Assessment of Molecular Biomarkers for Bladder Cancer Diagnosis, Prognosis and Therapy : Immune Checkpoint / Telomerase Network

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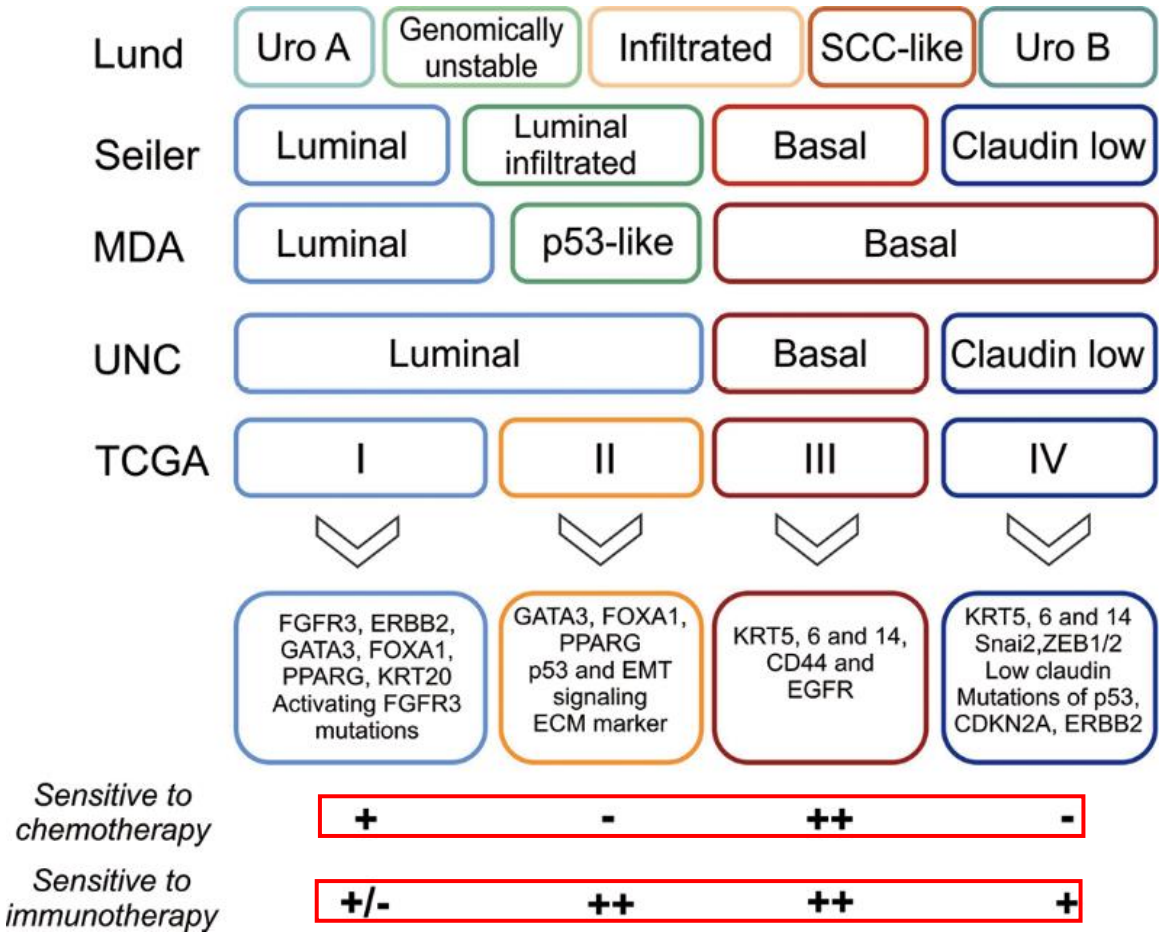
Global Congress on Bladder Cancer
Athens, 21-10-2022

Molecular Classification of Bladder Cancer



MDA: the MD Anderson Cancer Center;
UNC: the University of North Carolina;
TCGA: The Cancer Genome Atlas

Wezel et al., TAU, 2017

Research Objective

Study the behavior of Telomerase Reverse Transcriptase (TERT) genes in bladder cancer and its putative crosstalk with immune checkpoints

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Personalized medicine

↓

Improve patient's outcome

frontiers in Oncology

ORIGINAL RESEARCH
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Immune Checkpoint and Telomerase Crosstalk Is Mediated by miRNA-138 in Bladder Cancer

Hajar El Ahanidi[1,2,3], Meryem El Azzouzi[1,2], Chaimae Hafidi Alaoui[1,4], Mohammed Tetou[2,5], Mounia Bensaid[5], Imane Chaoui[1], Laila Benbacer[1], Ilias Hassan[2,5], Mohamed Oukabli[2,5], Katarzyna Michaud[6], Ahmed Ameur[1,5], Abderrahmane Al Bouzidi[2], Mohammed El Mzibri[1], Camilla Jandus[3,7†] and Mohammed Attaleb[1†]*

