



**ISTITUTO NAZIONALE PER LO
STUDIO E LA CURA DEI TUMORI
FONDAZIONE G. Pascale – NAPOLI
SC Biologia Cellulare e Bioterapie**

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Immuno-oncology biomarkers

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Immuno-oncology biomarkers

- **What is a cancer biomarker?**
- **Why biomarkers are important for cancer therapy?**
- **Why biomarkers are important for immunotherapy?**

What are cancer biomarkers?

- **A cancer biomarker is a characteristic of the tumor that can be objectively measured and evaluated (i.e. the levels of a protein, a sequence of DNA etc.)**
- **Biomarkers can be detected in the tumor tissue or in the blood**
- **Cancer biomarkers can provide important information for:**
 - **The diagnosis of the tumor and of its recurrence**
 - **The definition of the prognosis (i.e. may indicate the aggressiveness of the tumor)**
 - **The prediction of toxicity of therapeutics**
 - **The prediction of response to specific drugs**

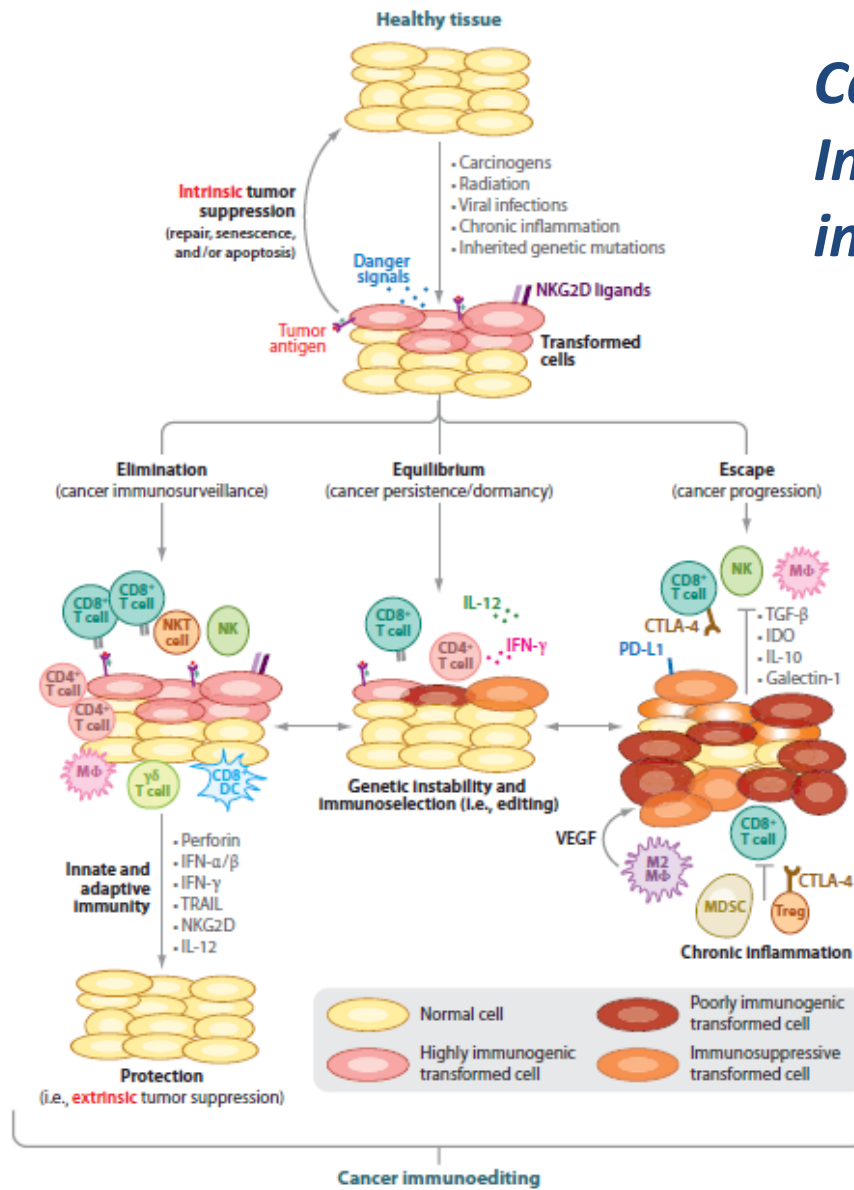
Target-based agents + predictive biomarkers: PRECISION MEDICINE



