

# Ricerca di nuovi marcatori diagnostici/prognostici ERA DEGLI “OMICs”

✓ GENOMICA

✓ ESPRESSIONE GENICA:

transcriptoma

miRNOMA

metilomica

✓ PROTEOMICA

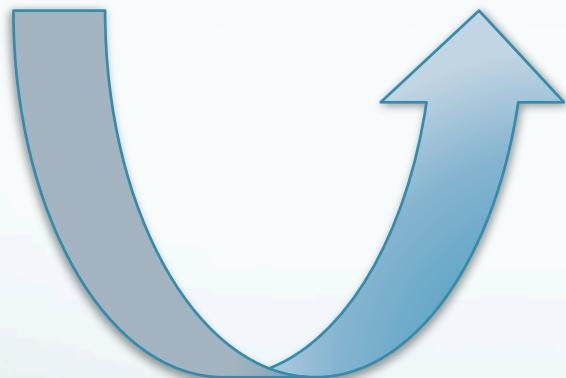
✓ METABOLOMICA

# **BIMARCATORI NON INVASIVI**

## **La Biopsia Liquida**

**TUMORE**

**sangue**



DNA libero circolante  
miRNA circolanti  
Cellule Tumorali Circolanti

# miR e ACC

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("micrornas" [MeSH Terms] OR "micrornas" [All Fields] OR "mirna" [All Fields]) AND ("adrenal gland neoplasms" [MeSH Terms] OR ("adrenal" [All Fields] AND "gland" [All Fields] AND "tumors" [All Fields]))

Next-generation sequencing reveals microRNA markers of adrenocortical tumors malignancy  
Lukasz Koperski, Marta Kotlarek, Michał Świerniak, Monika Kolanowska, Anna Kubiak, Barbara Górnicka, Krystian Jaźdżewski, Anna Wójcicka

ARTICLE IN PRESS

Molecular and Cellular Endocrinology xxx (2016) 1–8

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Elsevier

## The role of microRNAs in the pathophysiology of adrenal tumors

Nunki Hassan <sup>a, b</sup>, Jing Ting Zhao <sup>a, b</sup>, Stan B. Sidhu <sup>a, b, c, \*</sup>

<sup>a</sup> Cancer Genetics Laboratory, Kolling Institute, Northern Sydney Local Health District, St Leonards, NSW, Australia

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<sup>c</sup> University of Sydney Endocrine Surgery Unit, Royal North Shore Hospital, Sydney, St Leonards, Sydney, NSW, Australia

