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

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


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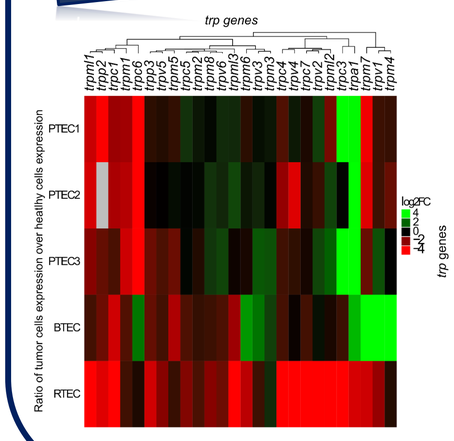
## INTRODUCTION

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.

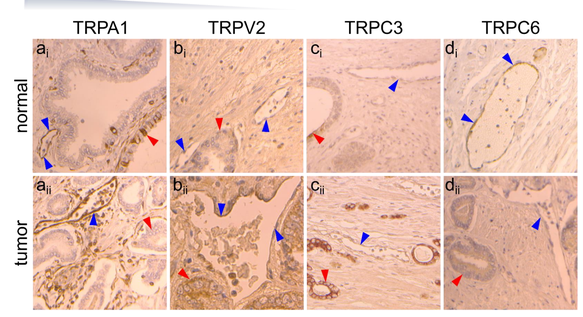
Our aim was to profile the expression of TRP channels during PCa angiogenesis and then to identify the specific molecular modulators of this process proving novel therapeutic targets.

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

### qPCR analysis

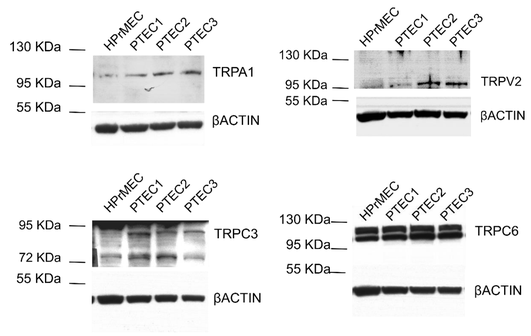



### Immunohistochemistry

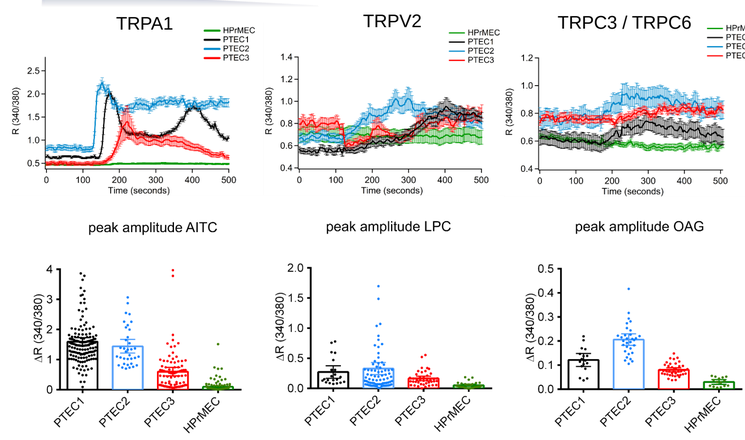



| | | TRPA1 | TRPV2 | TRPC3 | TRPC6 |
|---|---|---|---|---|---|
| normal | Epithelial cells | 10/10 (focal) | 0/10 | 10/10 (focal) | 0/10 |
| | ECs | 10/10 | 0/10 | 0/10 | 6/10 |
| tumor | PCa cells | 2/10 | 4/10 | 10/10 | 3/10 |
| | ECs | 10/10 | 7/10 | 1/10 | 0/10 |

