
SITC
2017
November 8-12
NATIONAL HARBOR
MARYLAND
Gaylord National Hotel
& Convention Center
sitc
Society for Immunotherapy of Cancer

November 8-12 • NATIONAL HARBOR, MD

SITC 2017

Multiplex IHC Immuno-Oncology Panel for standardized profiling based on spatial and functional characterization of the tumor microenvironment

Dr. Svenja Lippok (Definiens AG)

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Society for Immunotherapy of Cancer

#SITC2017

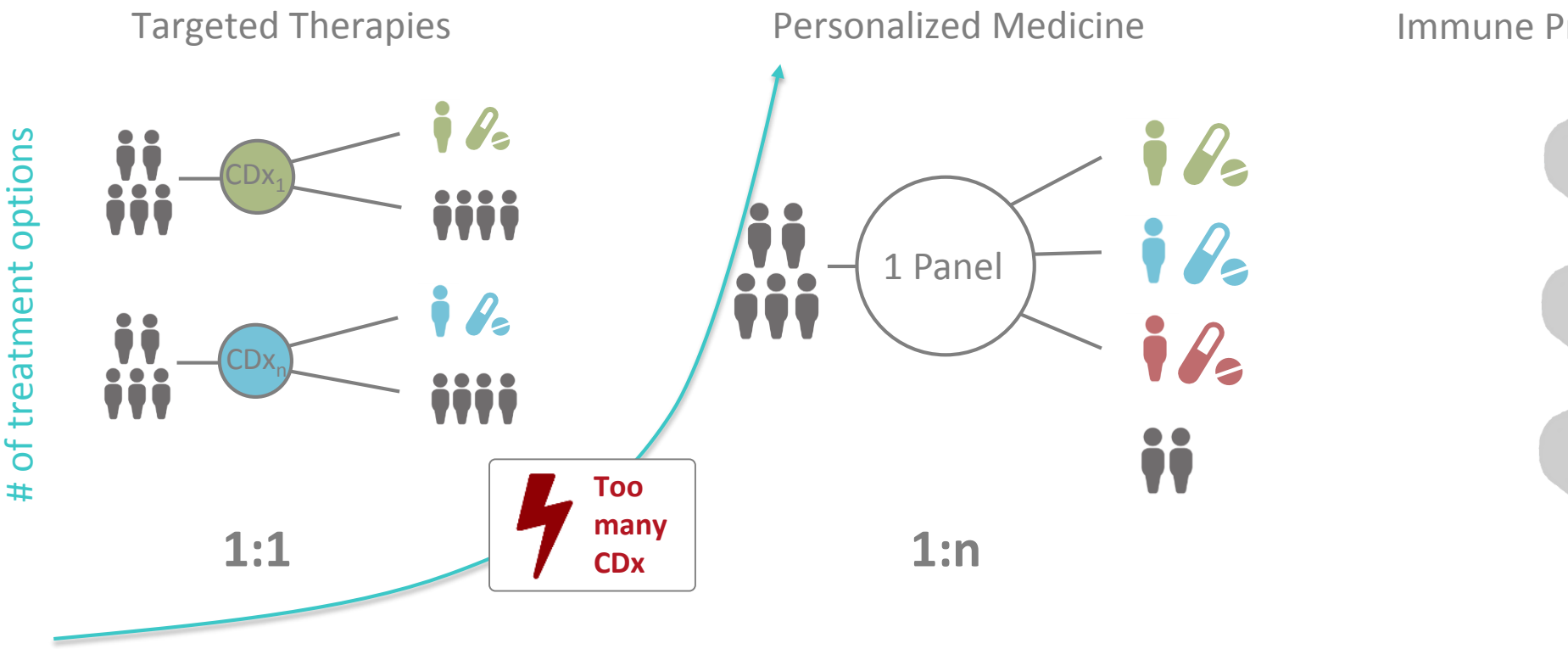
Presenter Disclosure Information

Dr. Svenja Lippok

The following relationships exist related to this presentation:

Svenja Lippok is a full-time employee of Definiens AG

Combinatorial & diagnostic challenge



Biomarkers for therapy & patient stratification*

CD8 (TE**)	CD8 (NE**)	PD-L1	FoxP3

Adaptive Immune Resistance

Immune Tolerance

Aquired Checkpoint Inhibitor Resistance

Impaired Tumor Parenchyma Infiltration

Immune Ignorance

Intrinsic Checkpoint Inhibitor Resistance

* In analogy to Teng et al *Cancer R* 2015 & Hedge et al Clin. *Cancer Res* 2016

** **TE**= Tumor Epithelium, **NE**: Non-Epithelium
Detected with automated AI-based approach

Biomarkers for therapy & patient stratification*

CD8 (TE**)	CD8 (NE**)	PD-L1	FoxP3

+	CD68	PD1	Granzyme B	(CD3)

AIR
IT
ACIR
ITPI
II
ICIR
Inflamed (Hot)
Non-Inflamed (Cold)