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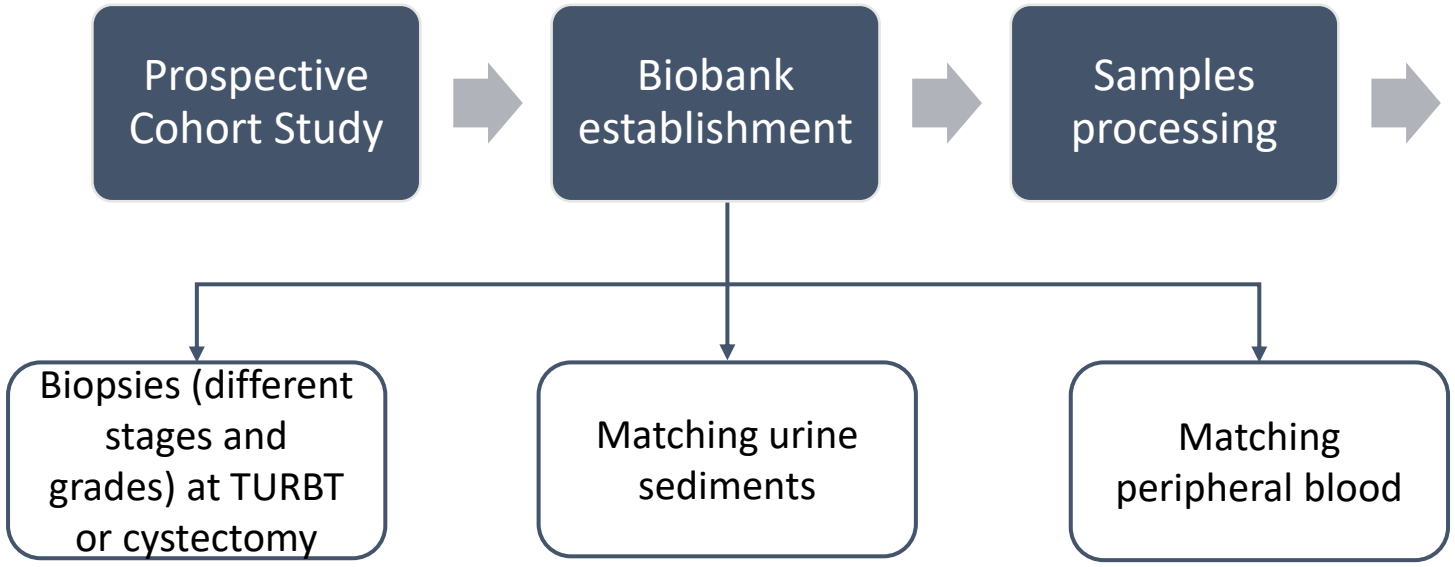
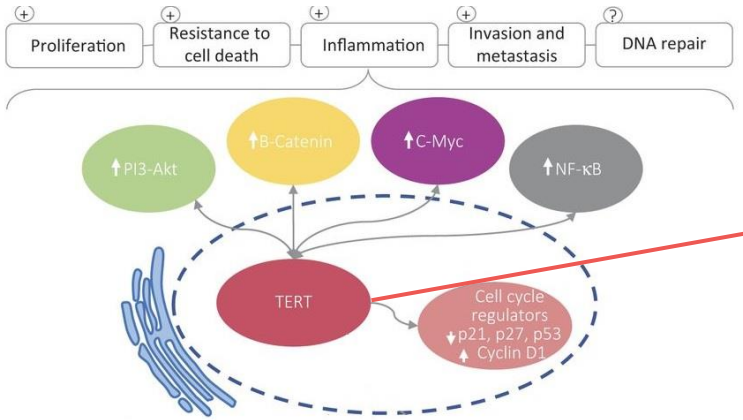
Project Workflow