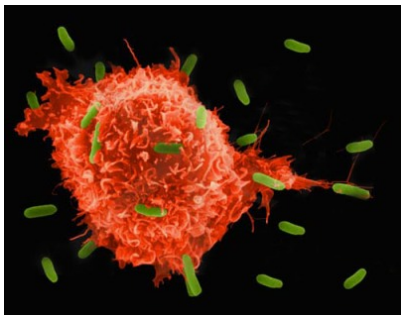
Most common predictive biomarkers for solid tumors

Drug	Biomarker	Tumor type
Cetuximab (Erbix), Panitumumab (Vectibix)	Absence of RAS mutations	Colorectal carcinoma
Crizotinib (Xalkori), Ceritinib (Zykadia), Alectinib (Alecensa)	Presence of ALK rearrangements	Non-small cell lung cancer
Gefitinib (Iressa), Erlotinib (Tarceva), Afatinib (Giotrif), Osimertinib (Tagrisso)	Presence of EGFR mutations	Non-small cell lung cancer
Trastuzumab (Herceptin)	Presence of HER2 amplification	Breast and gastric cancer
Vemurafenib (Zelboraf), Dabrafenib (Tafinlar), Trametinib (Mekinist)	Presence of BRAF mutations	Melanoma
Pembrolizumab	Expression of PD-L1	Non-small cell lung cancer

Cancer Immunoediting: immunoescape



Immune checkpoint inhibitors mechanism of action



Immune System

=



Cytokines



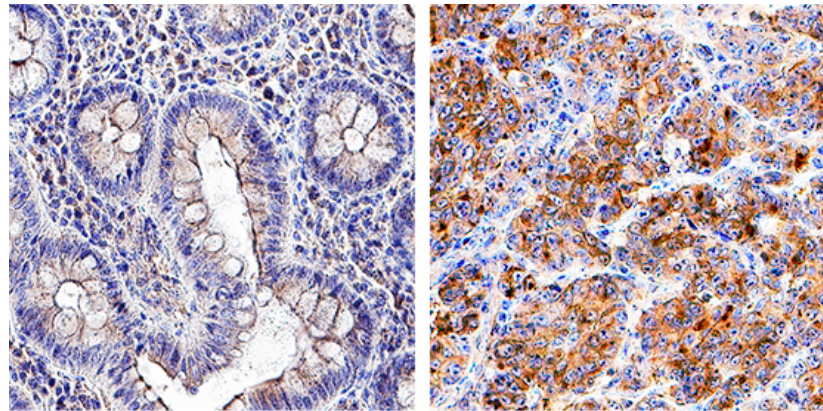
Antigens



Regulatory molecules
(CTLA-4, PD-1)

PD-L1 testing in cancer

- Measurement of the PD-L1 biomarker in the tumor tissue allows to identify patients who are more likely to respond to PD-1/PD-L1 drugs



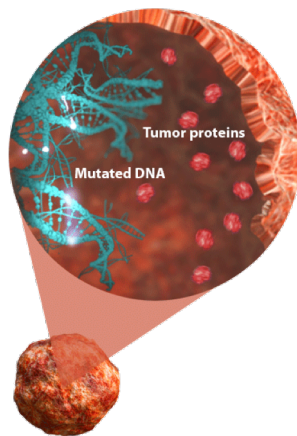
Normal Tissue

Cancer

Tumors With High Mutation Burden Are a Rational Target for I-O Therapy

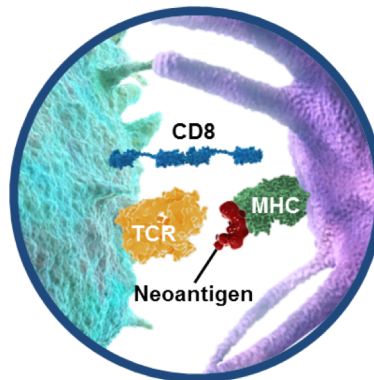
Tumor mutation burden (TMB): number of somatic mutations in the tumor genome

Tumor cells with high TMB...^{1,2}

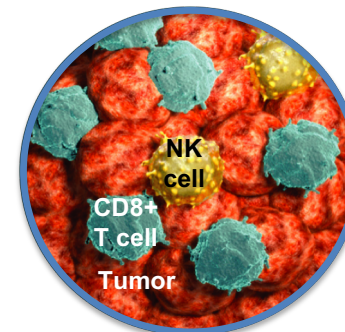


Tumor cell

...may have high neoantigen load ...^{1,2}



...which can lead to high tumor immunogenicity and increased T-cell reactivity and anti-tumor response²⁻⁵



