



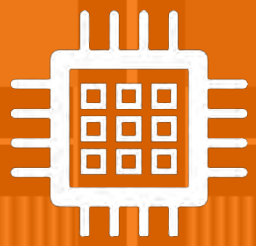
## Bristol-Myers Squibb

Bristol-Myers Squibb is actively conducting translational medicine research to further our understanding of cancer biology and to identify which patient populations may be more likely to derive benefit from Immuno-Oncology (I-O) agents.

**Biomarkers and  
Pharmacodiagnosics  
(PDx)**



**Imaging and  
Technologies**



**Bioinformatics and  
Integrated Sciences**



**Clinical  
Pharmacology and  
Pharmacometrics**



**Exploratory  
Translational  
Research**



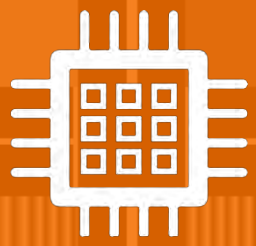
**Collaboration**



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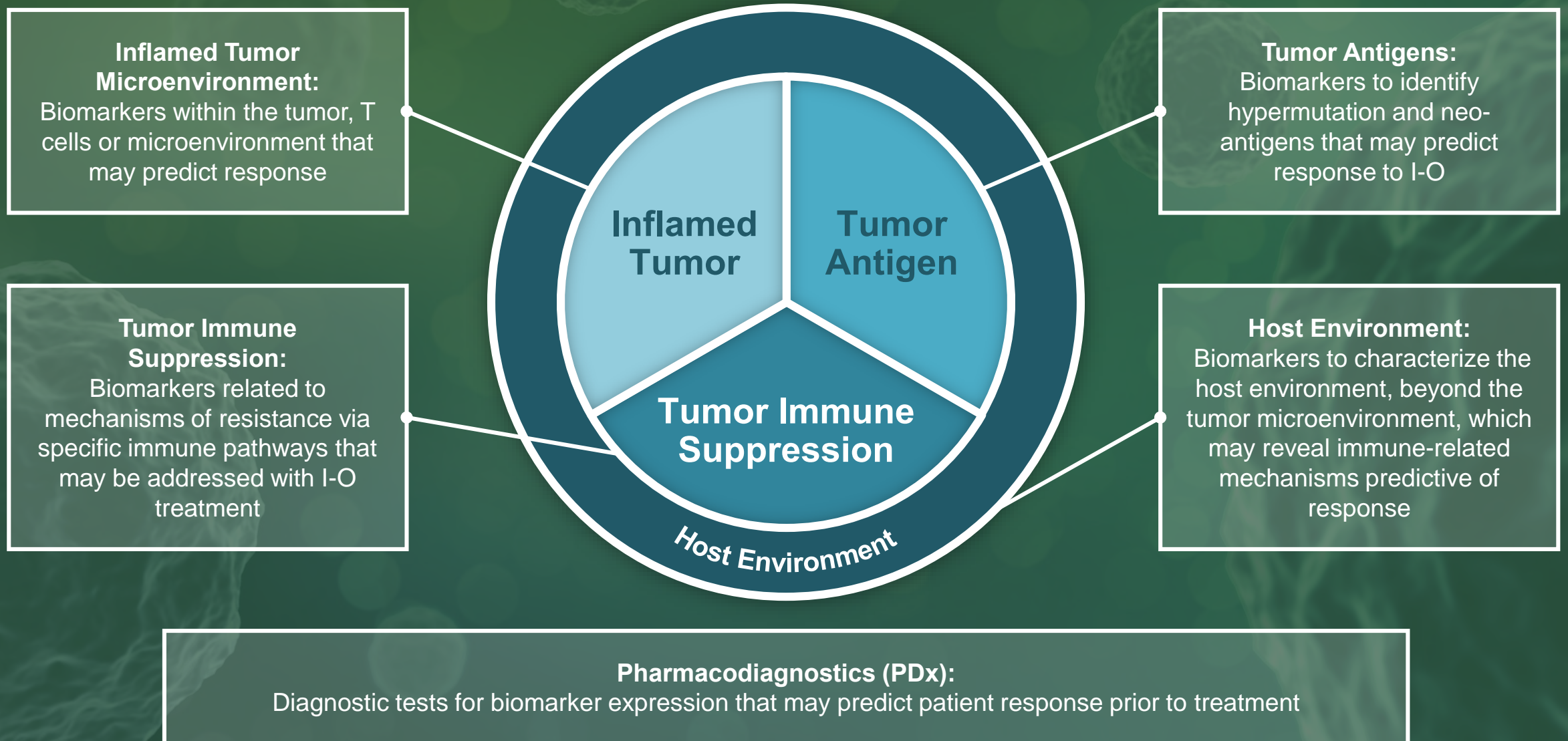