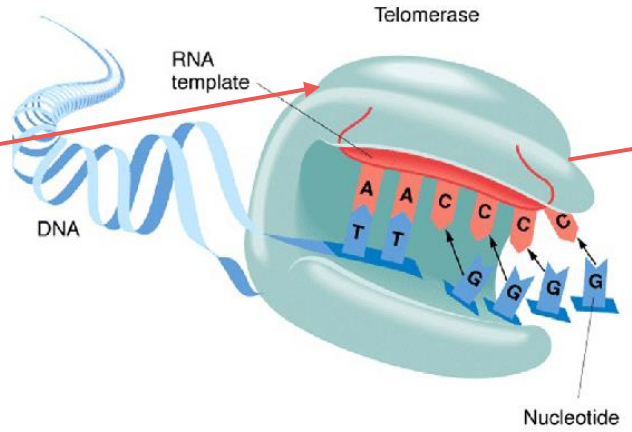


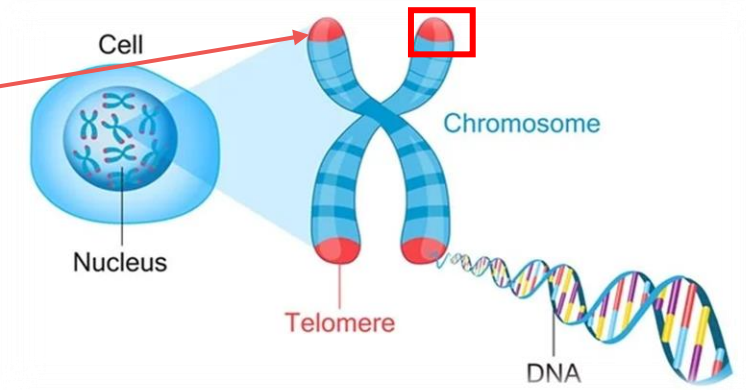
Parameter	Total cases	Percentage %
Sex		
Male	68	97.14
Female	2	2.86
Age		
<50	1	1.43
50–70	44	62.86
>70	25	35.71
Smoking history		
Yes	28	40
No	42	60
Tumor stage		
≤PT1	52	74.29
>PT1	18	25.71
Tumor grade		
Low grade	27	38.57
High grade	43	61.43
Tumor recurrence		
Yes	12	23.08
No	40	76.92
Tumor progression		
Yes	5	9.62
No	47	90.38

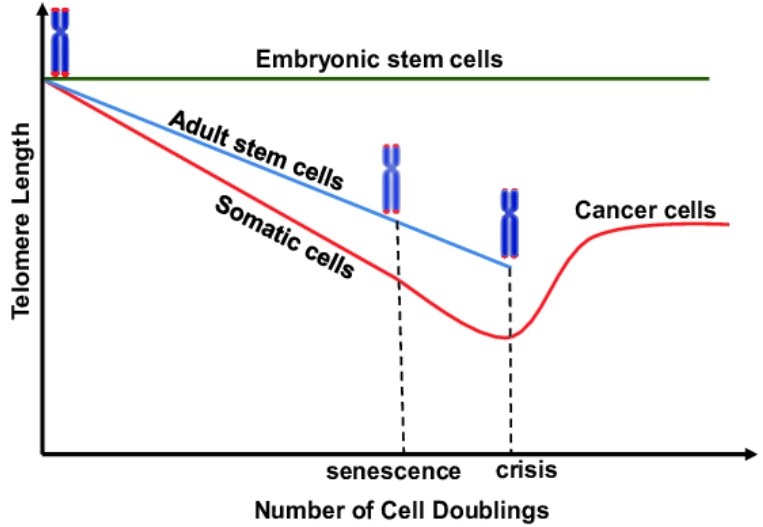
TERT and Telomeres

TERT: Telomerase Reverse Transcriptase





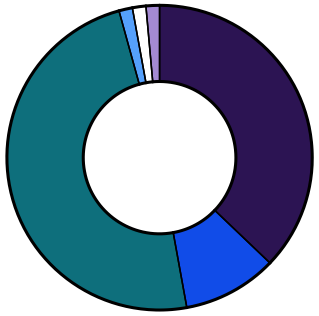




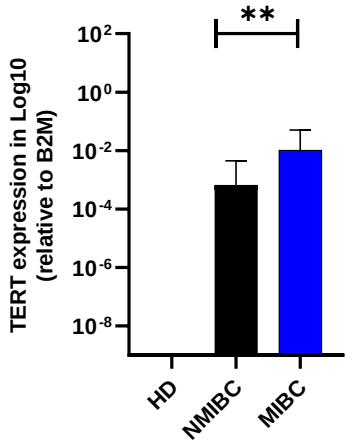
Adapted from: Pestana, JME, 2017

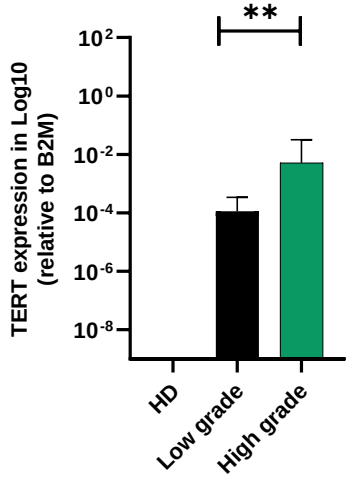
Markowetz, Sience, 2013
Zalzman et al., Cur Em Con, 2019