Adaptive Immune Resistance

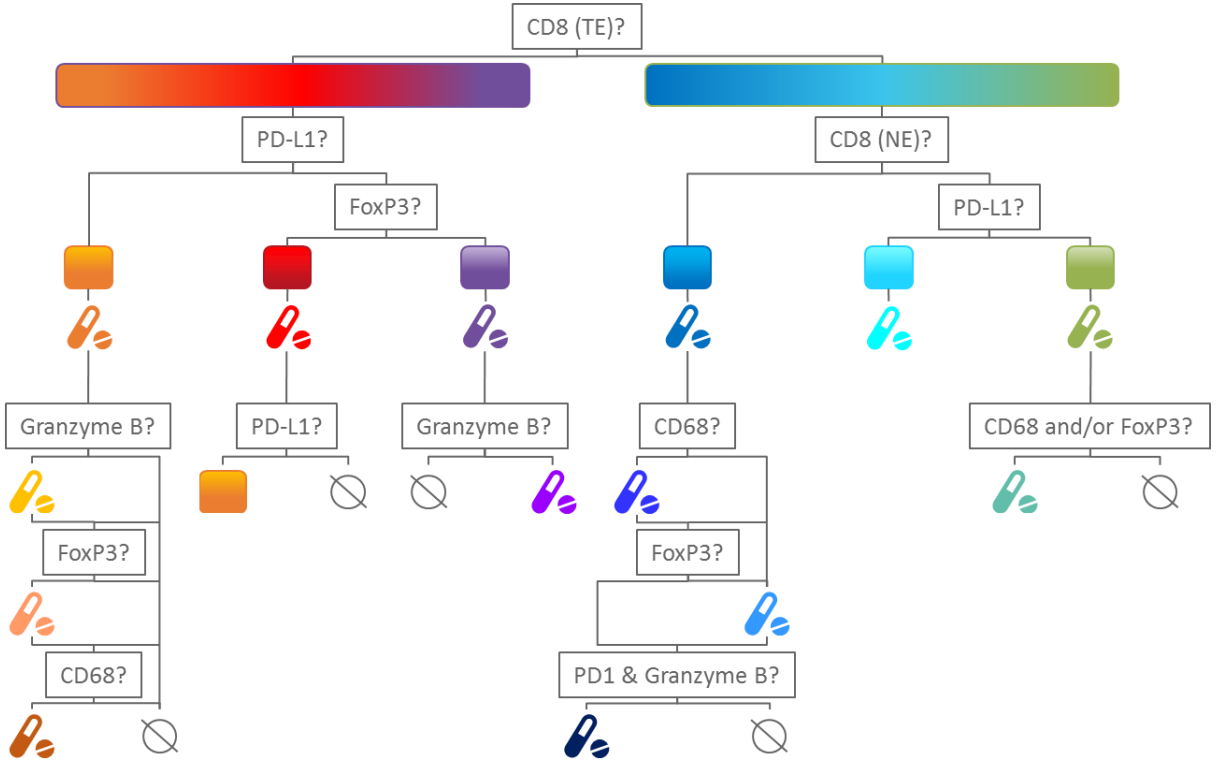
Immune Tolerance

Aquired Checkpoint Inhibitor Resistance

Impaired Tumor Parenchyma Infiltration

Immune Ignorance

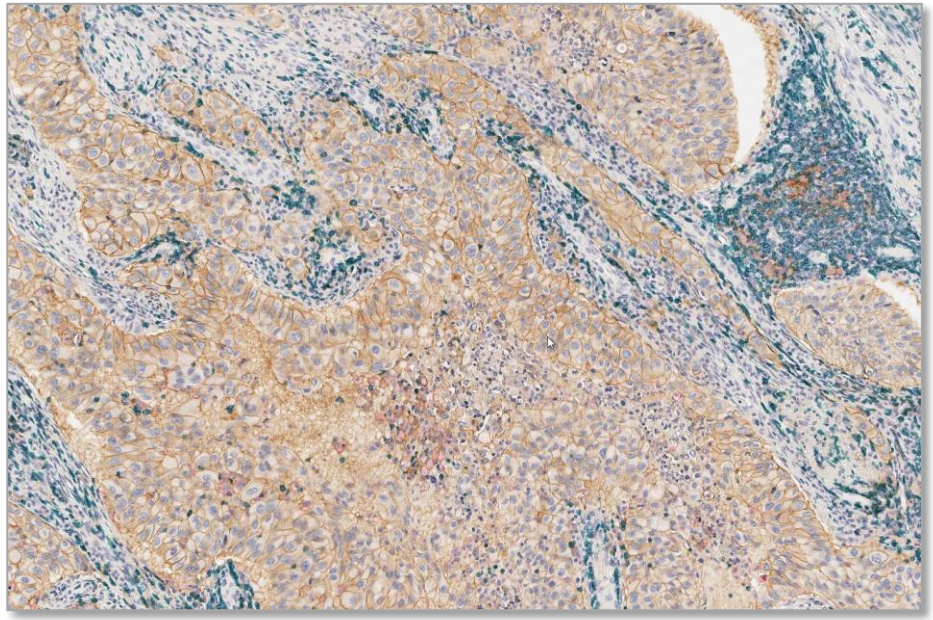
Intrinsic Checkpoint Inhibitor Resistance



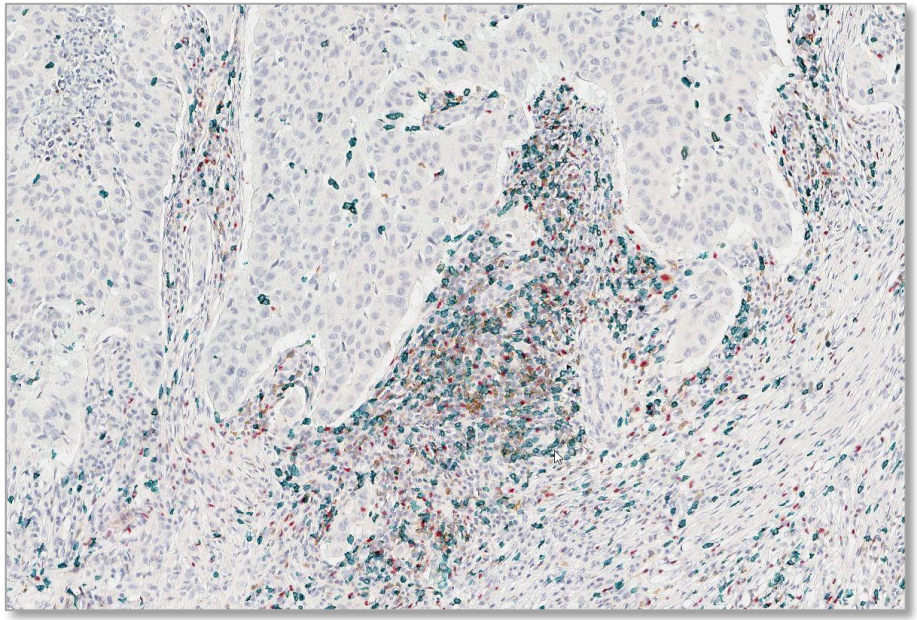
* In analogy to Teng et al *Cancer R* 2015 & Hedge et al Clin. *Cancer Res* 2016

** **TE**= Tumor Epithelium, **NE**: Non-Epithelium
Detected with automated AI-based approach

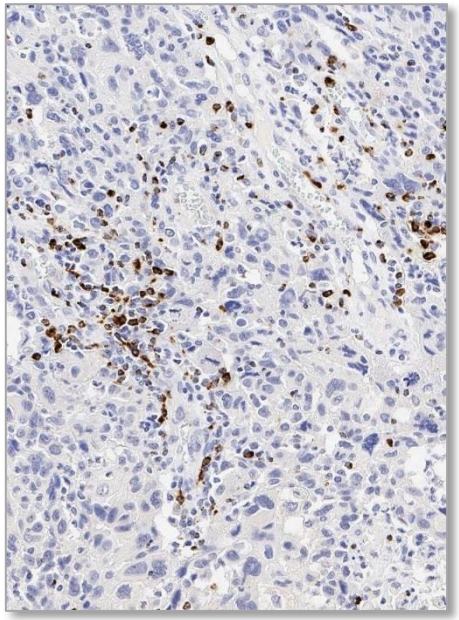
Multiplex approach optimizes spatial information



