The 26th Anti-Cancer Drug Development Forum

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Immunological resistance to Immune Checkpoint Inhibitor

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Disclosure Information

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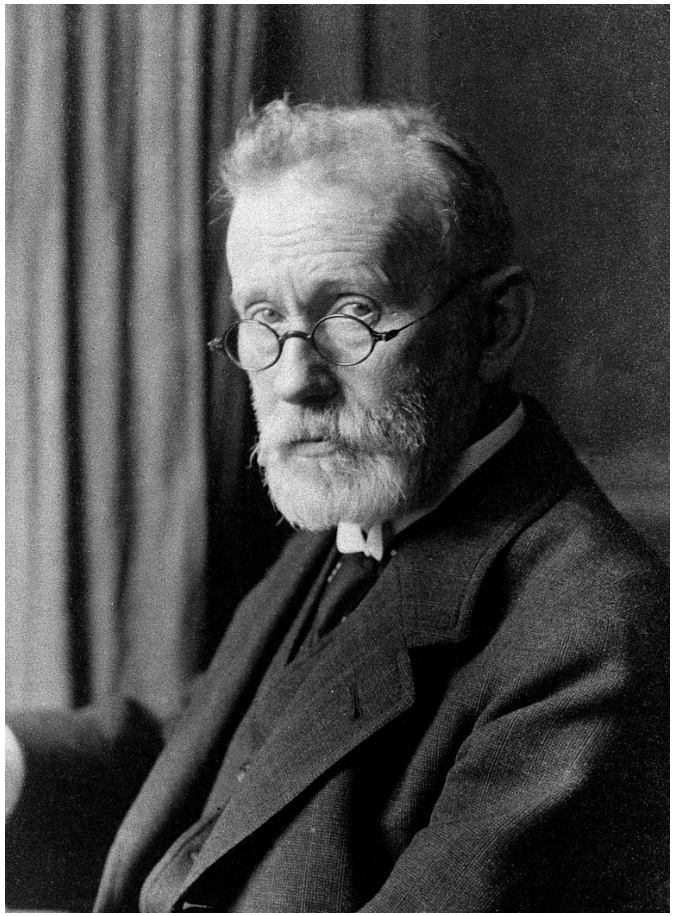
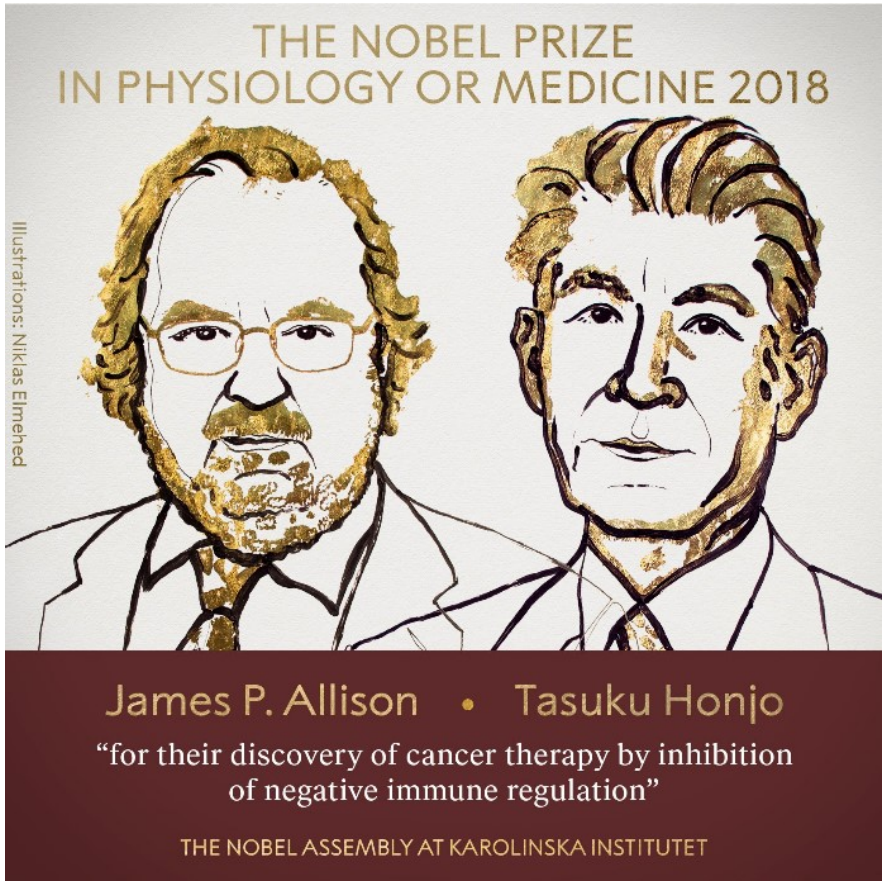
I have no financial relationships to disclose.

Cancer Immunotherapy
～the long journey to success～

William Coley
(1862-1936)

