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Society for Immunotherapy of Cancer



Altered T-cell clonotype composition is strongly associated with functional orientation of colon cancer microenvironment

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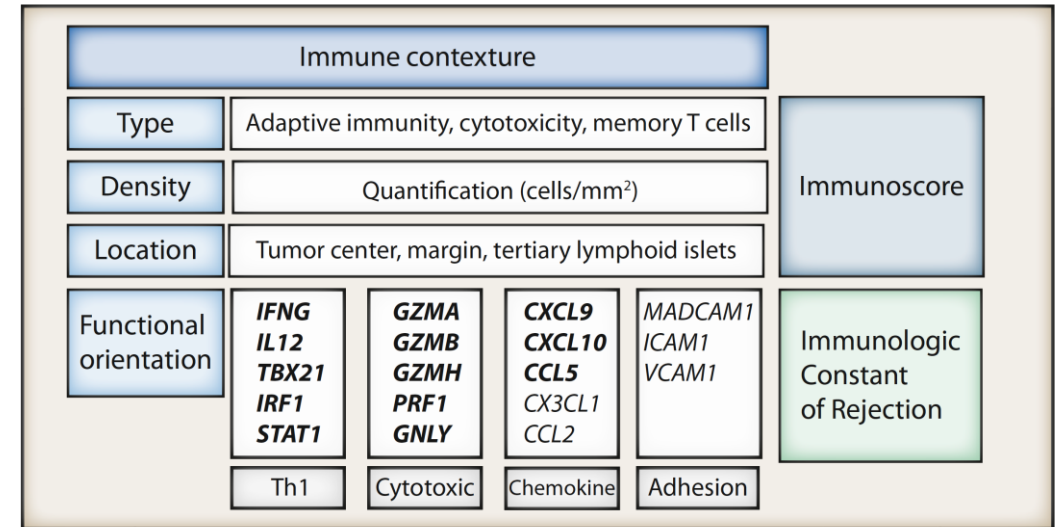
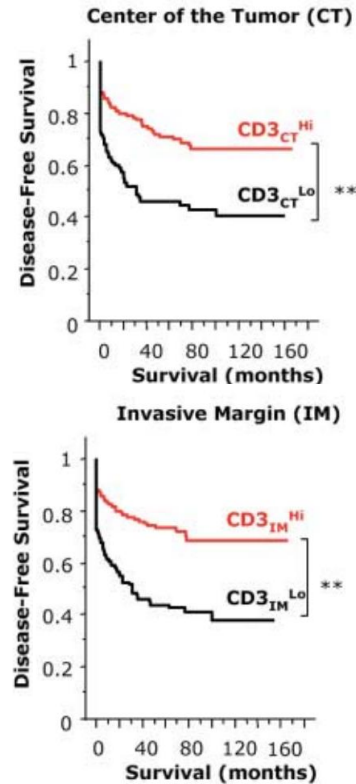
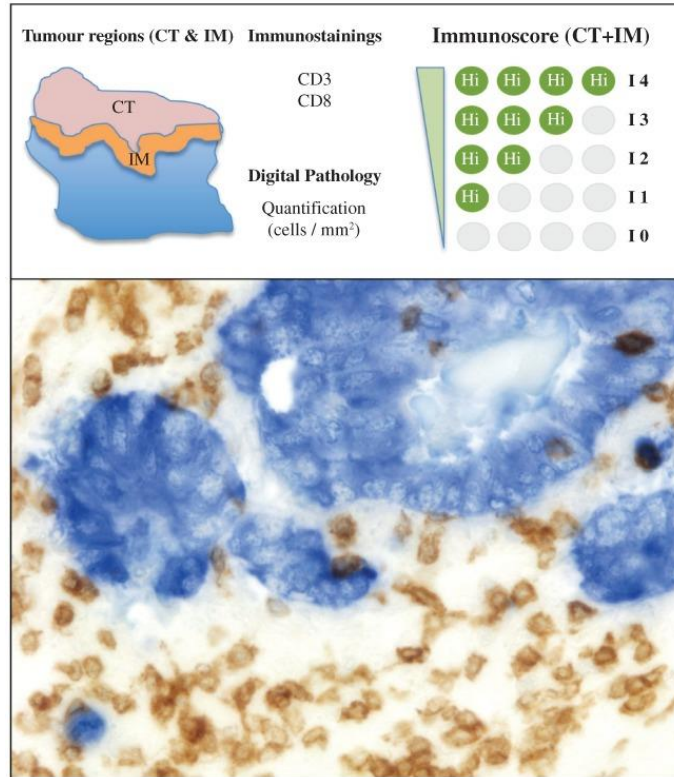
Disclosures

No disclosures.

Outline

- Background
- Colon cancer cohort for immunogenomic analyses
- T-cell receptor (TCR) clonality
- TCR sequences enriched in the tumor
- Lessons/ take home messages

Introduction



Galon, Angel, Bedognetti, Marincola, *Immunity*, 2016

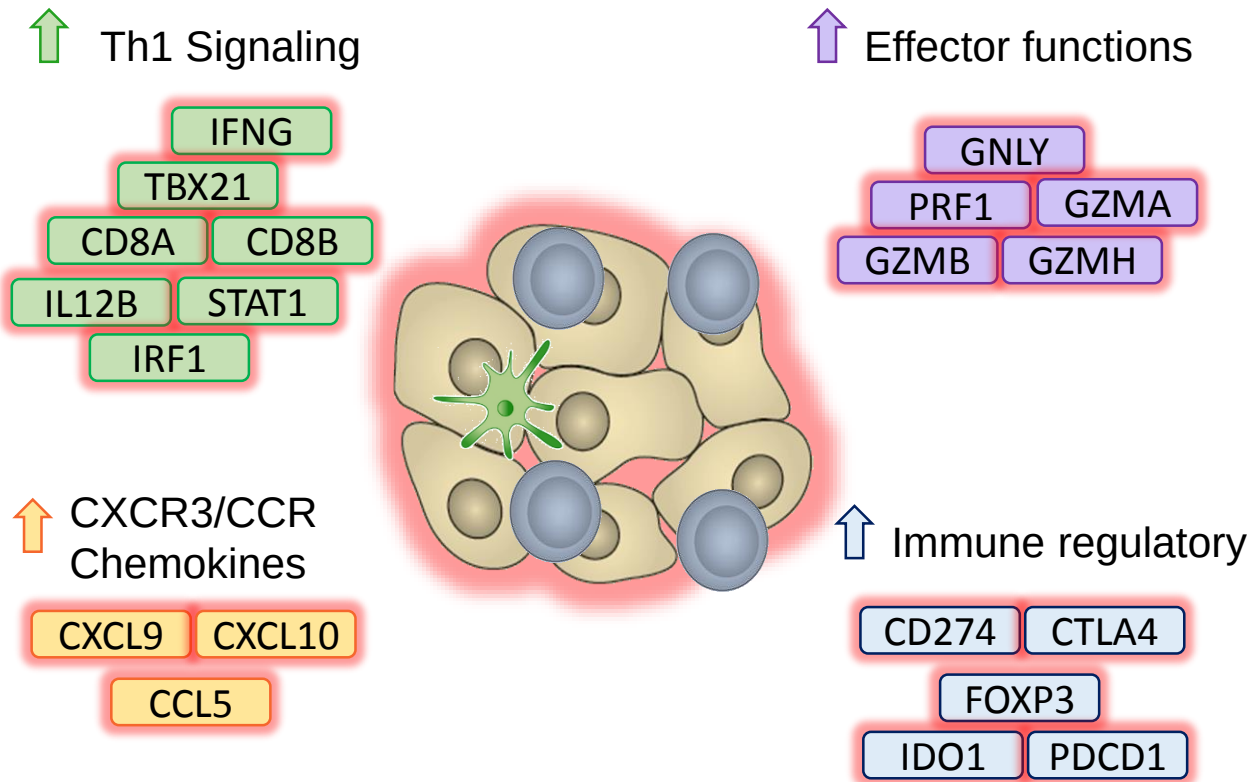
J  rome Galon, *Science* 2006; J  rome Galon, *J Pathology*, 2014.