Oncotarget, Advance Publications 2017

## Next-generation sequencing reveals microRNA markers of adrenocortical tumors malignancy

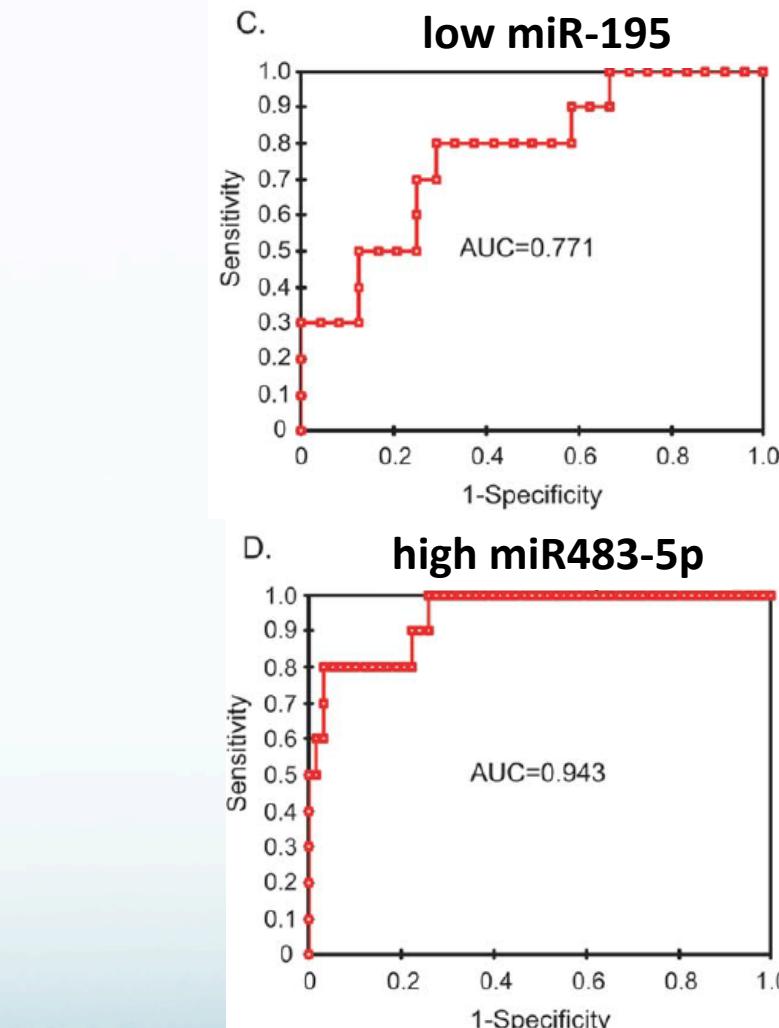
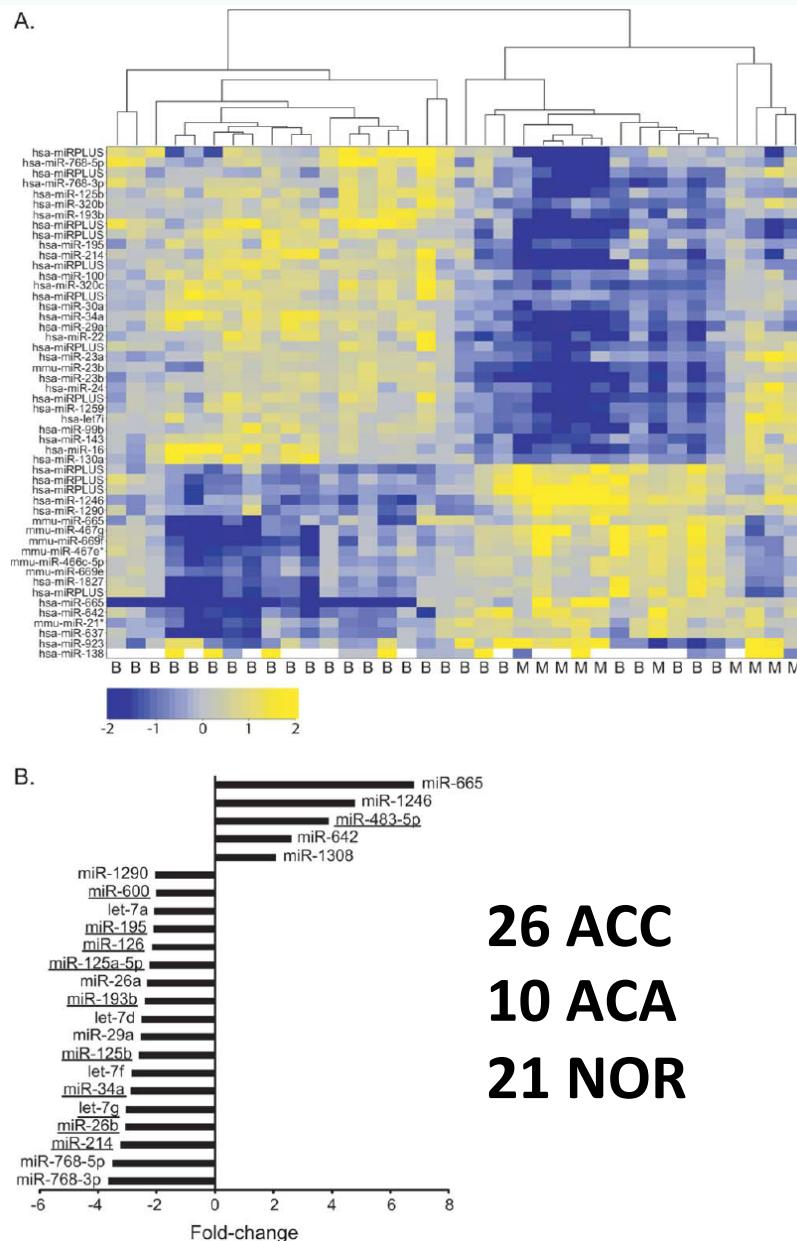
Lukasz Koperski<sup>1</sup>, Marta Kotlarek<sup>2</sup>, Michał Świerniak<sup>2,3</sup>, Monika Kolanowska<sup>2,3</sup>, Anna Kubiak<sup>2,3</sup>, Barbara Górnicka<sup>1</sup>, Krystian Jaźdżewski<sup>2,3</sup> and Anna Wójcicka<sup>2,3</sup>