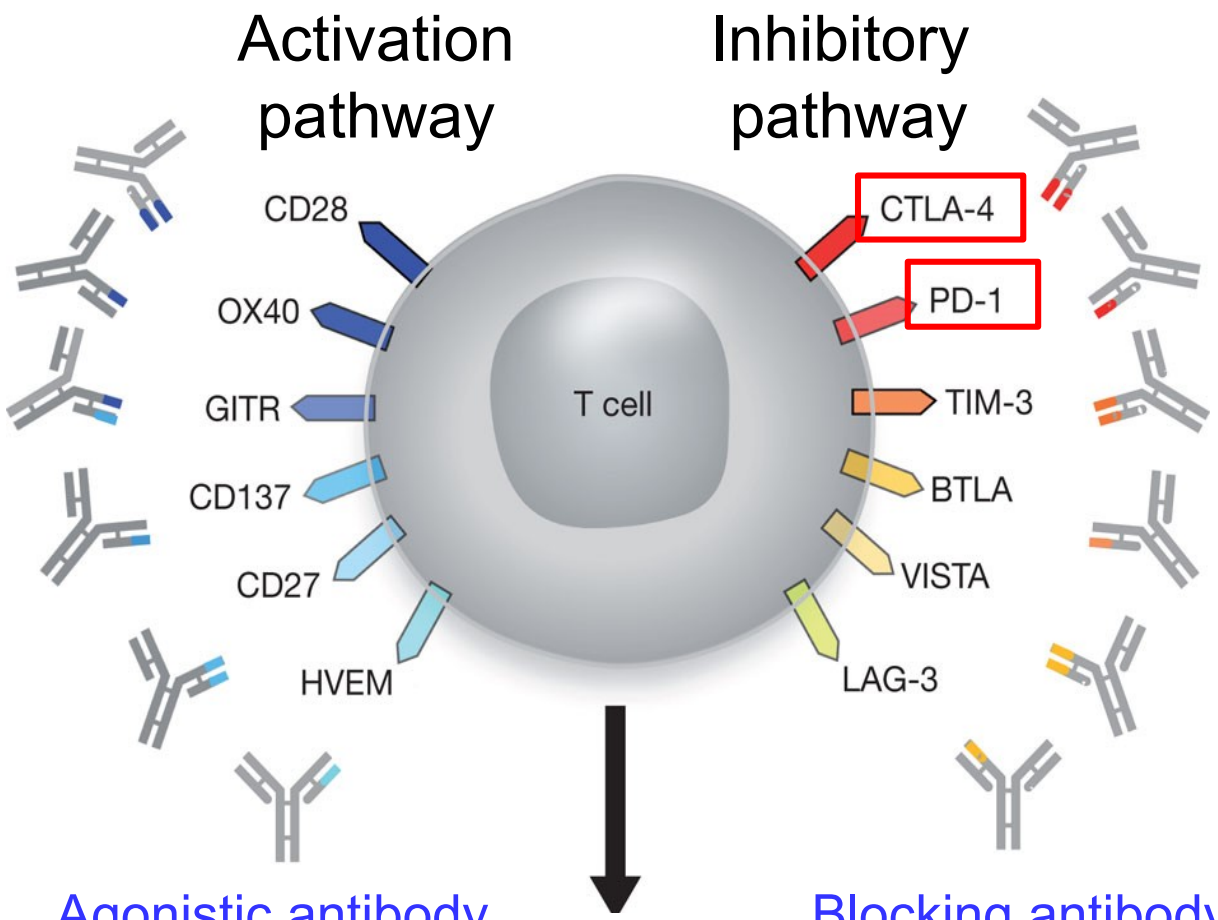


Paul Ehrlich
(1854-1915)



2018年

Current status of immunity checkpoint inhibitors



. Curr Opin Immunol 2016

T-cell activation

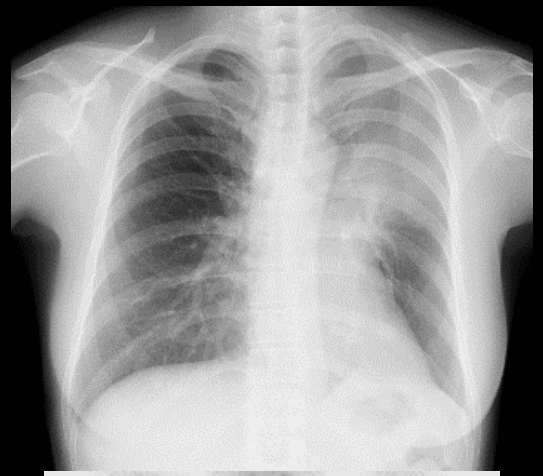
No dramatic therapeutic effect except anti-PD-1 and anti-CTLA-4

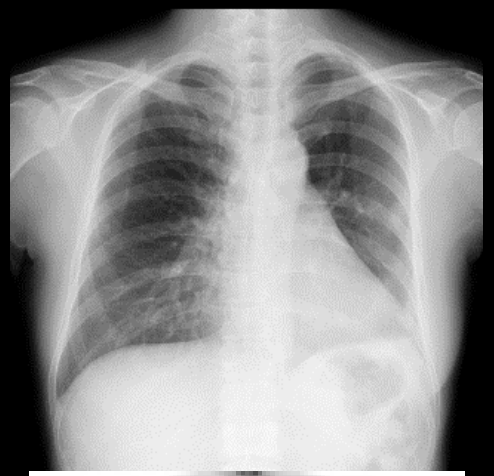
48yrs, female, NSCLC (Ad) cT3N2M1b stage IVa, EML4-ALK fusion (+)