Two opposite cancer immune phenotypes

Immune active (Th-1 inflamed)

Hot

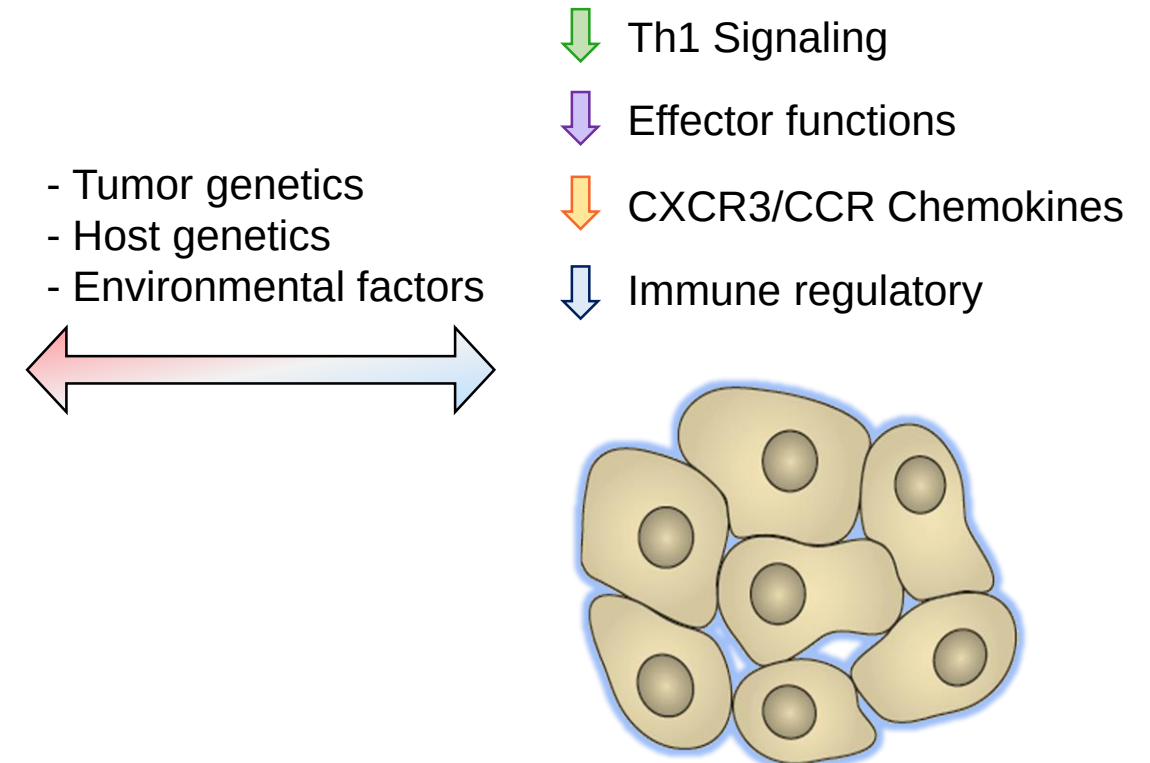
Immunologic Constant of Rejection (ICR) High



