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2017
November 8-12
NATIONAL HARBOR
MARYLAND
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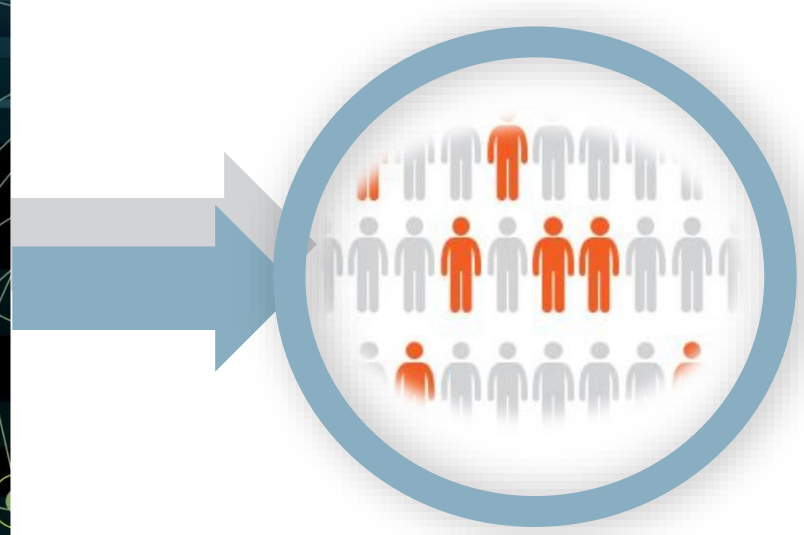
Society for Immunotherapy of Cancer

November 8-12 • NATIONAL HARBOR, MD

SITC 2017

A biomarker-driven approach for the development of the ICOS agonist antibody, JTX-2011



Heather A. Hirsch

On behalf of Jounce Therapeutics JTX-2011 team

Immuno-Oncology Biomarkers: Today's Imperatives for Tomorrow's Needs

November 8, 2017

National Harbor, MD

sitc

Society for Immunotherapy of Cancer

#SITC2017

Presenter Disclosure Information

Heather A. Hirsch

The following relationships exist related to this presentation:

Jounce Therapeutics, Inc. - Salary, Stock - Employee

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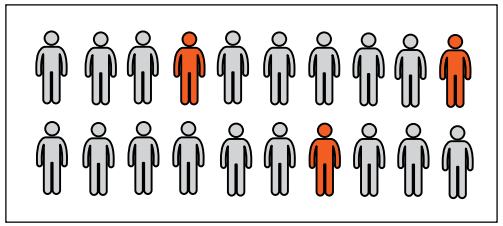
Rationale for Biomarkers and Complementary and/or Companion Diagnostics in Immunotherapy

(+) for predictive response biomarkers

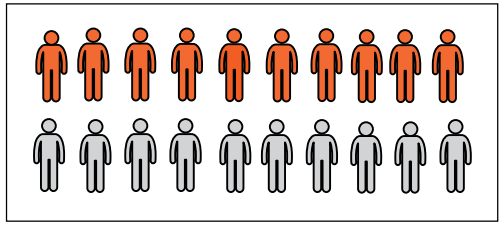
(-) for predictive response biomarkers

All-comers



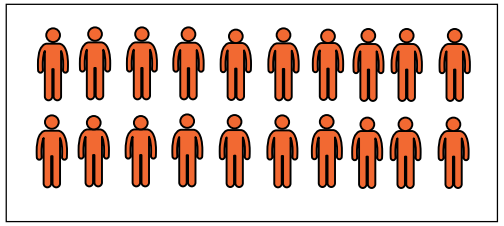
- No use of biomarkers for patient enrichment
- Minority of patients respond

Enrichment



- Use of biomarkers that may predict response
- Ensures sufficient number of biomarker (+) patients

Selection



- Biomarker expression required for enrollment
- Maximizes for potential responders

For illustrative purposes only, actual numbers may vary
Biomarker positive does not guarantee response to drug

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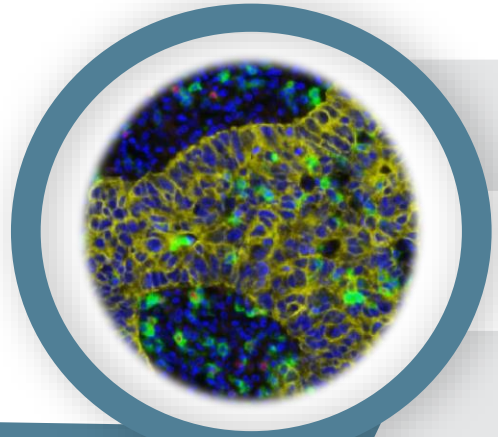
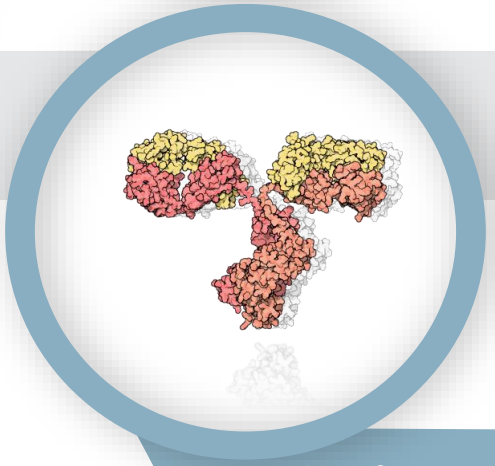
Translational Science Platform