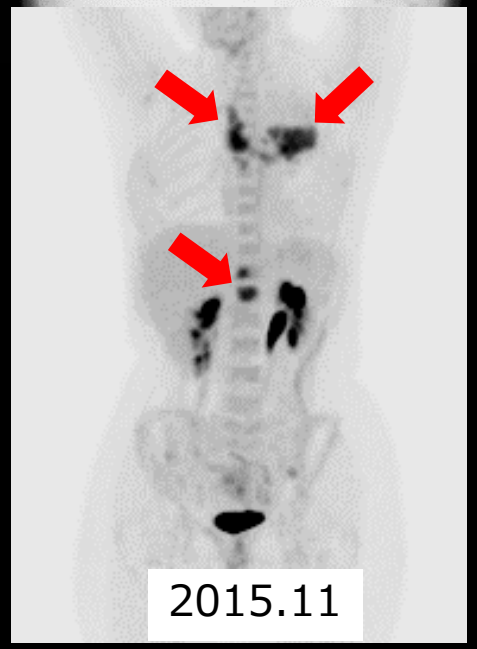
At diagnosis

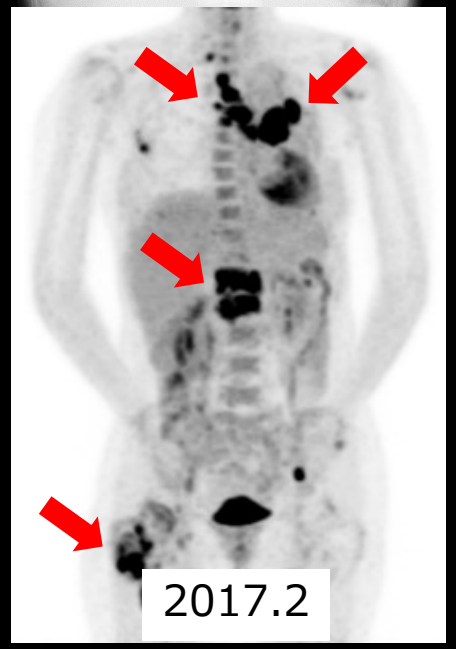
6th line
Pre anti-PD-1

Post anti-PD-1



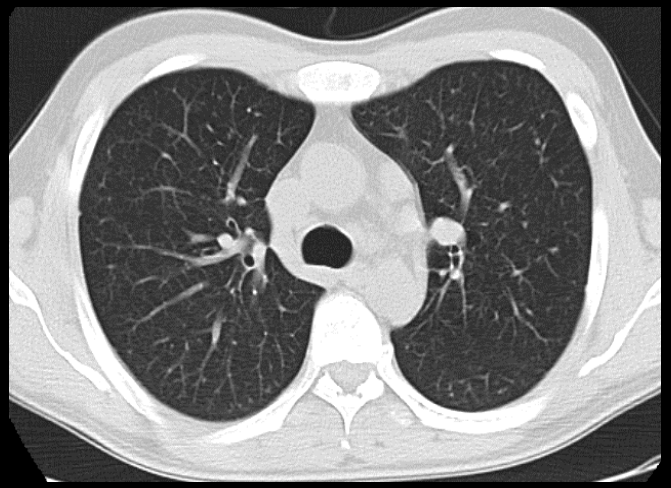




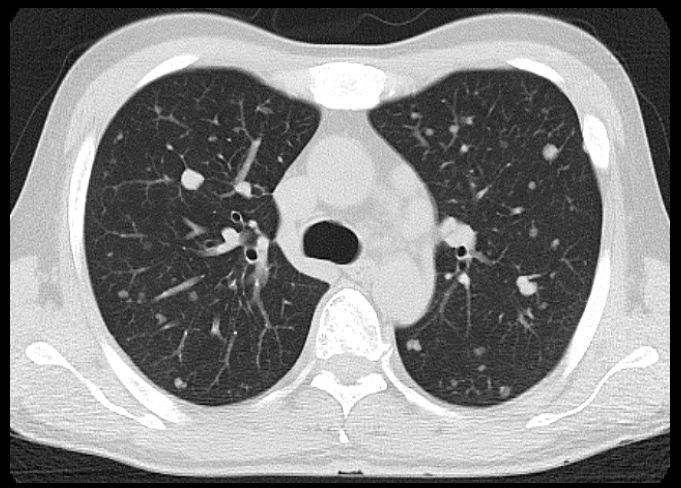


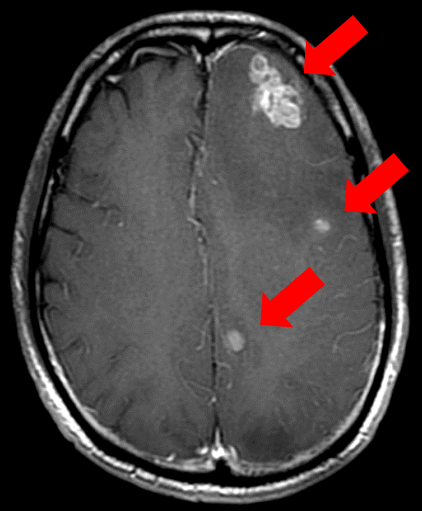
48yrs, male, NSCLC (Ad) cT1bN2M1b stage IVa,
EGFR mutaion (+)