Immune inactive

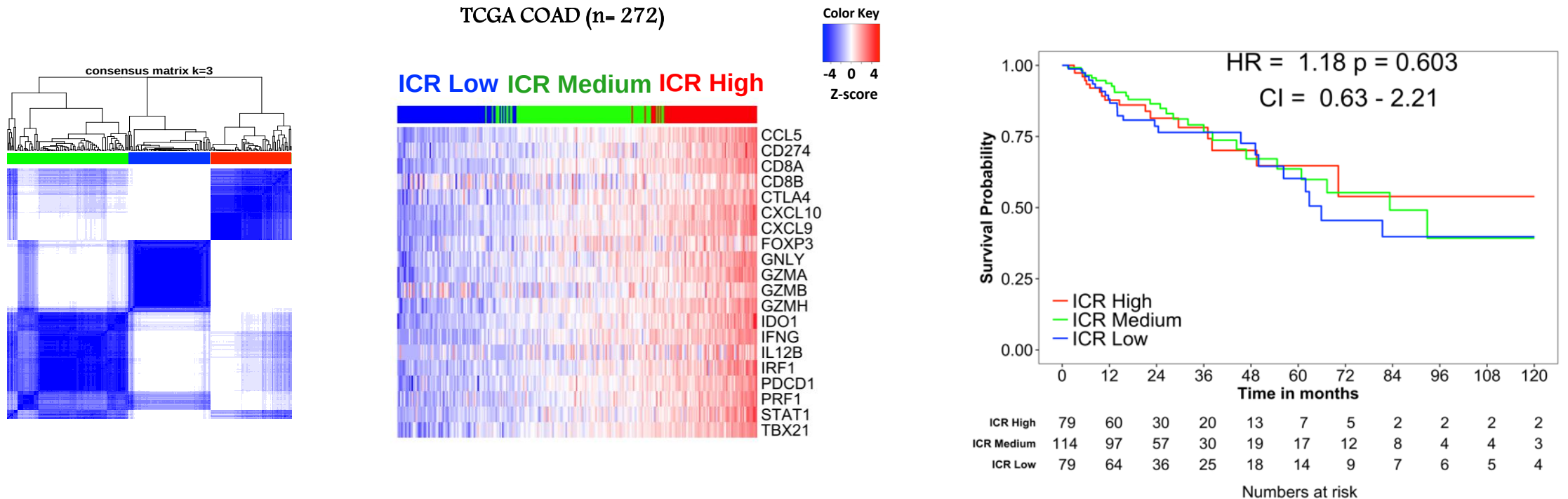
Cold

ICR Low

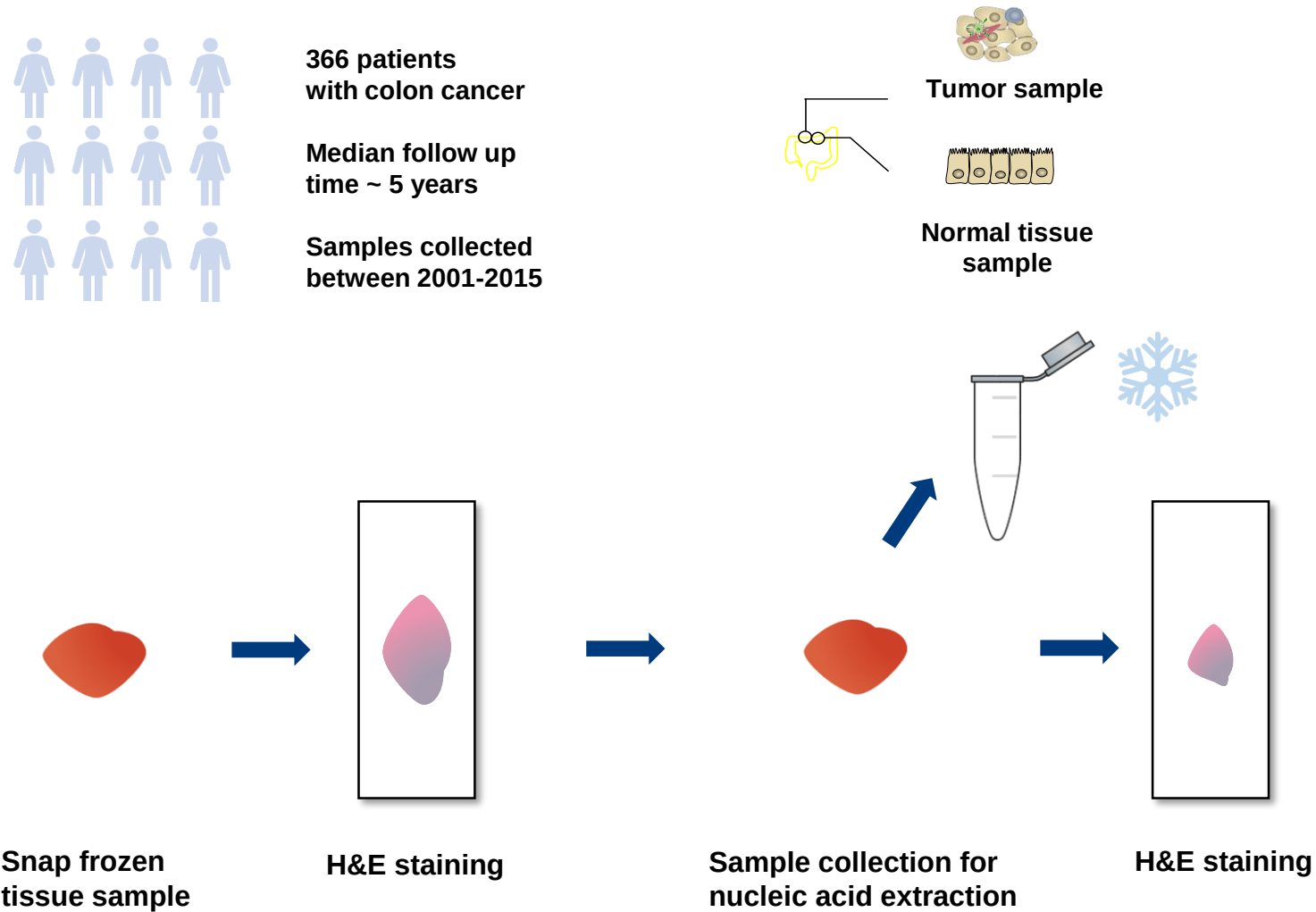


Bedognetti et al, *Curr Op Imm*, 2016; Roelands et al, *JITC*, 2019

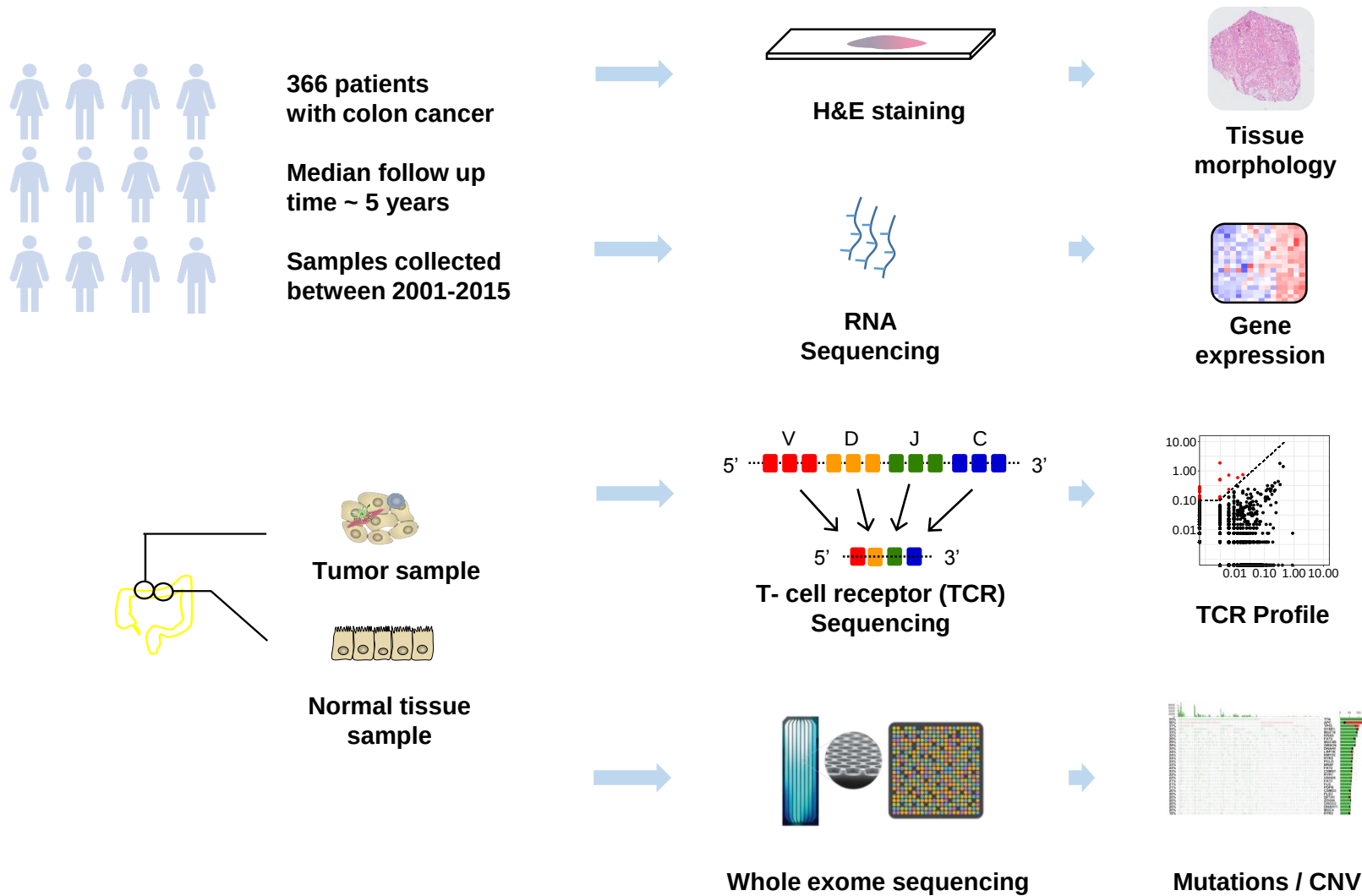
Absence of prognostic value of immune phenotypes in The Cancer Genome Atlas (TCGA) COAD cohort