CD3 CD68 PD-L1



CD8 FoxP3 PD1

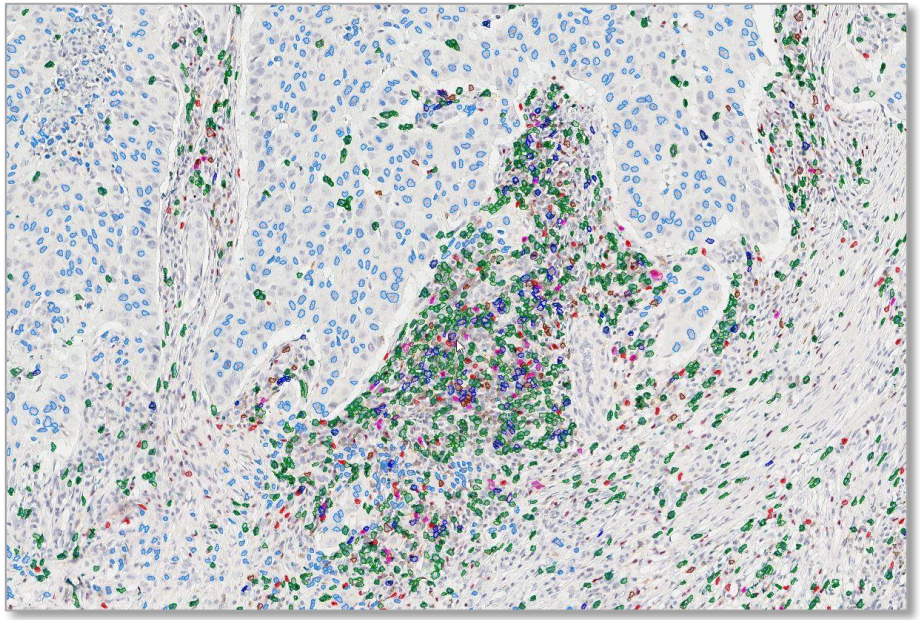


Granzyme B

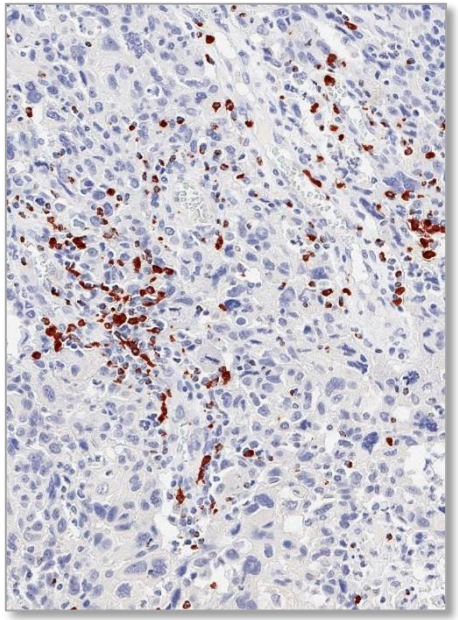
Slide Images: Courtesy Mosaic Laboratories, LLC, Lake Forest, CA

Multiplex approach optimizes spatial information

- CD68- PD-L1+ CD3-
- CD68+ PD-L1+ CD3-
- CD68- PD-L1- CD3+
- CD68- PD-L1+ CD3+
- CD68+ PD-L1- CD3-



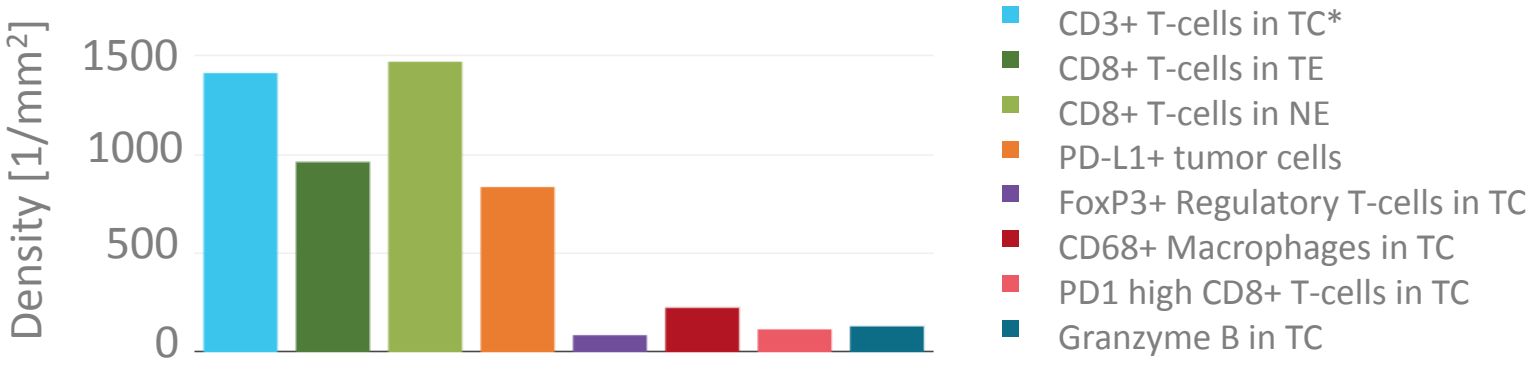
- FoxP3- PD1+ CD8-
- FoxP3+ PD1+ CD8-
- FoxP3 - PD1- CD8+
- FoxP3 - PD1+ CD8+
- FoxP3 + PD1- CD8-
- Negative cells TE
- Negative cells NE



- Granzyme B

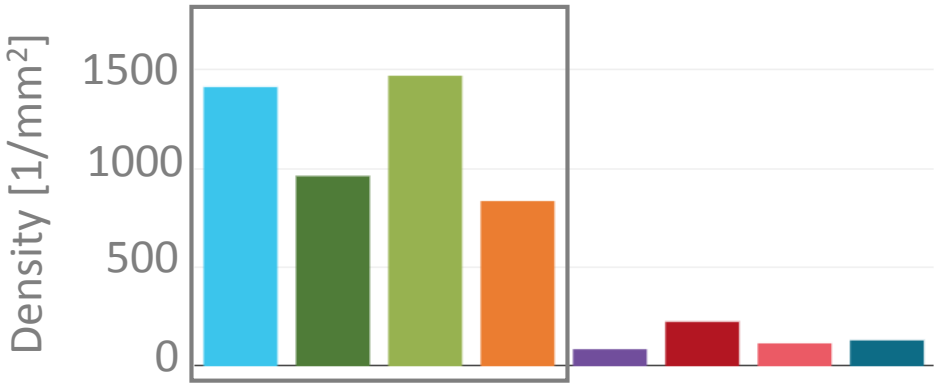
Slide Images: Courtesy Mosaic Laboratories, LLC, Lake Forest, CA

Case A



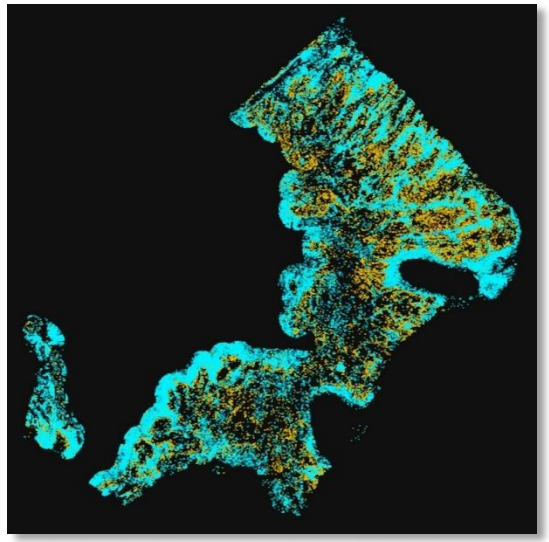
*TC = Tumor Center
IM = Invasive Margin
TE = Tumor Epithelium
NE = Non-Epithelium