Comprehensive interrogation of the TME

Patient enrichment strategies using predictive biomarkers



Identifying optimal immune cell targets and developing new immunotherapies

Sustainable immunotherapy pipeline

Transformative, long lasting treatments for patients

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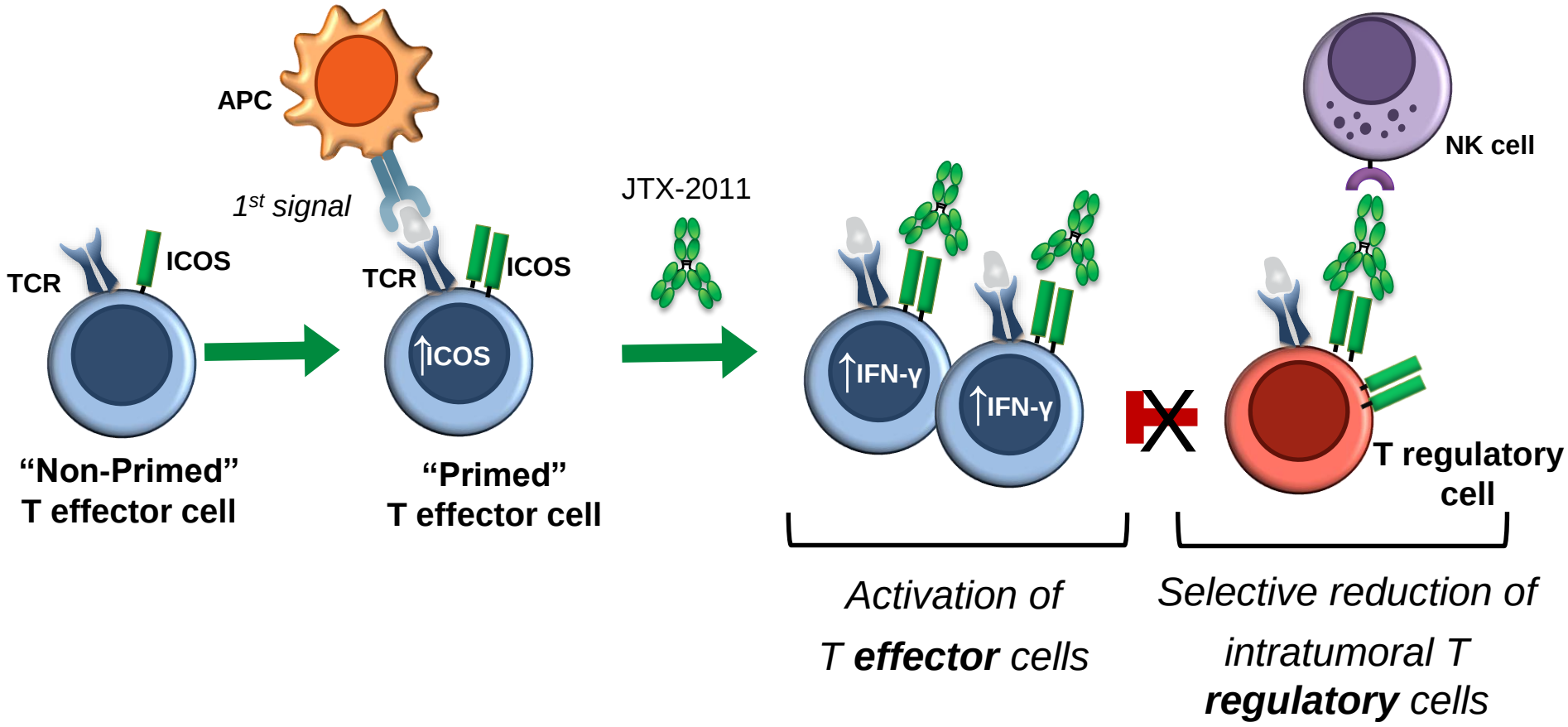
JTX-2011 Shifts Balance of T Cells Towards Anti-Tumor Activity



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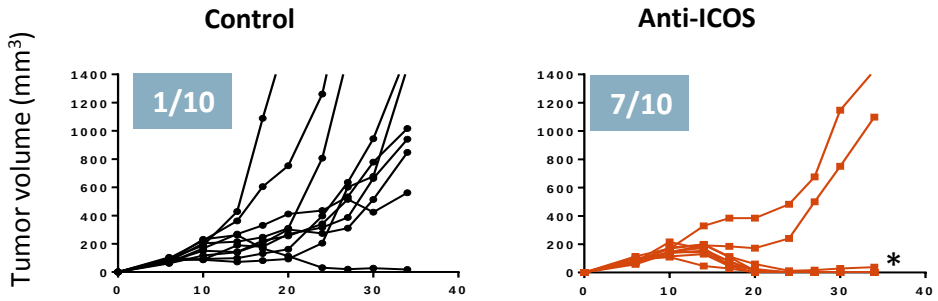
Critical Requirements for Preclinical Response to JTX-2011

1 Sustained target engagement in vivo: all available ICOS must be bound by JTX-2011

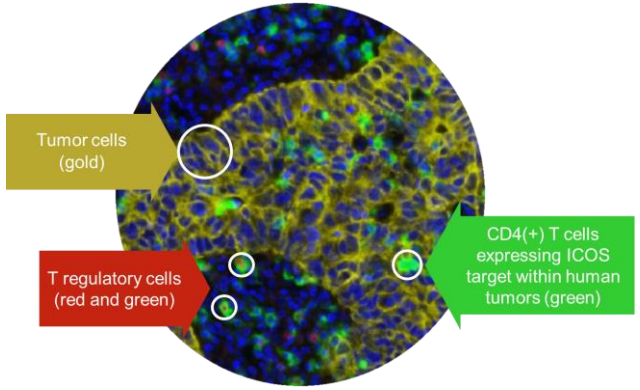


* Upon rechallenge "cured" mice reject tumors

Efficacy in mouse tumor models observed only at doses resulting in sustained target engagement

PK/PD model predicted human dose resulting in sustained target engagement

2 Efficacy in mouse tumor models requires ICOS(+) infiltrating immune cells within the tumor



ICOS biomarker scoring system developed to determine threshold to predict response

Biomarker translated to human tumors for patient enrichment in the clinic

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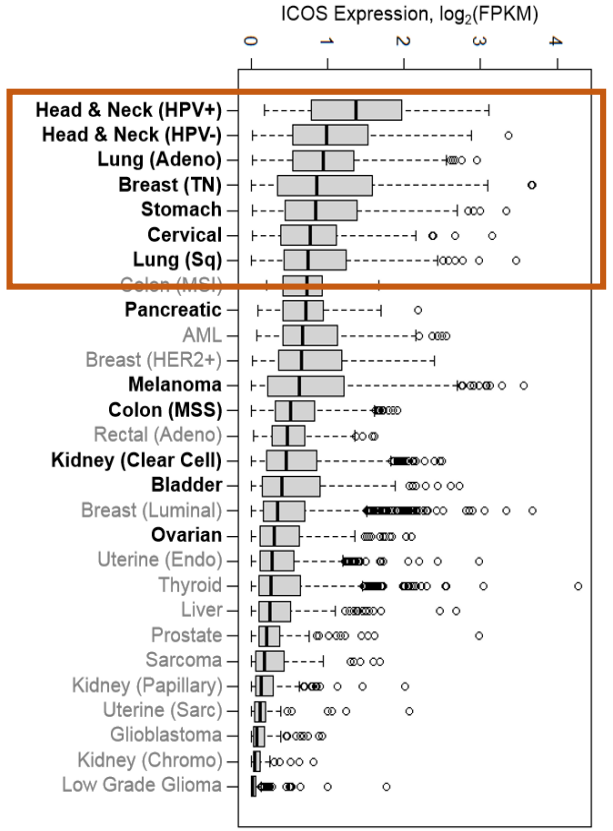
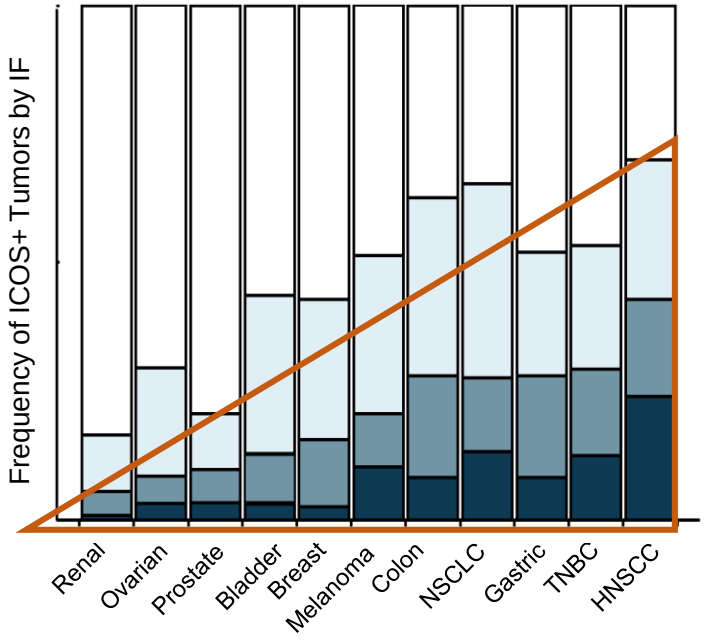
Phase 2 Indication Selection & Patient Enrichment via Biomarkers