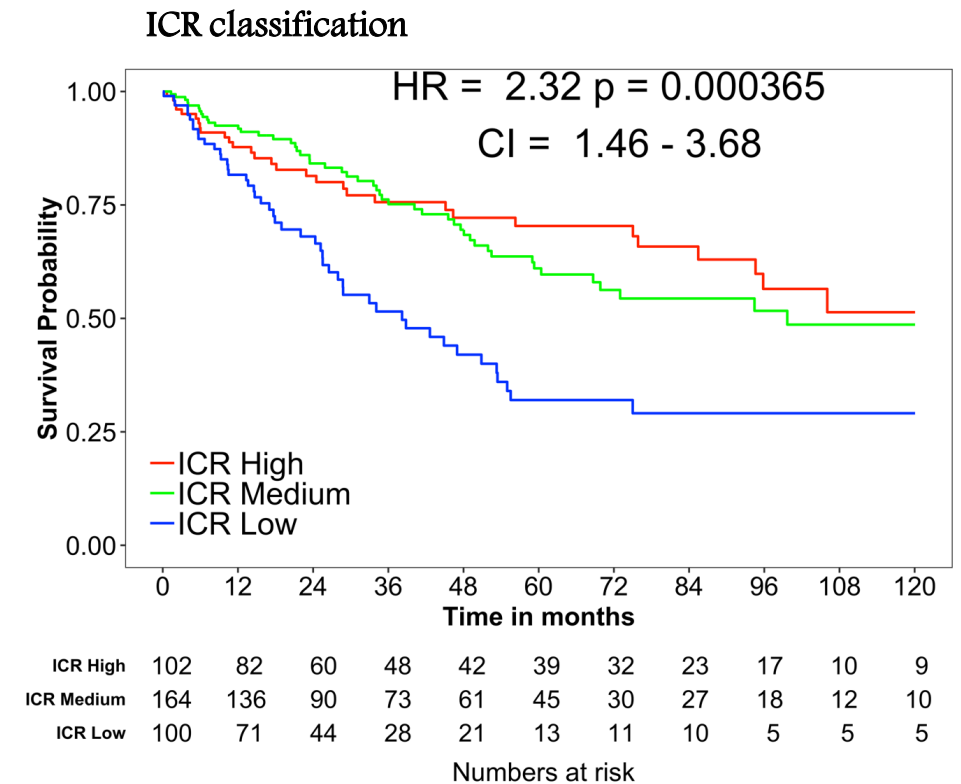
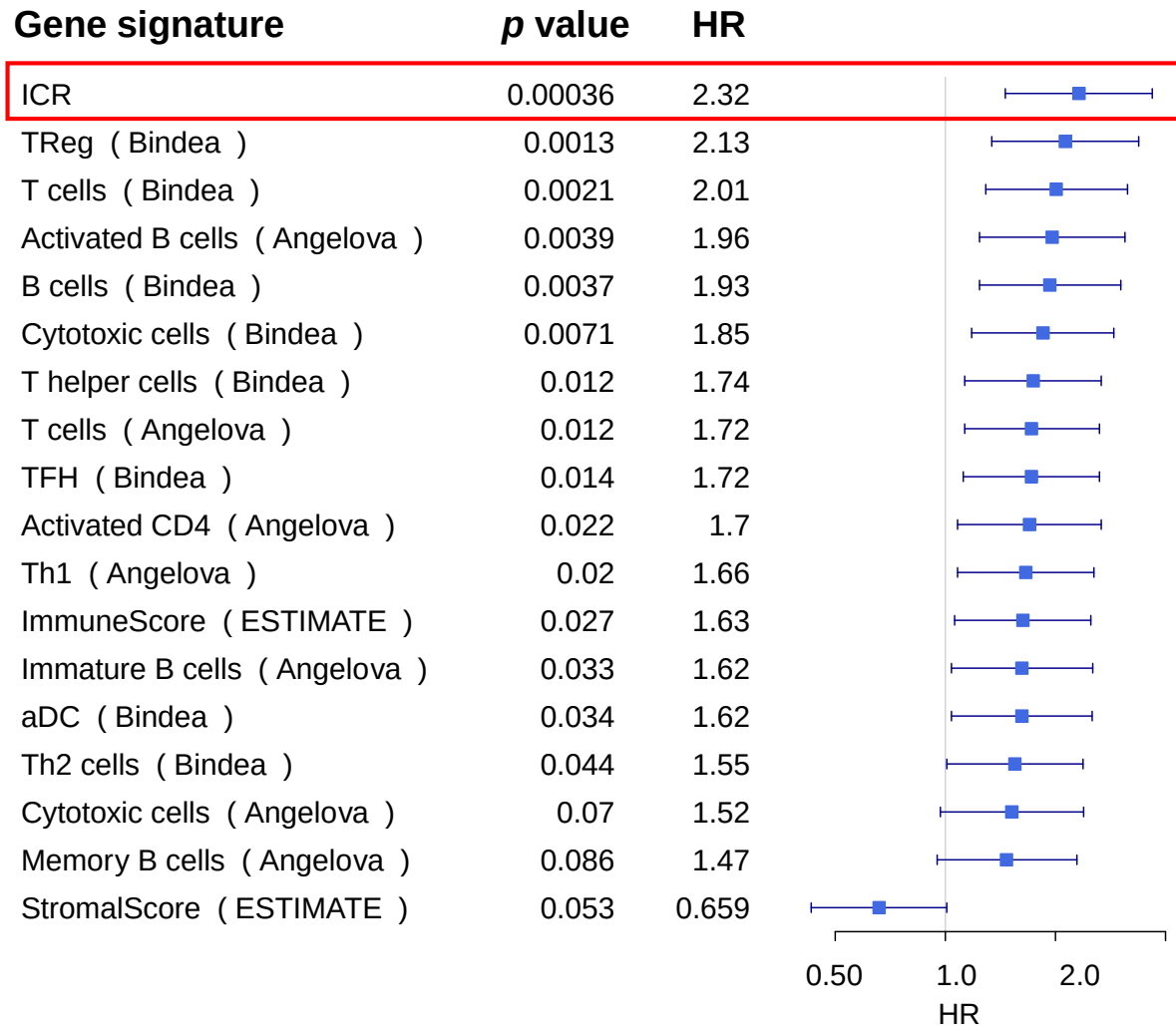
Sidra-LUMC colon cancer cohort