### Western Blot

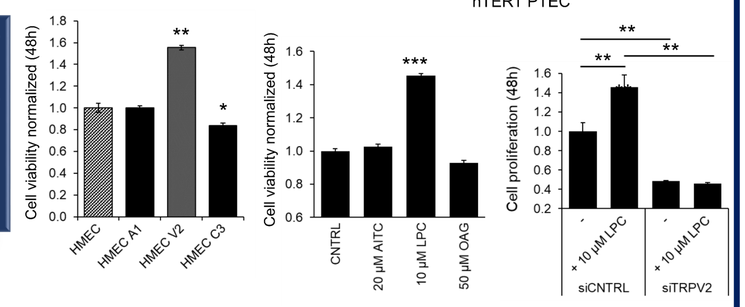



### $Ca^{2+}$ imaging

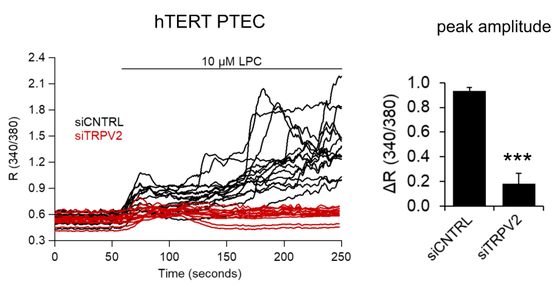



## '*Prostate-specific*' TRPV2 enhances EC proliferation

### Cell viability assay

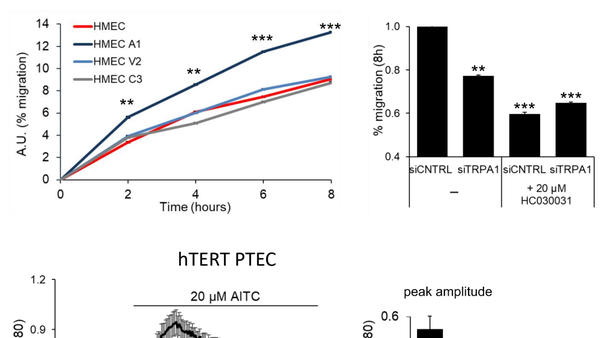



### $Ca^{2+}$ imaging

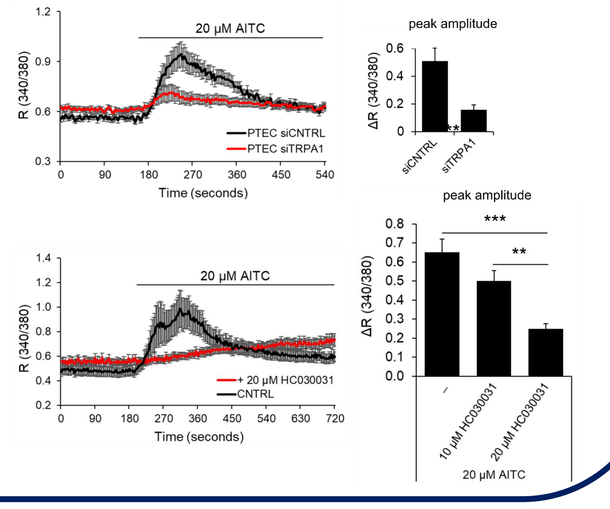



## '*Prostate-specific*' TRPA1 enhances EC migration

### Random migration assay

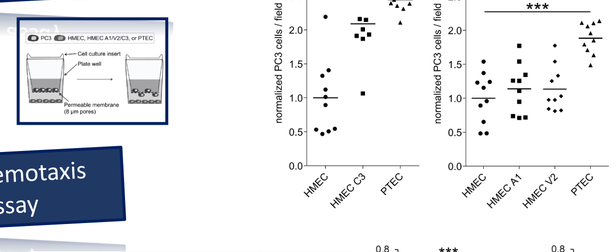



### $Ca^{2+}$ imaging

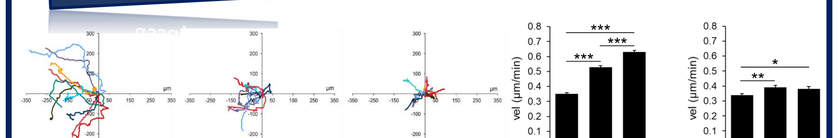



## '*Prostate-specific*' TRPC3 promotes Pca cell attraction

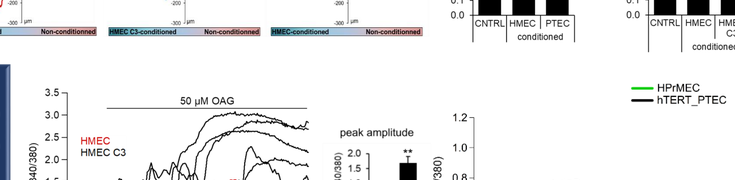
