

CARDIOVASCULAR REPAIR MECHANISMS: FROM STROMAL CELLS TO ncRNA

IBBC Seminar Series – February 1st 2021

Francesca Pagano
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Coupled RNA Processing and Transcription of Intergenic Primary MicroRNAs^{▽†}

Monica Ballarino,^{1‡} Francesca Pagano,^{1‡} Erika Girardi,¹ Mariangela Morlando,^{1,2} Davide Cacchiarelli,¹
Marcella Marchioni,¹ Nicholas J. Proudfoot,² and Irene Bozzoni^{1*}

*pienza University of Rome,
xford, South Parks Rd.,*

blood

Prepublished online August 16, 2012;
doi:10.1182/blood-2012-05-431791

JAK2V617F-homozygosity arises commonly and recurrently in PV and ET, but PV is characterized by expansion of a dominant homozygous subclone

Anna L. Godfrey, Edwin Chen, Francesca Pagano, Christina A. Ortmann, Yvonne Silber, Beatriz Bellosillo, Paola Guglielmelli, Claire N. Harrison, John T. Reilly, Frank Stegelmann, Fontanet Bijou, Eric Lippert, Mary F. McMullin, Jean-Michel Boiron, Konstanze Döhner, Alessandro M. Vannucchi, Carlos Besses, Peter J. Campbell and Anthony R. Green



UNIVERSITY OF
CAMBRIDGE

Leukemia
<https://doi.org/10.1038/s41375-018-0053-9>

BRIEF COMMUNICATION

Chronic myeloproliferative neoplasms

MicroRNA-101 expression is associated with JAK2V617F activity and regulates JAK2/STAT5 signaling

Francesca Pagano^{1,2} • Federico Comoglio^{1,2} • Jacob Grinfeld^{1,2,3} • Juan Li^{1,2} • Anna Godfrey³ • Joanna Baxter⁴ •
Yvonne Silber^{1,2} • Anthony R Green^{1,2,3}



EDITORIAL

Open Challenges and New Perspectives in Cardiac Regenerative Medicine

Francesca Pagano¹ and Isotta Chimenti^{2,3,*}

¹*Institute of Biochemistry and Cell Biology, National Council of Research (IBBC-CNR), Monterotondo (RM), Italy;*

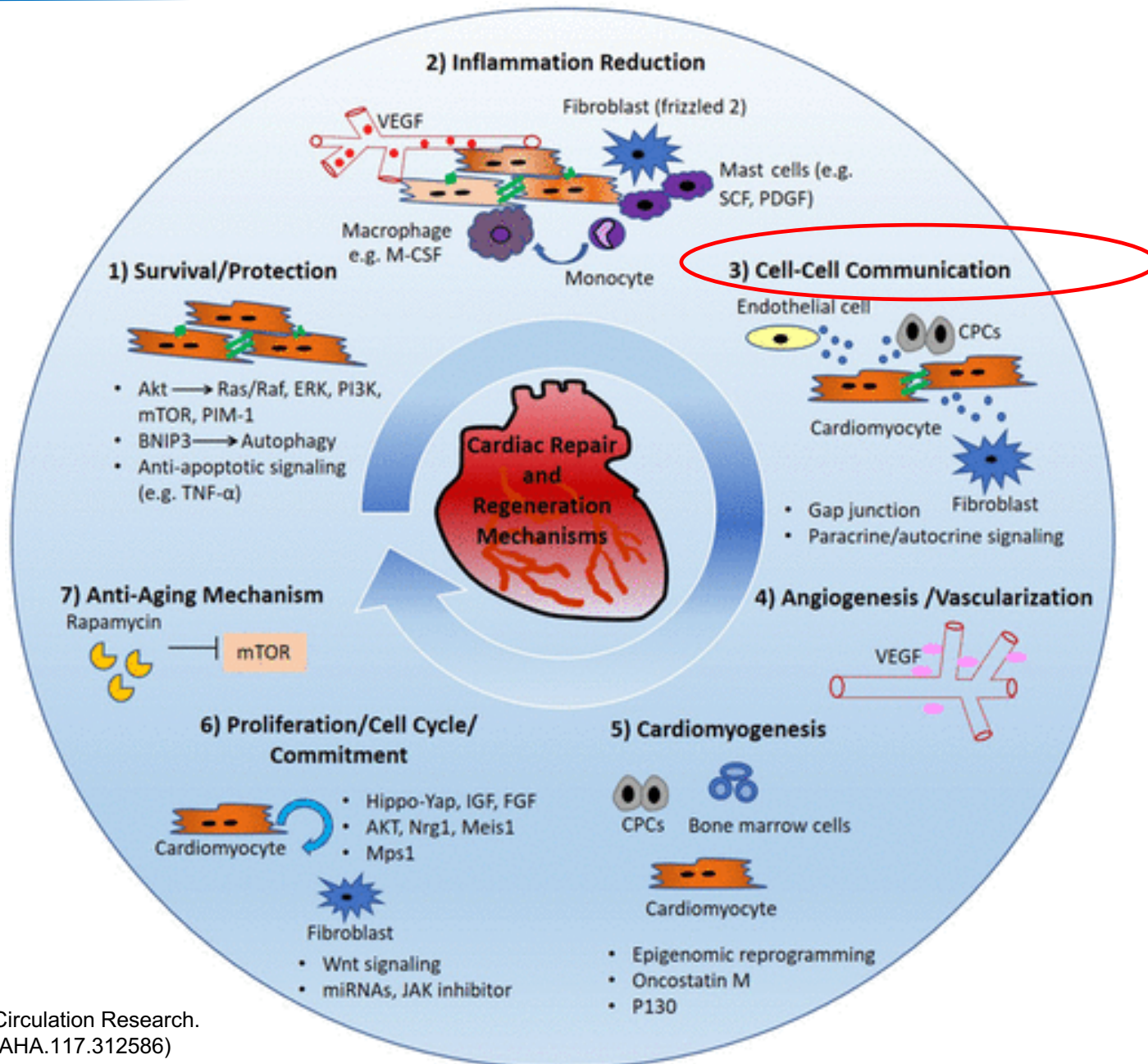
²*Mediterranea Cardiocentro, Napoli, Italy;* ³*Department of Medical Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy*

The Noncoding Side of Cardiac Differentiation and Regeneration

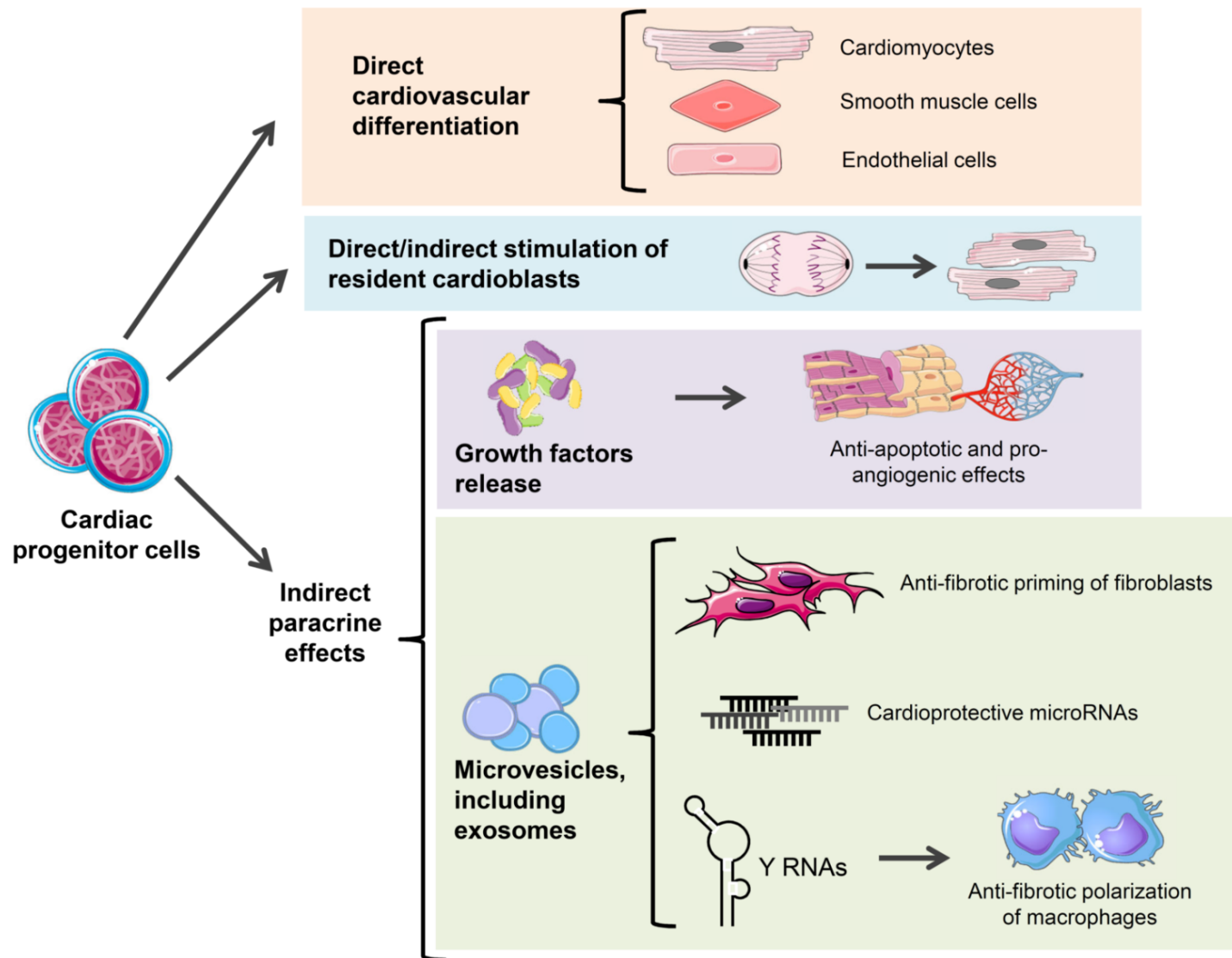
Francesca Pagano^{1,*}, Alessandro Calicchio², Vittorio Picchio¹ and Monica Ballarino^{2,*}