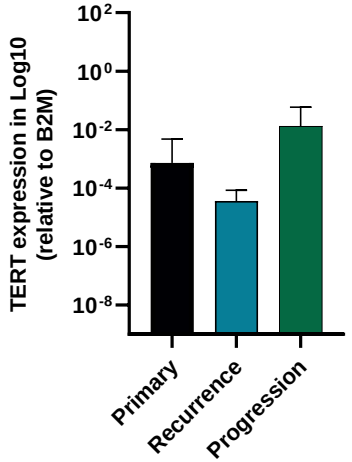
TERT Expression in Bladder Cancer

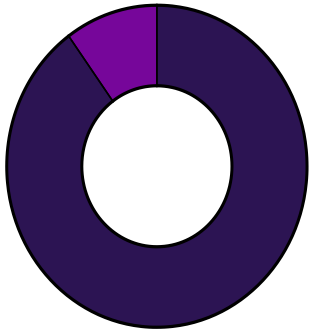


37.14% WT
10.00% C250T
48.57% C228T
1.43% A161C
1.43% G149T
1.43% C250T&C228T

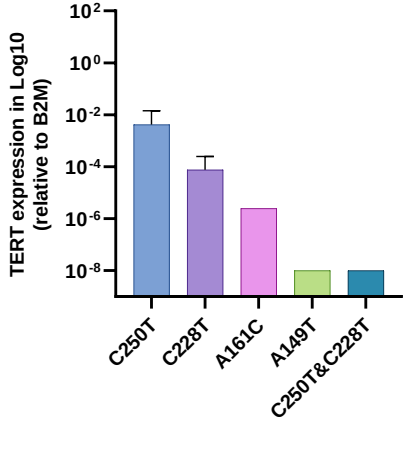


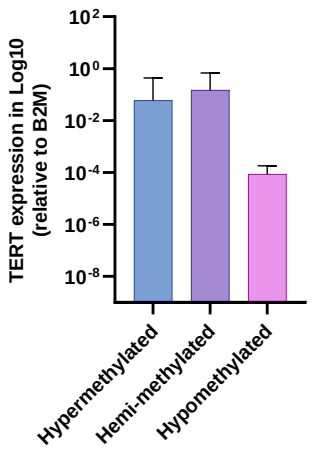




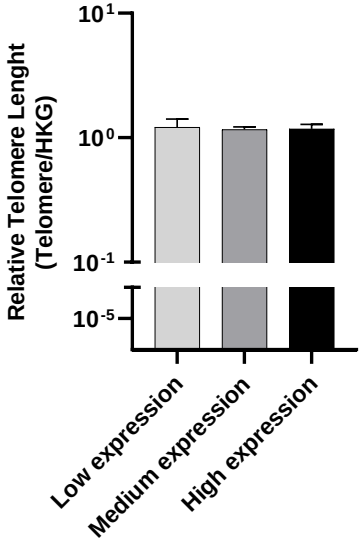


90.00% Hypermethylated
10.00% Hypomethylated





Effect on Telomere length ??



Immunotherapy Challenge in Bladder Cancer

Open access Original research

Journal for ImmunoTherapy of Cancer

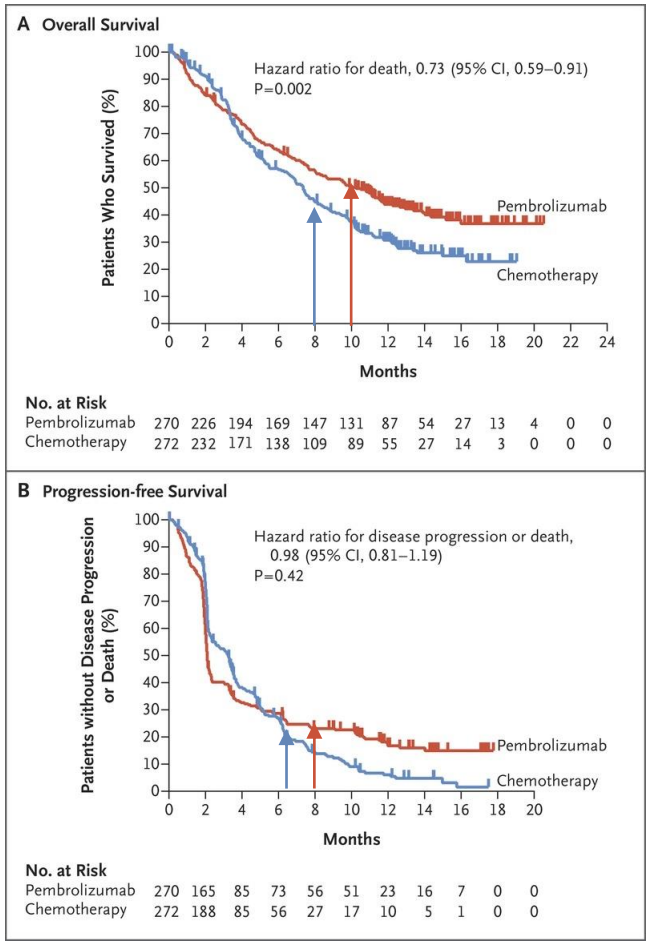
TERT promoter mutations and other prognostic factors in patients with advanced urothelial carcinoma treated with an immune checkpoint inhibitor