Sidra-LUMC colon cancer cohort



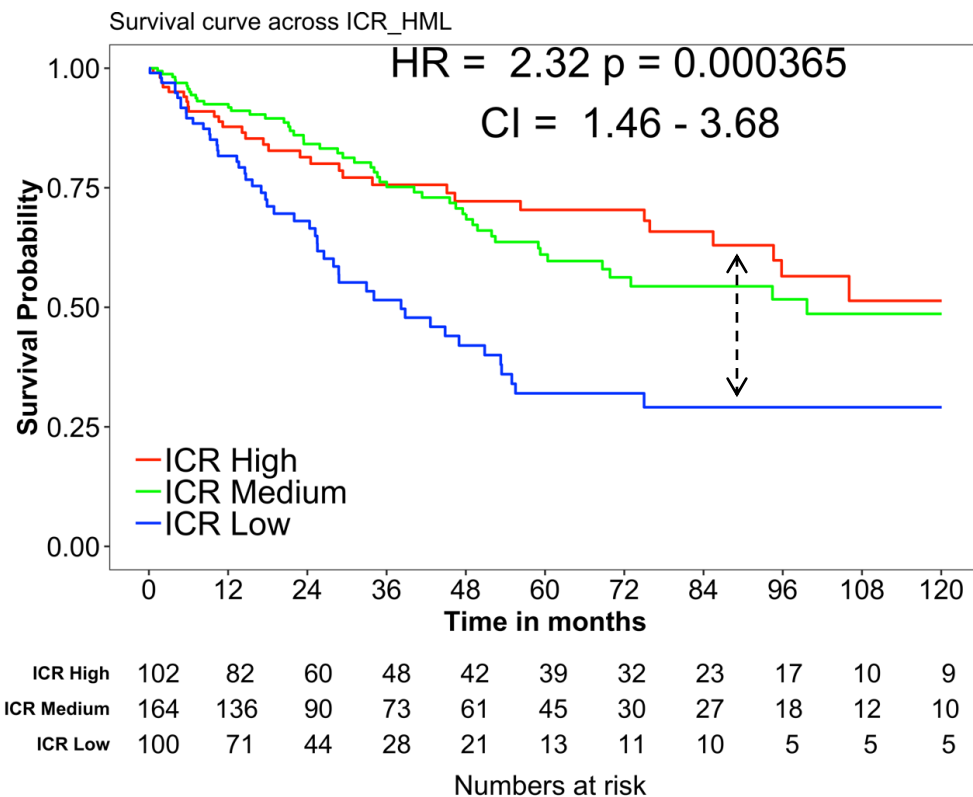
Prognostic signatures Sidra-LUMC cohort



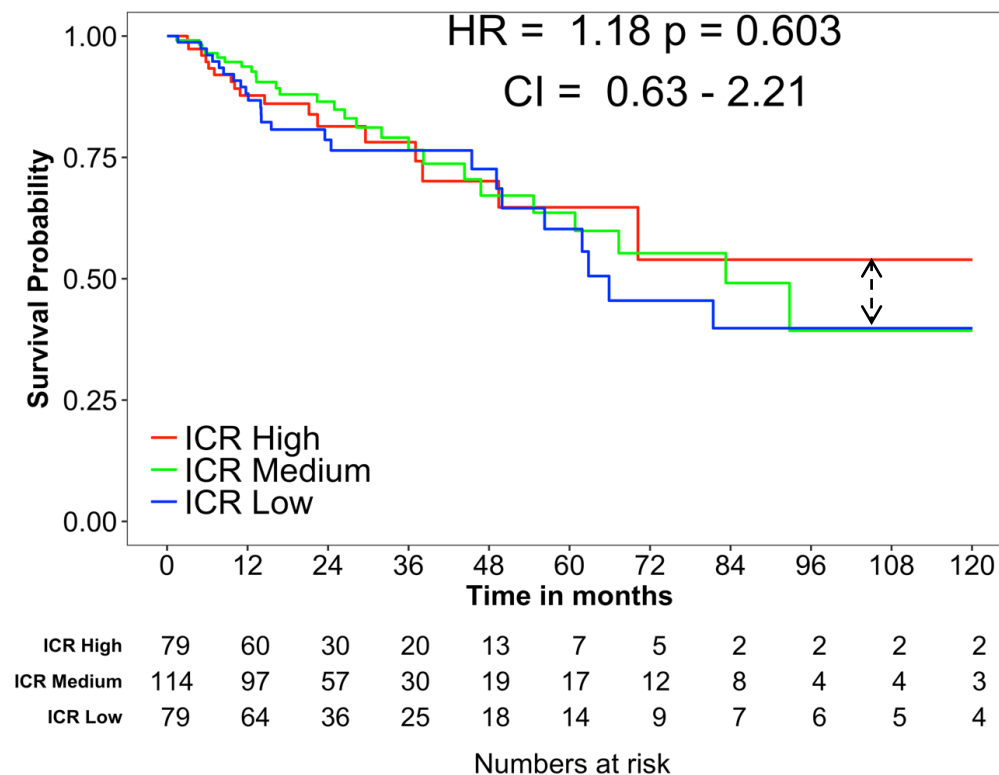
Bindea *et al*, *Cell*, 2013. Angelova *et al*, *Genome Biology*, 2015.
Yoshihara *et al*, *Nature Comm*, 2013

ICR in colon cancer

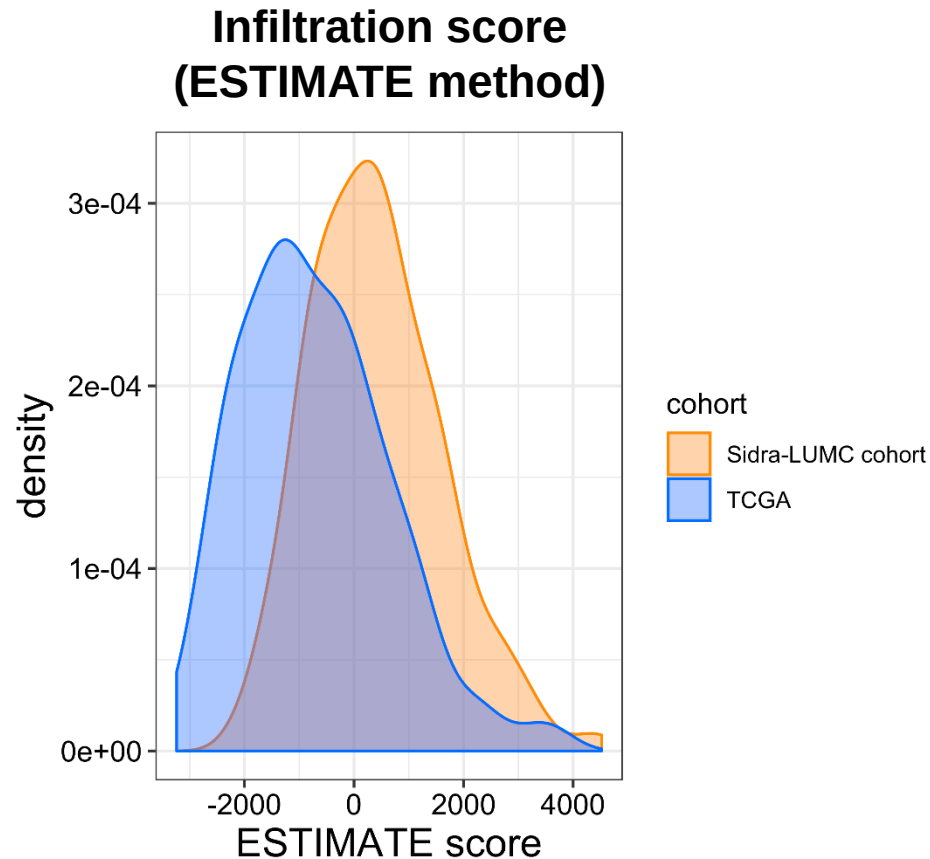
Sidra-LUMC cohort (n= 366)



TCGA COAD cohort (n= 272)



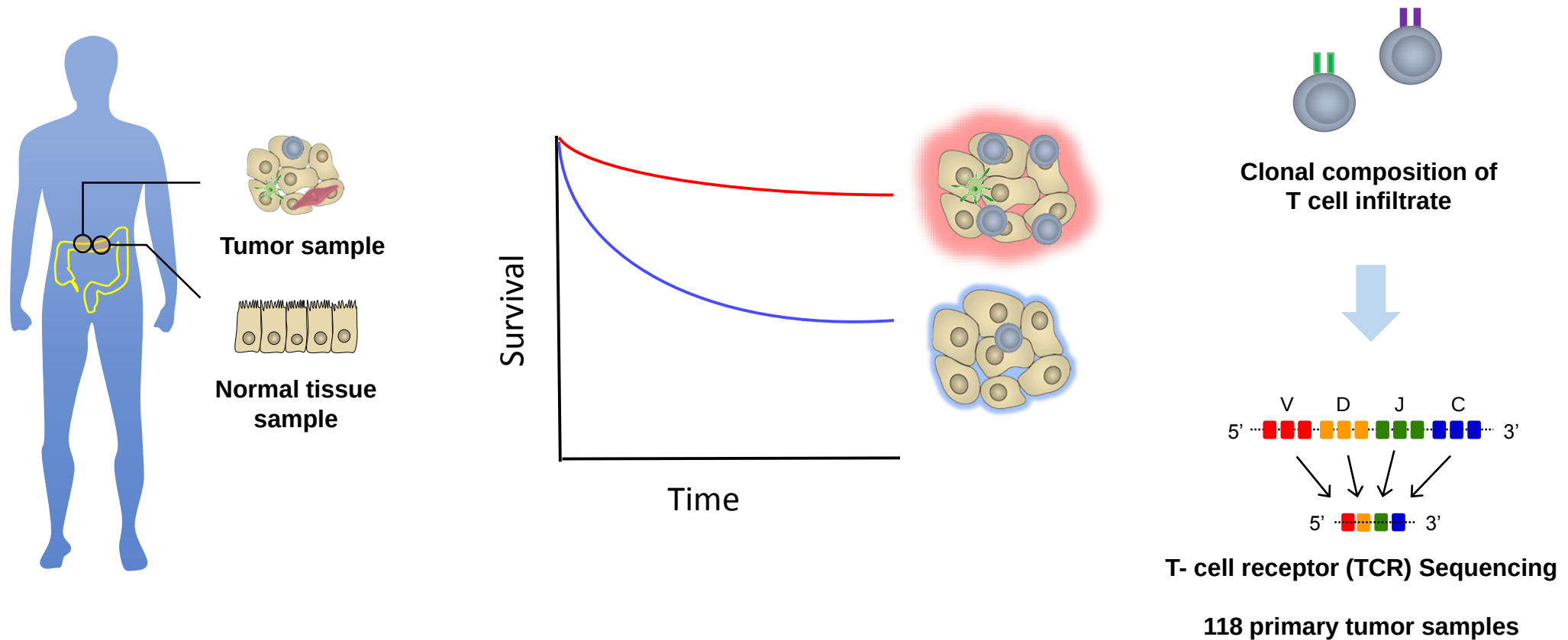
Infiltration to the tumor in colon cancer cohorts