<sup>1</sup> Department of Pathology, Medical University of Warsaw, Warsaw, Poland

<sup>2</sup> Laboratory of Human Cancer Genetics, Centre of New Technologies, CENT, University of Warsaw, Warsaw, Poland

<sup>3</sup> Genomic Medicine, Medical University of Warsaw, Warsaw, Poland

# miRNA in ACC

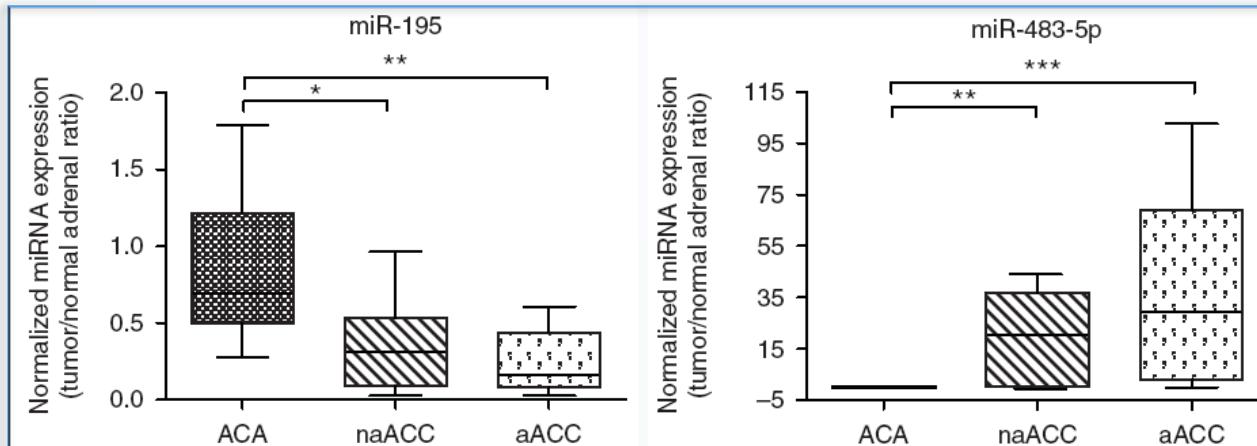


Patterson et al, Cancer 2010

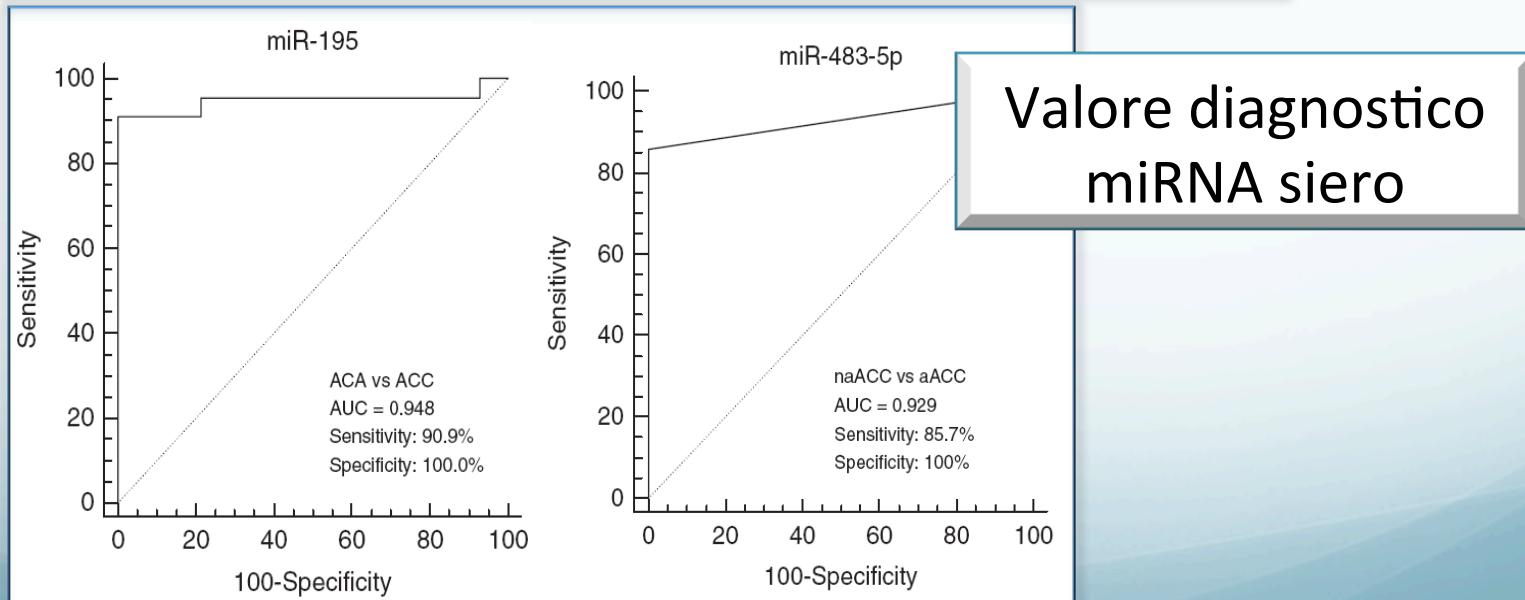
# Serum miR-483-5p and miR-195 are predictive of recurrence risk in adrenocortical cancer patients

Endocrine-Related Cancer  
(2013) 20, 579–594

O Chabre<sup>1,2,3,4</sup>, R Libé<sup>5,6,7</sup>, G Assie<sup>5,6,7</sup>, O Barreau<sup>5,6,7</sup>, J Bertherat<sup>5,6,7</sup>, X Bertagna<sup>5,6,7</sup>,  
J-J Feige<sup>1,3,4</sup> and N Cherradi<sup>1,3,4</sup>