Ivan de Kouchkovsky ,[1] Li Zhang,[1] Errol J Philip,[2] Francis Wright,[2] Daniel M Kim,[2] Divya Natesan,[1] Daniel Kwon,[1] Hansen Ho,[3] Son Ho,[3] Emily Chan,[4] Sima P Porten,[5] Anthony C Wong,[6] Arpita Desai,[1] Franklin W Huang,[1] Jonathan Chou,[1] David Y Oh,[1] Raj S Pruthi,[5] Lawrence Fong,[1] Eric J Small,[1] Terence W Friedlander,[1] Vadim S Koshkin[1]

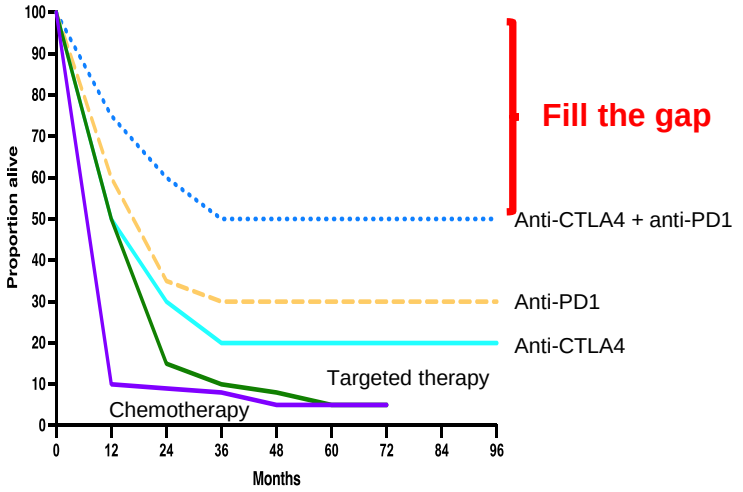
Bellmunt J.et al., NEJM, 2017

Model adapted from Emens L.A., et al, EJC, 2017

Immunotherapy Challenge in Bladder Cancer



Study number	Eligibility	Phase	Intervention
NCT01928394	Advanced or metastatic bladder cancer	Phase I/II	Nivolumab and Ipilimumab
NCT03084471	Advanced bladder cancer	Phase III	Durvalumab and Tremelimumab
NCT03219775	Metastatic or advanced transitional cell carcinoma	Phase II	Nivolumab and Ipilimumab
NCT03036098	Unresectable or metastatic UC	Phase III	Nivolumab, Ipilimumab, Gemcitabine/Cisplatin/Carboplatin
NCT02516241	Unresectable stage IV UC	Phase III	Durvalumab and Tremelimumab
NCT04223856	Advanced or metastatic UC	Phase III	EV and Pembrolizumab
NCT03519256	BCG unresponsive high-risk NMIBC	Phase II	Nivolumab, BMS-986205 and BCG
NCT02560636	Advanced bladder cancer	Phase I	Pembrolizumab and radiotherapy
NCT02643303	Bladder cancer	Phase I/II	Tremelimumab, Durvalumab and polyICLC
NCT03473743	Metastatic or advanced UC	Phase Ib-II	Erdafitinib, Cetrelimab and Platinum
NCT03473756	UC	Phase Ib/II	Rogaratinib and Atezolizumba
NCT04172675	High-risk NMIBC	Phase II	Erdafitinib, Gemcitabine/Mitomycin C
NCT03745911	Metastatic UC	Phase II	Paclitaxel and TAK-228
NCT02546661	MIBC	Phase I	Durvalumab, Olaparib, AZD1775 and Vistusertib
NCT03022825	BCG unresponsive high grade NMIBC	Phase II	ALT-803 and BCG