- ESTIMATE (Estimation of STromal and Immune cells in MAlignant Tumor tissues using Expression data)
- Infiltration is higher in Sidra-LUMC cohort
- Sidra-LUMC cohort more suitable for immunogenomic studies

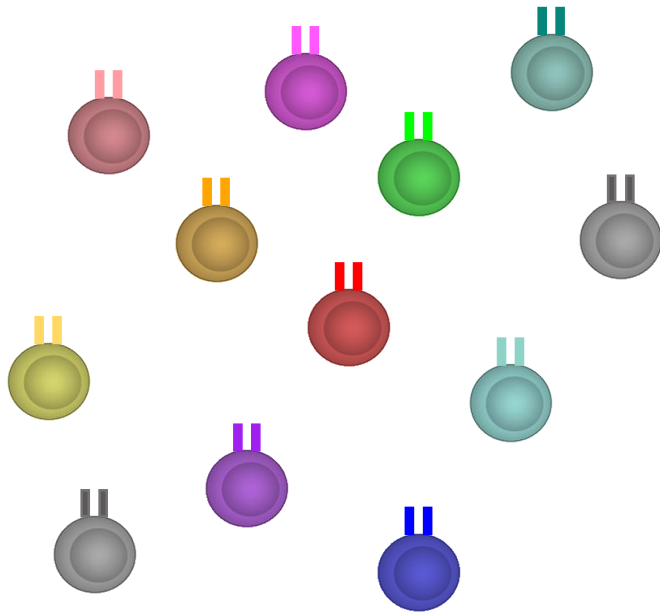
ESTIMATE algorithm: Yoshihara *et al*, *Nature Comm*, 2013

