20/35	9/22
Hypertension	22/35	14/22
Smokers:		
- Current	12/35	7/22
- Former	20/35	12/22
COPD	16/35	7/22
Diabetes	3/35	5/22
Hyperlipidemia	23/35	13/22
Statins	19/35	12/22
β-Blocker	11/35	6/22
Calcium channel blocker	4/35	4/22
ACEI	4/35	2/22
NSAID	0/35	1/22

Uptake of FDG measured

=

Standardized Uptake
Value (SUV)



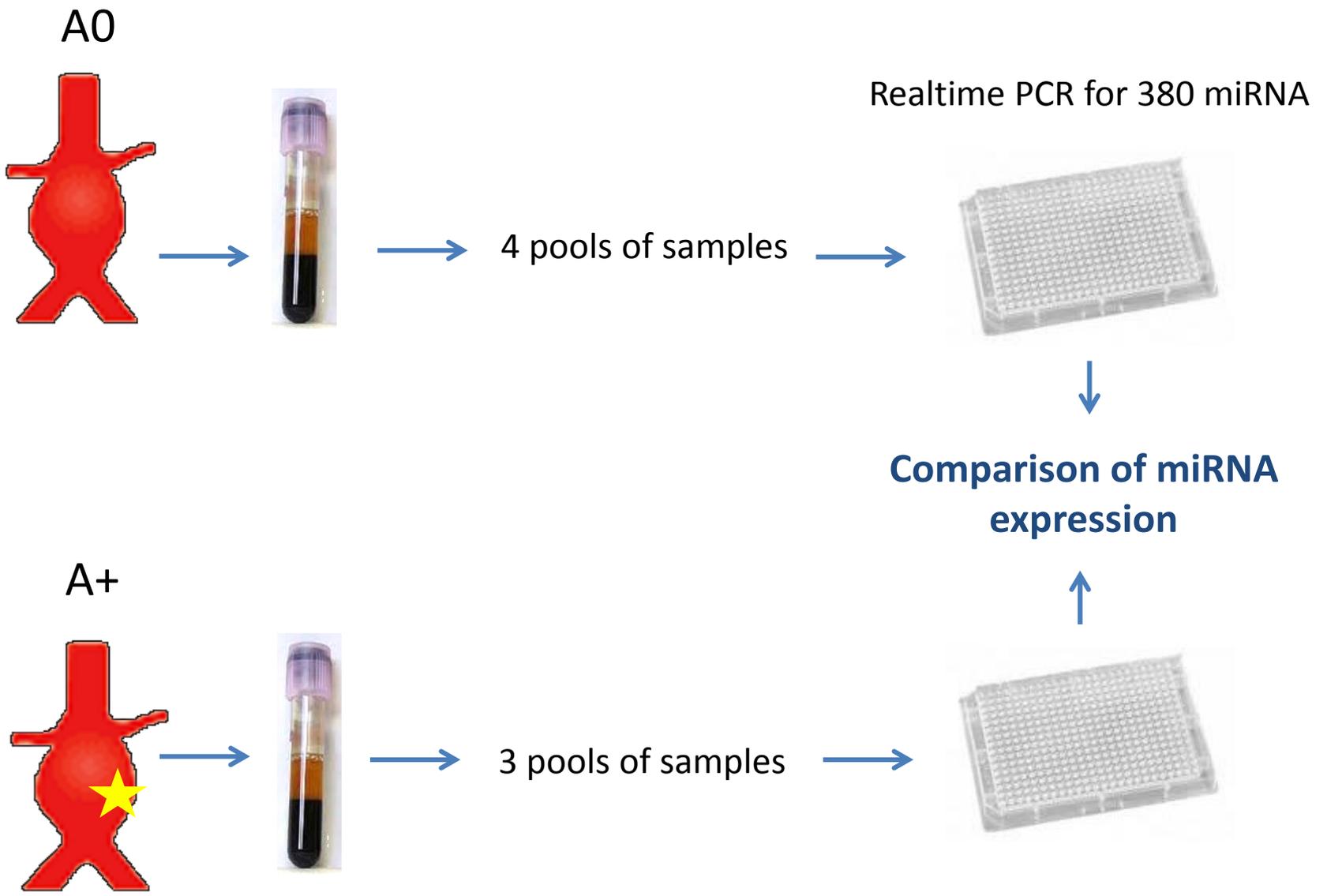
SUV

=

SUV AAA/ SUV
Liver

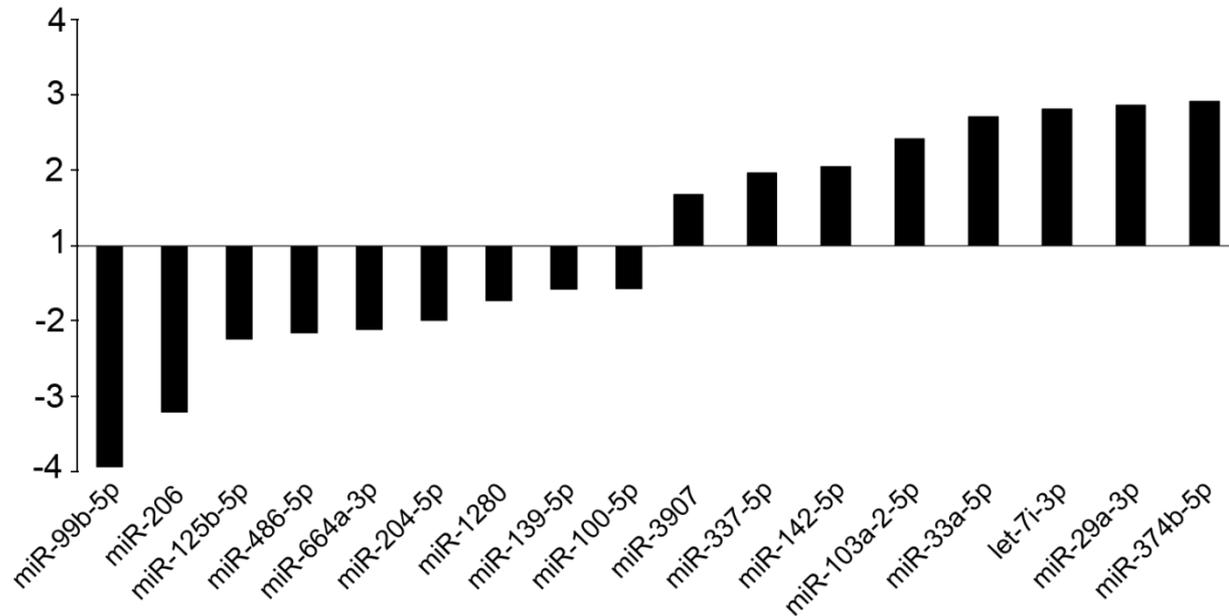


First experiment on plasma samples from A0 and A+ patients



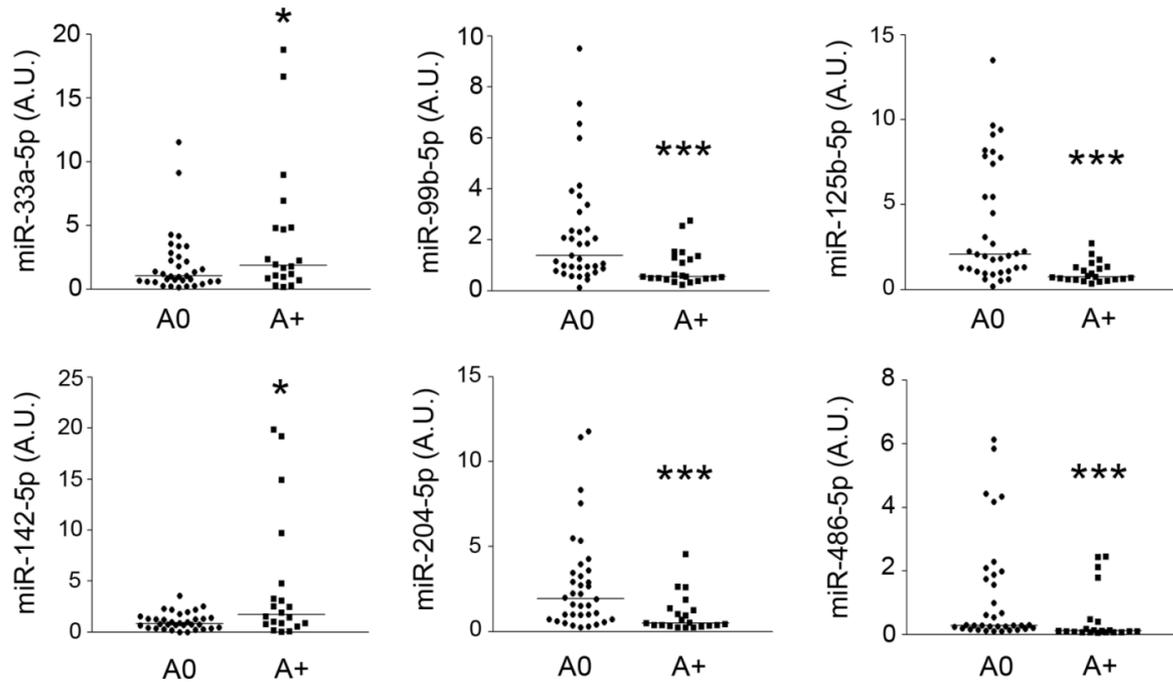
❖ 17 miRNA were modulated in the plasma of patients A+ as compared to patients A0 by miRNA array:

- 9 miRNA were downregulated
- 8 miRNA were upregulated





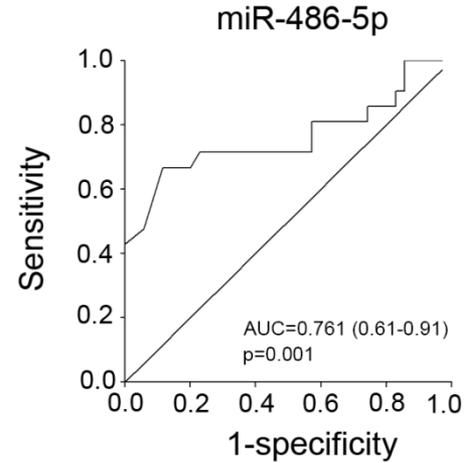
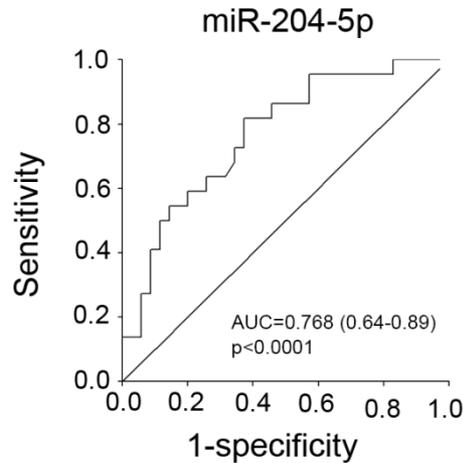
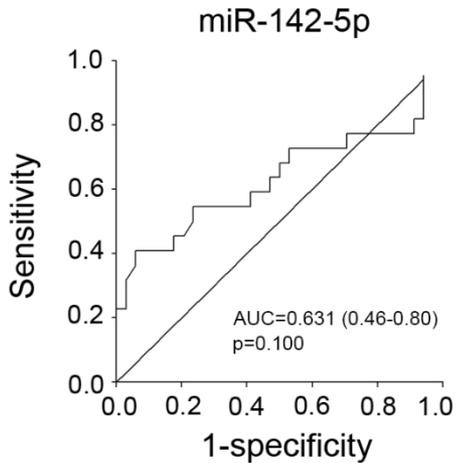
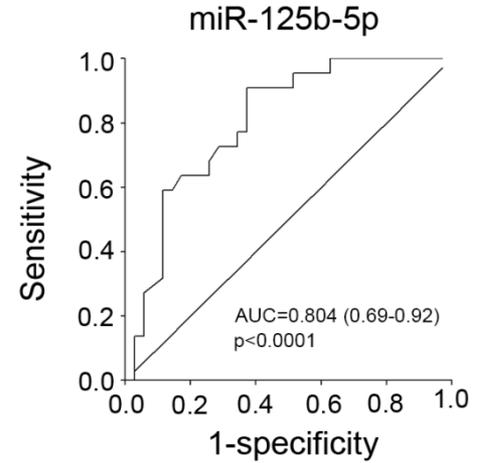
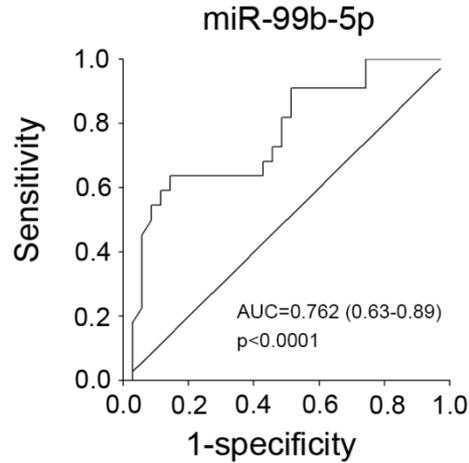
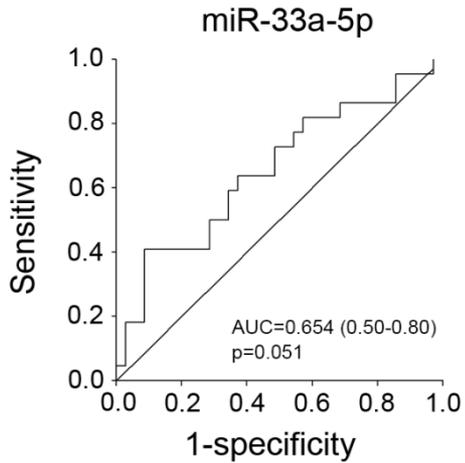
❖ 6 miRNA were significantly modulated in A+ patients as compared to A0 patients