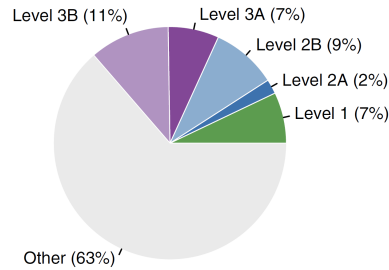
The high immunogenicity of tumors with high mutation burden makes them a rational target for treatment with I-O therapies^{1,2}

1. Schumacher TN, Schreiber RD. *Science*. 2015;348(6230):69-74. 2. Kim JM, Chen DS. *Ann Oncol*. 2016;27(8):1492-1504. 3. Liontos M et al. *Ann Transl Med*. 2016; 4(14):264. 4. Sharma P, Allison JP. *Science*. 2015;348(6230):56-61. 5. Giannakis M et al. *Cell Rep*. 2016;15:857-865.

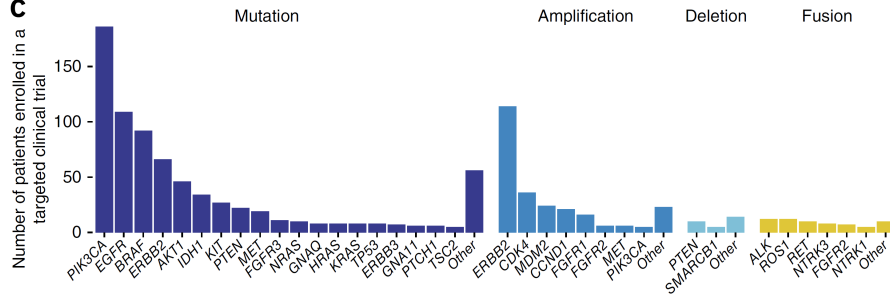
“Actionable” somatic alterations identified in different tumor types

a

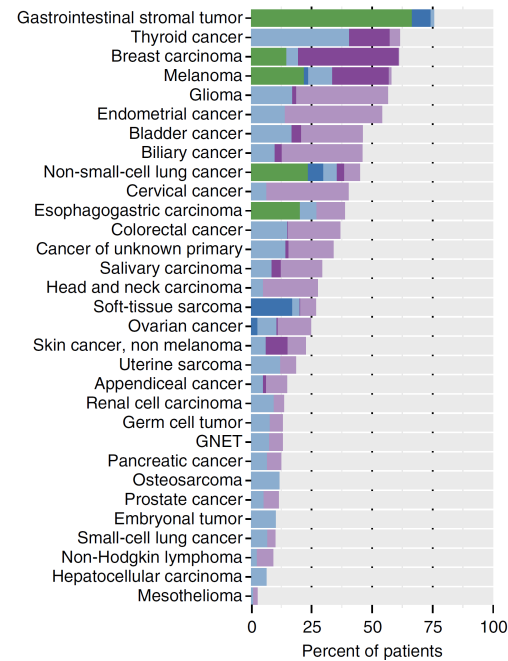
Level 1	FDA-recognized biomarker for an FDA-approved drug in the same indication
Level 2A	Standard of care biomarker for an FDA-approved drug in the same indication
Level 2B	Standard of care biomarker for an FDA-approved drug in another indication
Level 3A	Compelling clinical evidence supporting the biomarker as being predictive of drug response in the same indication
Level 3B	Compelling clinical evidence supporting the biomarker as being predictive of drug response in another indication