9th line
Pre anti-PD-1

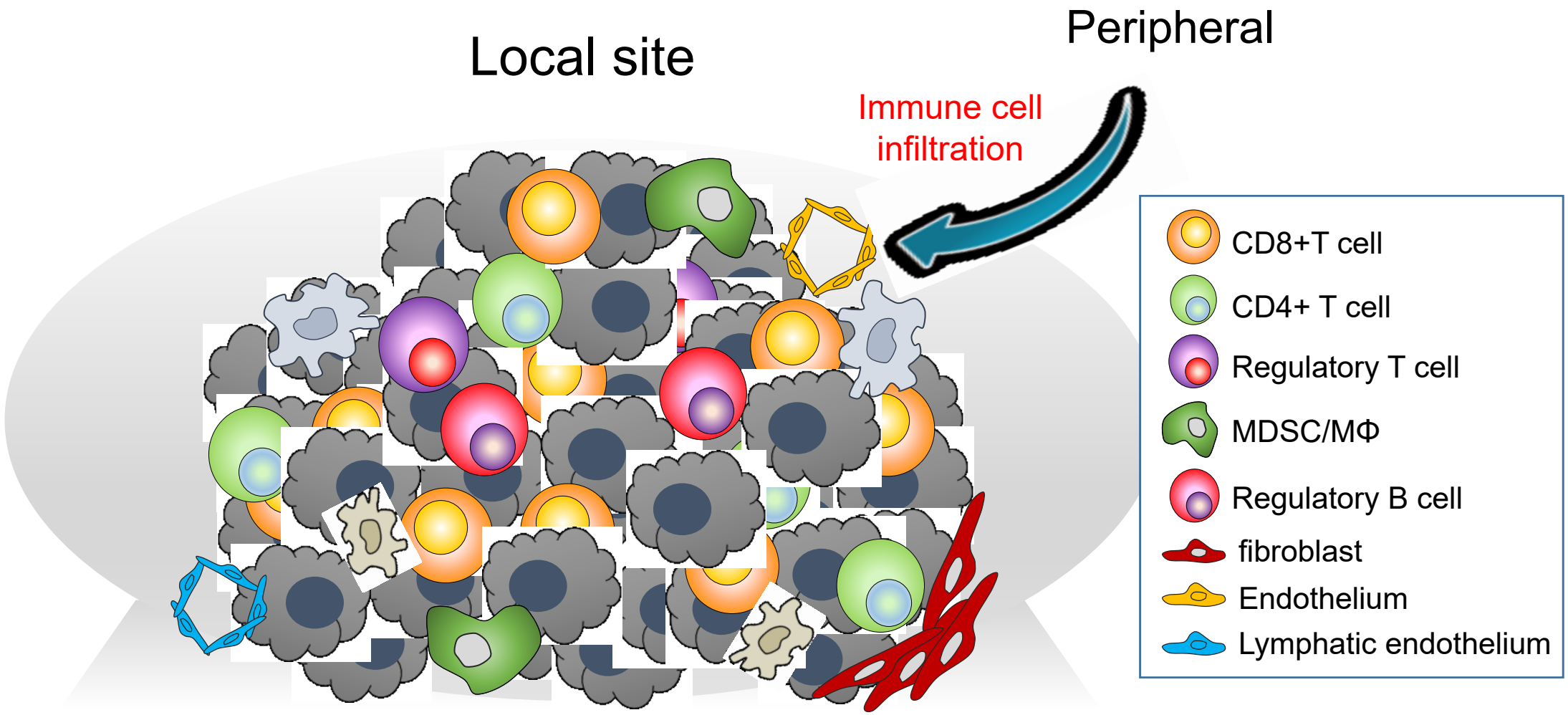


Post anti-PD-1





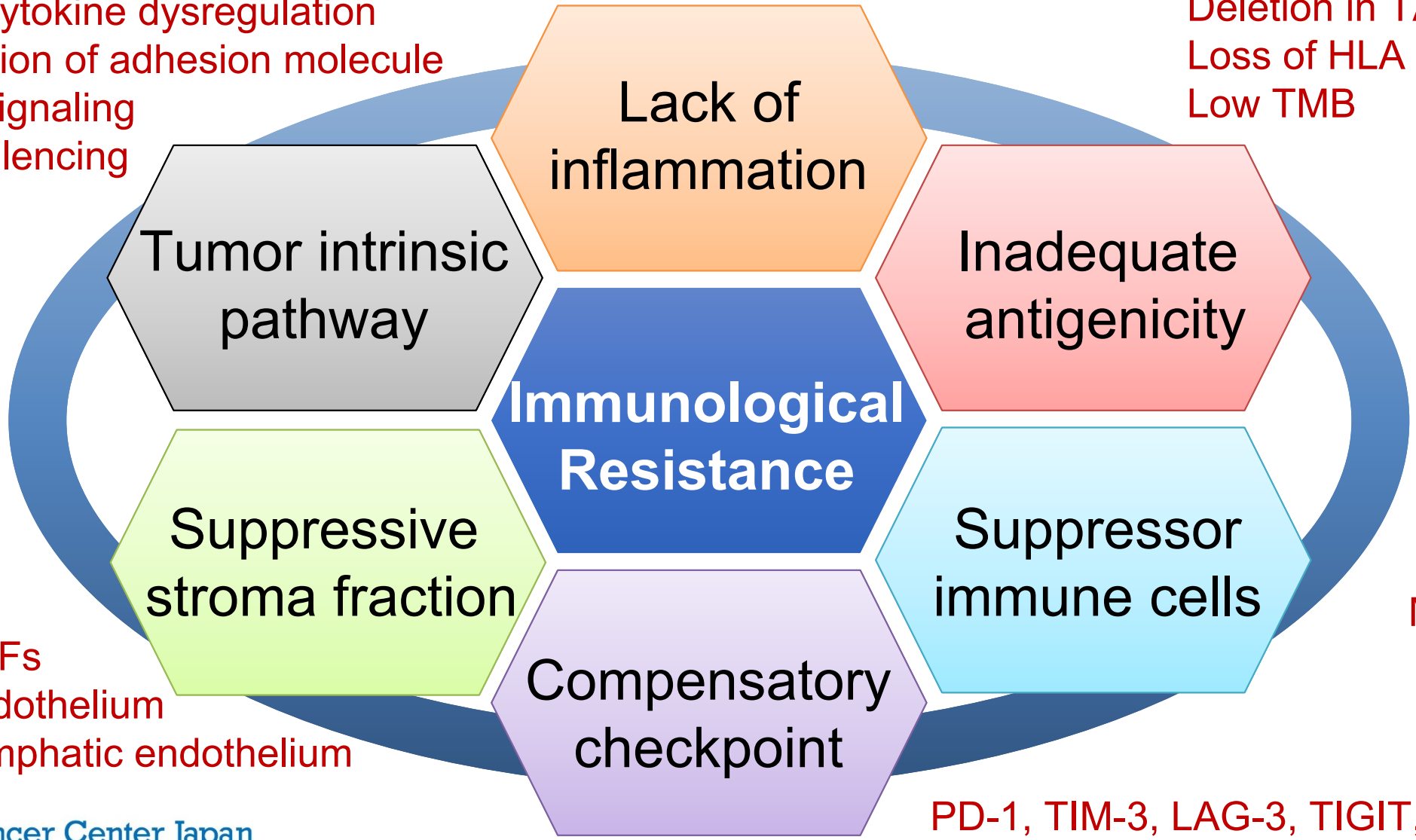
Tumor microenvironment



Cause of immunological resistance to anti-tumor immunity

Mutation in IFNg signaling
Metabolite/Cytokine dysregulation
Downregulation of adhesion molecule
Oncogenic signaling
Epigenetic silencing

