TRP EXPRESSION SIGNATURE IN TUMOR-DERIVED ENDOTHELIAL CELLS: FUNCTIONAL ROLES IN PROSTATE CANCER ANGIOGENESIS

(Article begins on next page)

TRP expression signature in tumor-derived endothelial cells: functional roles in prostate cancer angiogenesis

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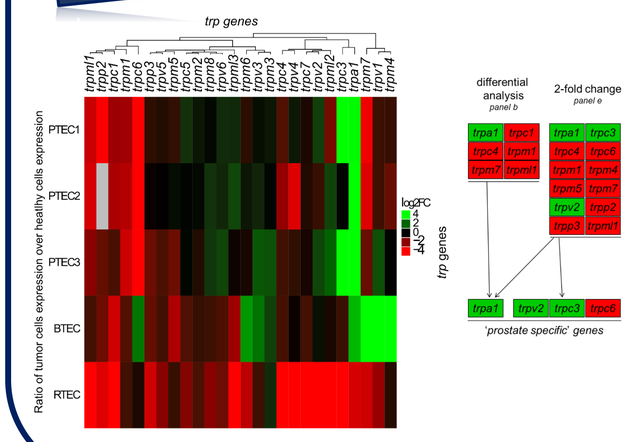
INTRODUCTION

TRP channels play a key role in cancer progression, modulating cell proliferation and survival, cancer invasion of surrounding tissues and angiogenesis. TRP expression could therefore characterize the prostate cancer (PCa) cell phenotype. Another well-established concept is that TRPs deeply modulate endothelial cell (EC) biology and tumor angiogenesis. However, a specific TRP expression signature of PCa angiogenesis is still lacking.

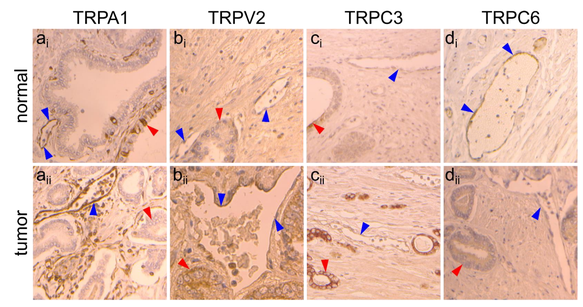
Our aim was to profile the expression of TRP channels during PCa angiogenesis and then to identify the specific molecular modulators of this process proving novel therapeutic targets.

TRP channel expression profile in normal and tumor-derived EC highlights a '*Prostate specific*' pattern

qPCR analysis

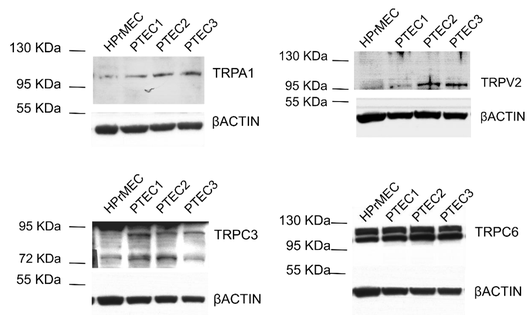


Immunohistochemistry

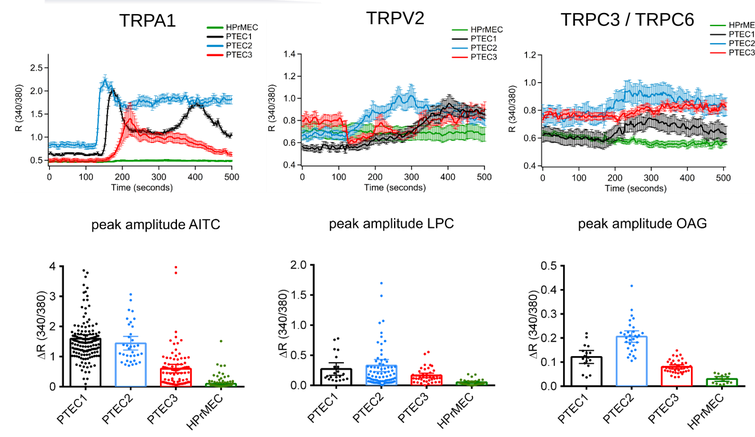


		TRPA1	TRPV2	TRPC3	TRPC6
normal	Epithelial cells	10/10 (focal)	0/10	10/10 (focal)	0/10
	ECs	10/10	0/10	0/10	6/10
tumor	PCa cells	2/10	4/10	10/10	3/10
	ECs	10/10	7/10	1/10	0/10