¹*Department of Medico-Surgical Sciences and Biotechnology, Sapienza University of Rome, C.so della Repubblica 79, 04100 Latina, Italy;* ²*Department of Biology and Biotechnology "Charles Darwin", Sapienza University of Rome, P.le A. Moro 5, 00185 Rome, Italy*

Cardiac repair is a complex and multifaceted matter

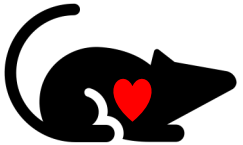
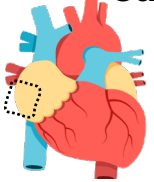


Stromal Progenitor Cells: Mechanisms Of Action

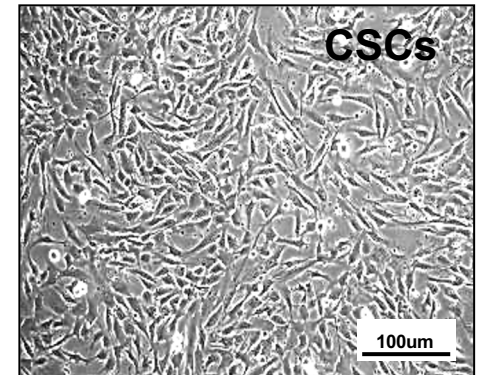
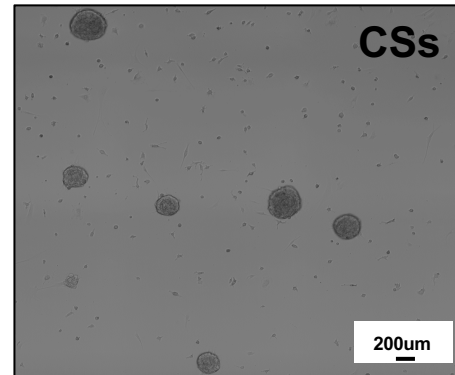
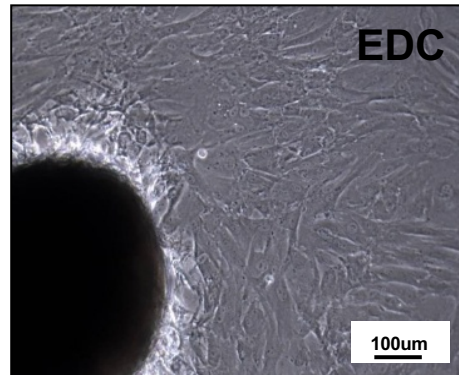
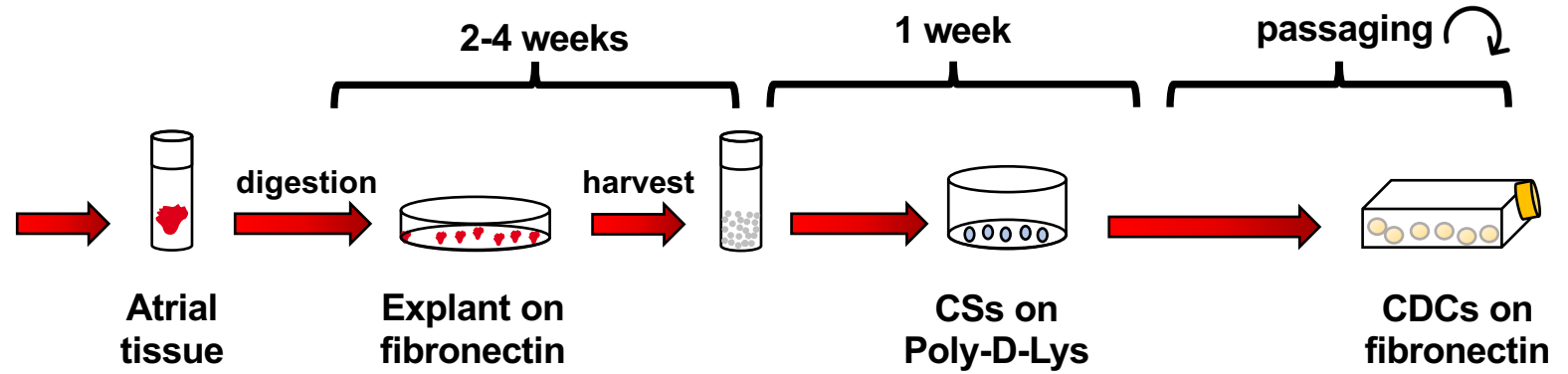


Stromal Cells Culture System

HUMAN
Cardiac Biopsy



C57BL/6J
4weeks



Micro-Environment and CSCs: patient clinical history

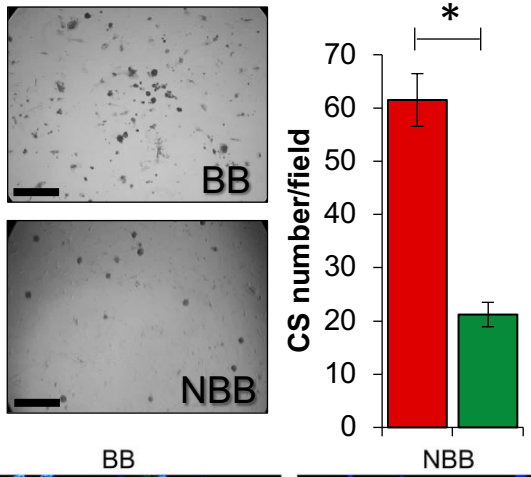
Variable*	No beta-blocker therapy NBB	Beta-blocker therapy BB	p†
Cardiospheres	7/19 (36.8%)	18/22 (81.2%)	0.005
Cumulative yield (EDCs/mg)	0 (0; 1,308)	3,319 (464; 6,012)	0.010

Cardioselective Beta Blockers

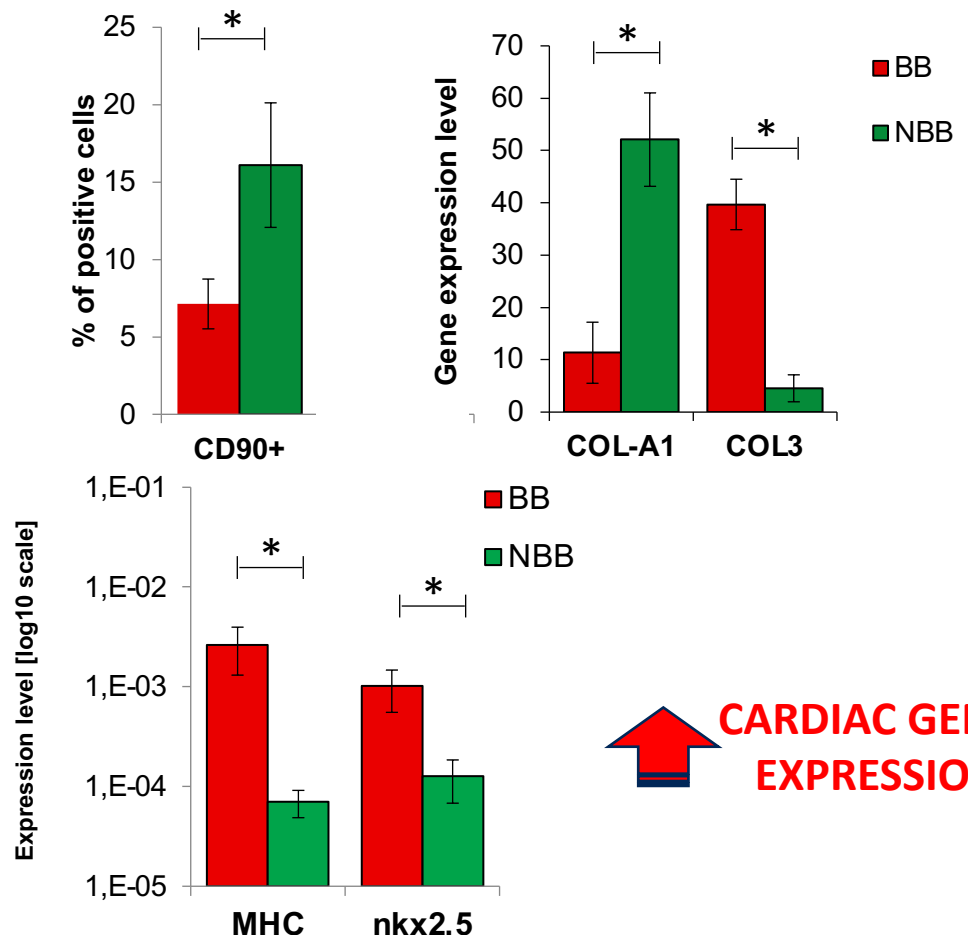
- Metoprolol
- Atenolol
- Nebivolol
- Bisoprolol
- Acebutolol
- Betaxolol
- Esmolol

β1
"MANBABE"