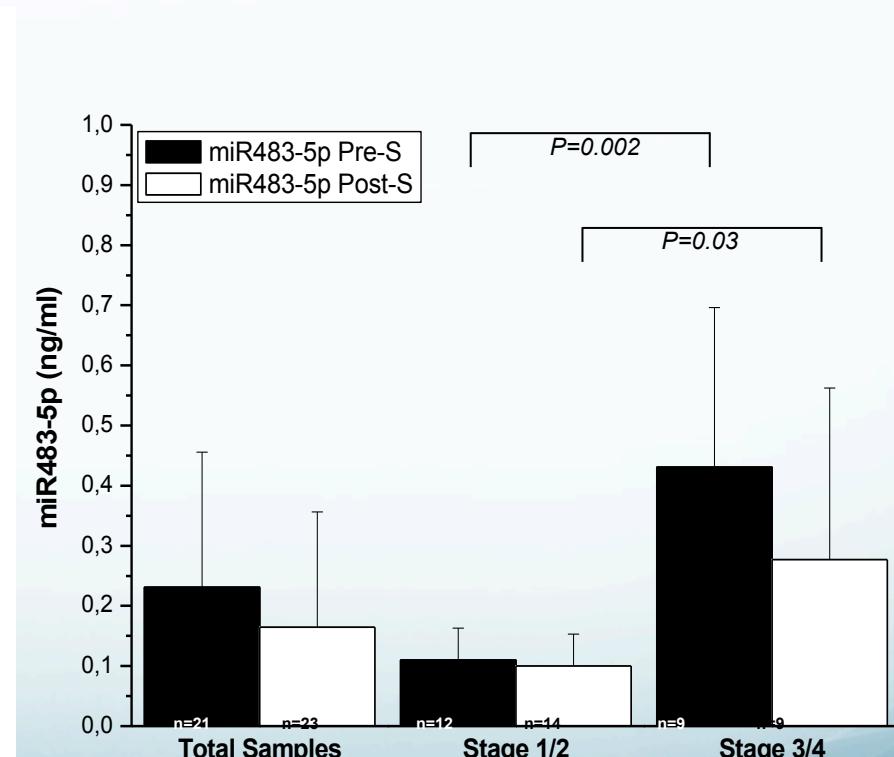
**9 naACC  
14 aACC  
14 ACA  
19 NOR**



## New insights in the clinical and translational relevance of miR483-5p in adrenocortical cancer

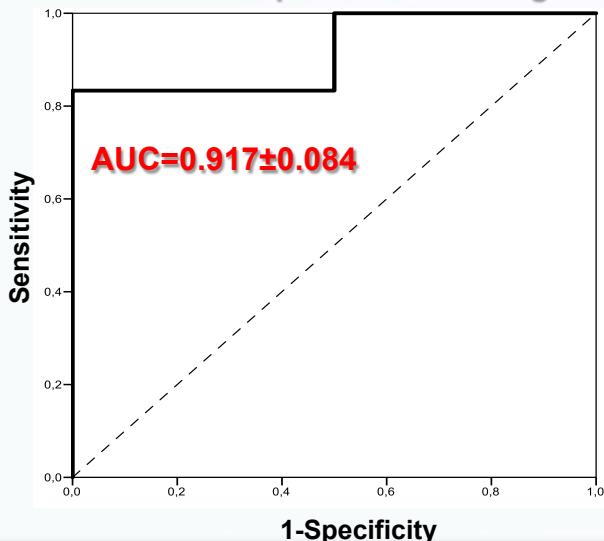
**Francesca Salvianti<sup>1,\*</sup>, Letizia Canu<sup>1,\*</sup>, Giada Poli<sup>1</sup>, Roberta Armignacco<sup>1</sup>, Cristian Scatena<sup>2</sup>, Giulia Cantini<sup>1</sup>, Alessandra Di Franco<sup>1</sup>, Stefania Gelmini<sup>1</sup>, Tonino Ercolino<sup>1</sup>, Mario Pazzaglia<sup>1</sup>, Gabriella Nesi<sup>3</sup>, Massimo Mannelli<sup>1</sup>, Pamela Pinzani<sup>1,\*</sup> and Michaela Luconi<sup>1,\*</sup>**

	Mean (SD)	N Patients	%
Age at surgery (years)	45.3(16.2)	27	100
Sex			
Male	11	41	
Female	18	59	
Secretion	17	63	
Cortisol	10	37	
Androgens	8	30	
DHEAS	2	7	
Progesterins	1	4	
Tumor Diameter (cm)	8.8(4.9)	27	100
Ki67 (%)	26.8(24.7)	25	92.6
WEISS	6.5(1.9)	24	88.9
Stage			
1	6	22	
2	12	44	
3	4	15	
4	5	19	
Metastases	Lung, liver, bone, pancreas, contralateral adrenal	5	18.5
Surgery	27	100	
Surgery Resection	R0	18	67
	R2	5	22
	nd	3	11
Mitotane therapy	21	78	
Other Chemotherapies (Etoposide-Doxorubicin-Cisplatin, taxol)	10	37	
Radiotherapy	0	0	
Follow-up from surgery (months)	17.6(17.3)	27	100
Survival	21	78	