Western Blot

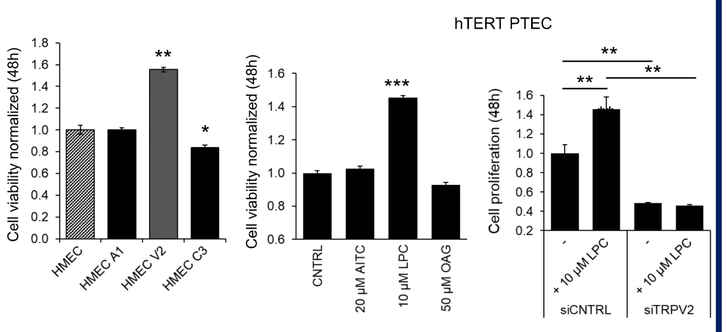


Ca^{2+} imaging

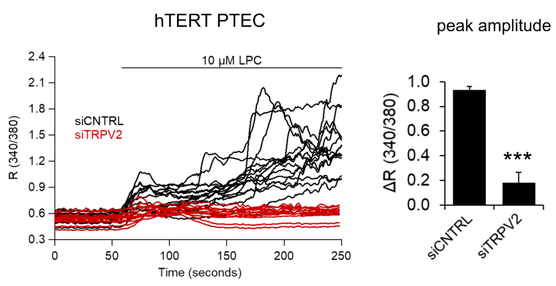


'*Prostate-specific*' TRPV2 enhances EC proliferation

Cell viability assay

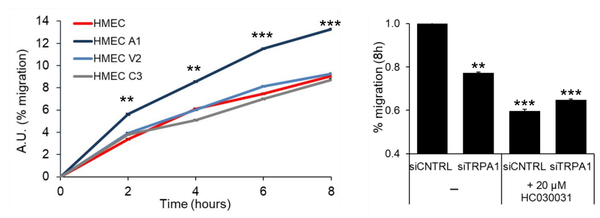


Ca^{2+} imaging

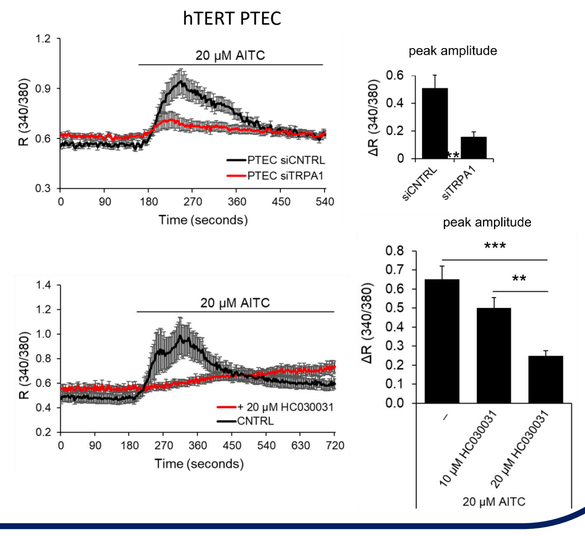


'*Prostate-specific*' TRPA1 enhances EC migration

Random migration assay

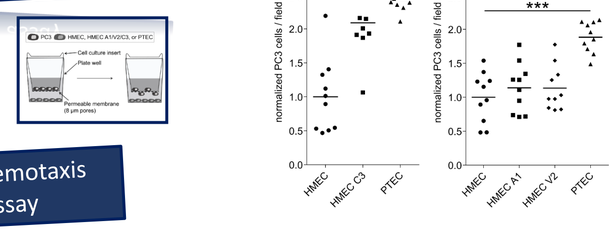


Ca^{2+} imaging

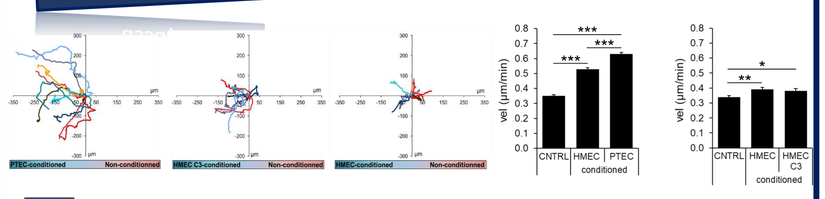


'*Prostate-specific*' TRPC3 promotes Pca cell attraction

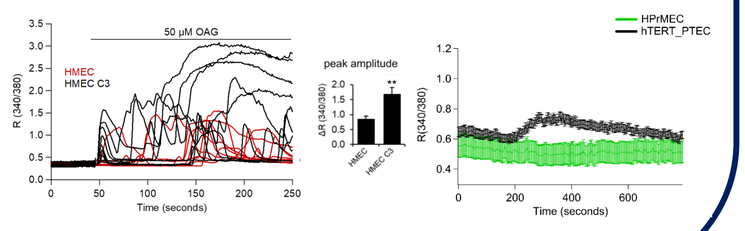
Co-colture transwell assay



2D chemotaxis assay

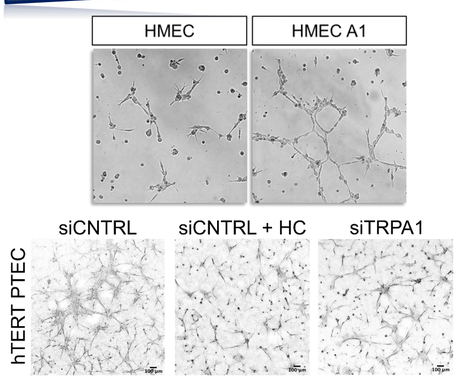


Ca^{2+} imaging

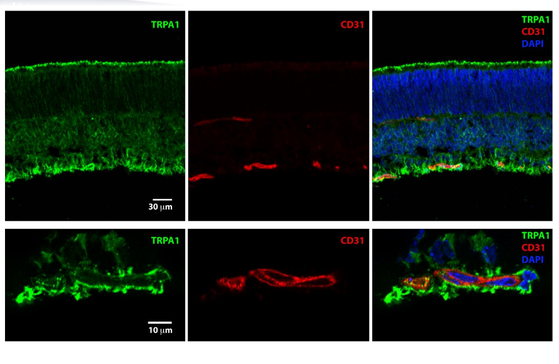


TRPA1 promotes EC tubulogenesis *in vitro* and angiogenesis *in vivo*

In vitro tubulogenesis

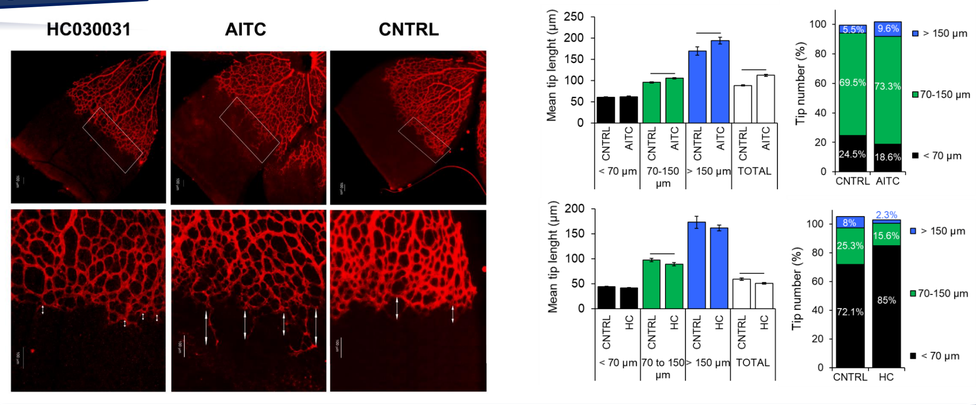


Immunohistochemistry