	SUV max AAA		rSUV AAA/liver		Diameter	
miR-33a-5p	r= +0.313	p=0.01*	r= +0.258	p=0.03*	r= +0.173	p=0.105
miR-99b-5p	r= -0.267	p=0.022*	r= -0.251	p=0.03*	r= -0.118	p=0.19
miR-125b-5p	r= -0.392	p=0.002**	r= -0.365	p=0.003**	r= -0.278	p=0.018*
miR-142-5p	r= +0.179	p=0.091	r= +0.242	p=0.035*	r= -0.138	p=0.153
miR-204-5p	r= -0.277	p=0.018*	r= -0.279	p=0.018*	r= -0.22	p=0.05
miR-486-5p	r= -0.336	p=0.006**	r= -0.29	p=0.015*	r= -0.269	p=0.023*



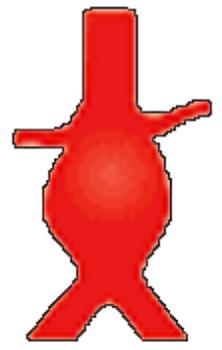
❖ The ROC curves show the discriminating powerfull of the four downregulated miRNAs



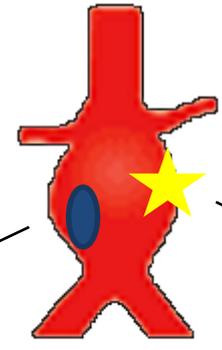


And in the wall:

A0 (n=12)

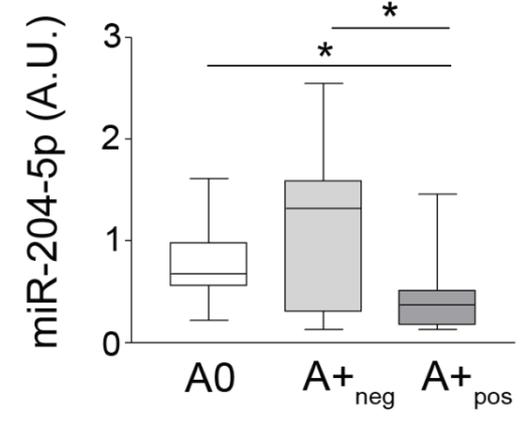
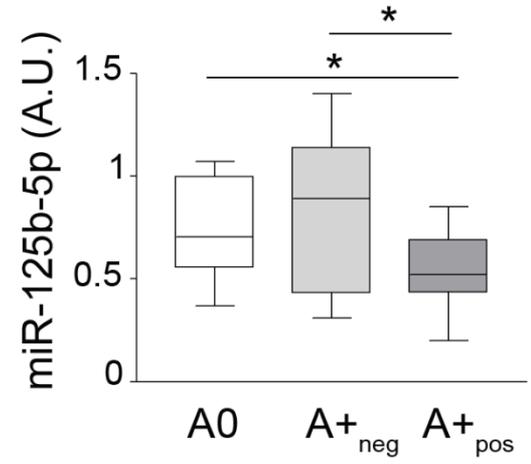
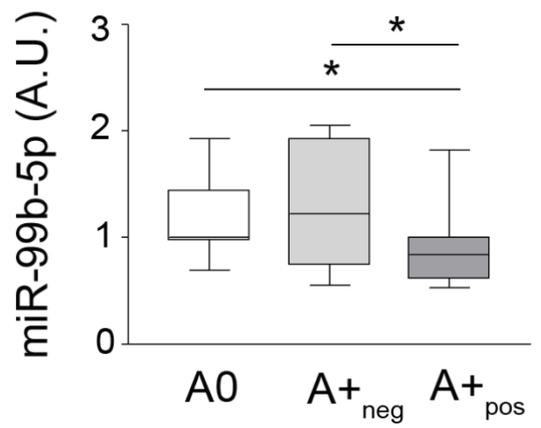