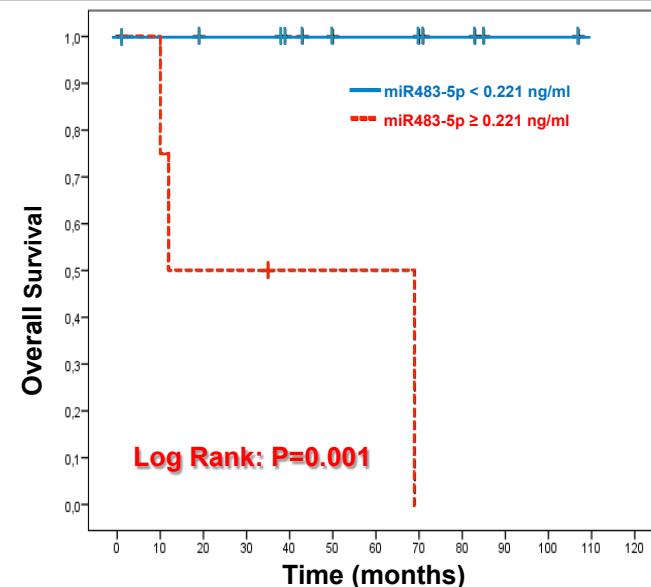
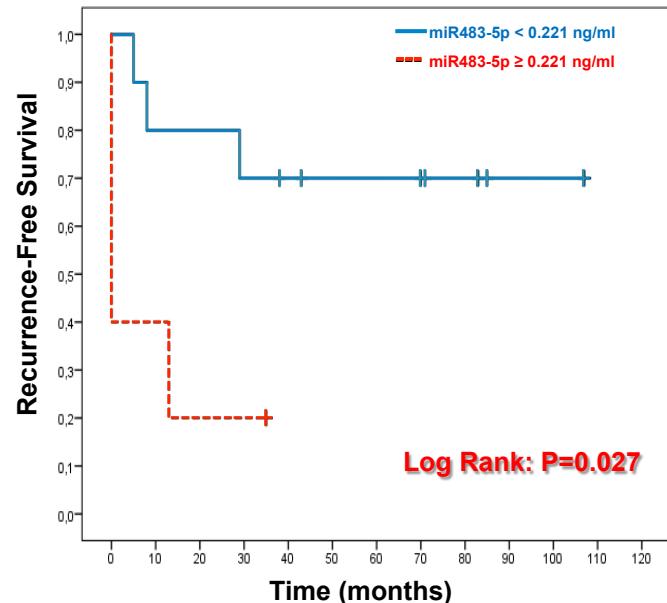
# miR483-5p predice OS e RFS