Case A

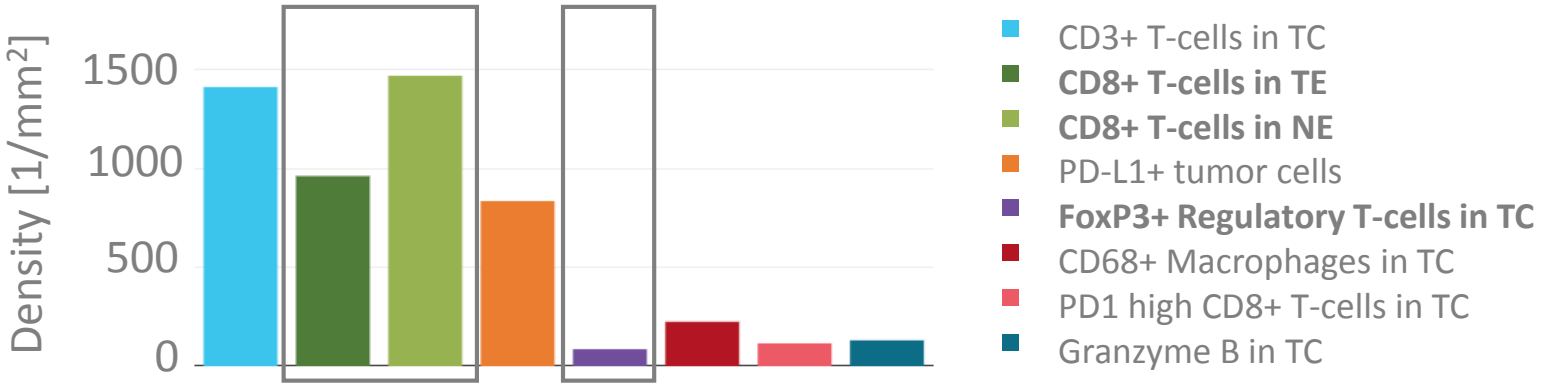


- **CD3+ T-cells in TC**
- **CD8+ T-cells in TE**
- **CD8+ T-cells in NE**
- **PD-L1+ tumor cells**
- FoxP3+ Regulatory T-cells in TC
- CD68+ Macrophages in TC
- PD1 high CD8+ T-cells in TC
- Granzyme B in TC

Adjacent localization
- CD3+ T-cells and
- PD-L1+ tumor cells

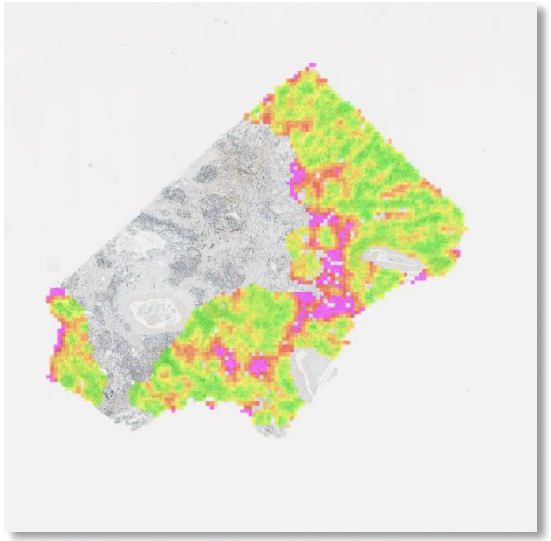


Case A



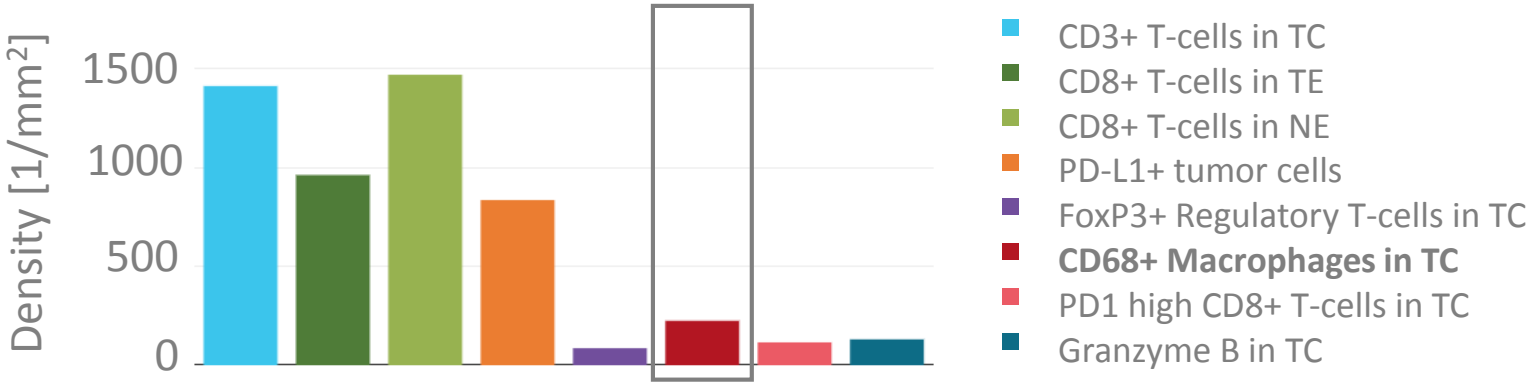
Distance of CD8+ to neighboring FoxP3+ cells