**Exploratory  
Translational  
Research**



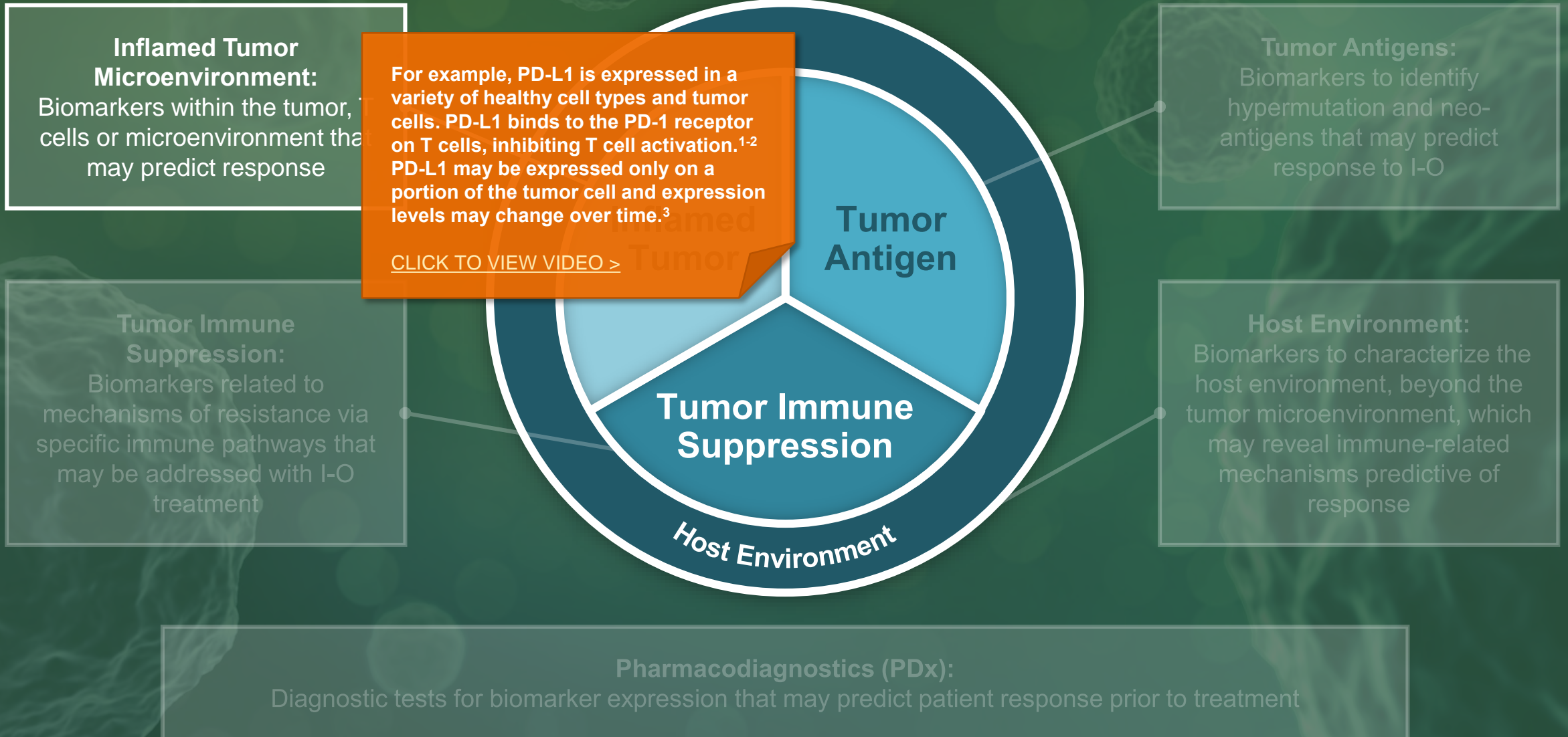
**Collaboration**

# Areas of Focus in Biomarker Research

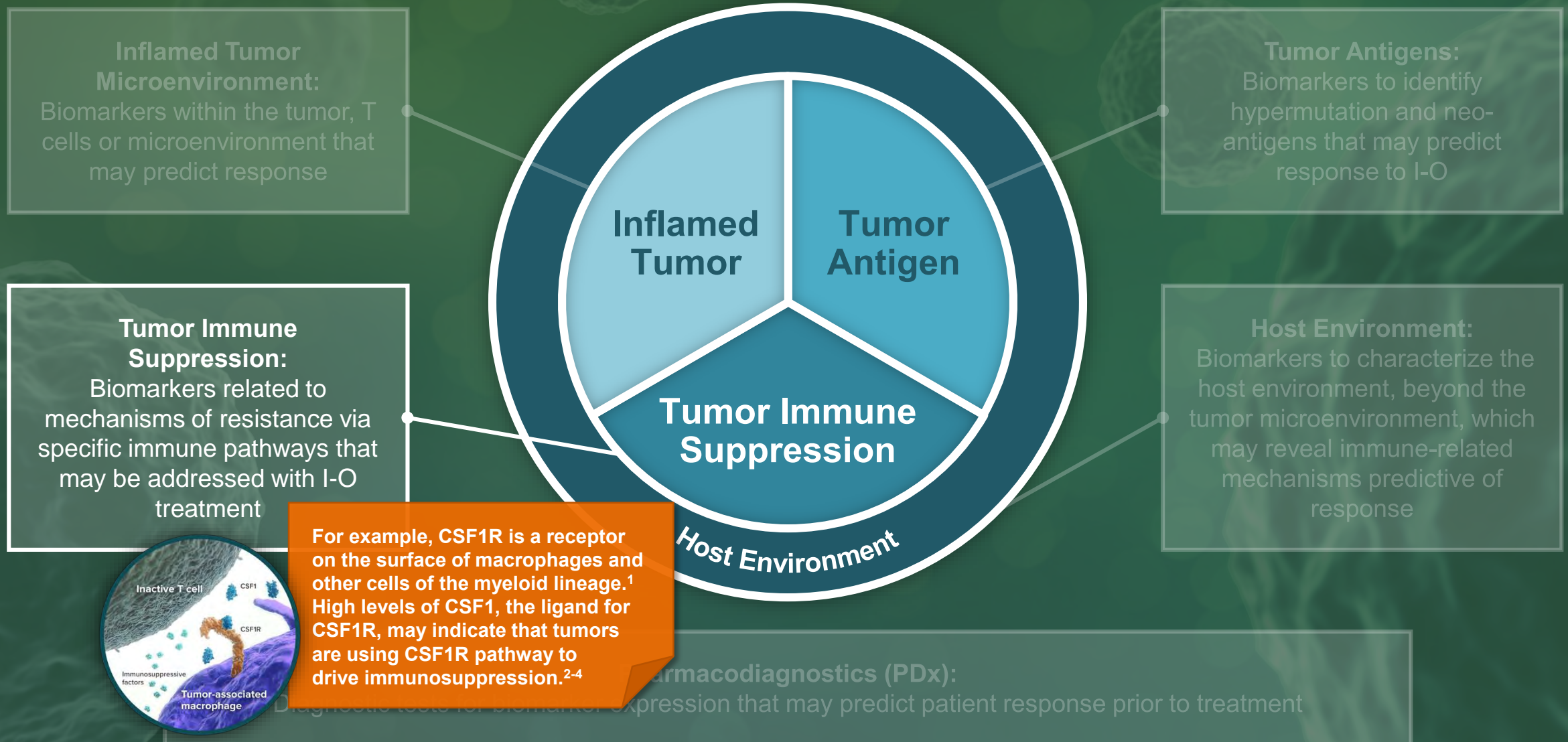