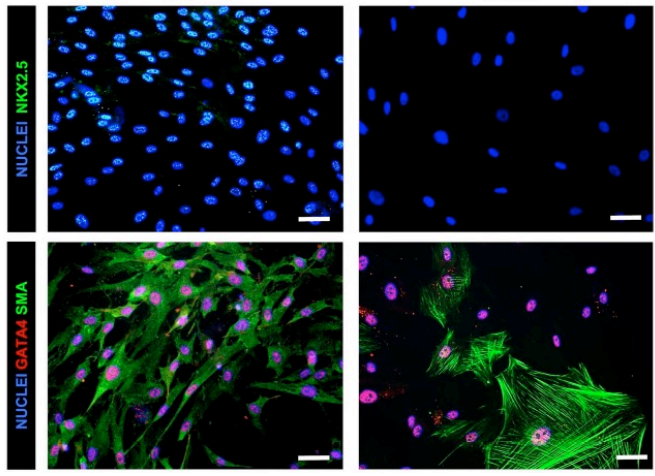
PROLIFERATIVE POTENTIAL



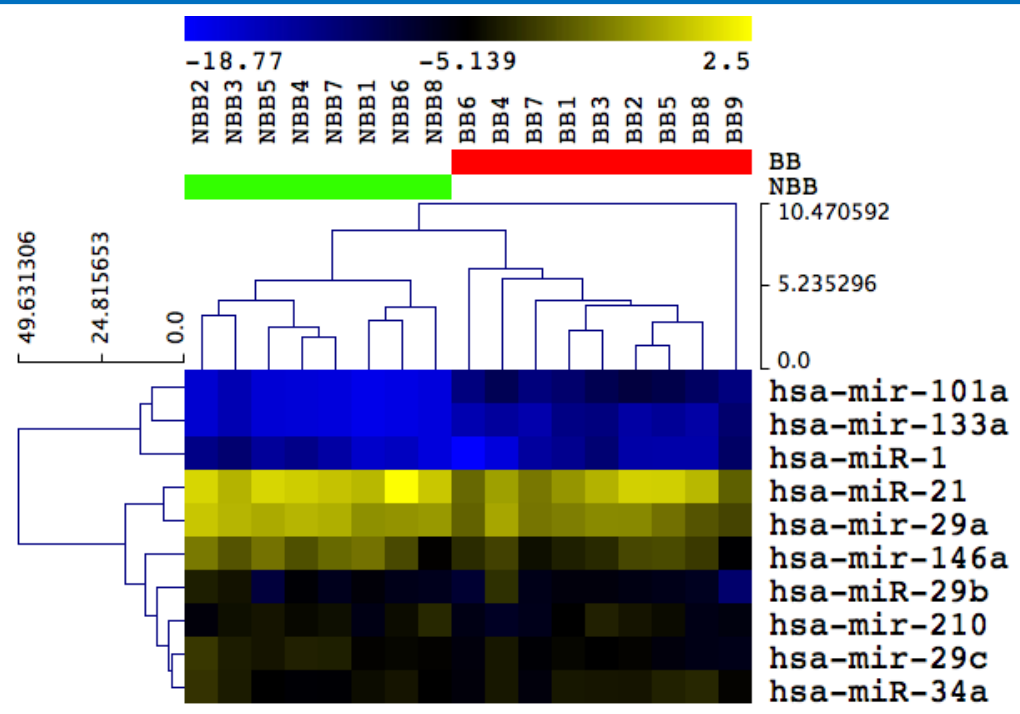
FIBROTIC PHENOTYPE



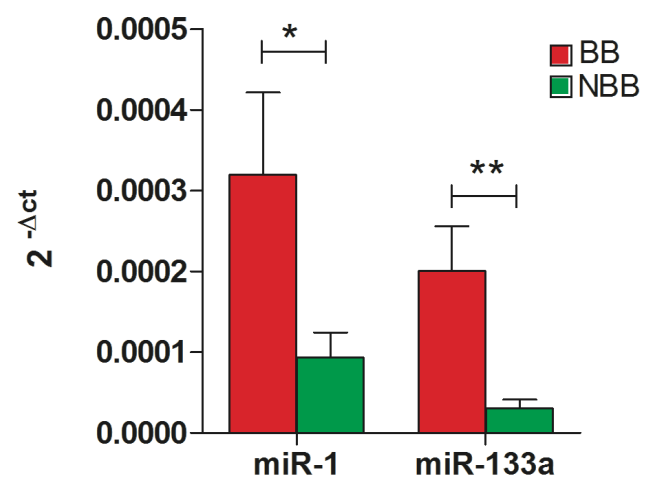
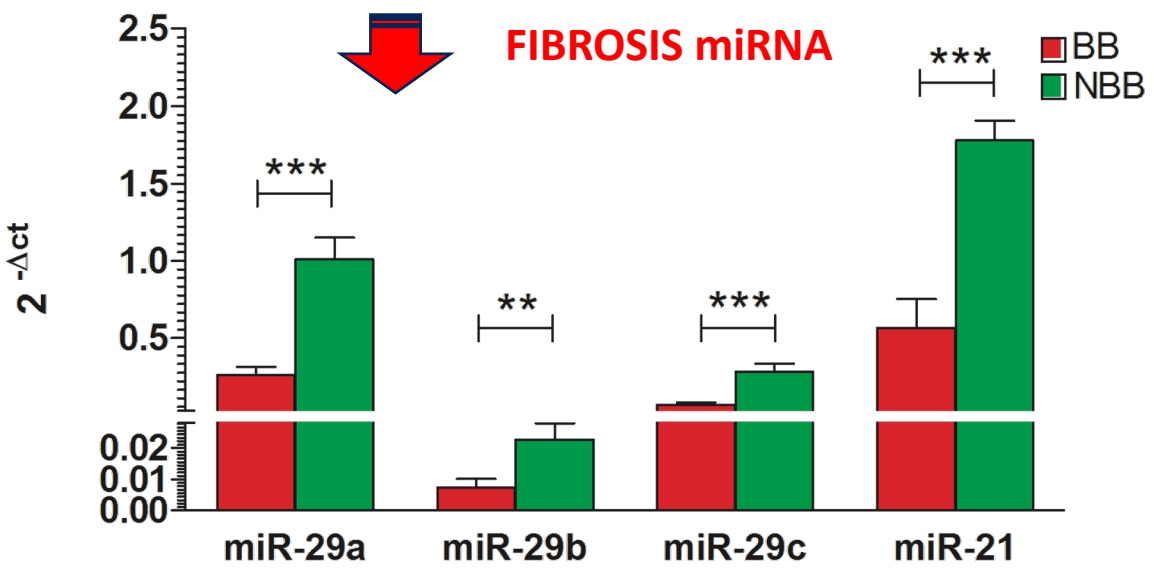
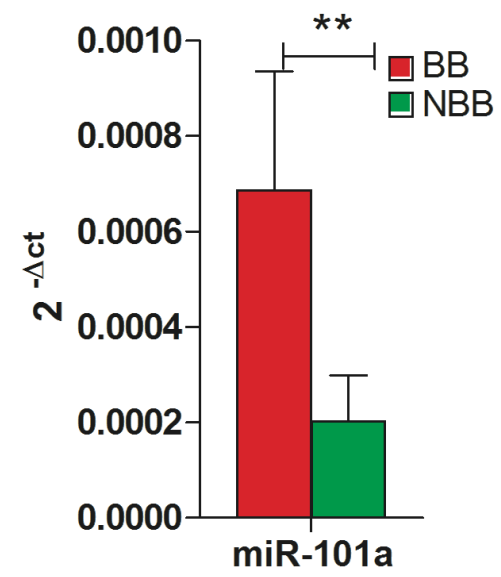
CARDIAC GENES EXPRESSION



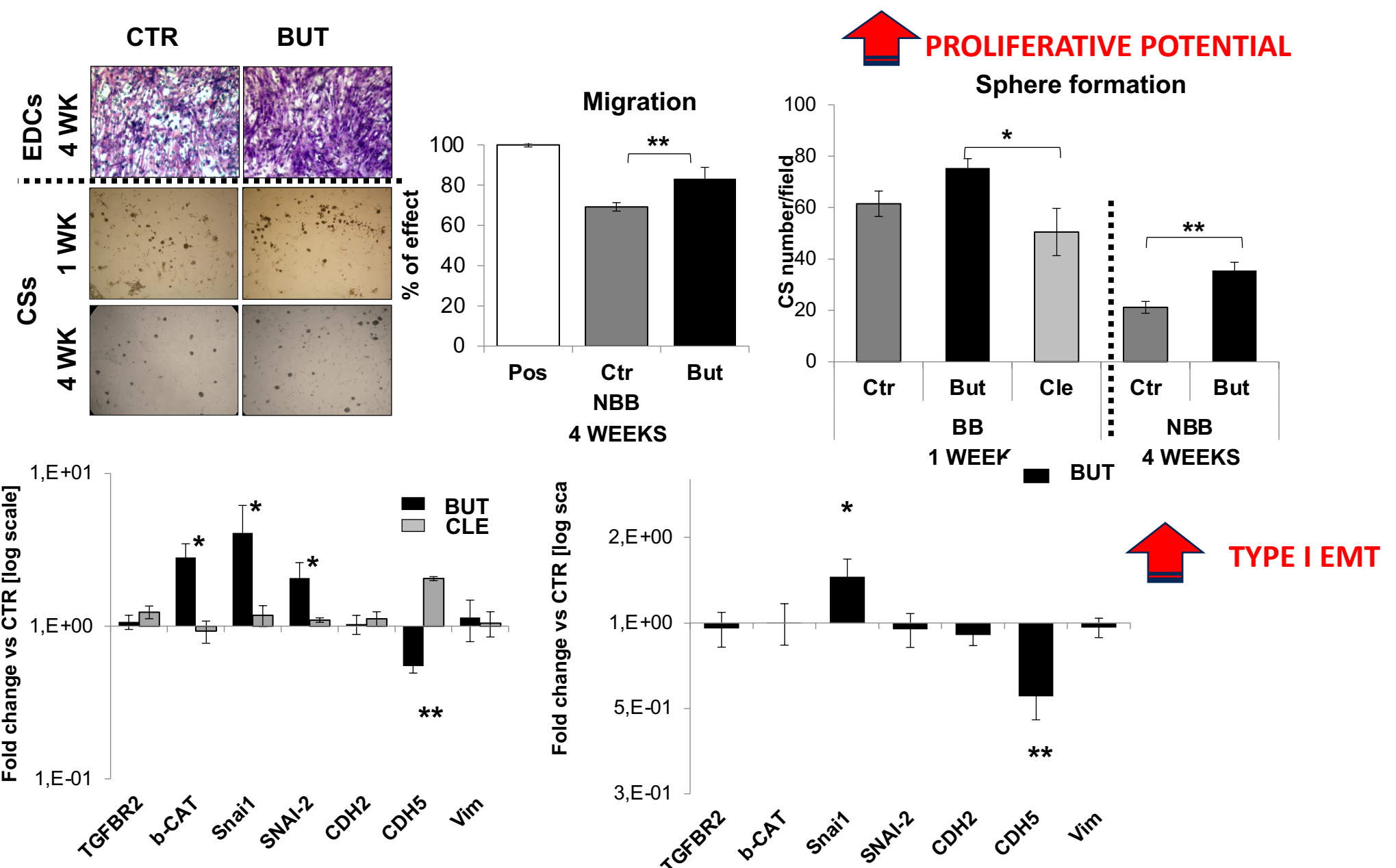
Micro-Environment and CSCs: patient clinical history