12% of CD8+ T-cells might be inhibited in TE*

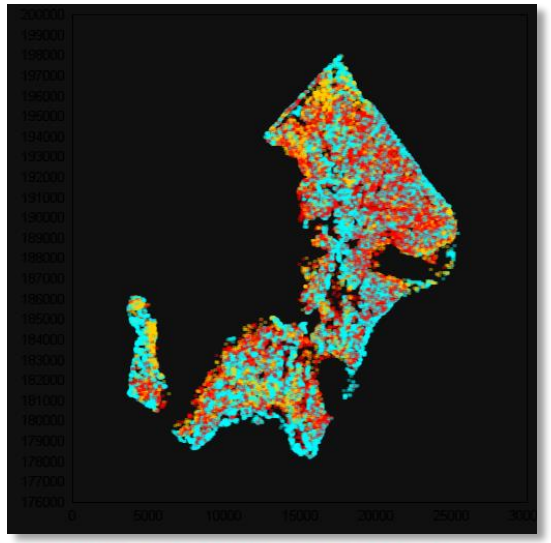


* CD8+ T-cells within <30µm distance of a FoxP3+ T-cell

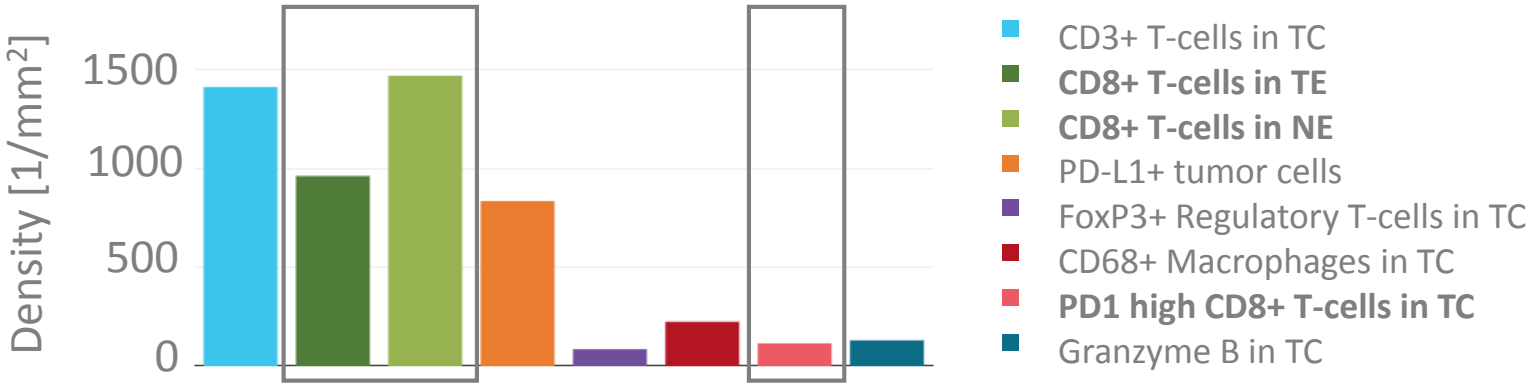
Case A



Macrophages sparsely populate the tumor



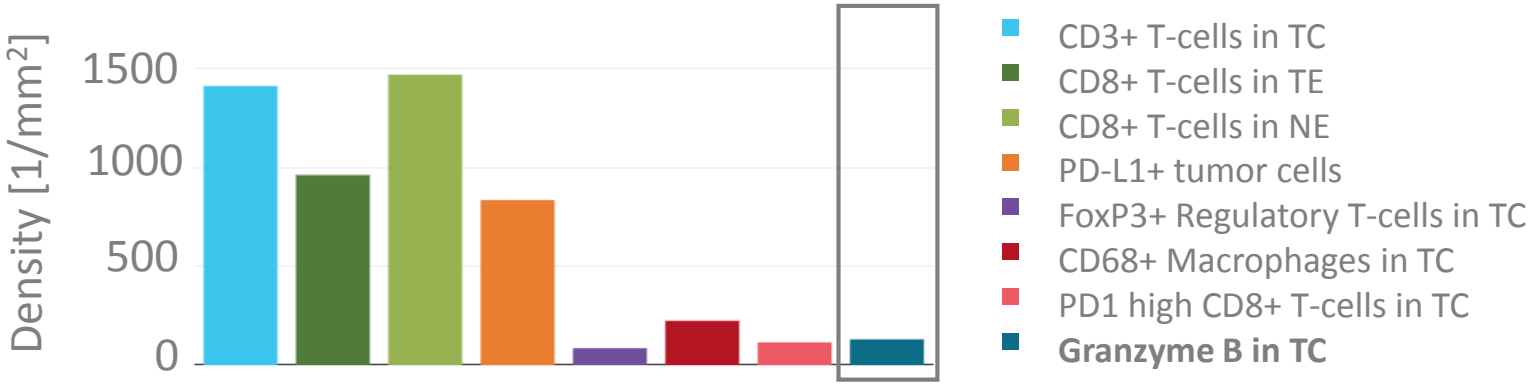
Case A



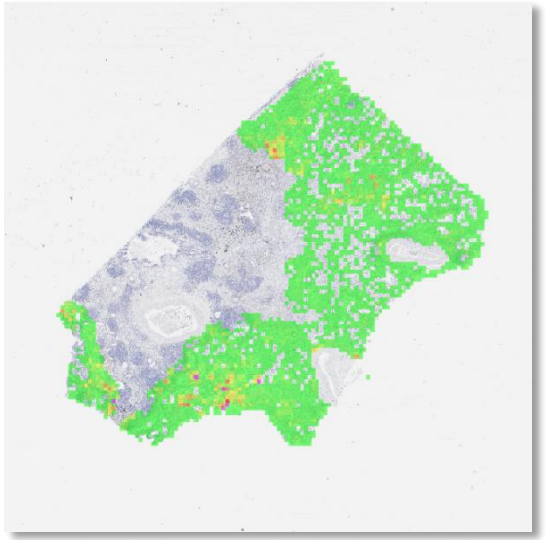
Visualization of the ratio CD8+PD1 low/CD8+PD1 high

10% of all CD8+ T-cells are PD1 high

Case A



Granzyme B
Coverage Score*: 1



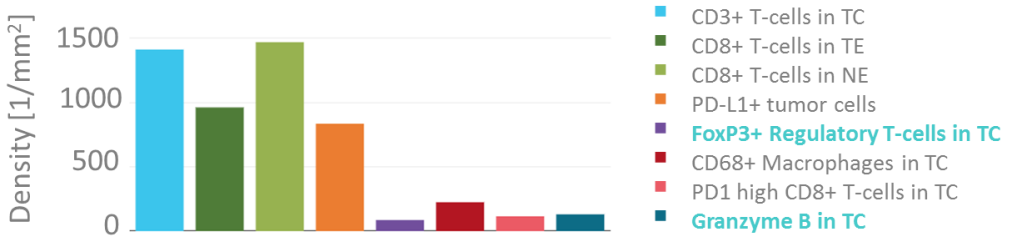
low high

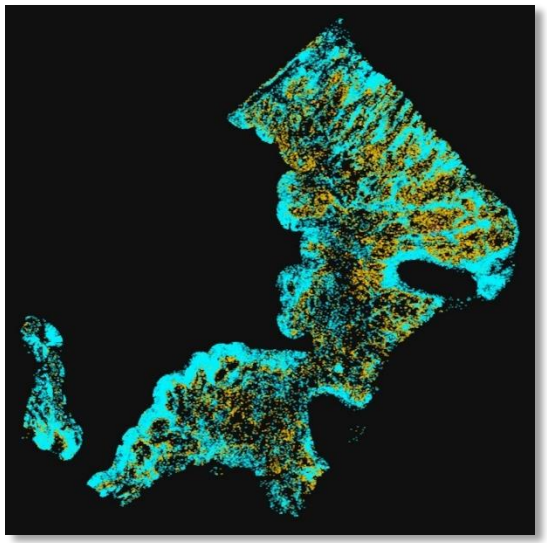
* Score [0:4]: GranzB+ area related to number of CD8+ T-cells