Deletion in TAP, β2M
Loss of HLA
Low TMB



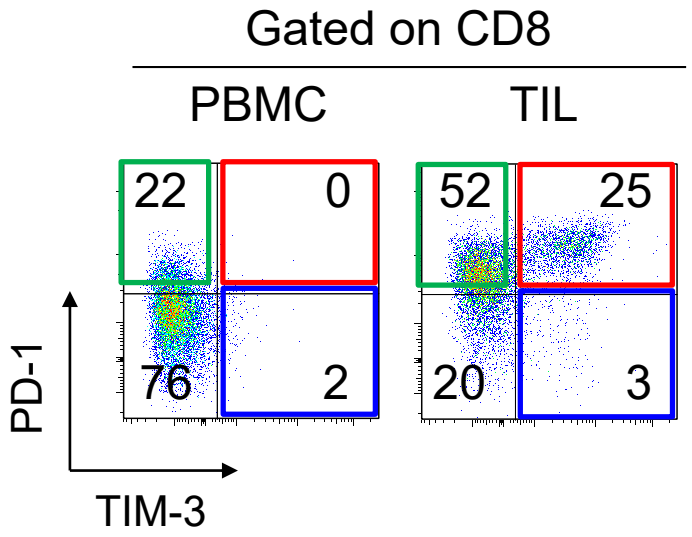
Treg
Breg
MDSC
TAM

CAFs
Endothelium
Lymphatic endothelium

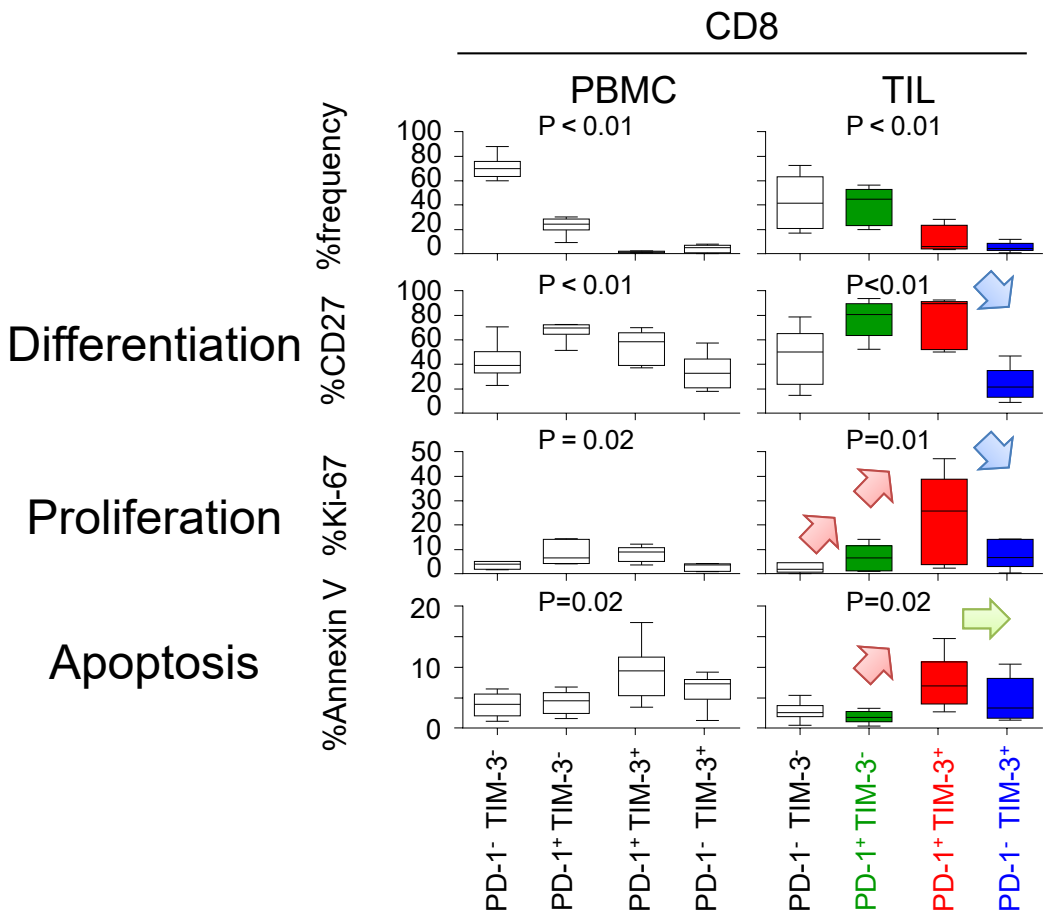
PD-1, TIM-3, LAG-3, TIGIT, VISTA

Correlation of PD-L1 and Galectin-9 expression, and TIL

Flow cytometry



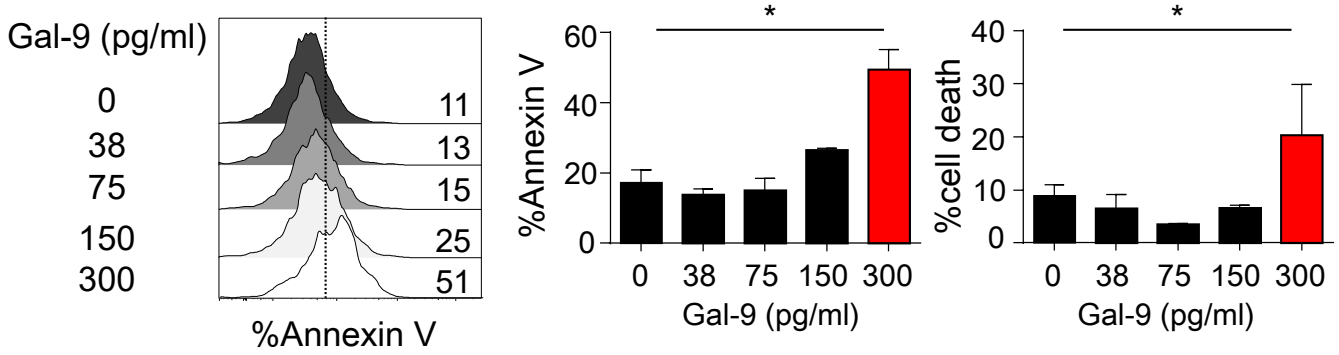
Analysis of each fraction



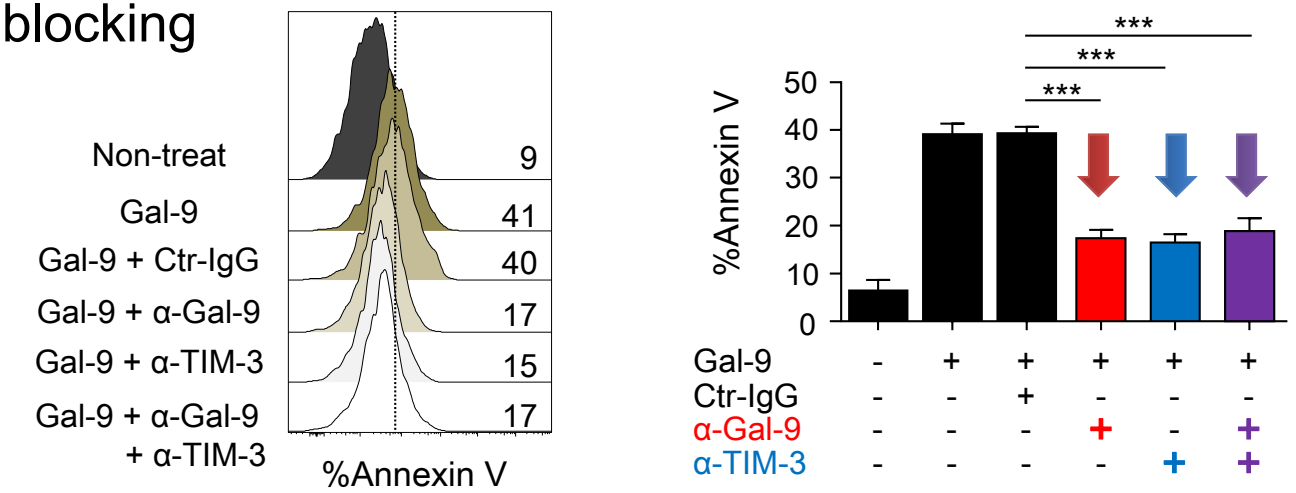
Ohue Y, et, al. **Cancer Immunol Res**. 2016