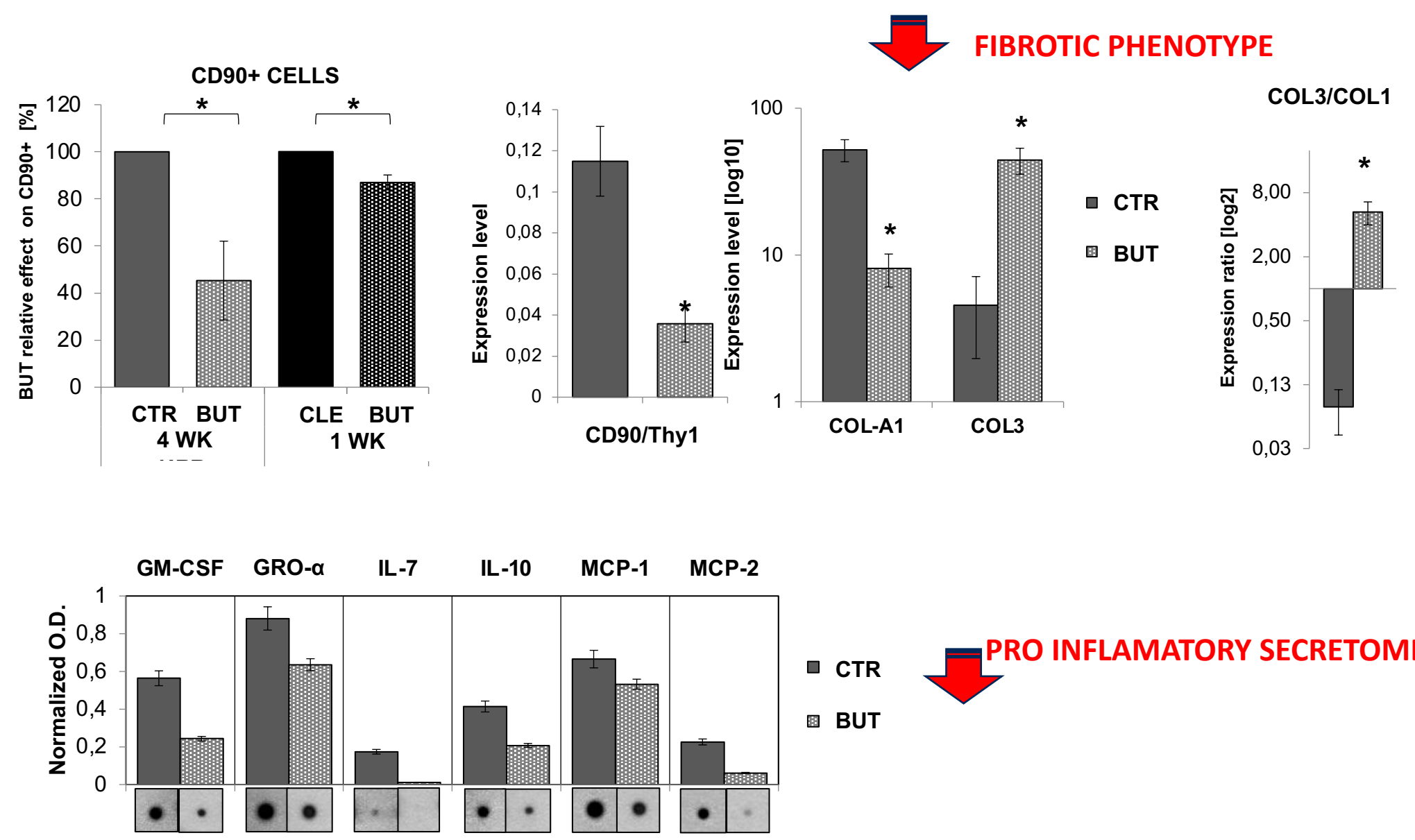
 **CARDIAC FUNCTION RECOVERY AND PROTECTION**



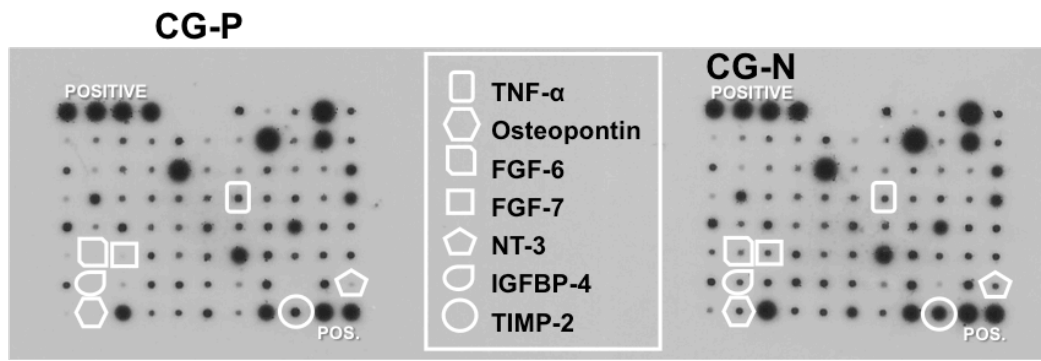
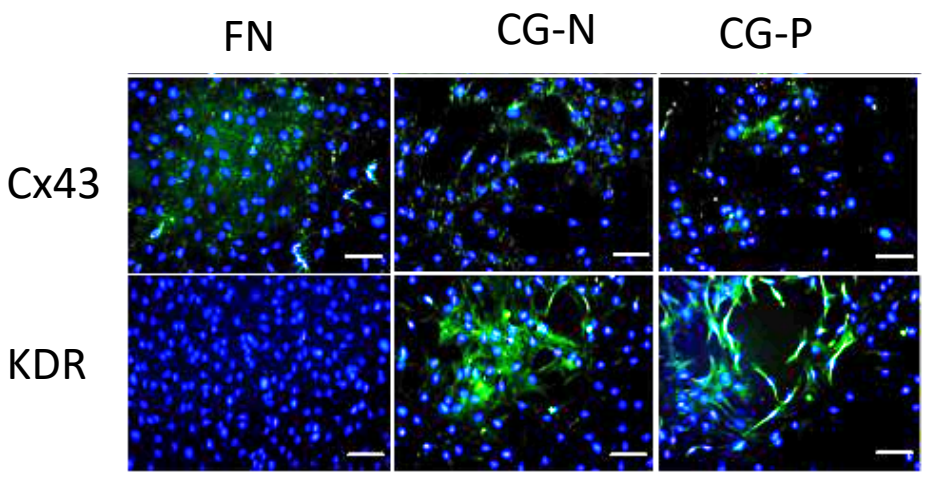
Micro-Environment and CSCs: **in vitro** manipulation