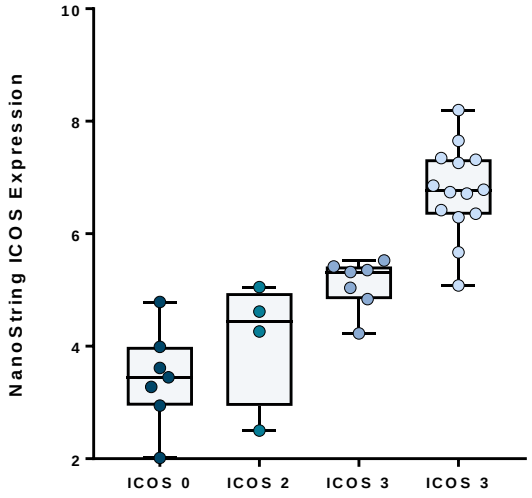
Rank order of tumor indications based on ICOS RNA expression in TCGA



ICOS protein levels vary across indications and within individual indications



ICOS RNA levels correlate well with ICOS protein levels via IHC



IHC and NanoString analysis of HNSCC histoculture samples

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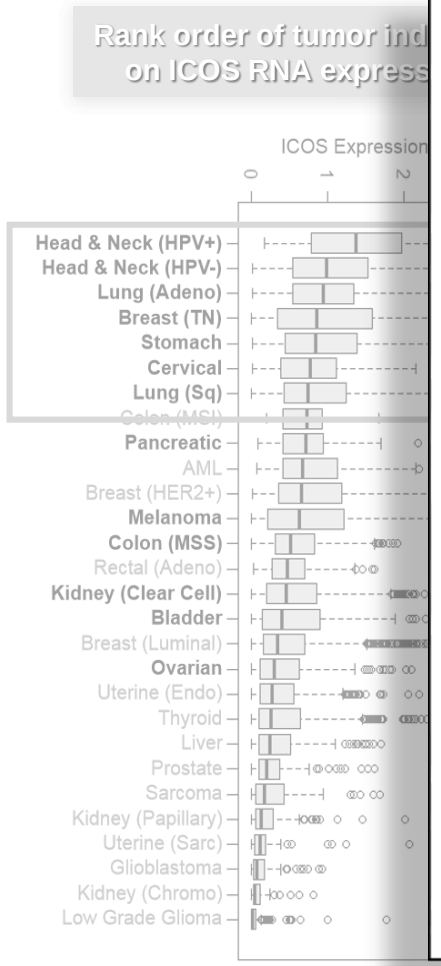
Phase 2 Indication Selection & Patient Enrichment via Biomarkers



1 Select indication priorities

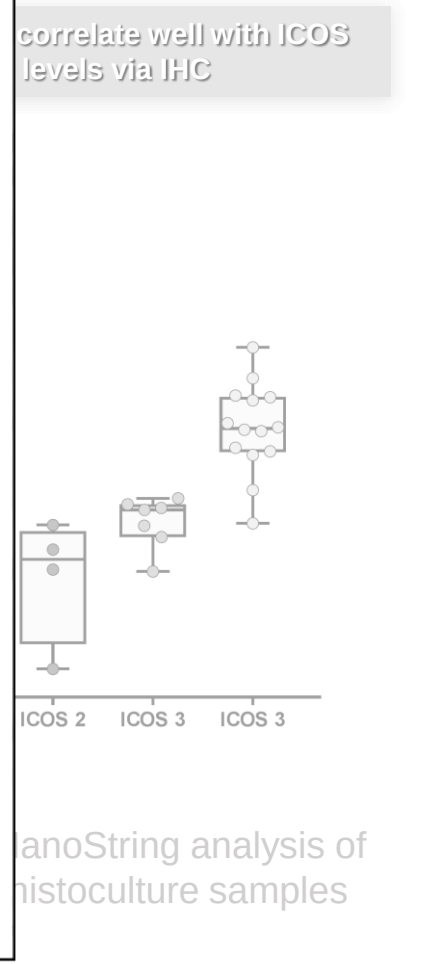
HNSCC, NSCLC, TNBC, melanoma, gastric, plus undisclosed "niche" indications

Includes IO naïve and IO failures

2 Prospective enrichment of biomarker high patients into study cohorts

10 patients in each cohort ICOS 2/3

ICOS 2/3 required for preclinical efficacy



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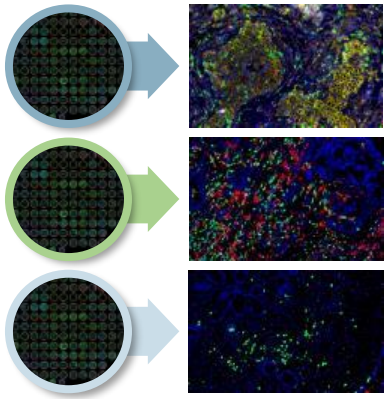
Integrated Approach to Understanding ICOS in the Context of Immune Oncology Landscape

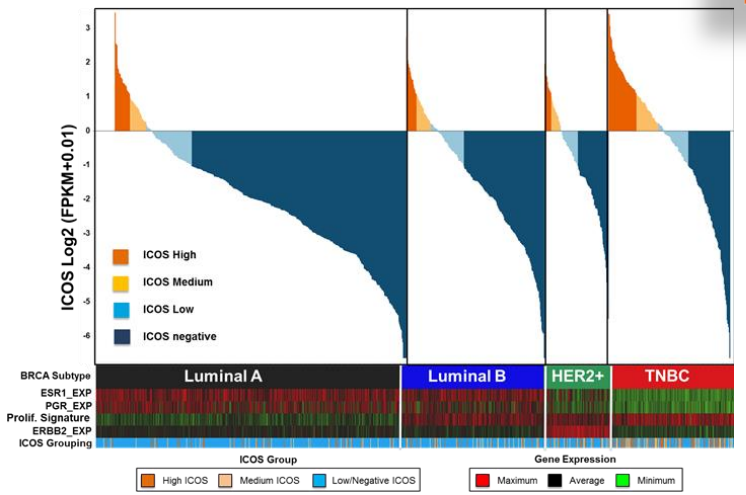
Collaborations with premier institutions