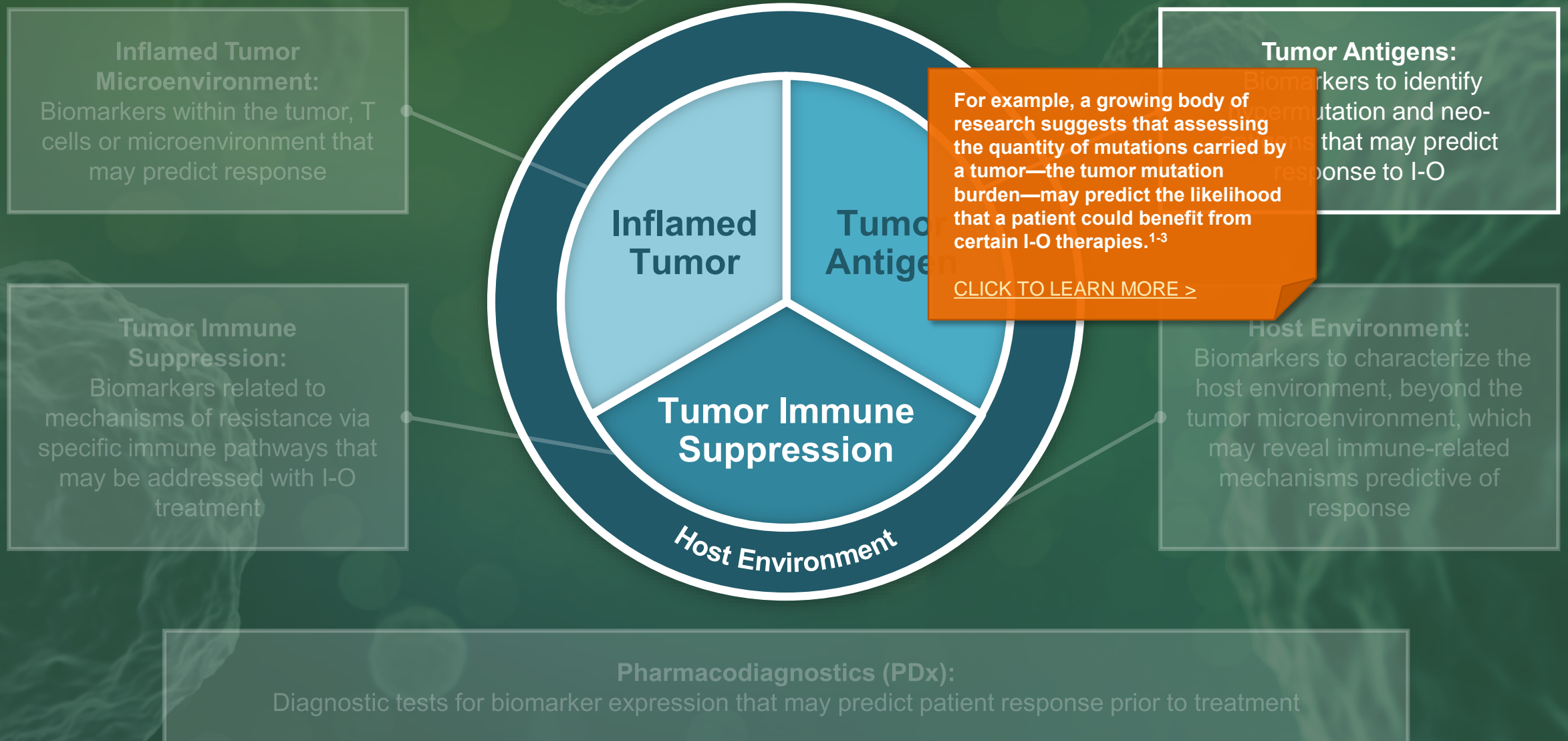
# Areas of Focus in Biomarker Research



# Areas of Focus in Biomarker Research

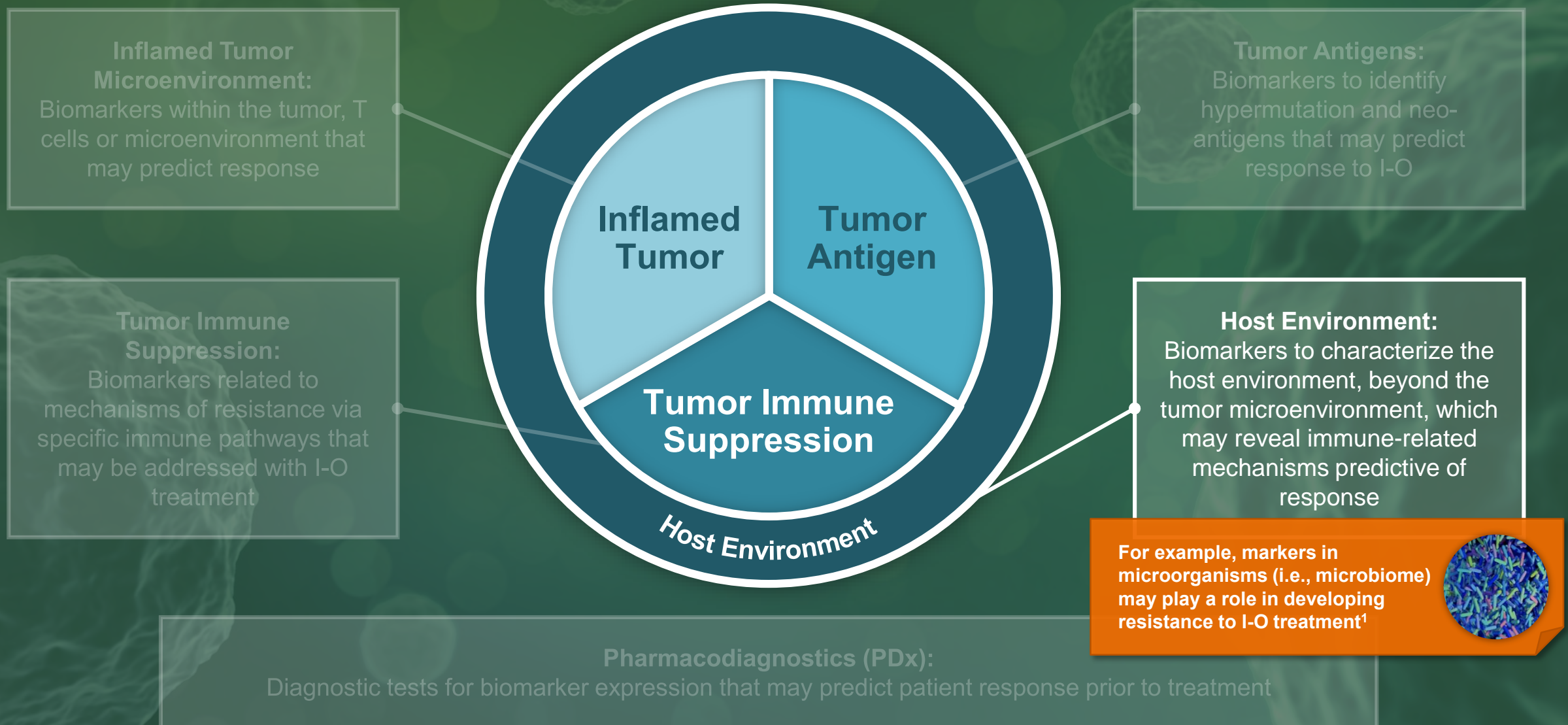


# Areas of Focus in Biomarker Research



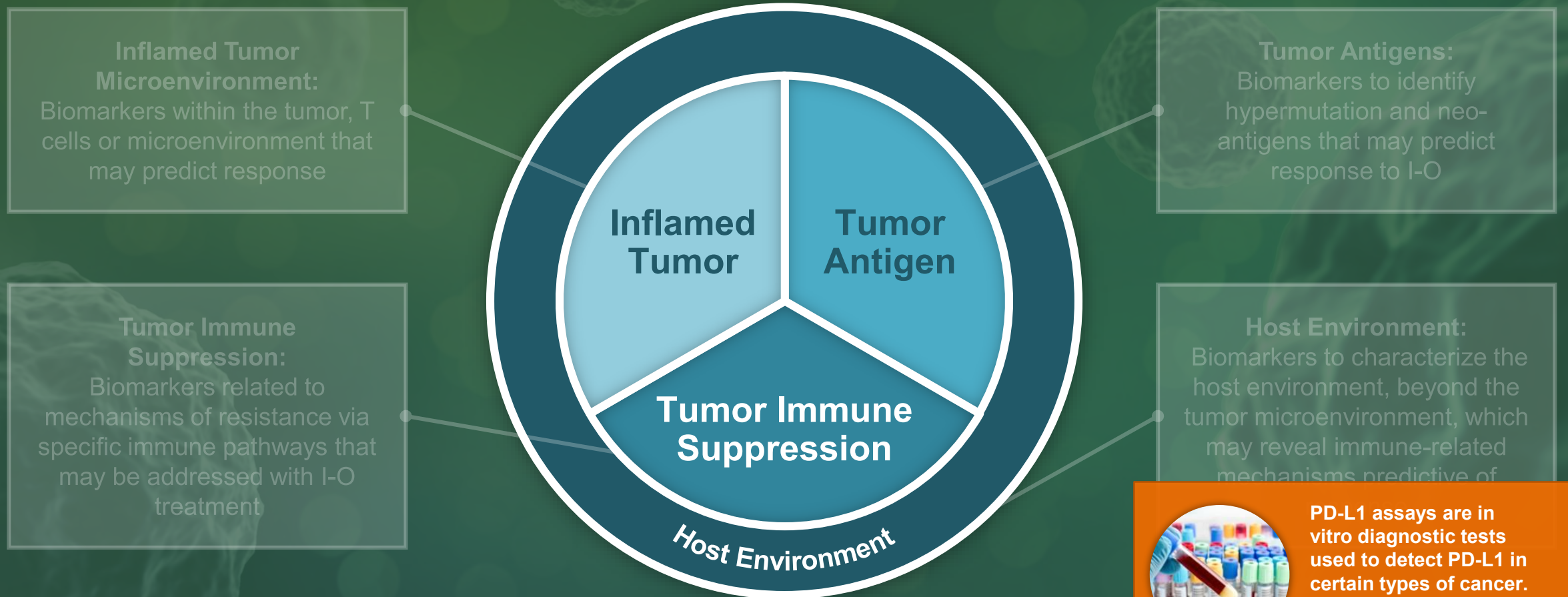