T cell clonal composition

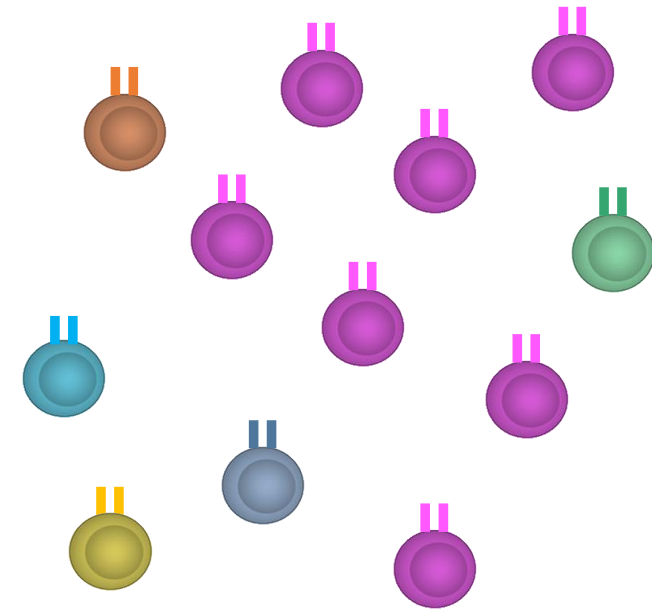


T-cell receptor (TCR) clonality

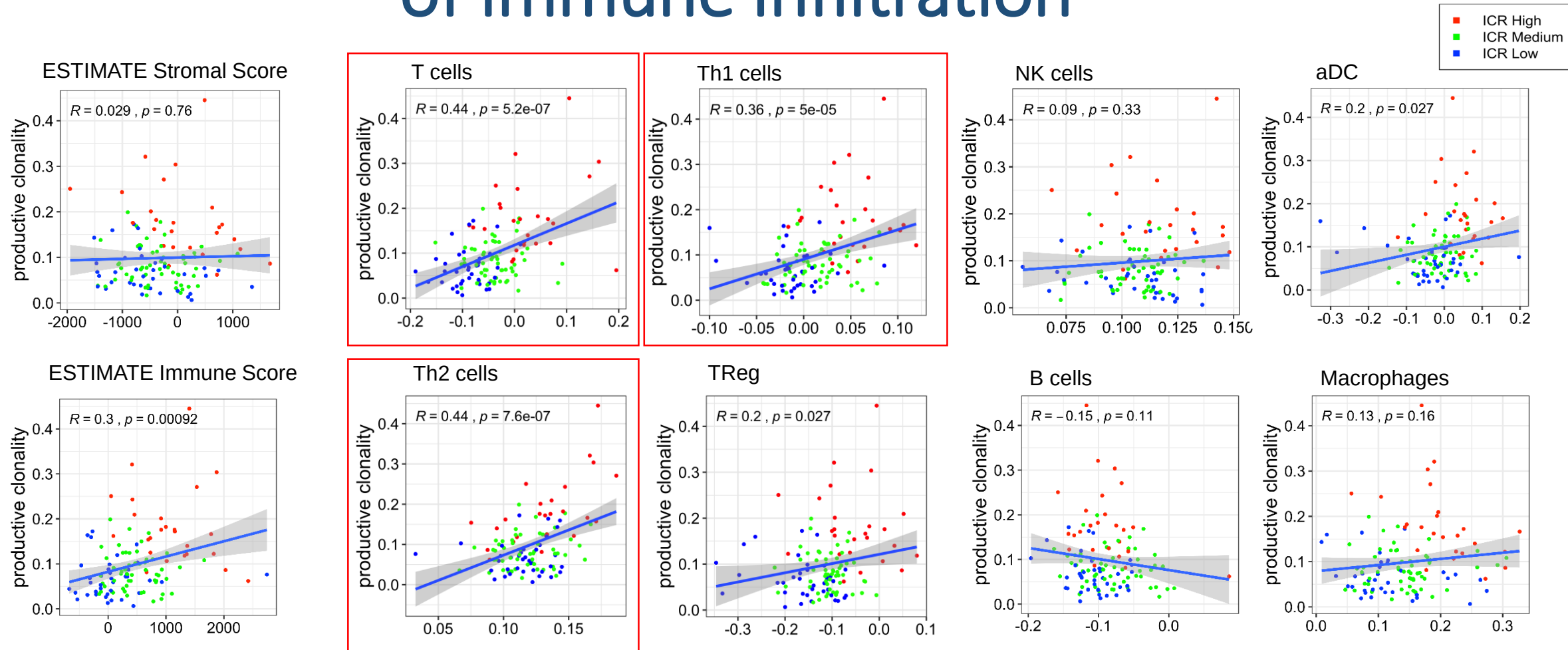
Low clonality



High clonality



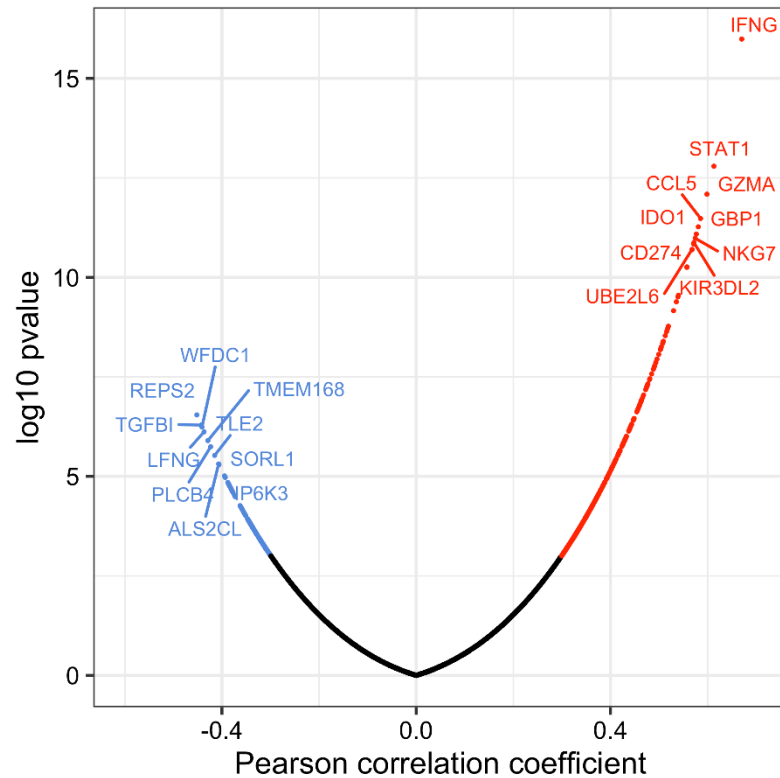
TCR clonality correlates with transcriptomic measures of immune infiltration



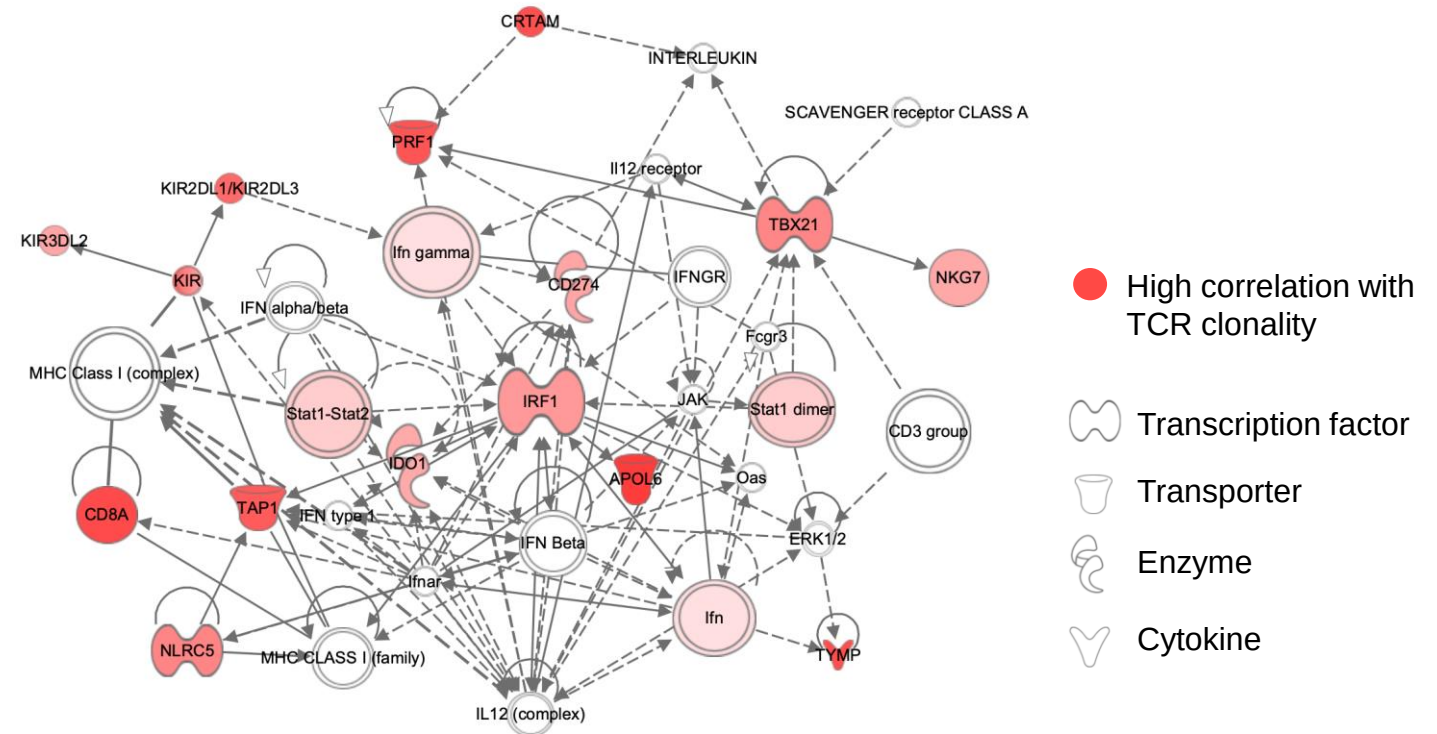
ESTIMATE algorithm: Yoshihara *et al*, *Nature Comm*, 2013

Immune cell population signatures from: Bindea *et al*, *Cell*, 2013

TCR clonality is associated with upregulation of immune transcripts



Pearson correlation between TCR clonality and expression of individual genes (n=18302 genes) in 118 primary colon cancer samples