1000s of human tumors interrogated



Adaptive immune cells
Innate immune cells
Stromal cells

Integrated TCGA and internal data analysis



Enriching patients for our clinical trials

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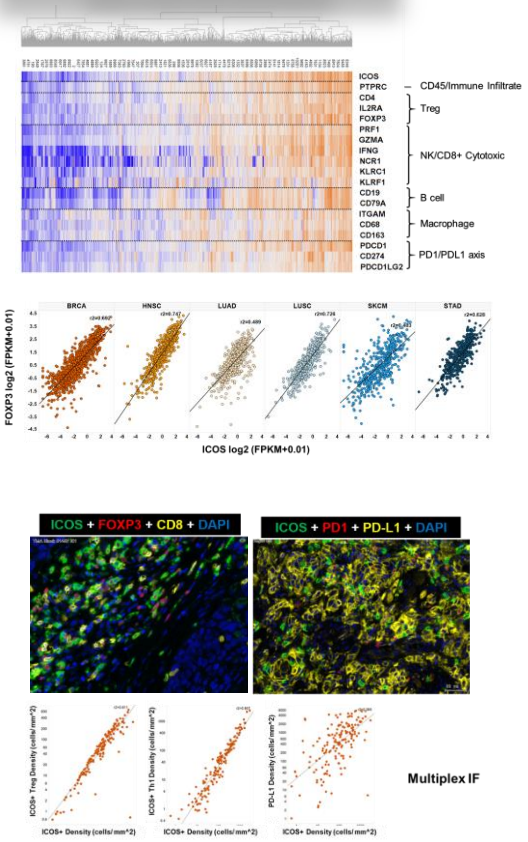
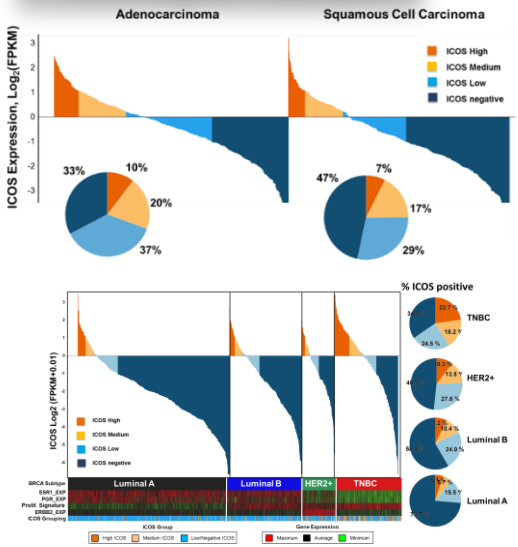
Integrated Approach to Understanding ICOS in the Context of Immune Oncology Landscape

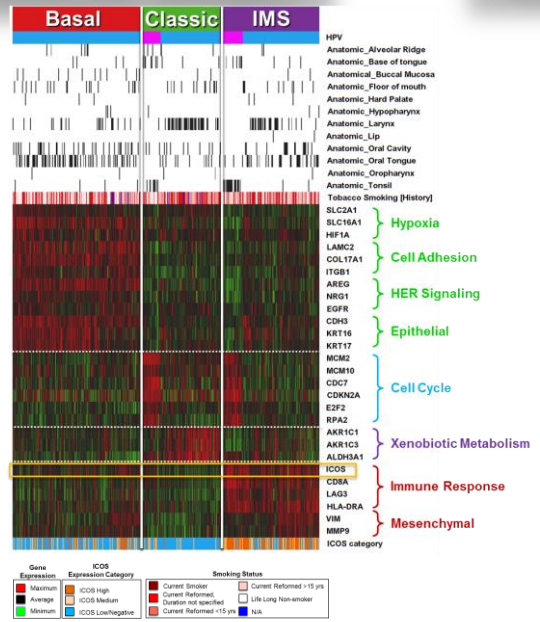
Characterization within microenvironment



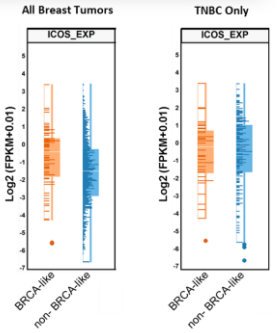
Histological Subtypes



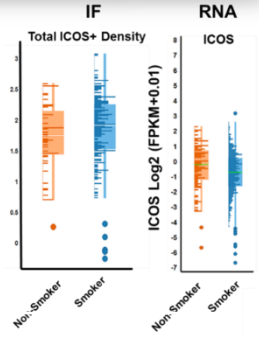
Molecular Subtypes



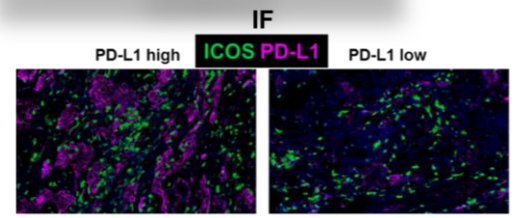
Known Mutations

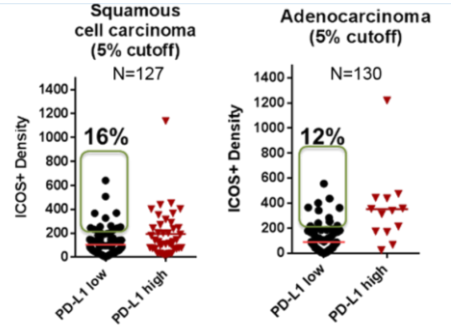


Smoking Status

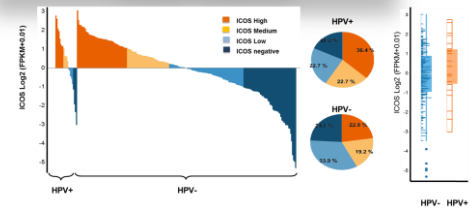


Context with Checkpoint inhibitors

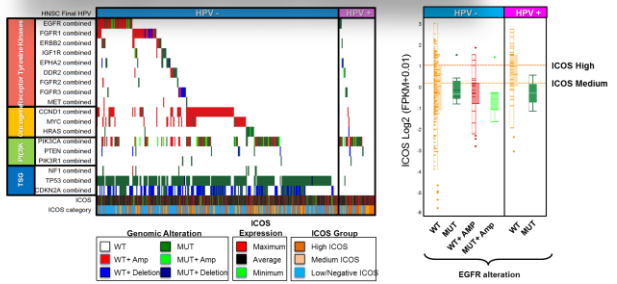




Viral Status



Oncogenes/Tumor Suppressors



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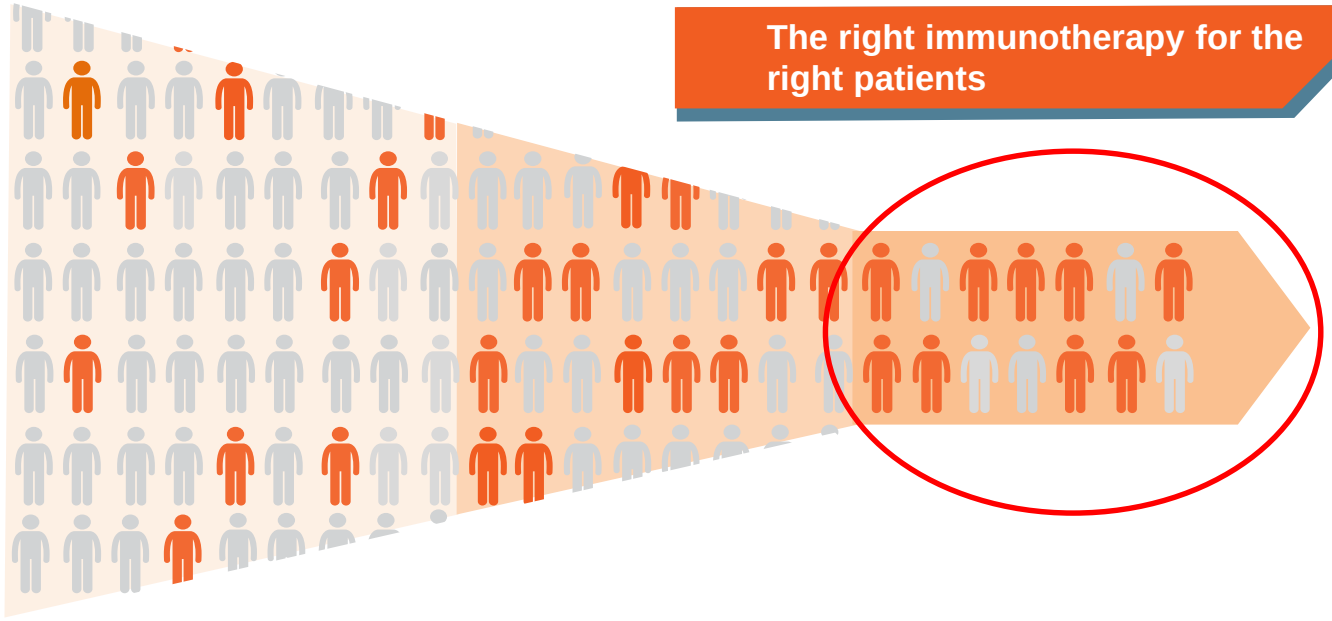
ICONIC: Adaptive, Biomarker-Driven Clinical Study