# Areas of Focus in Biomarker Research





# Pharmacodiagnosics



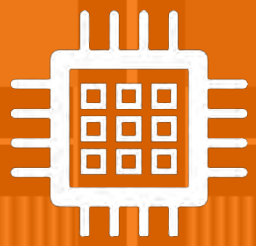
**PD-L1 assays** are in vitro diagnostic tests used to detect PD-L1 in certain types of cancer. This test can help determine appropriate treatment. <sup>1</sup>

**Pharmacodiagnosics (PDx):**  
Diagnostic tests for biomarker expression that may predict patient response prior to treatment

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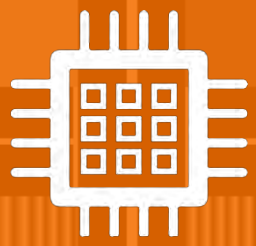
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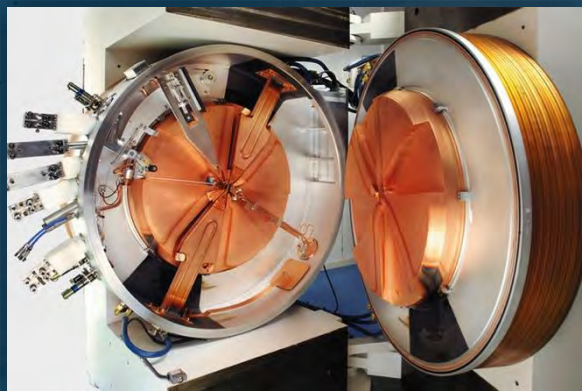