IPA Core network analysis with top 50 genes correlated with TCR clonality

TCR clonality is associated with tumor immune phenotype

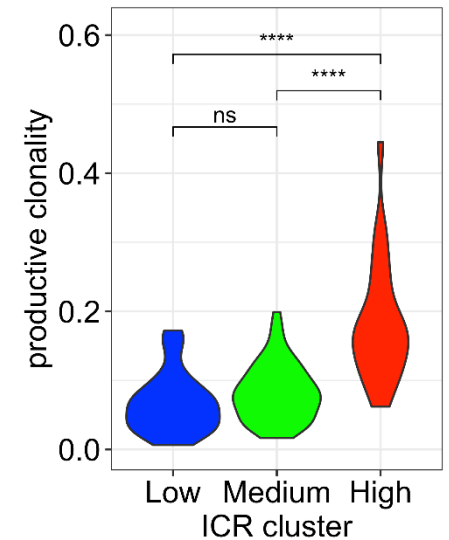
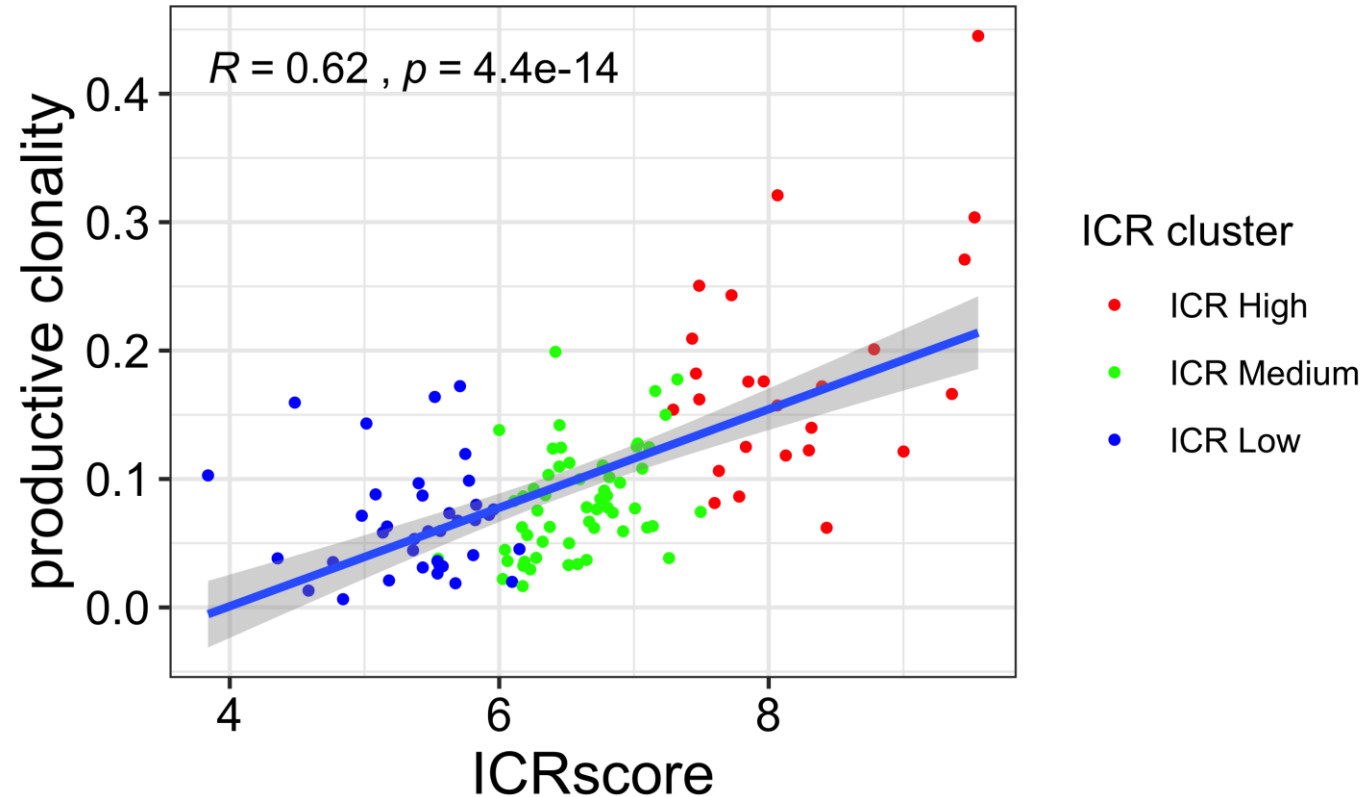
High clonality



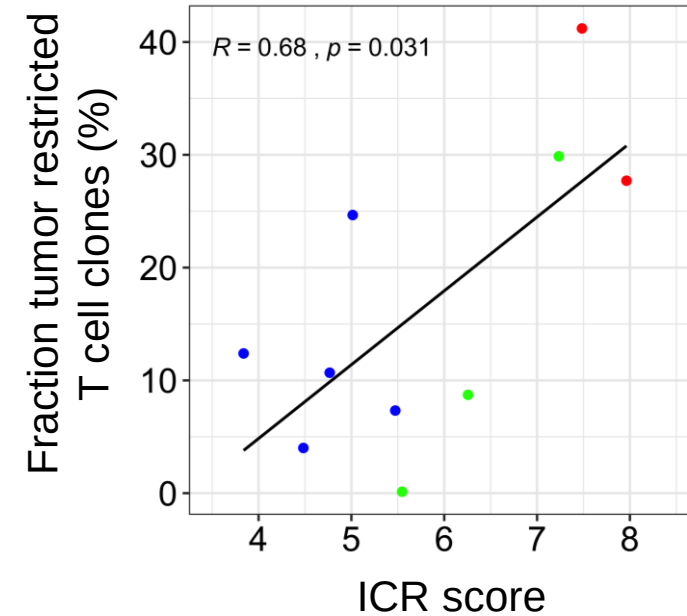
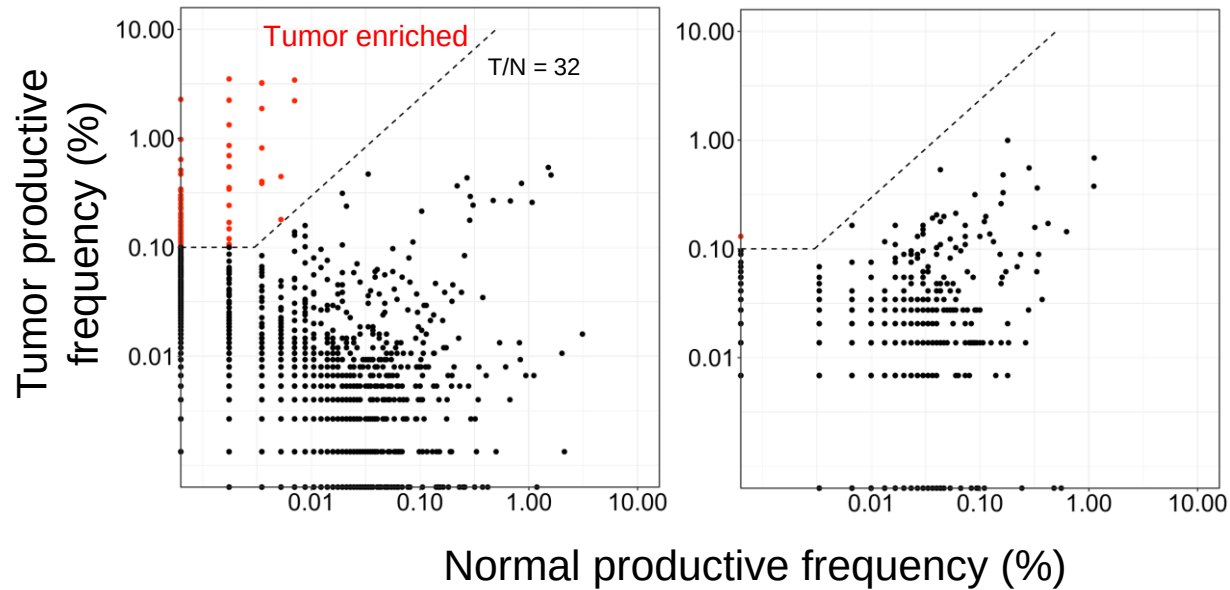
Low clonality



Clonality of TCR repertoire (n=118)



TCR sequences in 10 tumor *versus* 10 normal colon samples



Take home messages

- Colon tumors with an active Th1-oriented immune contexture are characterized by increased T cell clonality, suggesting clonal expansion of antigen-specific T cell subsets.
- Comparison of T cell receptor (TCR) sequences in tumor versus normal colon tissues reveals that the fraction of tumor-enriched sequences is higher in immune active tumors

Poster P93 The advanced immune-centric NGS cohort for colon cancer.

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