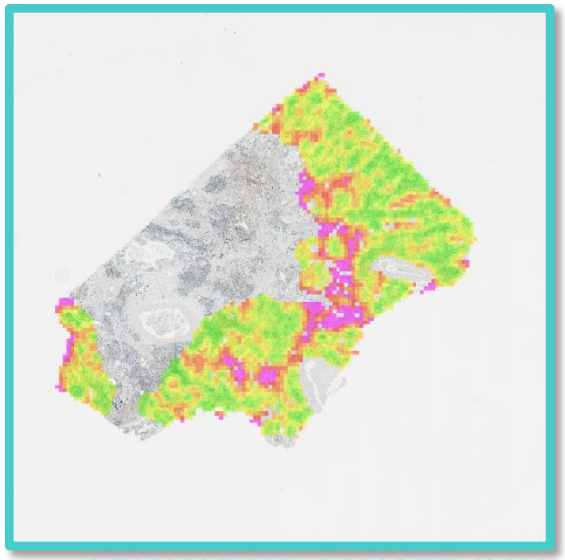
Case A

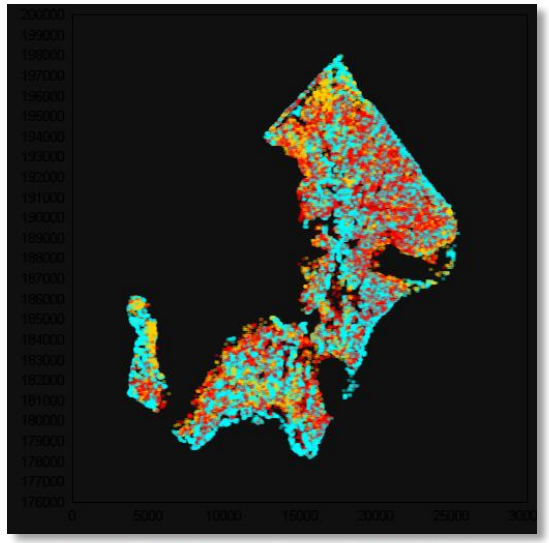
Inflamed (Hot)		
AIR	IT	ACIR
Non-Inflammed (Cold)		
ITPI	II	ICIR

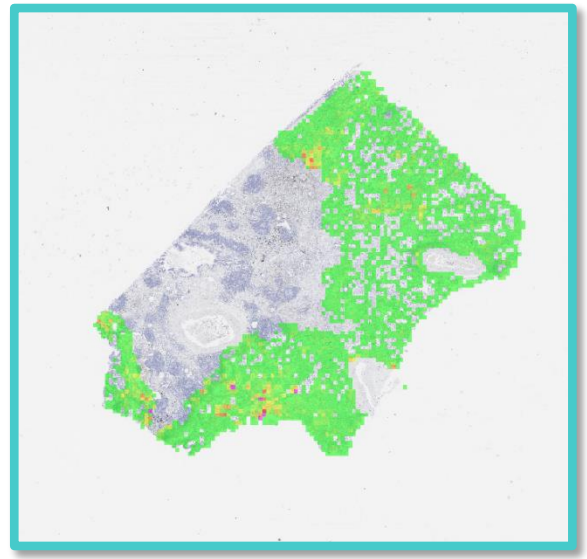
Adaptive Immune Resistance
CD8 (TE): ↑ PD-L1 : ↑



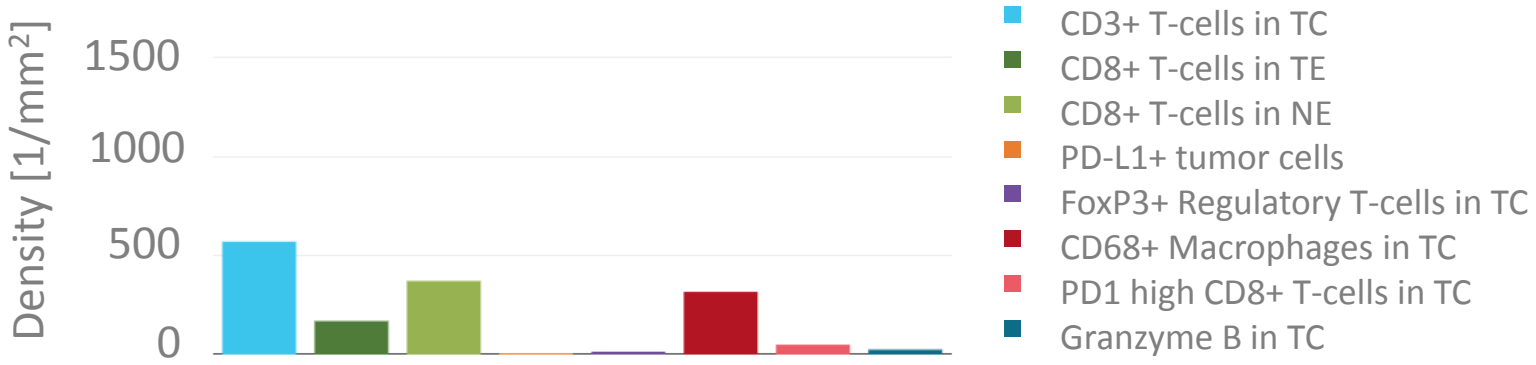




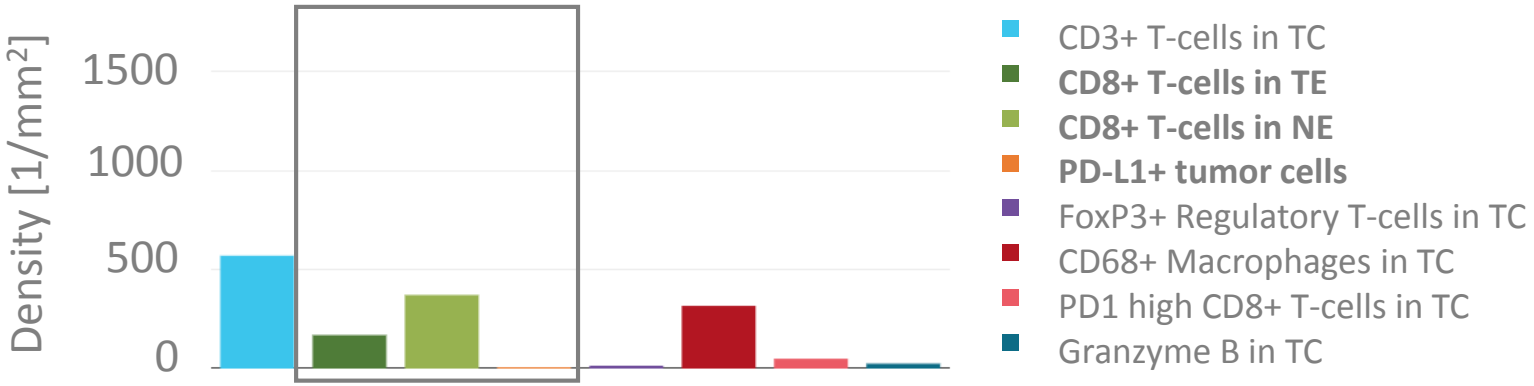




Case B

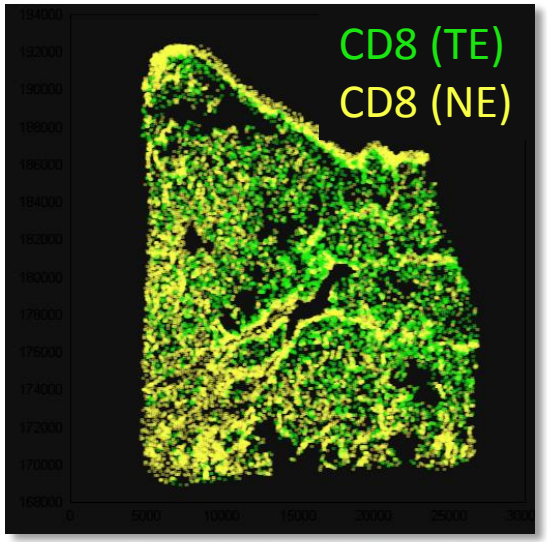

Density [1/mm²]
1500
1000
500
0
CD3+ T-cells in TC
CD8+ T-cells in TE
CD8+ T-cells in NE
PD-L1+ tumor cells
FoxP3+ Regulatory T-cells in TC
CD68+ Macrophages in TC
PD1 high CD8+ T-cells in TC
Granzyme B in TC