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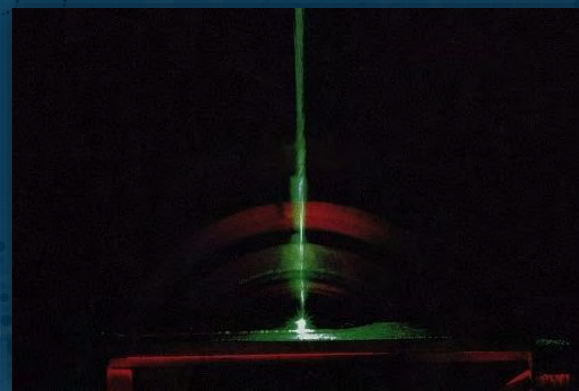
## IMAGING

Molecular imaging allows researchers to study specific targets and guide treatment decisions without invasive procedures



## GENOMICS & GENETICS

Mapping, characterizing and quantifying gene expression and mutations to allow for a deeper understanding of disease biology and mechanisms of drug response



## FLOW CYTOMETRY & FUNCTIONAL BIOLOGY

Method of single-cell analysis that allows for cell sorting, detection of disease biomarkers and a better understanding of cell biology



## SAMPLE MANAGEMENT

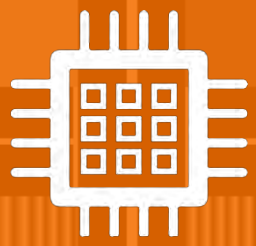
System for storing and organizing samples for efficient future use



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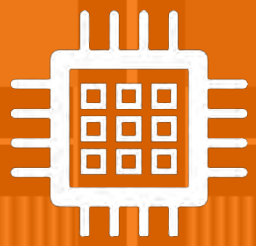


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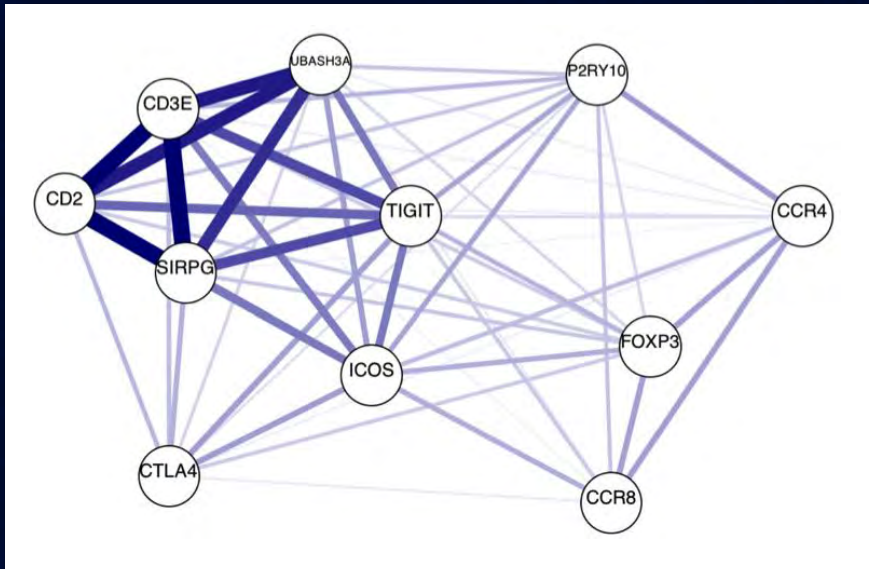


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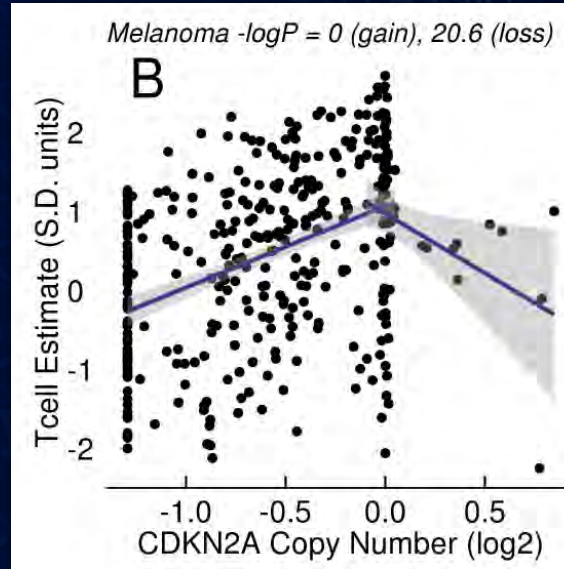