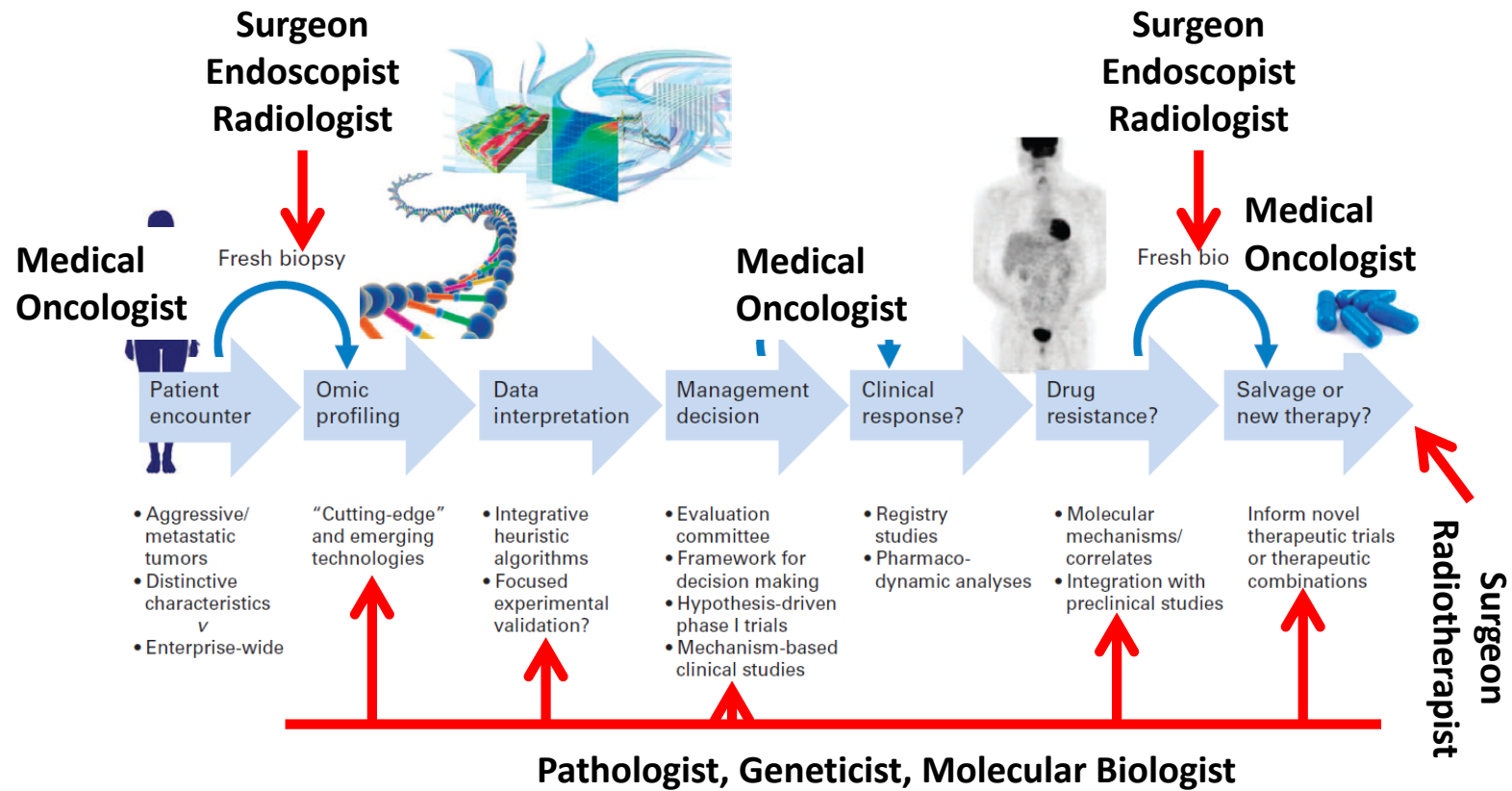
c



b



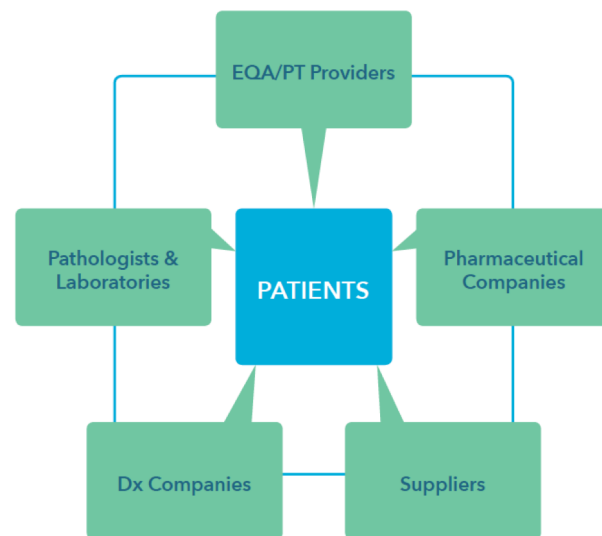
Precision Oncology



Garraway JCO 2013

IQNPath

International Quality Network for Pathology



Quality biomarker testing for patients

*EQA = External Quality Assessment, PT = Proficiency Testing

Mission

- International multi-stakeholder expert group for improving quality of clinical biomarker testing in pathology

Organisation

- Non-profit association (network)
- EQA provider members
- Corporate sponsors

Activities

- **Publications, guidelines & training:**
Advocate EQA/PT & education
- **Multi-stakeholder Communication:**
Working Groups, Workshops
- **Best practice for EQA: Scheme badging**
- **Verification/endorsement:**
Badging standards, controls, tools
- **EQA data sharing for research in EQA design: Database**

EQA Members