Phase 2 Patient Enrichment



The right immunotherapy for the right patients

Indication Selection

Patient Screening / Enrichment

Phase 2
Preliminary Efficacy

Preliminary Efficacy readout expected 1H 2018

Enriched for pts with high ICOS expression

C **Single agent**

- NSCLC
- HNSCC
- Any solid tumor type
- New indications based on emerging science

D **Combo with nivolumab**

- NSCLC
- HNSCC
- TNBC
- Melanoma
- Gastric
- New indications based on emerging science

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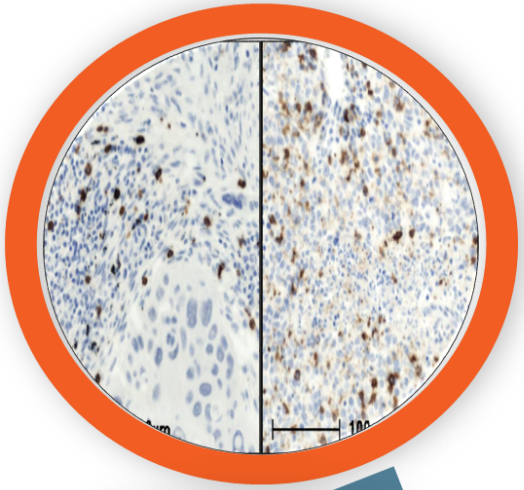
Developing predictive biomarker assays for the ICONIC trial

Potential predictive biomarkers to be correlated with efficacy:

1. ICOS by IHC
2. ICOS gene signature by qPCR
3. Exploration of alternative gene signatures (NanoString analysis)

ICOS IHC



ICOS gene signature qPCR

New gene signature (Nanostring)

Correlate with clinical activity

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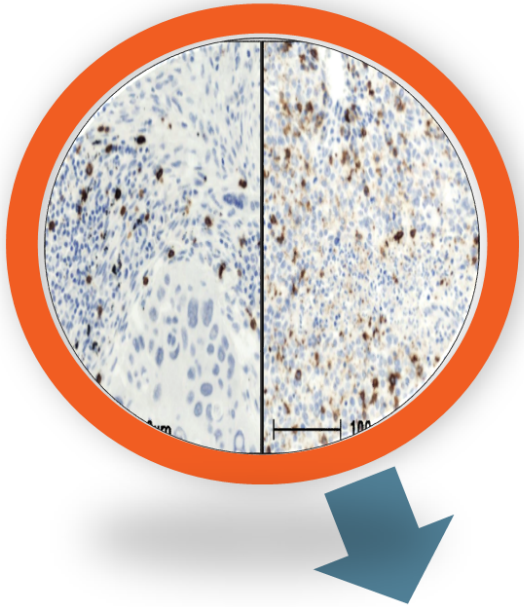
ICOS IHC



ICOS gene signature qPCR

New gene signature (Nanostring)

Correlate with clinical activity

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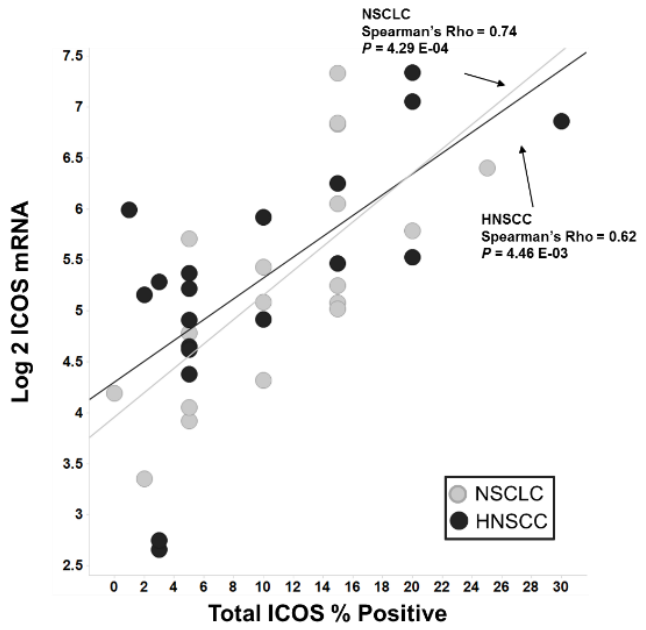
Development of an ICOS IHC assay for ICONIC enrollment

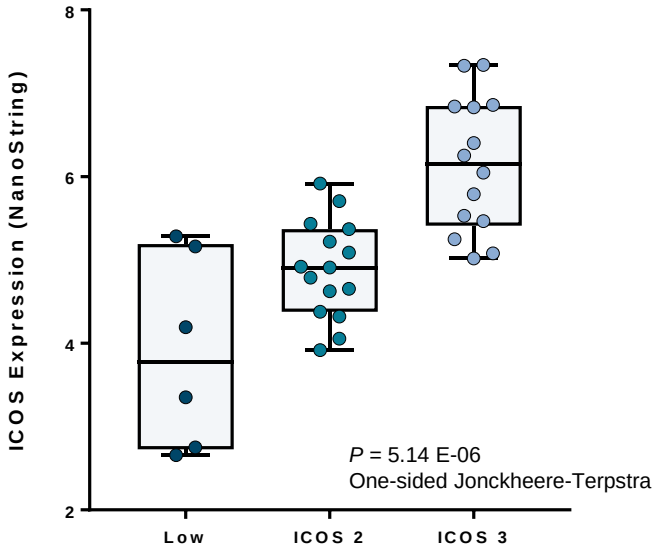
ICOS Scoring Criteria	
< 1%	0
≥ 1% but < 5%	1
≥ 5% but <15%	2
≥ 15%	3
*in carcinoma region only	

- Chromogenic IHC assay developed in house with proprietary anti-ICOS antibody
- Developed for the Leica Bond III platform
- Assay transferred to and validated at CLIA lab
- Currently in use for ICONIC clinical trial patient stratification

