

Con il Patrocinio di





CORSO DI IMMUNOTERAPIA IN ONCOLOGIA "CARCINOMA DEL RENE E DELLA VESCICA"

 NEGRAR (VR)

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 Cancer Care Center

 "Sacro Cuore - Don Calabria"

 Centro Formazione - Aula 1

# IMMUNOTERAPIA Razionale e Basi Biologiche

Alessandro Inno

Oncologia Medica Ospedale Sacro Cuore Don Calabria Negrar - Verona



#### **Immune System Functions**

#### Identify and destroy foreign pathogens or abnormal cells in the body

#### **Innate Immunity**



#### **Non Specific**

First line of defense

Activation of adaptive response

#### **Immune System Functions**

Identify and destroy foreign pathogens or abnormal cells in the body



### Immune System identifies tumor antigens

Antigen-specific T cells and antibodies at tumor site, draining LN and peripheral blood of cancer patients

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### **T** Cell Activation



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# **T Cell Exhaustion**



### **Cancer Immunoediting**



Modified from Schreiber D et al. Science 2011 Mar 25;331(6024):1565-70.

#### **Immune Escape**



#### Immune responses promoting tumor growth



#### **Goal of Cancer Immunotherapy**



#### **T Cell Co-Receptors**



#### **Resistance to Endogenous Immunity**



#### a Innate immune resistance

#### **Immune Checkpoints**



#### **Immune Checkpoints**



## T-cell targets for immunoregulatory antibody therapy



#### **Cancer Vaccines**



#### **CAR-T**





#### **Cancer Immunity Cycle**



### **Tumor Immunity Continuum**







#### Immune desert

Chemotherapy Radiotherapy Target therapy Epigenetic modifiers Vaccines Oncolytic viruses Cytokines Anti-CTLA4 Anti-CD40 (agonist) Anti-CD137 (agonist) Anti-OX40 (agonist)



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Chemotherapy Radiotherapy Target therapy Epigenetic modifiers Vaccines Oncolytic viruses Cytokines Anti-CTLA4 Anti-CD40 (agonist) Anti-CD27 (agonist) Anti-CD137 (agonist)



Vaccines

#### Modified from Chen DS et al. Immunity 2013 Jul 25;39(1):1-10.





Tumor-Immunity is a complex relationship that can lead to immune escape and tumor growth



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Immunotherapy can induce or restore antitumor immunity



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**Cancer-immune phenotypes could guide personalized immunotherapy strategies** 





alessandro.inno@sacrocuore.it

### **Anticancer Immunity Matters**

 T-cell infiltration within tumors predicts overall survival (OS) in multiple cancer types including bladder cancer<sup>1-3</sup>



- 1. Sharma P, Sato E, et al. *Proc Natl Acad Sci U S A*. 2007;104(10): 3967-3972.
- 2. Zhang L, Coukos G, et al. *N Engl J Med*. 2003;348(3):203-213.
- 3. Galon J, Pagès F, et al. Science. 2006;313(5795):1960-1964.

#### **Anticancer Immunity Matters**

 Treg infiltration within tumors is associated with worse prognosis in RCC



#### Immunoscore



#### Immunoscore validation task force



Mlecniq B et al. *Immunity* 2016;44(3):698-711. Galon J et al. *J Pathol* 2014;232(2):199-209.