miR483-5p: cut off 0.221 ng/ml

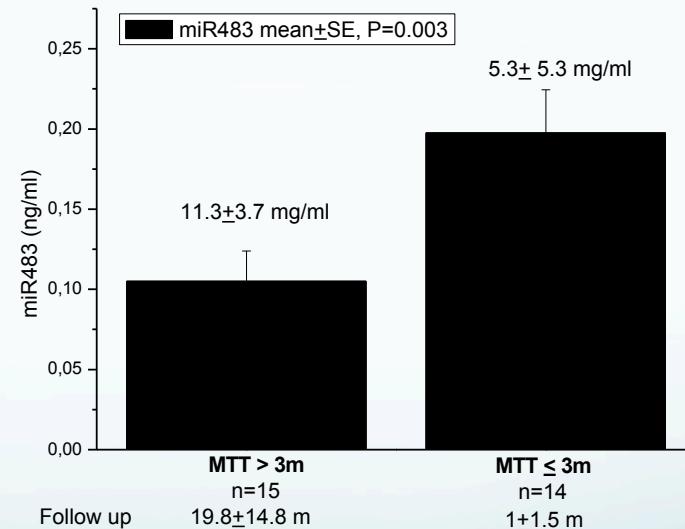
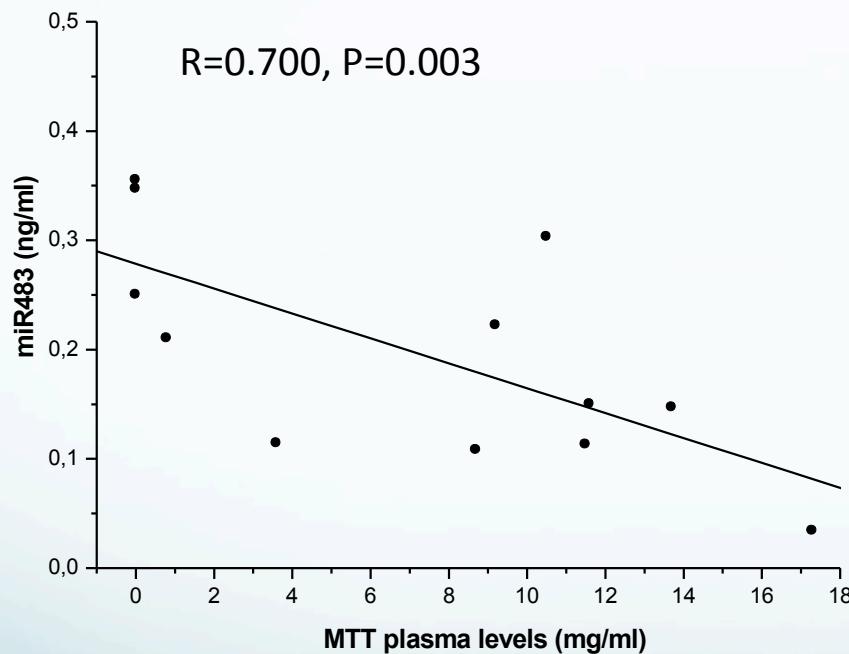


The range of the standard curve obtained on miR from H295R was 0.00523-5.23-pg miRNA. The quantity of miR483 and miR483-5p was calculated by interpolating the Cq values of qPCR on the standard curve and expressed as total miRNA equivalents. The results were normalized for the volume of plasma and expressed as ng equivalents/ml plasma

Taqman Small RNA assays (Life Technologies, USA):  
hsa-miR483 and hsa-miR483-5p on plasma samples



# miR483 correla negativamente con MTT levels



# miR483-5p e MTT

Studio pilota osservazionale:

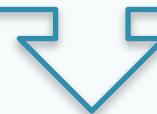
**HP: livelli plasmatici miR483-5p correlano inversamente con livelli**

- ✓ Campioni di plasma (500ul)
- ✓ Criteri di inclusione: pz ACC stadio 4  
trattamento MTT
- ✓ Prima e dopo inizio MTT
- ✓ Valori di MTT negli stessi prelievi

# CONCLUSIONI

- Nuovi markers diagnostici/prognostici a livello tumorale
- Nuovi markers diagnostici/prognostici non invasivi per diagnosi preoperatoria e follow-up

validare su casistiche estese



Club surrene & ENSAT  
combinazione nuovi markers  
in associazione con diagnostica classica

# Cellule Tumorali Circolanti in ACC

*J Clin Endocrinol Metab* 98: 3731–3738, 2013

ORIGINAL ARTICLE

Endocrine Research

## Detection of Circulating Tumor Cells in Patients With Adrenocortical Carcinoma: A Monocentric Preliminary Study

Pamela Pinzani,\* Cristian Scatena,\* Francesca Salvianti, Elisa Corsini, Letizia Canu, Giada Poli, Milena Paglierani, Valentina Piccini, Mario Pazzagli, Gabriella Nesi, Massimo Mannelli, and Michaela Luconi

Clinical Biochemistry (P.P., F.S., M.Paz.) and Endocrinology (E.C., L.C., G.P., V.P., M.M., M.L.) Units, Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence 50139, Italy; Division of Pathological Anatomy (C.S., M.Pag., G.N.), Department of Surgery and Translational Medicine, University of Florence, Florence 50139, Italy; and Istituto Toscano Tumori (M.M.), Florence 50139, Italy

# miR483-5p predice OS e FS