T-cell apoptosis by soluble Galectin-9

Apoptosis by galectin-9



Antibody blocking



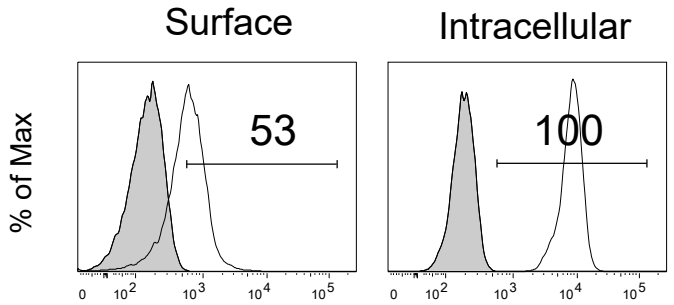
Ohue Y, et, al. **Cancer Immunol Res**. 2016

Release of soluble Galectin-9 from tumor cells

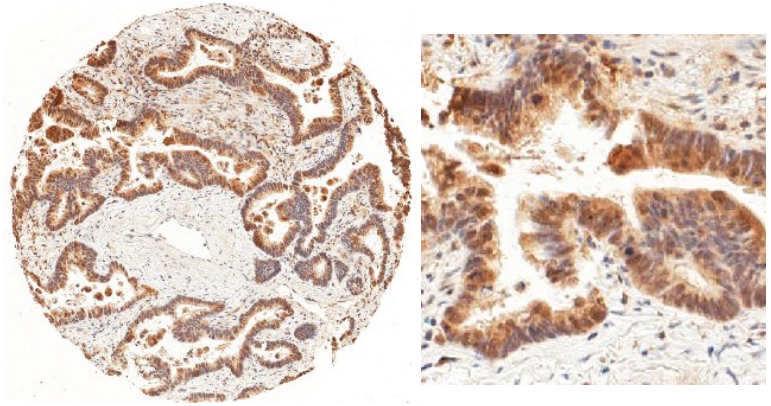
A

Galectin-9 expression

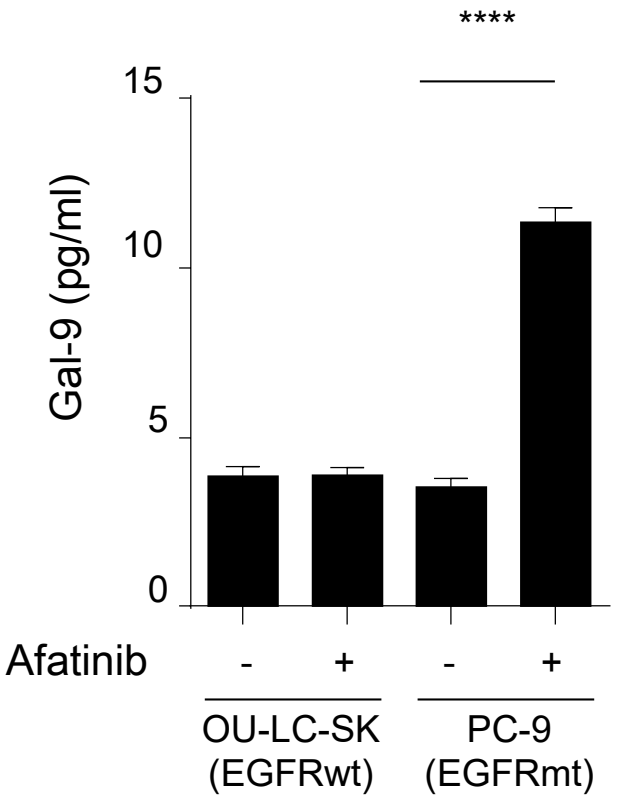
Cell line (OU-LC-SK)