A+ (n=9)



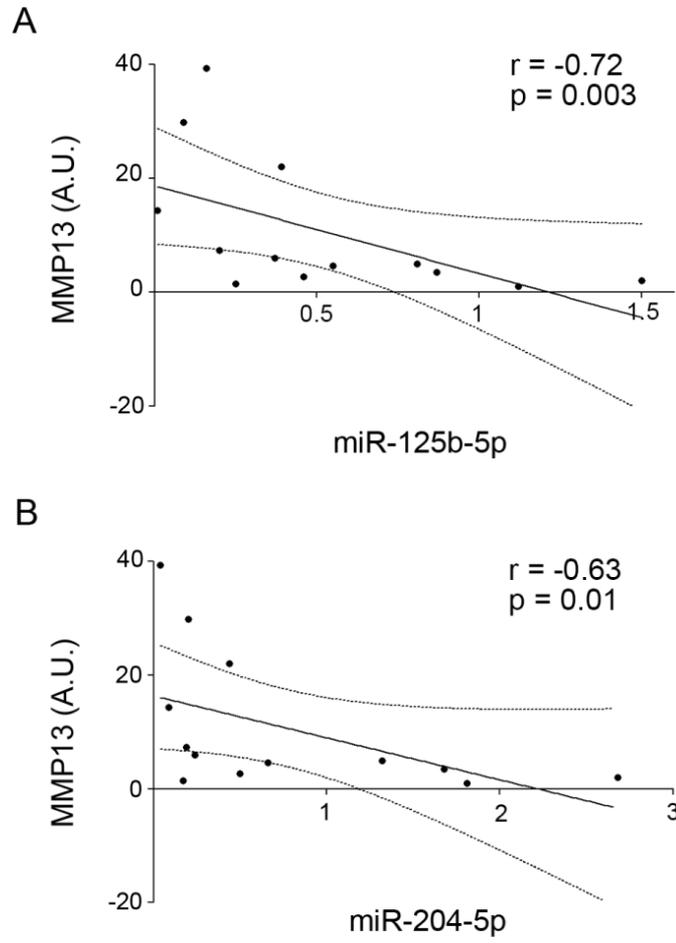
A+_{neg}

A+_{pos}





❖ MMP13 is a validated target of miR-125b-5p and was previously showed to be increased in the A+pos site of aneurysm



❖ In the media of A+ patients, miR-125b-5p and miR-204-5p were significantly and negatively correlated with MMP13



CONCLUSION

- ❖ 17 circulating miRNA were modulated between A0 and A+ patients and 6 of them were validated by realtime PCR
- ❖ The 6 miRNA modulated were significantly correlated with the SUV (AAA/liver) while two miRNA were correlated with the diameter of AAA
- ❖ miR-125b-5p has the higher AUC calculated on ROC curves
- ❖ miR-99b-5p, miR-125b-5p and miR-204-5p were downregulated in the aneurysmal wall at the specific FDG uptake site
- ❖ MMP13, a validated target of miR-125b-5p involved in the progression of AAA, was negatively correlated with this miRNA and with miR-204-5p



miR-125b-5p could represent a new potential biomarkers of the degradation of AAA leading to rupture



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