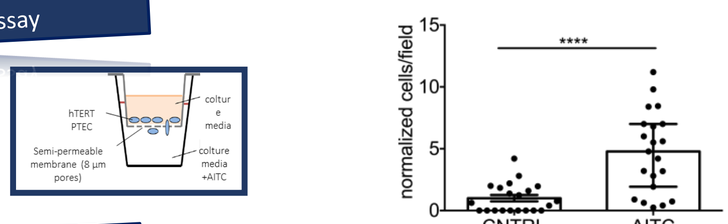
qPCR analysis

In vivo angiogenesis

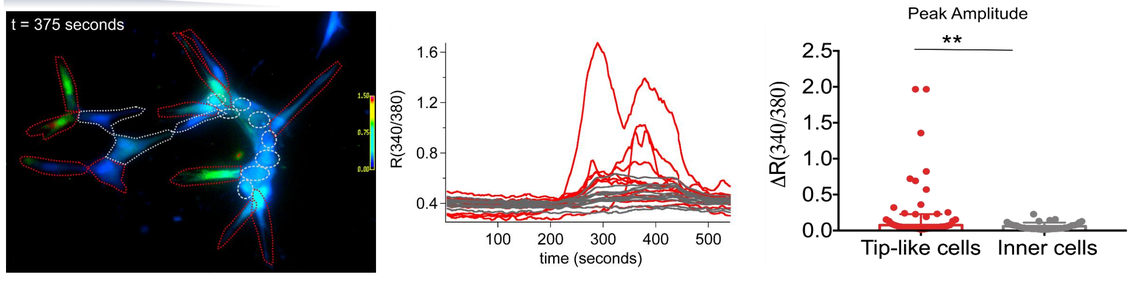


TRPA1 is implicated in PTEC chemotaxis and function in tip-like cells

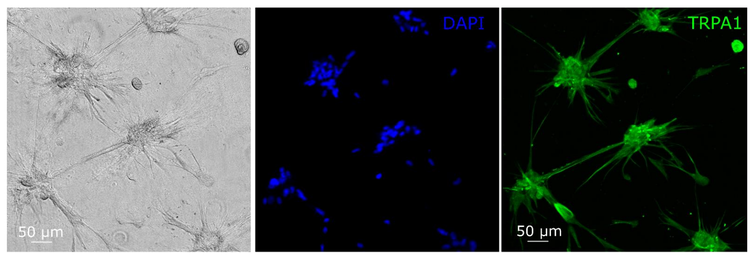
Migration transwell assay



Ca^{2+} imaging



Immunostaining



CONCLUSION

It was previously shown that PTEC exhibit the aggressive phenotype typical of TECs (Fiorio Pla et al. 2014). Here we identified three 'prostate specific' TEC overexpressed TRPs: TRPV2, TRPC3 and TRPA1 involved in different aspects of the angiogenic process. Taken together, our expression profiling and functional data could explain the transition of prostate endothelial cells to their aggressive tumor phenotype, proposing novel molecular players to selectively target PCa progression and angiogenesis. Results recently published (Bernardini *et al., Cancers* 2019).