### Co-colture transwell assay




### 2D chemotaxis assay

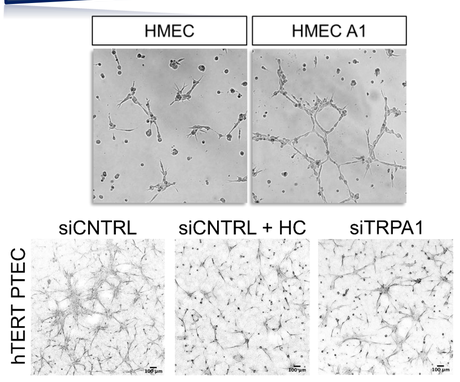



### $Ca^{2+}$ imaging

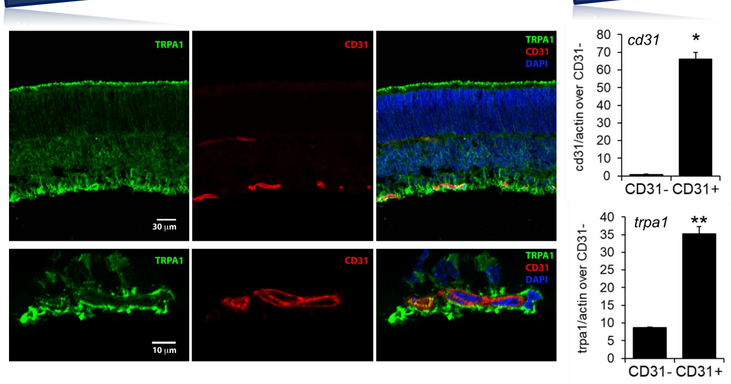



## TRPA1 promotes EC tubulogenesis *in vitro* and angiogenesis *in vivo*

### *In vitro* tubulogenesis



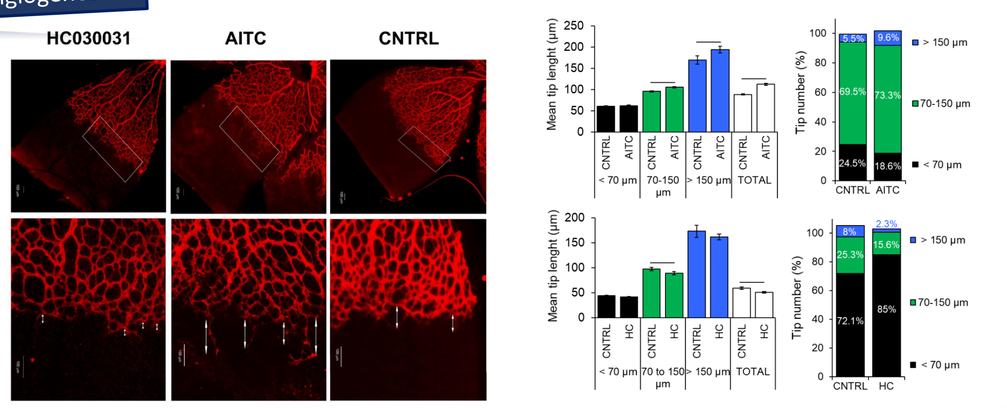

### Immunohistochemistry




### qPCR analysis

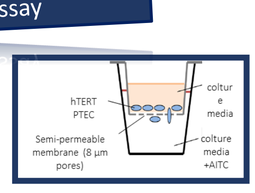



### *In vivo* angiogenesis

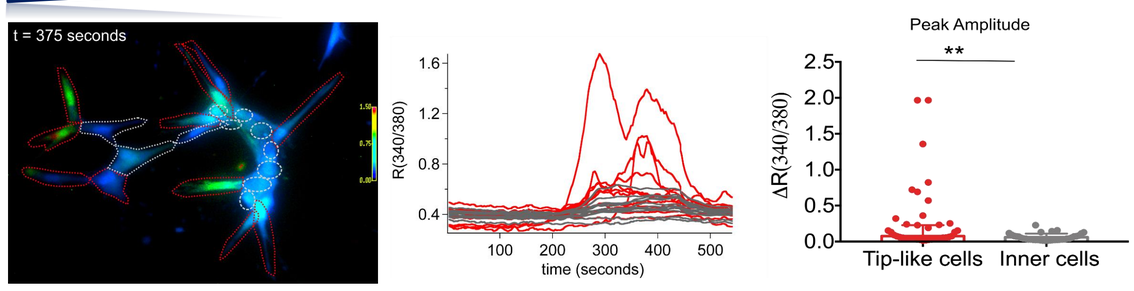



## TRPA1 is implicated in PTEC chemotaxis and function in tip-like cells

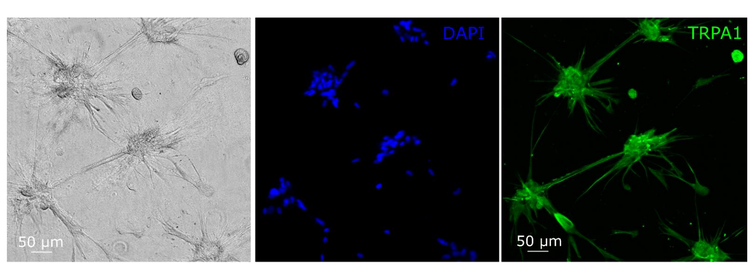
### Migration transwell assay




### $Ca^{2+}$ 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).