Micro-Environment and CSCs: **in vitro** manipulation

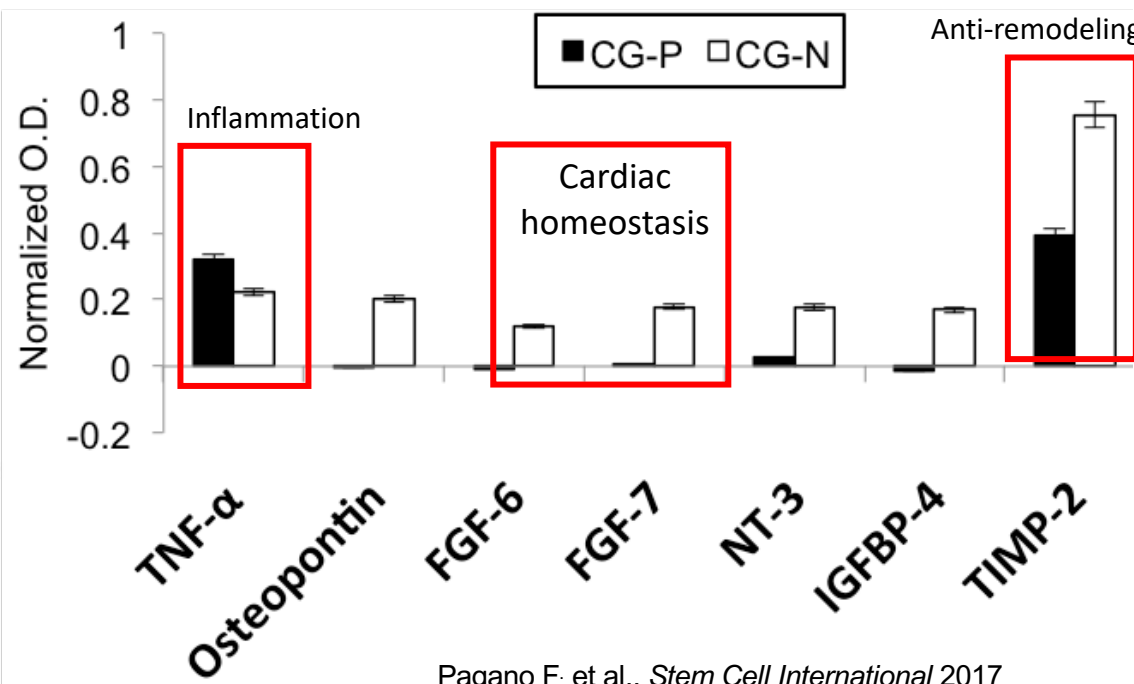
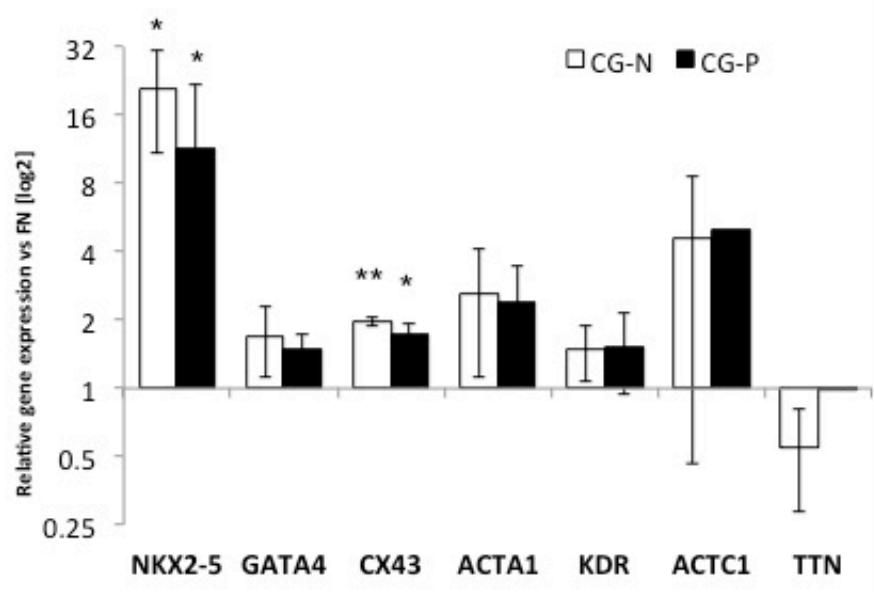


Micro-Environment and CSCs: Fibroblast derived ECM-CARDIOGEL

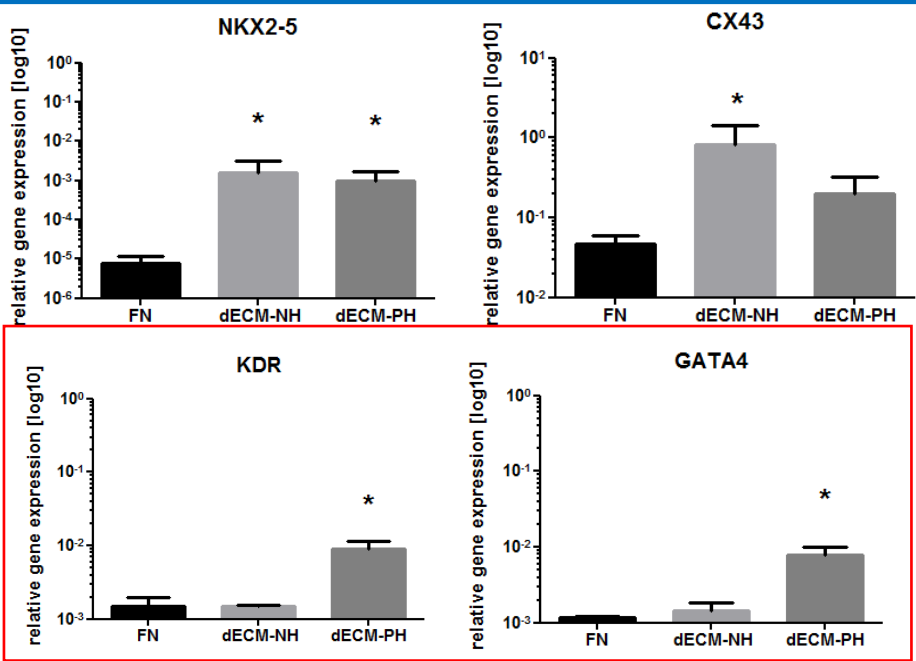
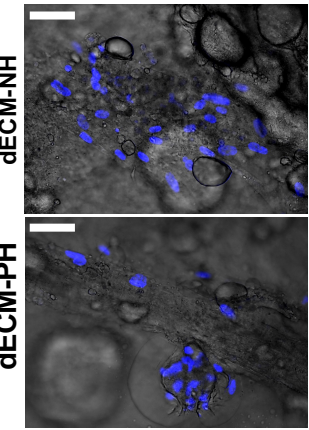


SPECIFIC SECRETOME PROFILE

CARDIAC GENES EXPRESSION



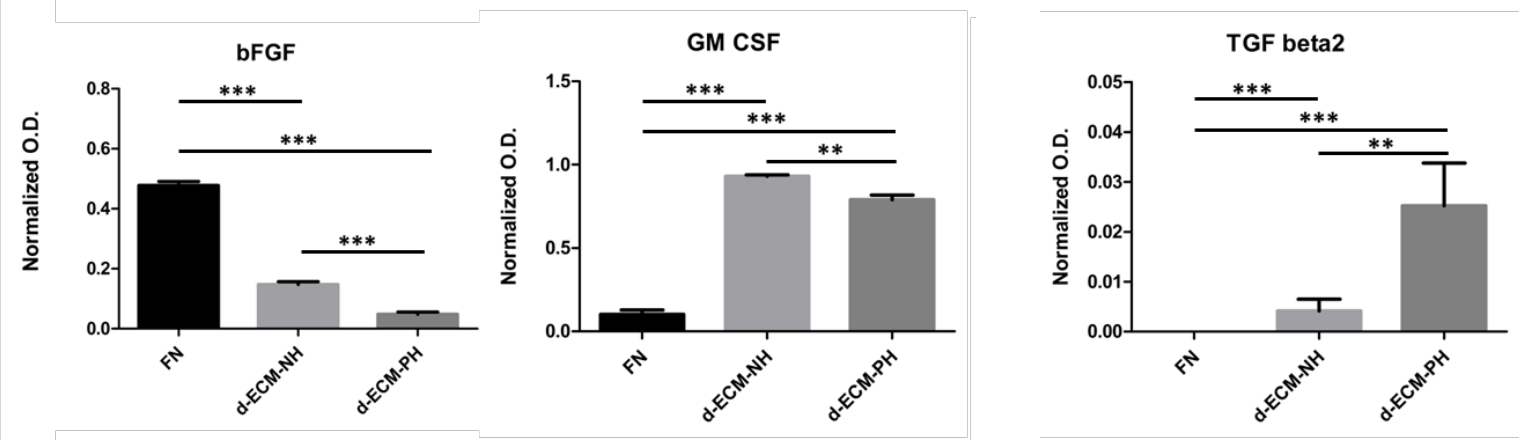
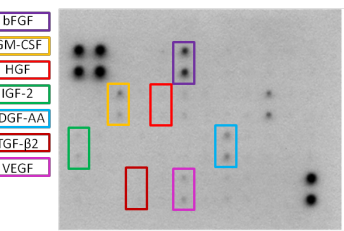
Micro-Environment and CSCs: cardiac de-cellularized ECM



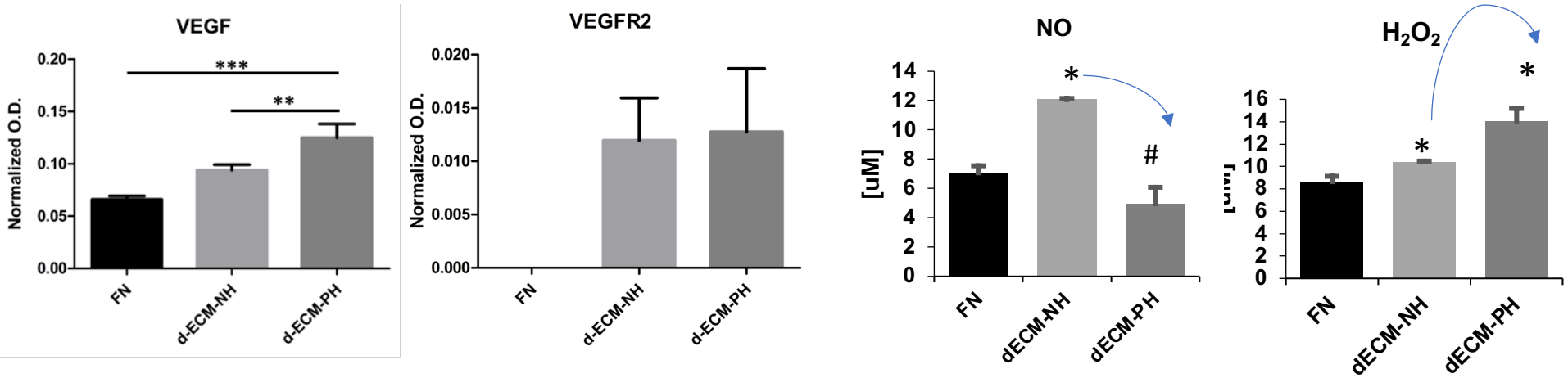
CARDIAC GENES EXPRESSION

ISCHEMIA «RESCUE GENES»