Percent positive ICOS correlates to ICOS RNA expression in HNSCC and NSCLC



Total ICOS IHC score correlates to ICOS RNA expression in HNSCC and NSCLC



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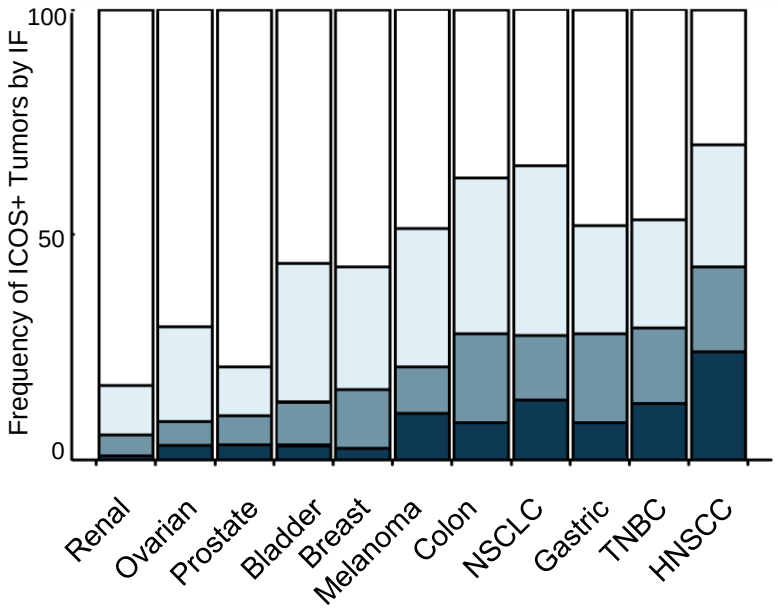
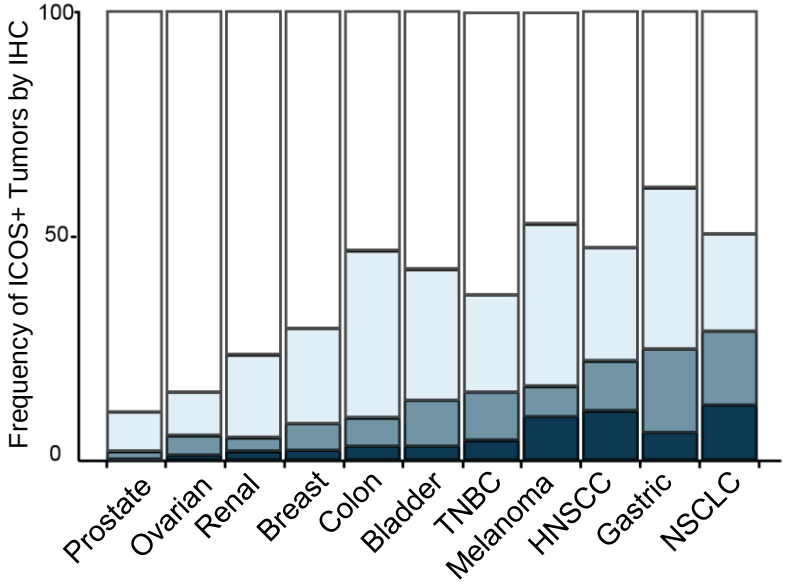
Frequency of ICOS positivity in tissue microarrays and ICONIC patient samples

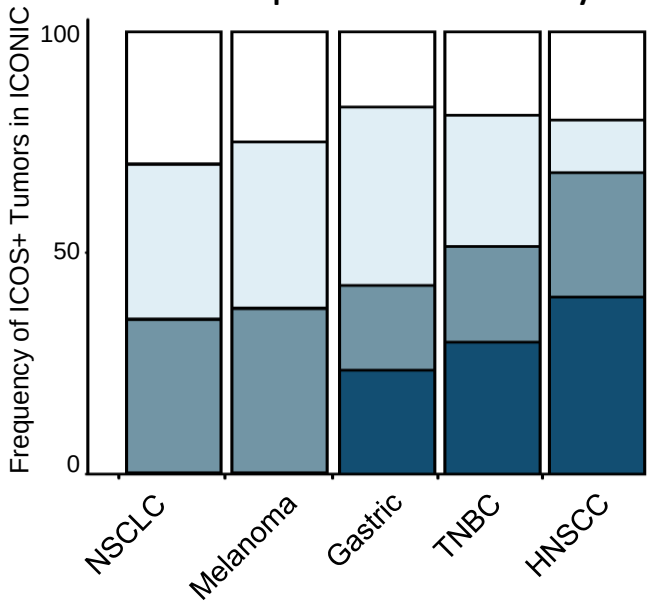
Immunofluorescence



Chromogenic IHC assay



Patient samples screened by IHC



Developing predictive biomarker assays for the ICONIC trial

Potential predictive biomarkers to be correlated with efficacy:

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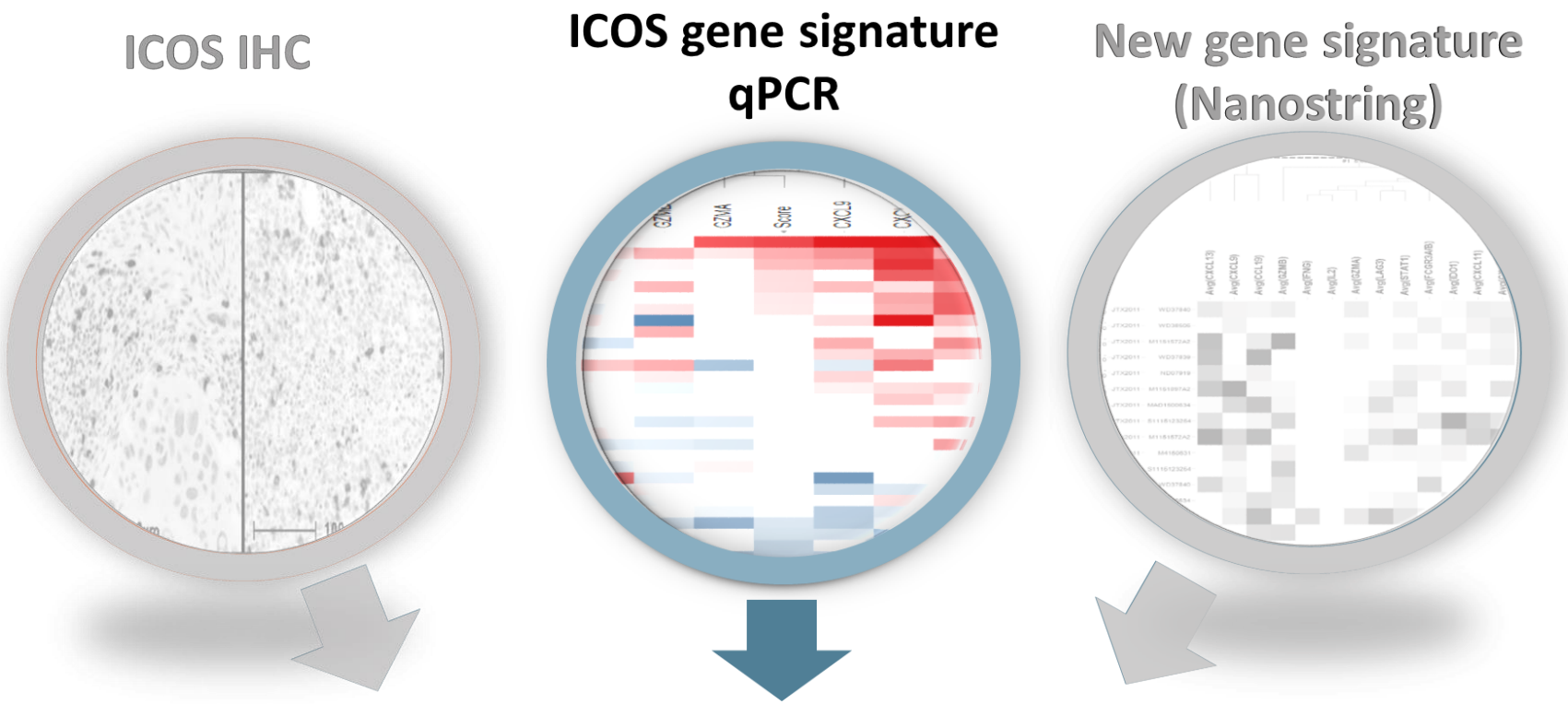
2. ICOS gene signature by qPCR
3. Exploration of alternative gene signatures (NanoString analysis)