Bellmunt J.et al., NEJM, 2017

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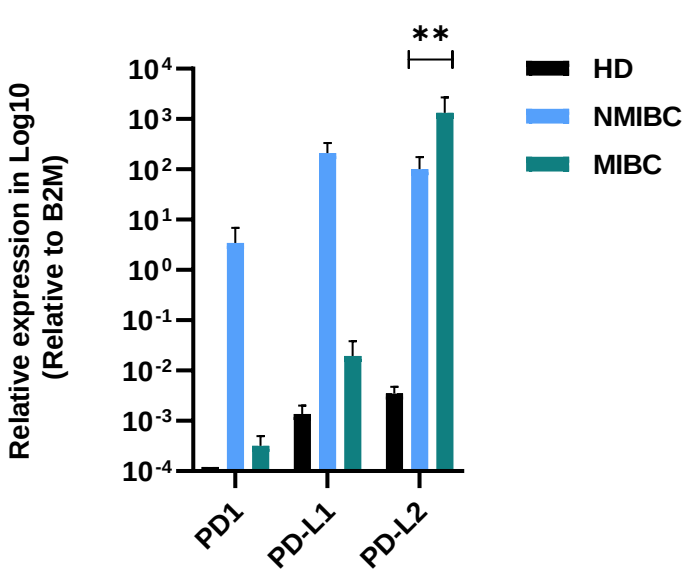
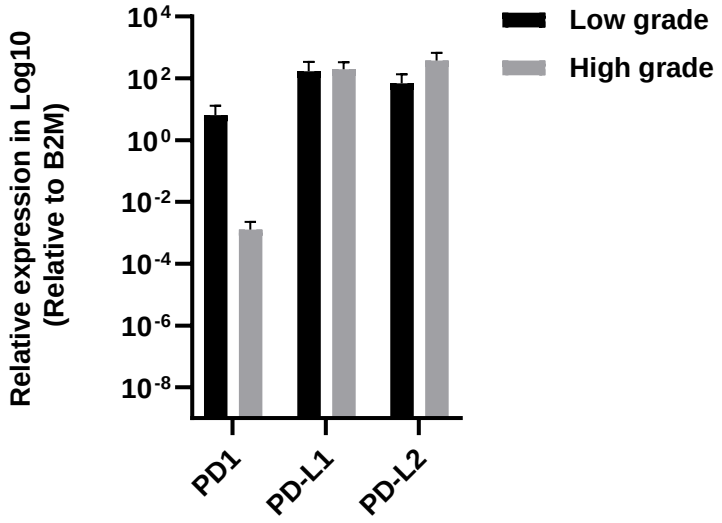
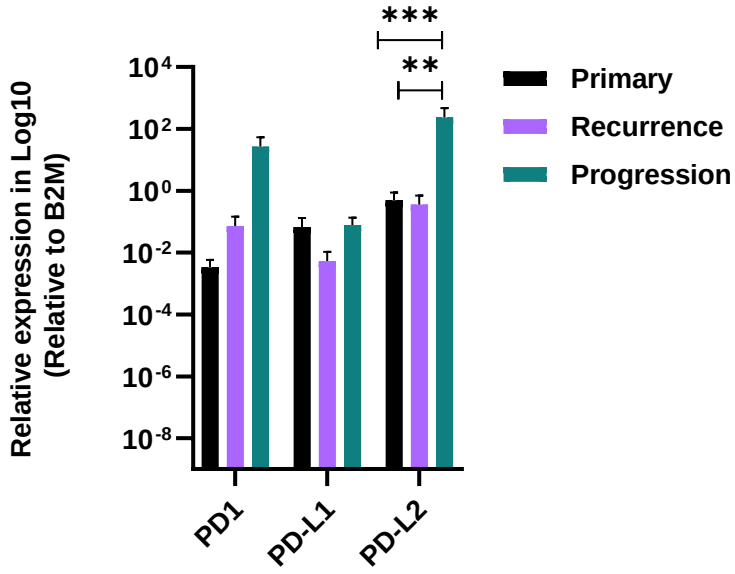
Immune Checkpoints Expression in Bladder Cancer







TERT and PD-Ls Regulation by miRNAs

RESEARCH ARTICLE

Hsa_circ_0020397 regulates colorectal cancer cell viability, apoptosis and invasion by promoting the expression of the miR-138 targets TERT and PD-L1

Xiu-li Zhang [1]*, Ling-ling Xu [1] and Fang Wang [2]

1 Oncology Department, Yidu Central Hospital of Weifang, 4138# Linglong Mountain Road, Qingzhou, Weifang 262500 Shandong, P.R. China
2 Medical-Record Department, Yidu Central Hospital of Weifang, Weifang 262500 Shandong, China

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www.impactjournals.com/oncotarget/ Oncotarget, Vol. 7, No. 29

Research Paper

The tumor suppressor miR-138-5p targets PD-L1 in colorectal cancer

Lian Zhao[1,2], Haibo Yu[3], Shuijing Yi[4], Xiaowei Peng[5], Peng Su[1,2], Zhiming Xiao[1], Rui Liu[1], Anliu Tang [1,2], Xiayu Li[1,2], Fen Liu[1,2], Shourong Shen[1,2]