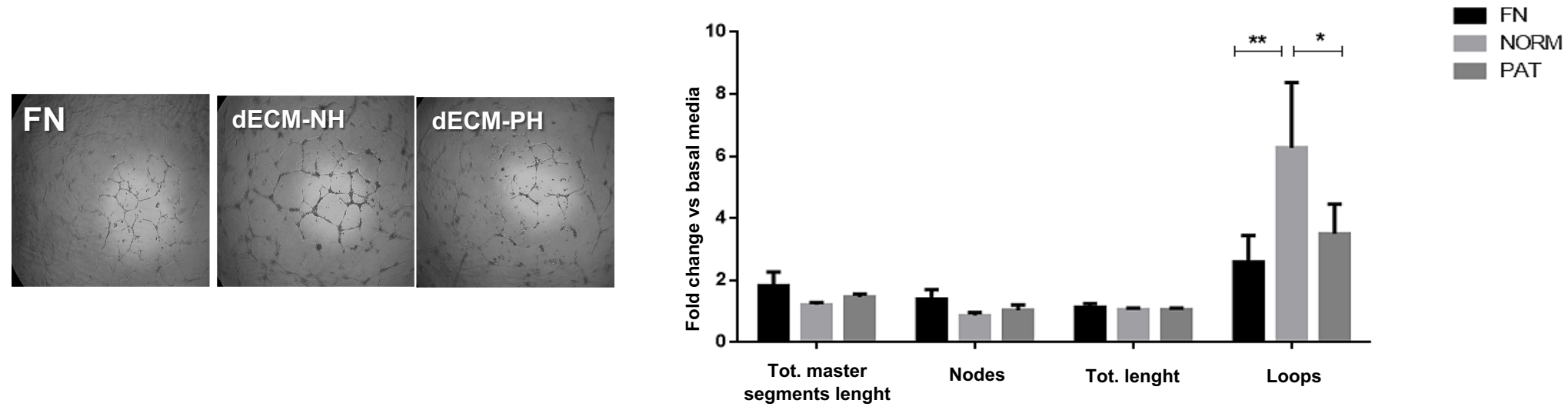
**LOW REGENERATIVE POTENTIAL
PARACRINE PROFILE**



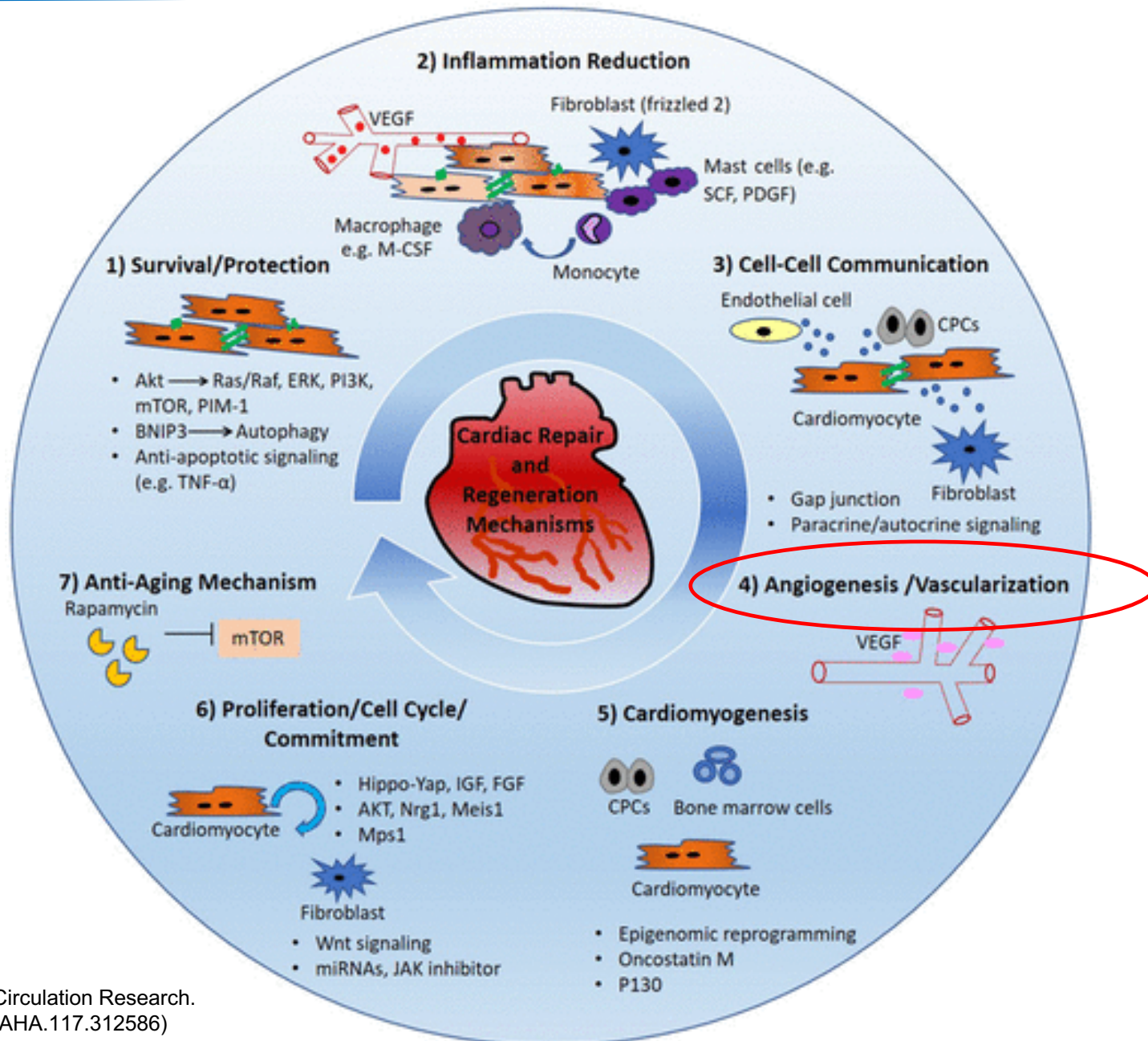
Micro-Environment and CSCs: cardiac de-cellularized ECM



PECULIAR MODULATION of ANGIOGENESIS DRIVE



Cardiac repair is a complex and multifaceted matter



LATEST NEWS

Molecular Effects of Cardiovascular risk factors Cigarette Smoke and the Cardiovascular System

The American Journal of Cardiology (www.ajconline.org)

Impact of Tobacco Versus Electronic Cigarette Smoking on Platelet Function



Cristina Nocella, PhD^a, Giuseppe Biondi-Zoccai, MD, MStat^{a,b}, Sebastiano Sciarretta, MD^{a,b},
Mariangela Peruzzi, MD^b, Francesca Pagano, PhD^b, Lorenzo Loffredo, MD^c, Pasquale Pignatelli, MD^c,
Chris Bullen, MD^d, Giacomo Frati, MD, MSc^{a,b}, and Roberto Carnevale, PhD^{b,*}

Journal of the American Heart Association

Chapter 2

ORIGINAL RESEARCH

Inhibition of miR-155 Attenuates Detrimental Vascular Effects of Tobacco Cigarette Smoking

Giacomo Frati, MD^{*}; Maurizio Forte, PhD^{*}; Flavio di Nonno, MS; Antonella Bordin, PhD; Isotta Chimenti, PhD;
Vittorio Picchio, PhD; Elena Cavarretta , MD, PhD; Rosita Stanzione, MS; Franca Bianchi, MS;
Roberto Carnevale , PhD; Cristina Nocella, PhD; Sonia Schiavon , MS; Daniele Vecchio , MS;
Simona Marchitti , MS; Elena De Falco, PhD; Speranza Rubattu, MD; Francesco Paneni, MD, PhD;
Giuseppe Biondi-Zoccai, MD; Francesco Versaci, MD; Massimo Volpe, MD; Francesca Pagano, PhD[†];
Sebastiano Sciarretta , MD, PhD[†]



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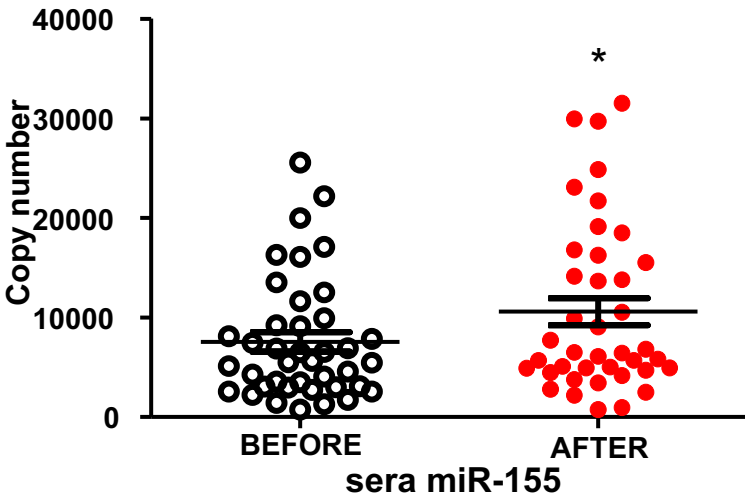
Effects of Smoking on Oxidative Stress and Vascular Function