Correlate with clinical activity

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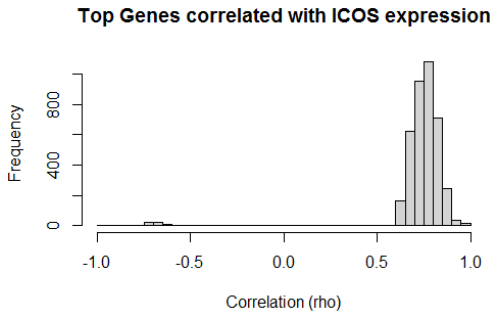
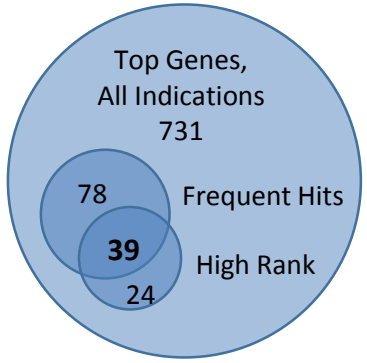
Developing an ICOS RNA gene signature

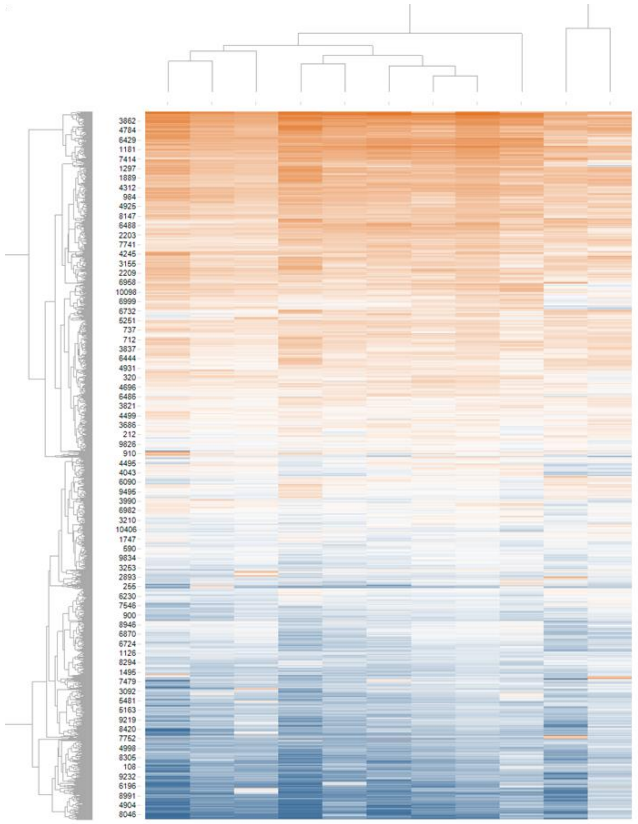
Criteria for gene selection:

- Frequently found
  - Must be in the top 300 genes in at least 10 indications
- Highly ranked on average
  - Within the top 75 genes identified on average across indications

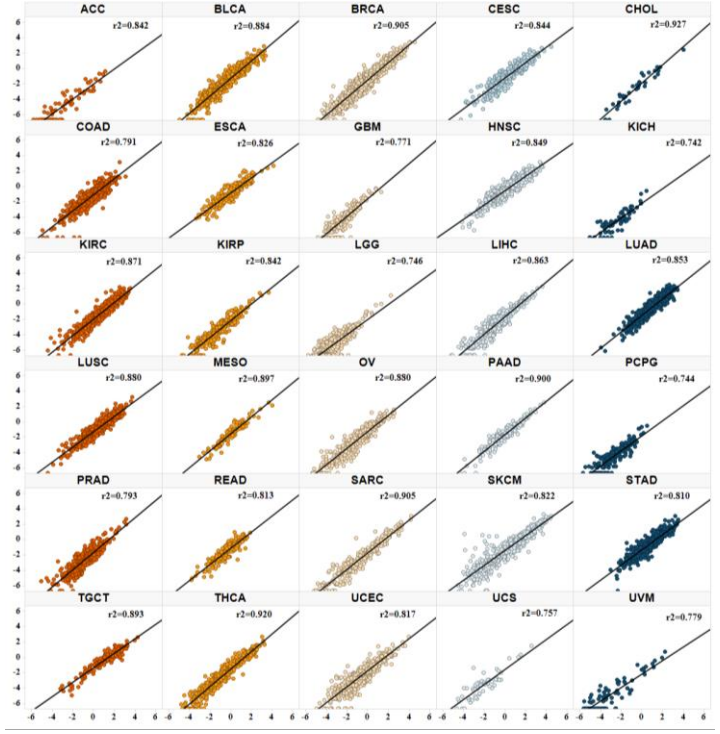




The 11 gene ICOS signature is coherent across all solid tumors in TCGA



ICOS signature is highly correlated to ICOS gene expression across tumors types



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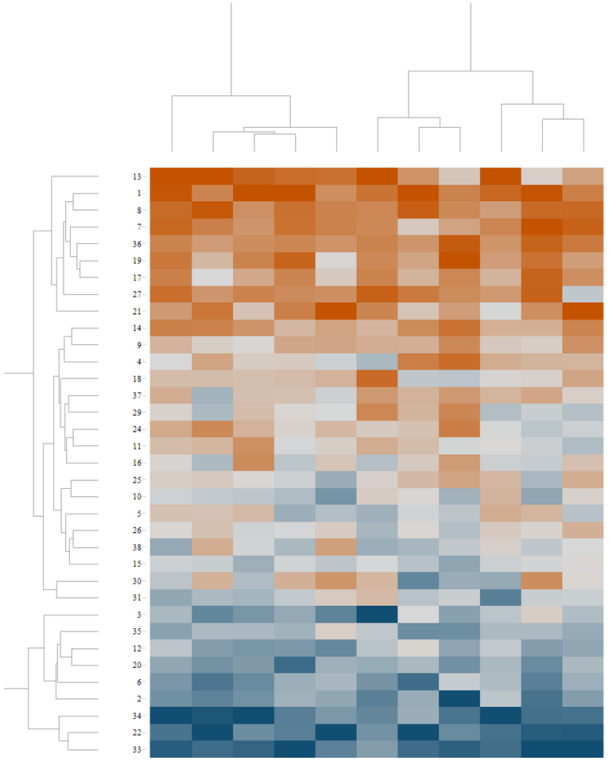
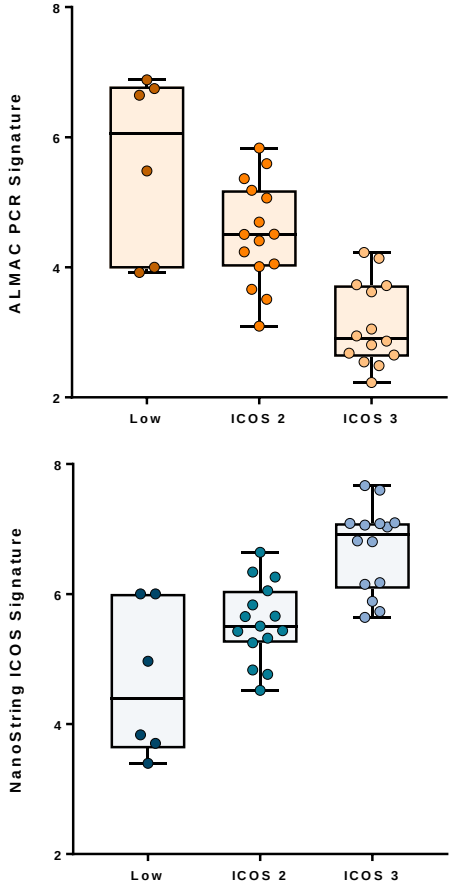
Developing an ICOS RNA gene Signature