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APMIS JOURNAL OF PATHOLOGY, MICROBIOLOGY AND IMMUNOLOGY

APMIS 127: 545–553

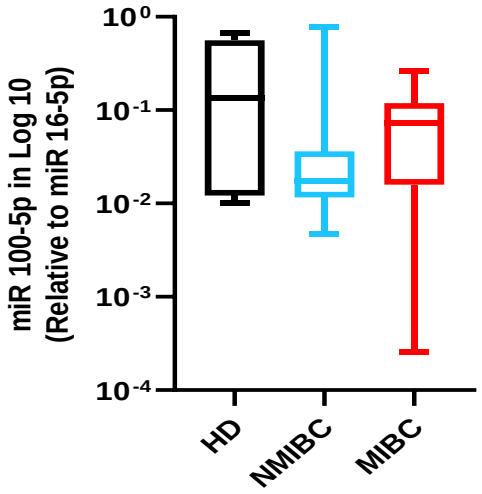
DOI 10.1111/apm.12973

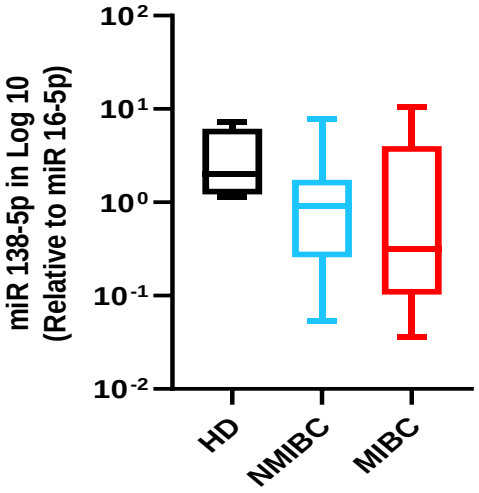
Expression of miR-100 and miR-138 as prognostic biomarkers in non-muscle-invasive bladder cancer

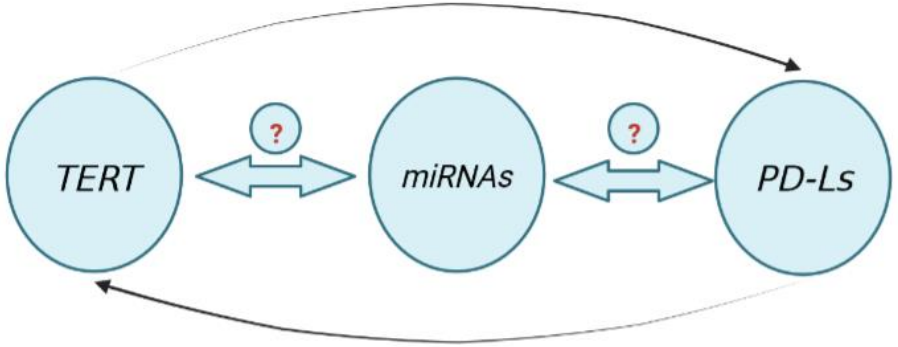
ANA BLANCA,[1]* ALVARO SANCHEZ-GONZALEZ,[1]* MARIA J. REQUENA,[1] JULIA CARRASCO-VALIENTE,[1] ENRIQUE GOMEZ-GOMEZ,[1] LIANG CHENG,[2] ALESSIA CIMADAMORE,[3] RODOLFO MONTIRONI[3] and ANTONIO LOPEZ-BELTRAN[4]

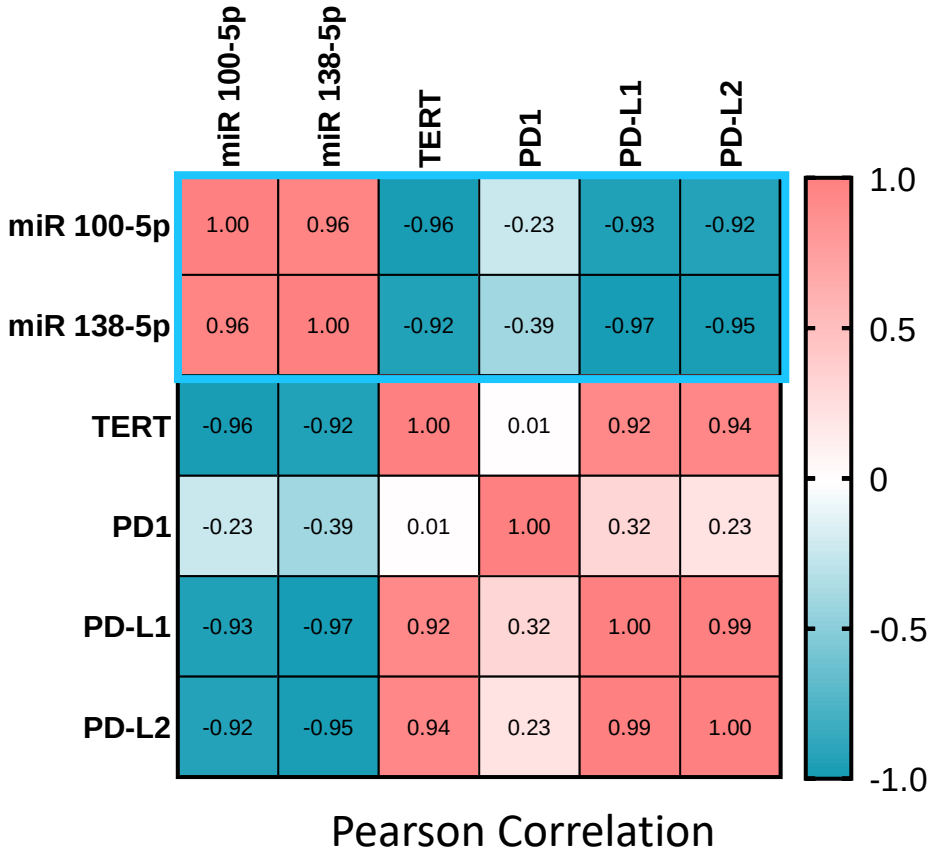
[1]Urology Department, Maimonides Institute of Biomedical Research (IMIBIC), Reina Sofía Hospital, University of Córdoba, Córdoba, Spain; [2]Departments of Pathology and Laboratory Medicine, and Urology, Indiana University School of Medicine, Indianapolis, IN, USA; [3]Institute of Pathological Anatomy and Histopathology, Polytechnic University of the Marche Region, Ancona, Italy; and [4]Department of Pathology and Surgery, Cordoba University Medical School, Cordoba, Spain