Lung cancer tissue



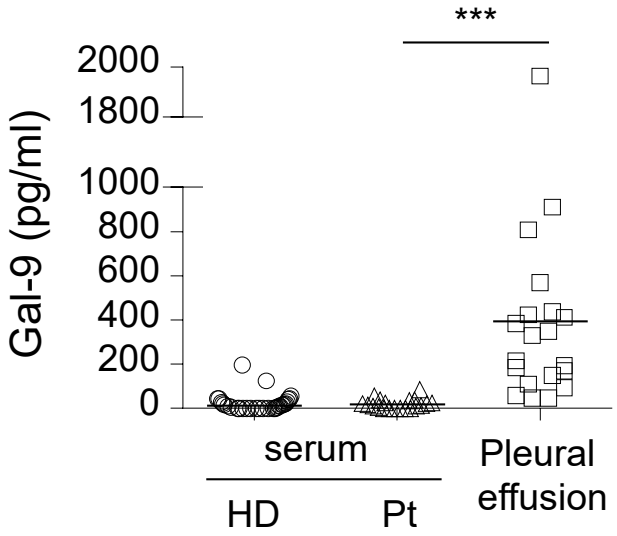
B



**** $p < 0.0001$

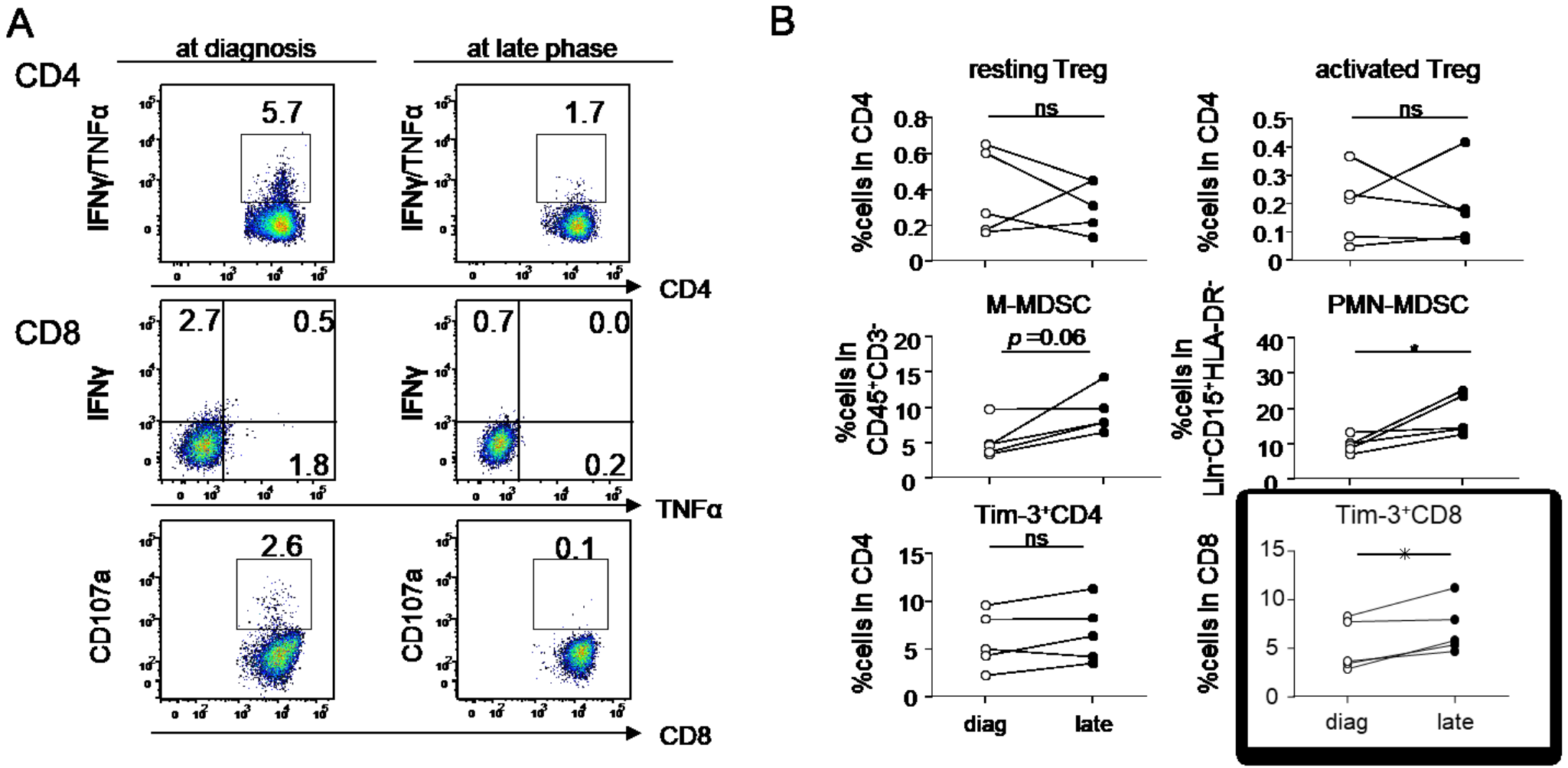
C

Galectin-9
in clinical samples



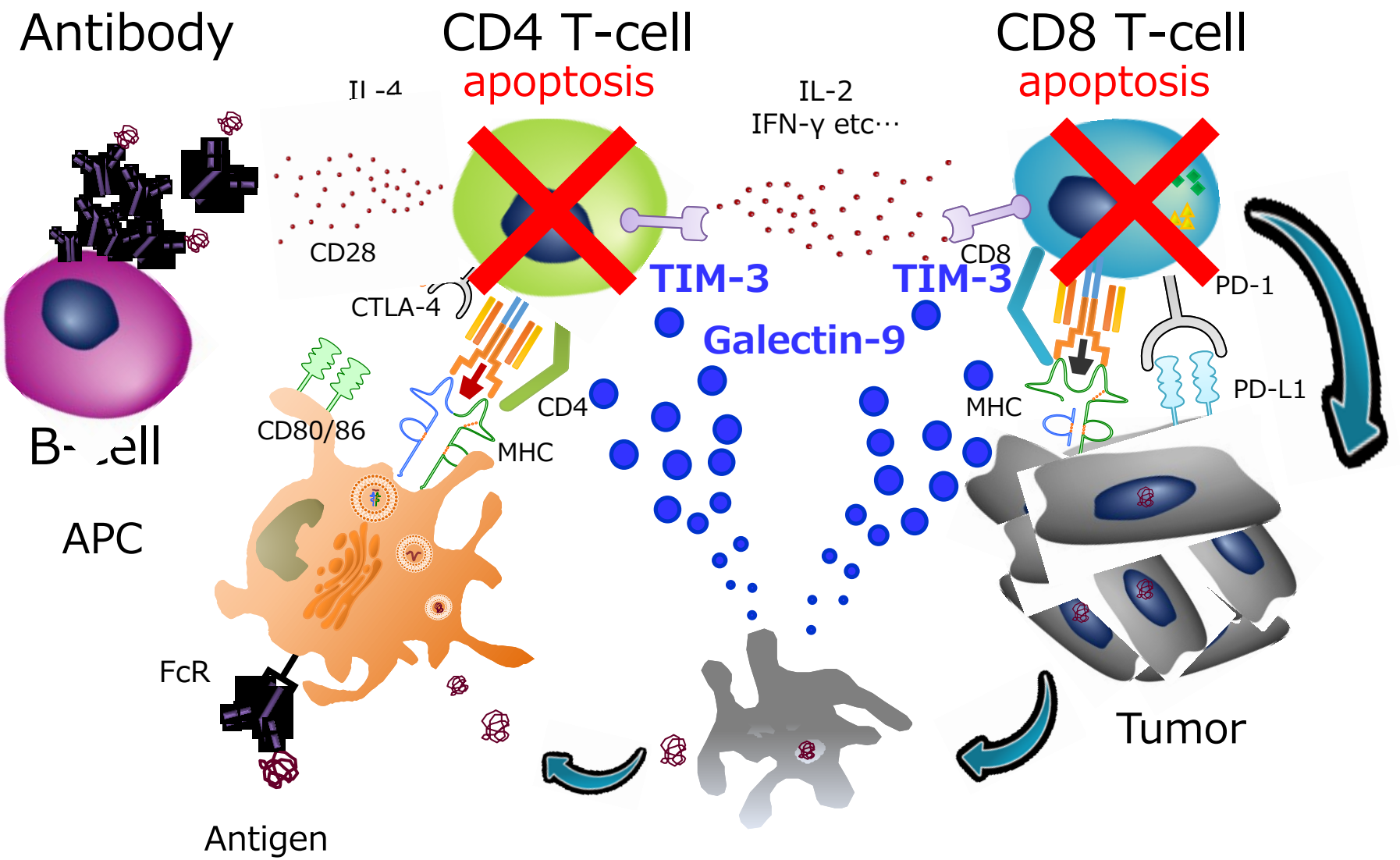
Ohue Y, et, al. **Cancer Immunol Res**. 2016

Involvement of immune checkpoint molecules at the late phase of disease progression