- Transferred 11 gene signature to CLIA lab
- Developed with 4 house keeping controls in FFPE tumor material in multiple indications
- Is currently in use for retrospective testing in the ICONIC trial

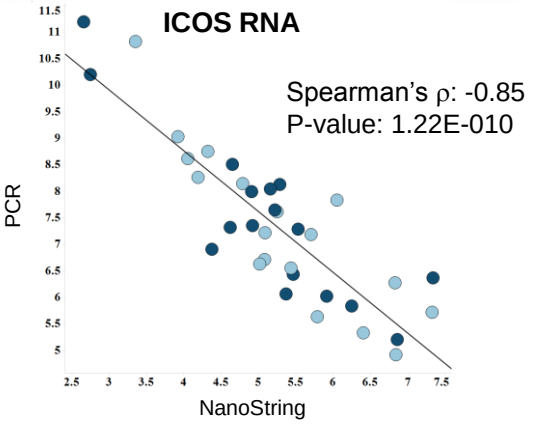
The 11 gene ICOS signature is coherent in the PCR assay

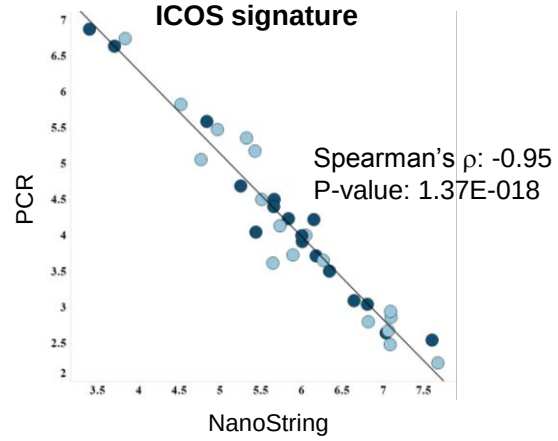


ICOS RNA signature by both PCR and NanoString correlates with ICOS IHC



ICOS expression and ICOS signature are highly correlated between PCR and NanoString platforms





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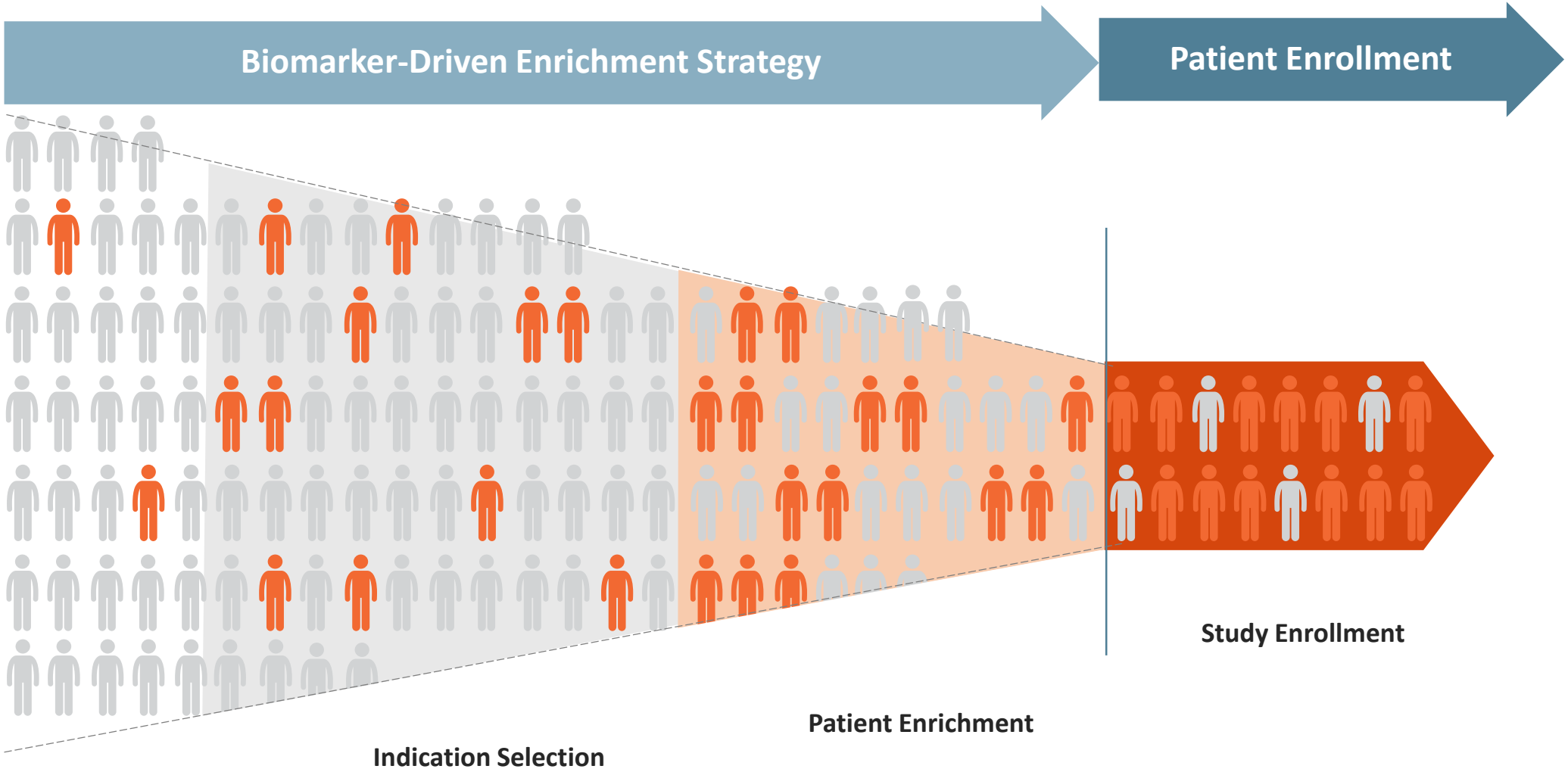
Biomarker-Driven Strategy for Patient Enrichment

Potential for Establishing Complementary and/or Companion Diagnostics



Thank You

As always, Jounce is exceptionally thankful to all of the patients and families participating in the ICONIC clinical trial.

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Making Cancer History®

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Pam Sharma

Jounce Therapeutics

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Myles Clancy
Amit Deshpande
Bayou Ding
Alison Duarte
Courtney Hart
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