Roberto Carnevale, Vittoria Cammisotto,
Francesca Pagano and Cristina Nocella

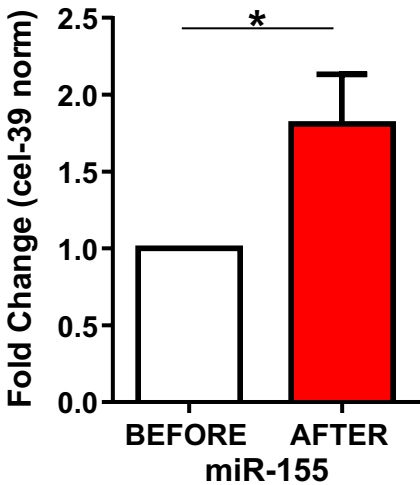
IntechOpen

Cigarette Smoke effects on Vascular Cells Function

Selected circulating microRNAs	BEFORE		AFTER		Wilcoxon matched-pairs signed rank test	
	Mean	S.E.M.	Mean	S.E.M.	P value	
hsa-mir-101a	6.50E-10	1.20E-10	5.71E-10	1.02E-10	0.4639	ns
hsa-miR126	6.07E-09	1.32E-09	6.49E-09	8.00E-10	0.0892	ns
hsa-miR-138	n.d.		n.d.		NA	
hsa-miR-15a	n.d.		n.d.		NA	
hsa-miR-155	3.13E-10	3.91E-11	4.35E-10	5.44E-11	0.0215	*
hsa-miR-181	1.14E-09	1.20E-10	1.13E-09	1.23E-10	0.7346	ns
hsa-miR-200b	n.d.		n.d.		NA	
hsa-miR-21	3.09E-08	7.78E-09	2.10E-08	3.20E-09	0.4125	ns
hsa-miR-212	1.24E-09	2.86E-10	9.06E-10	1.67E-10	0.8264	ns
hsa-mir-29a	1.19E-09	4.94E-10	8.66E-10	1.22E-10	0.1119	ns
hsa-miR-29b	n.d.		n.d.		NA	
hsa-mir-29c	7.31E-10	3.87E-10	4.69E-10	8.64E-11	0.1139	ns
hsa-miR-223	5.87E-06	1.45E-06	6.15E-06	1.26E-06	0.2479	ns
hsa-miR-365	1.56E-09	2.79E-10	1.79E-09	3.09E-10	0.7146	ns
hsa-miR-370	n.d.		n.d.		NA	
hsa-miR-495	n.d.		n.d.		NA	

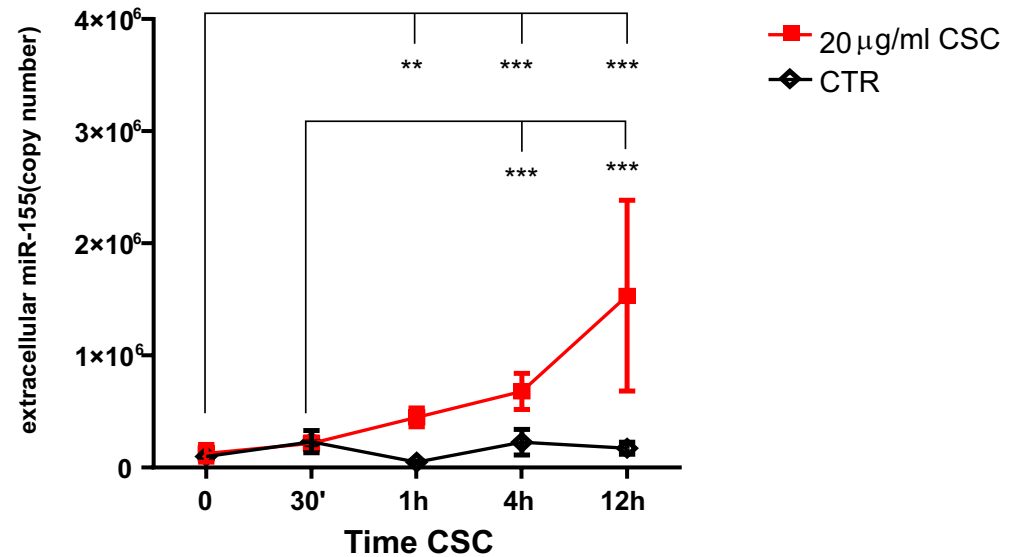


miR-155 is doubled after smoking one cigarette

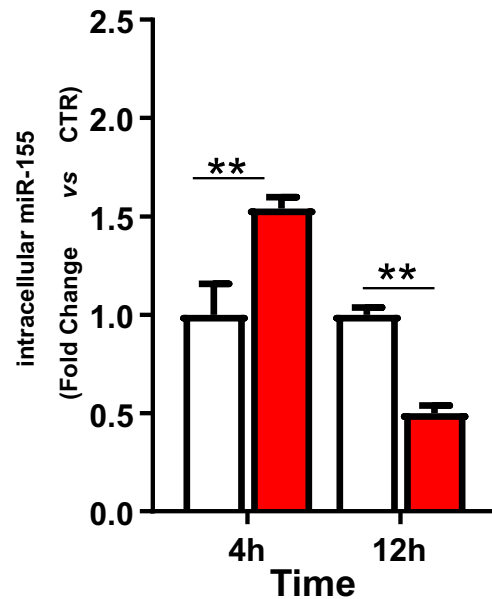


Cigarette Smoke effects on Vascular Cells Function

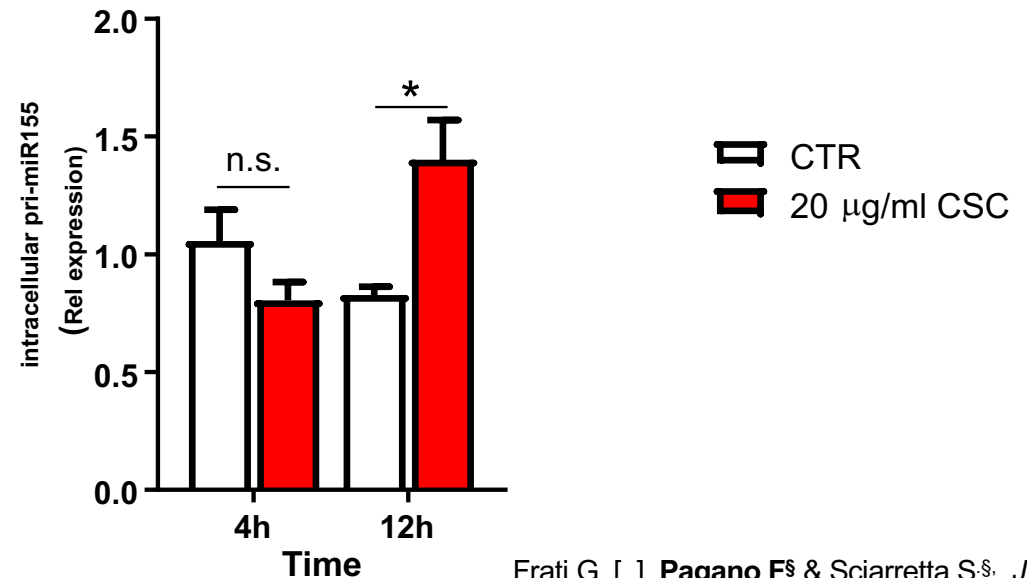
Extracellular miR-155
Increases upon Condensed Smoke treatment
In HUVECs



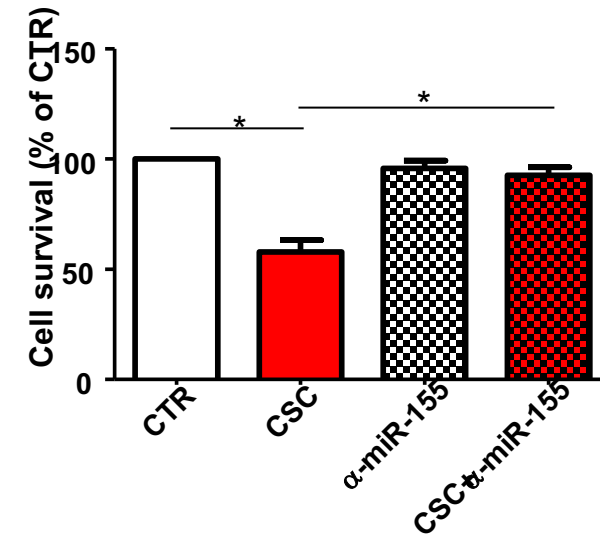
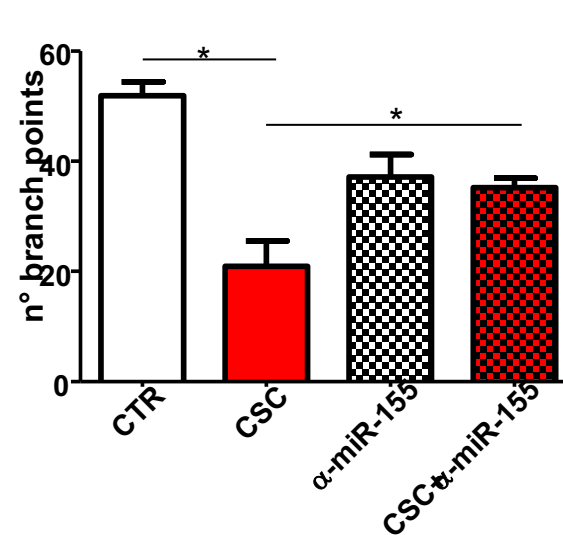
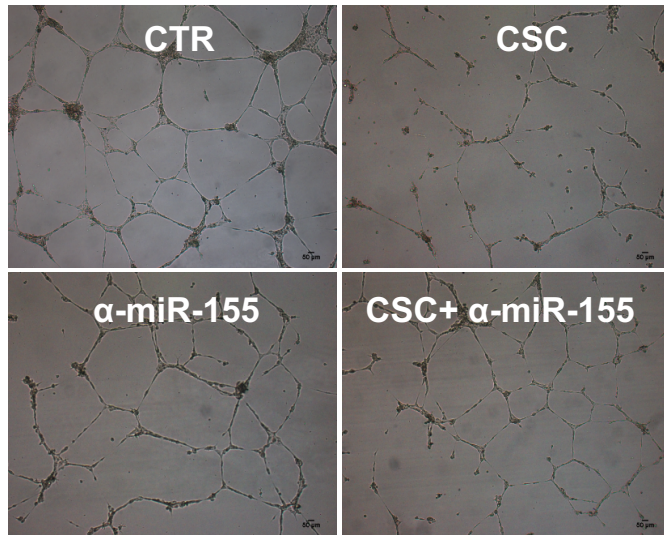
Intracellular miR-155 is increased ...