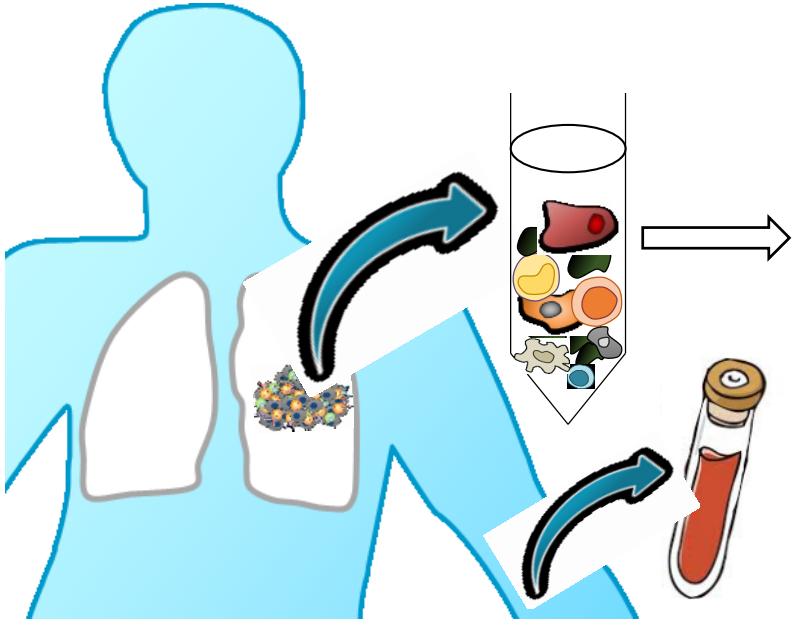
Ohue Y, et, al. **Clin Cancer Res.** 2014

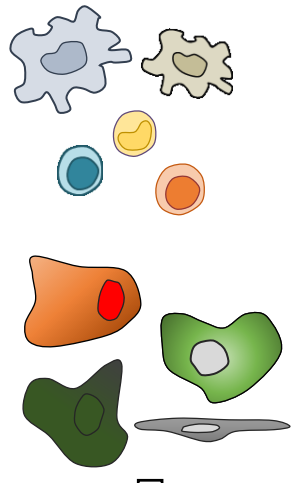
Tumor immune microenvironment

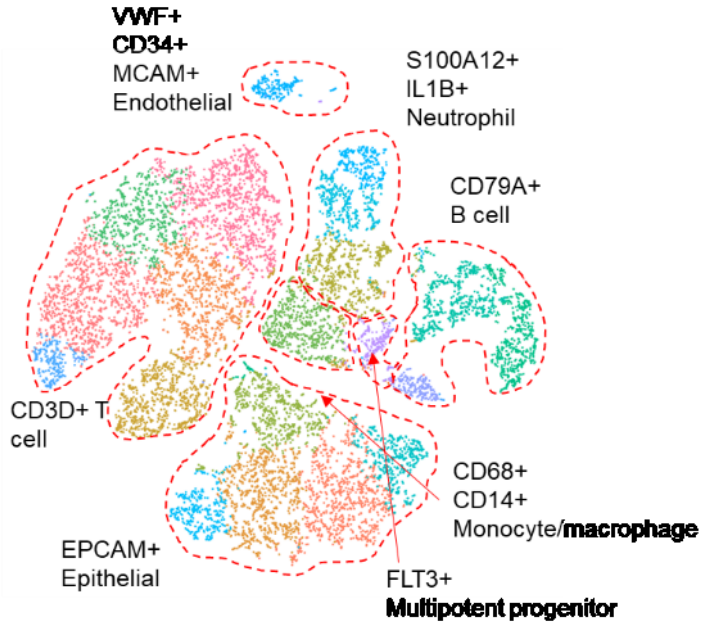


Ohue Y, et, al. **OncoImmunol**. 2014

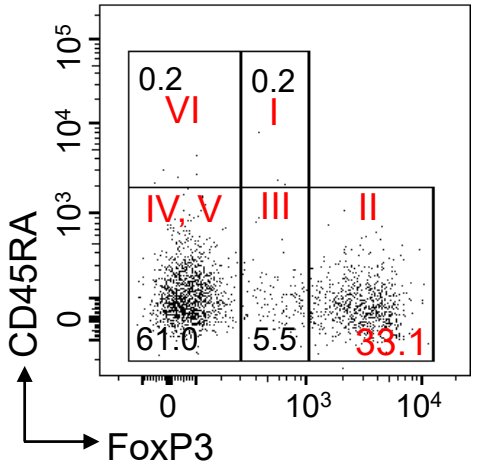
Comprehensive Analysis of Tumor Immunity

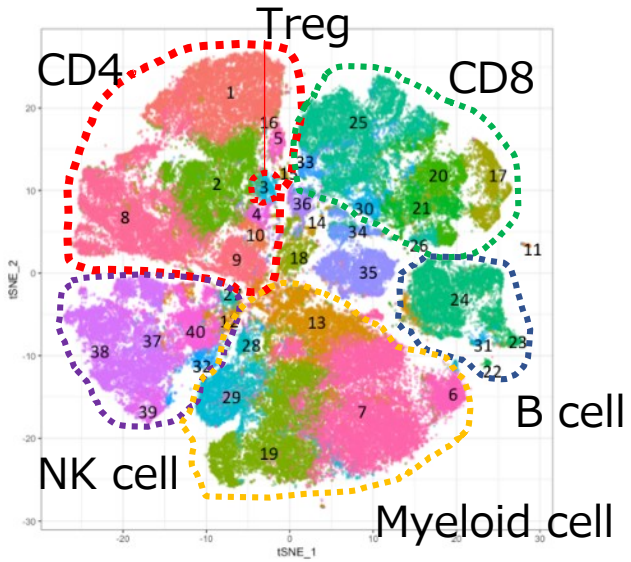






Fr. I: Naive Treg cells
Fr. II: Effector Treg cells
Fr. III: Non-Treg cells





National Cancer Center Japan

Acknowledgements

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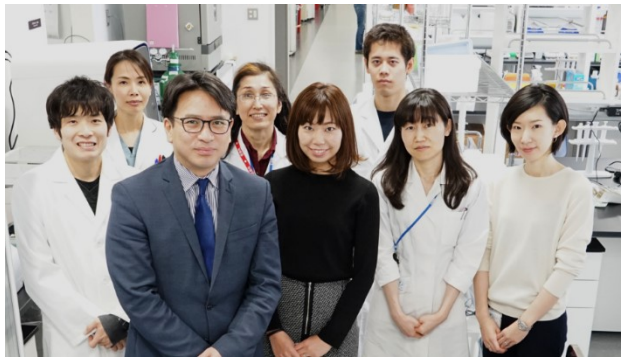

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