Case B

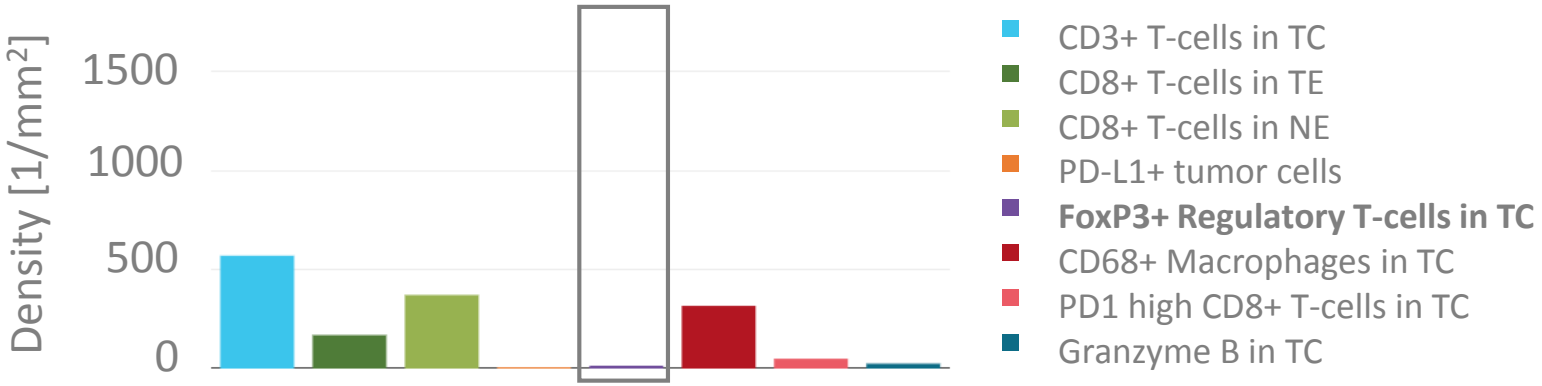


Ratio of CD8+ T-cells:

NE/TE = 2.2
IM/TC = 2.2

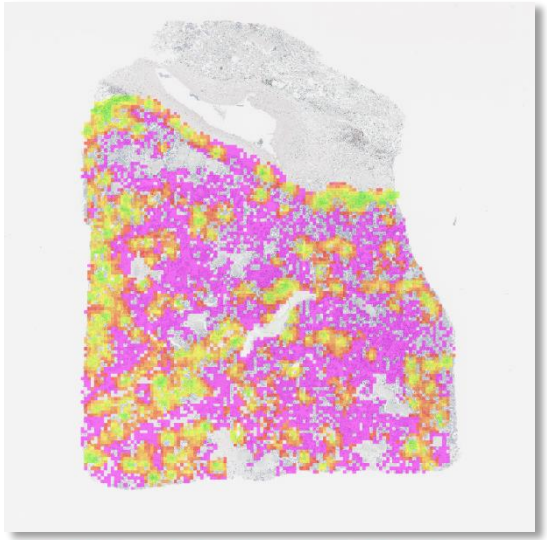


Case B

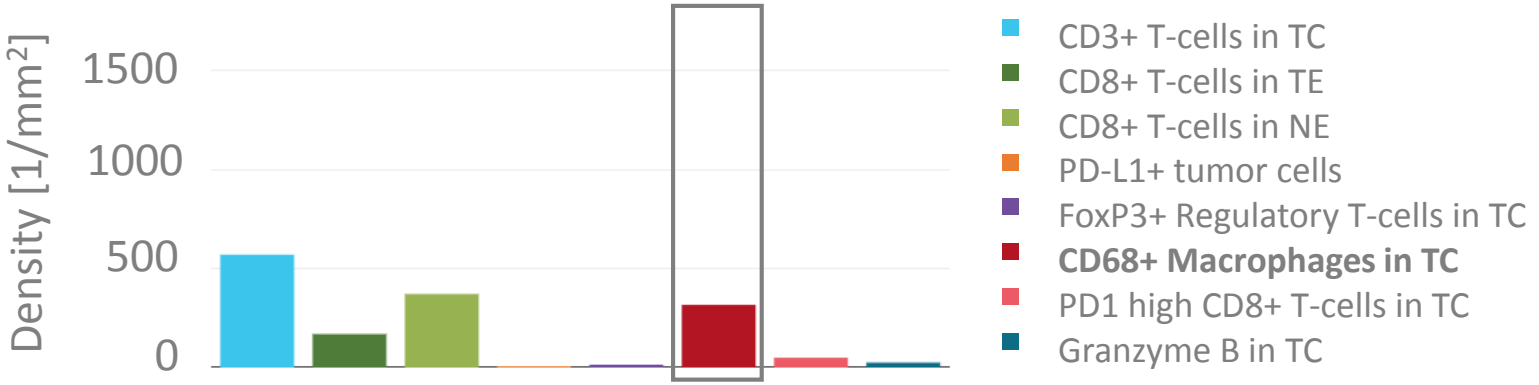


Distance of CD8+ to neighboring FoxP3 cells

4% (TE), 8% (NE) and 19% (IM) of CD8+ T-cells might be inhibited

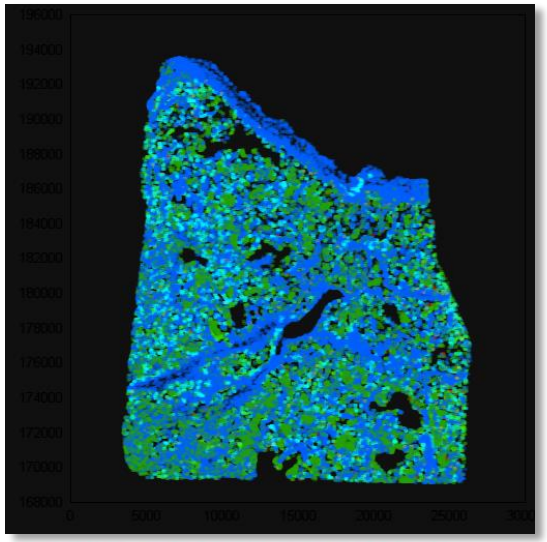


Case B

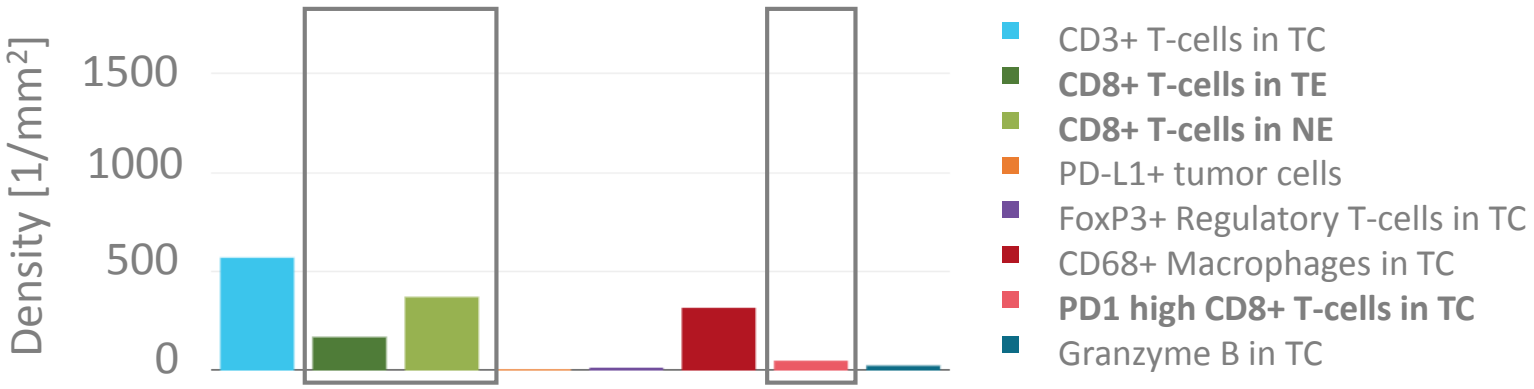


Ratio Macrophages TC/IM = 6.6

40% (TC), 48% (IM) of Macrophages PD-L1+



Case B



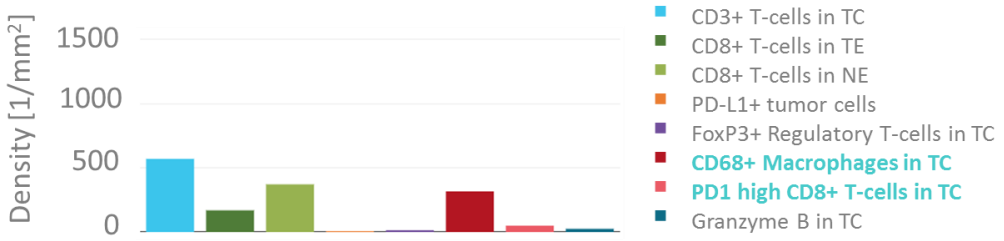
Visualization of the ratio CD8+PD1 low/CD8+PD1 high

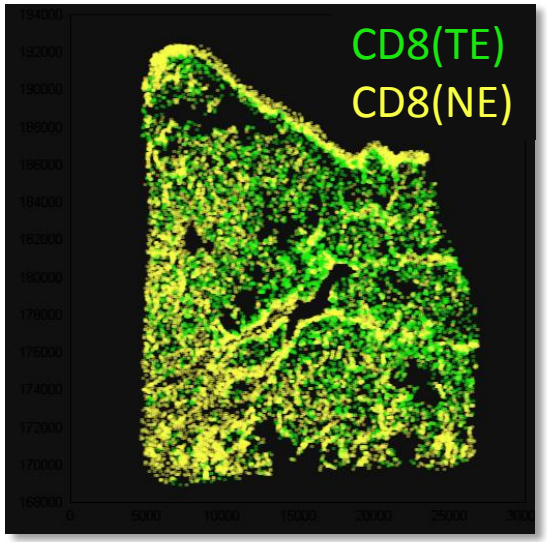
19% PD1 high of all CD8+ cells

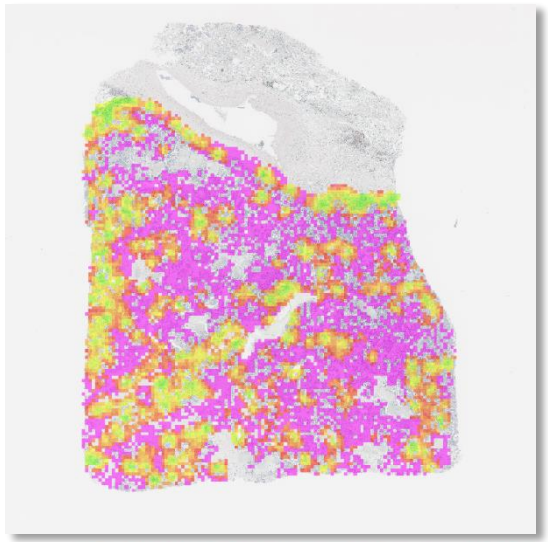
Case B

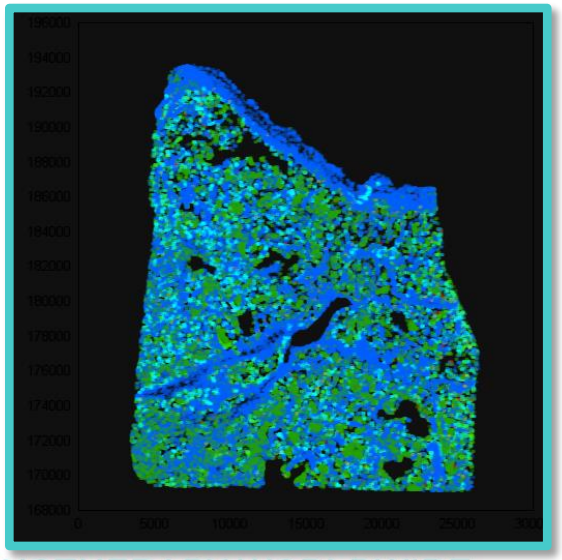
Inflamed (Hot)		
AIR	IT	ACIR
Non-Inflammed (Cold)		
ITPI	II	ICIR

Immune Ignorance
CD8 (TE): ↓ PD-L1 : ↓









Lessons and Take Home Messages

Definiens IO-Panel enables:

- **Quantitative analysis** of immune cells **in the context of tumor tissue** from multiplex IHC assays provided by Mosaic Laboratories
- Identification of **interactions** between the immune system and the tumor on a **single-cell resolution level**
- **Construction of immune landscapes** within the tumor-microenvironment
- Visualization of **prevalent immune populations**, hotspots **of interaction** and **tumor heterogeneity**

Generated **insights** provide a comprehensive assessment of a **patient's tumor immune status** and provide indispensable **information for personalized medicine**

Acknowledgements

Definiens AG

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Mosaic Laboratories LLC

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