miRNAs Expression in Bladder Cancer





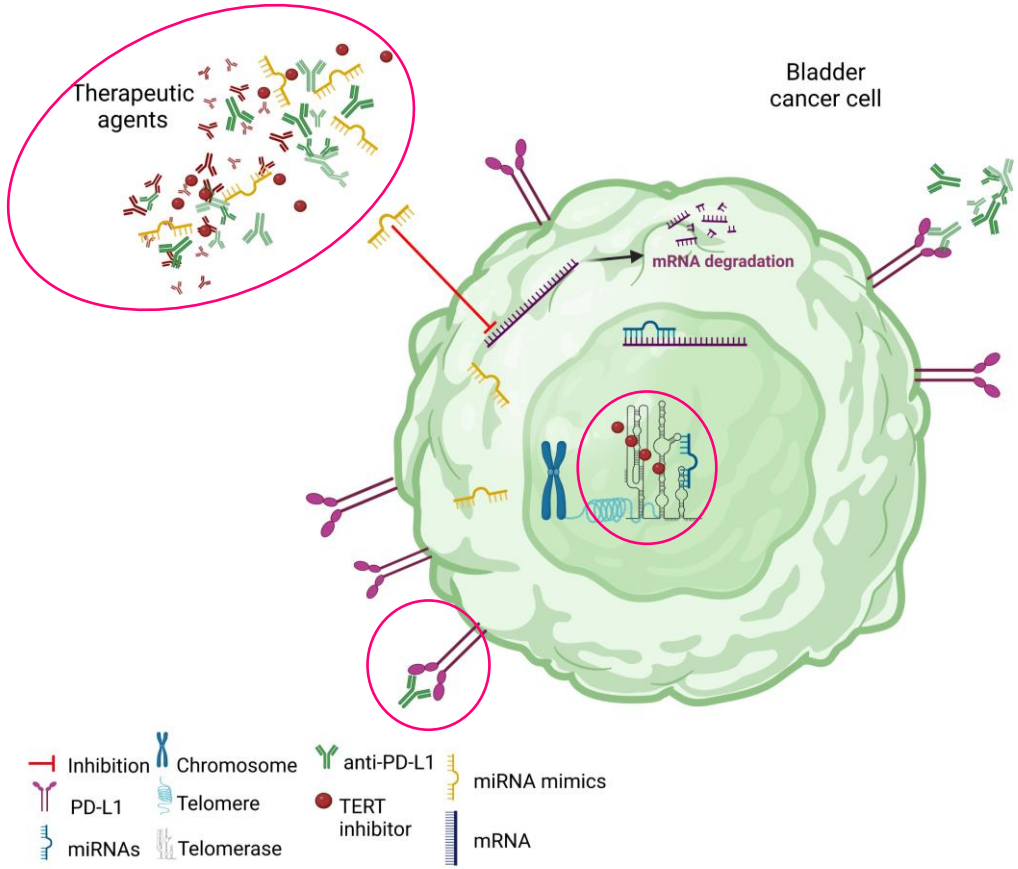




Main findings & Conclusion

- ✓ TERT, PD-Ls, miR-138-5p, and miR-100-5p expression might be used as diagnosis and prognosis biomarkers for better patients' stratification and follow-up

- ✓ The identified network could be a promising therapeutic target



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Dr M. Attaleb
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The patients

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