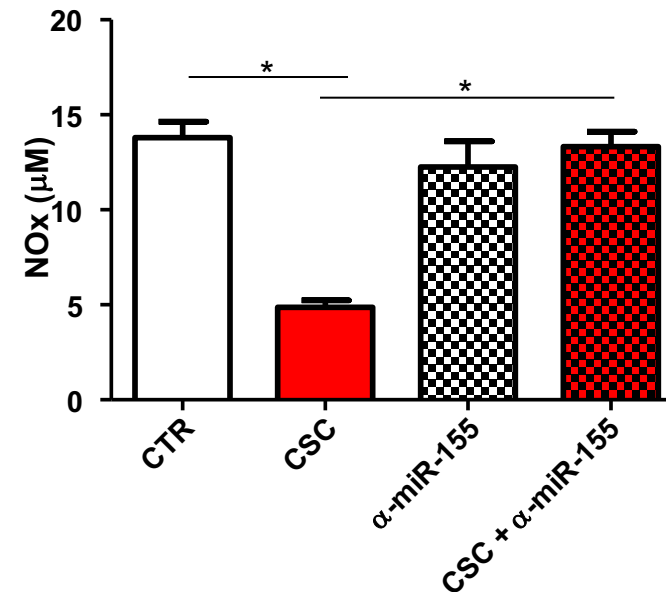
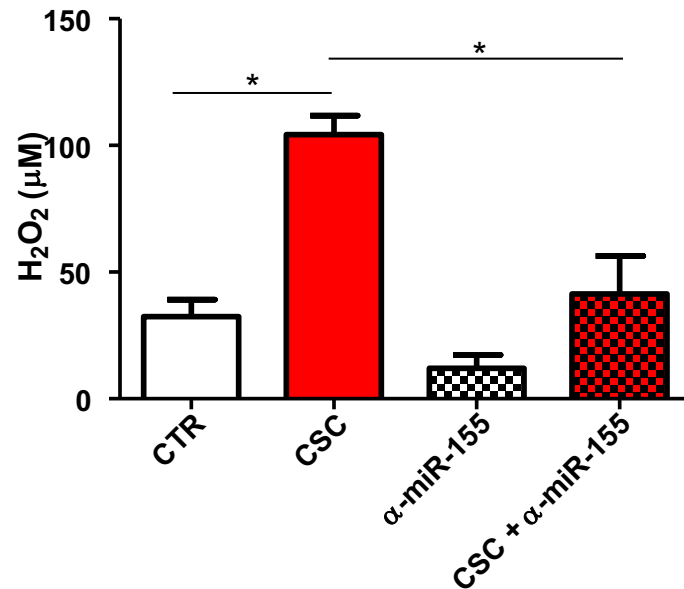
..with transcriptional activation in the long term



Cigarette Smoke effects on Vascular Cells Function

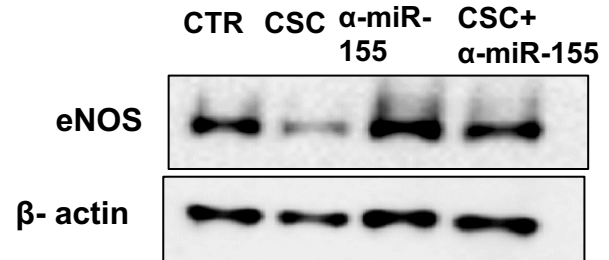
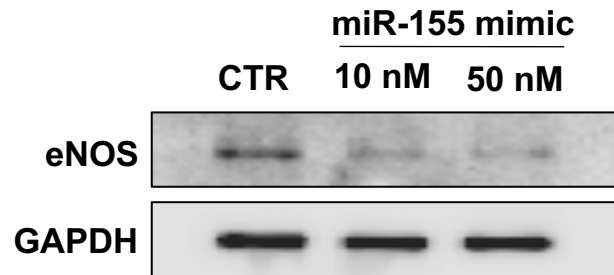
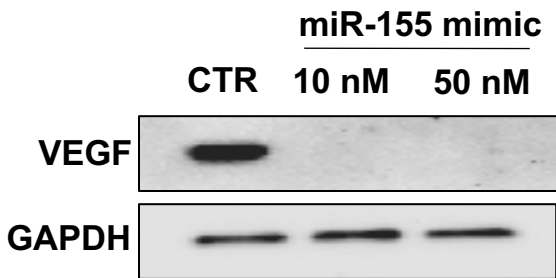
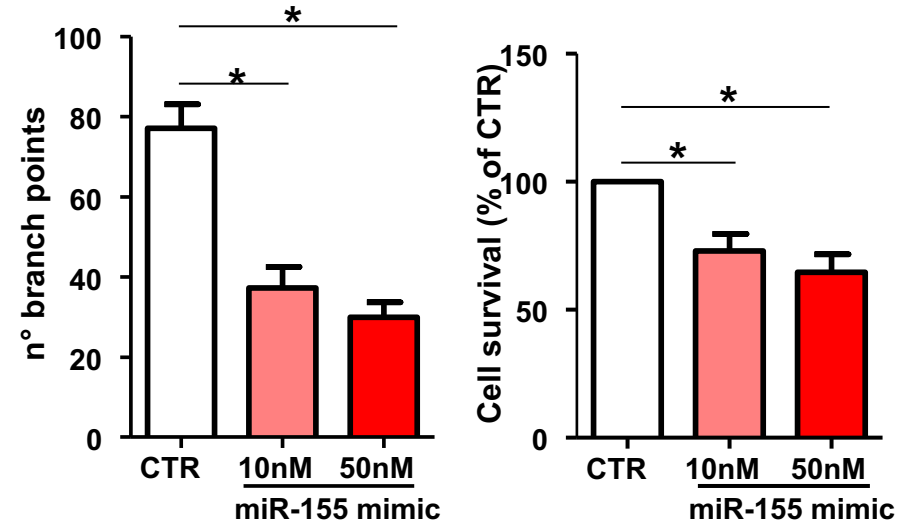
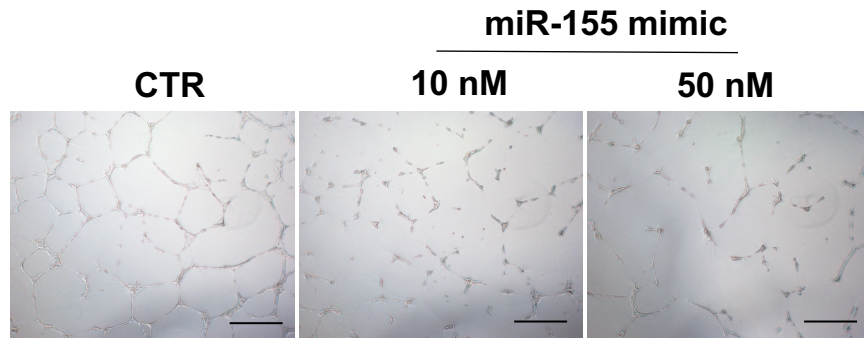


miR-155 inhibition reverts CSC detrimental effects on angiogenesis in vitro

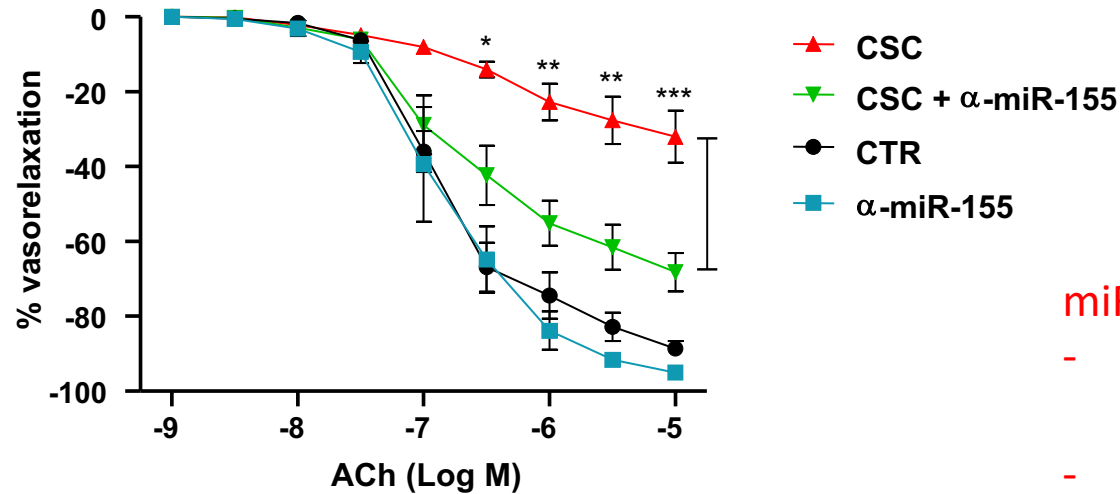


Cigarette Smoke effects on Vascular Cells Function

miR-155 incRease mimics CSC detrimental effects on angiogenesis in vitro



Cigarette Smoke effects on Vascular Cells Function



miR-155 depletion reverts

- CSC induced low arterial vasorelaxation (decreased elasticity)
- Oxidative stress