**Collaboration**





*Gene expression network derived from analysis of TCGA RNA sequencing data*

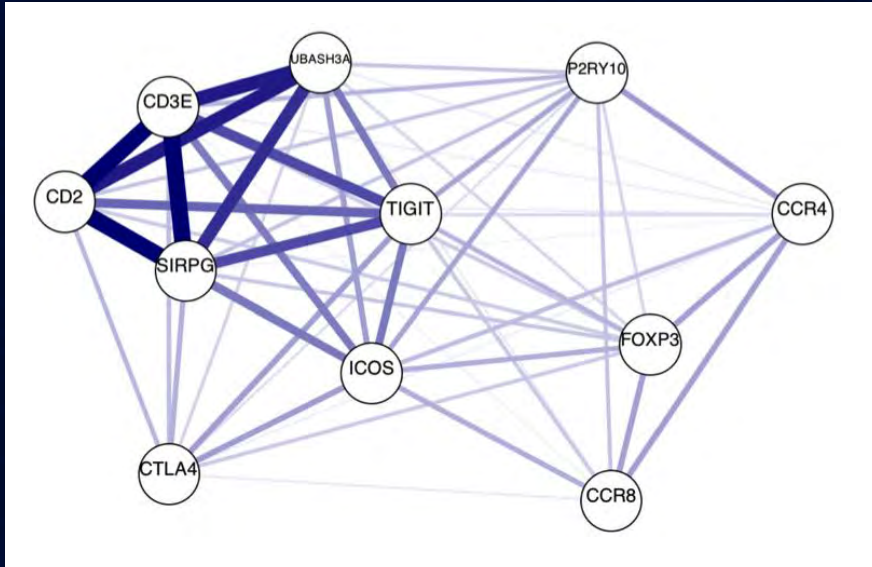


*Loss of CDKN2A is associated with reduced estimates of T cells in the tumor microenvironment in some cancers*

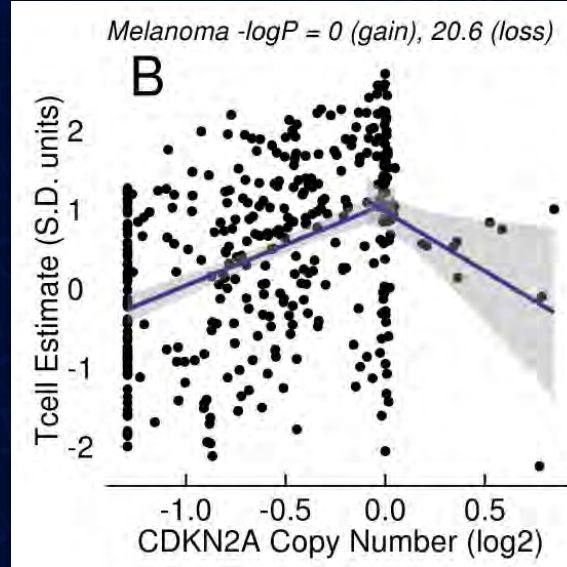
Our Translational Bioinformatics team uses cutting-edge methods to perform integrative data analysis. We study the interplay of tumor genomes, their regulation and the tumor microenvironment to further our understanding of response to I-O agents.

Our comprehensive analysis of The Cancer Genome Atlas (TCGA) identified networks of co-expressed genes that can be used to identify specific types of immune cells in the tumor microenvironment. In some tumors, certain genetic mutations correlate with the abundance of such cells.





*Gene expression network derived from analysis of TCGA RNA sequencing data*



*Loss of CDKN2A is associated with reduced estimates of T cells in the tumor microenvironment in some cancers*

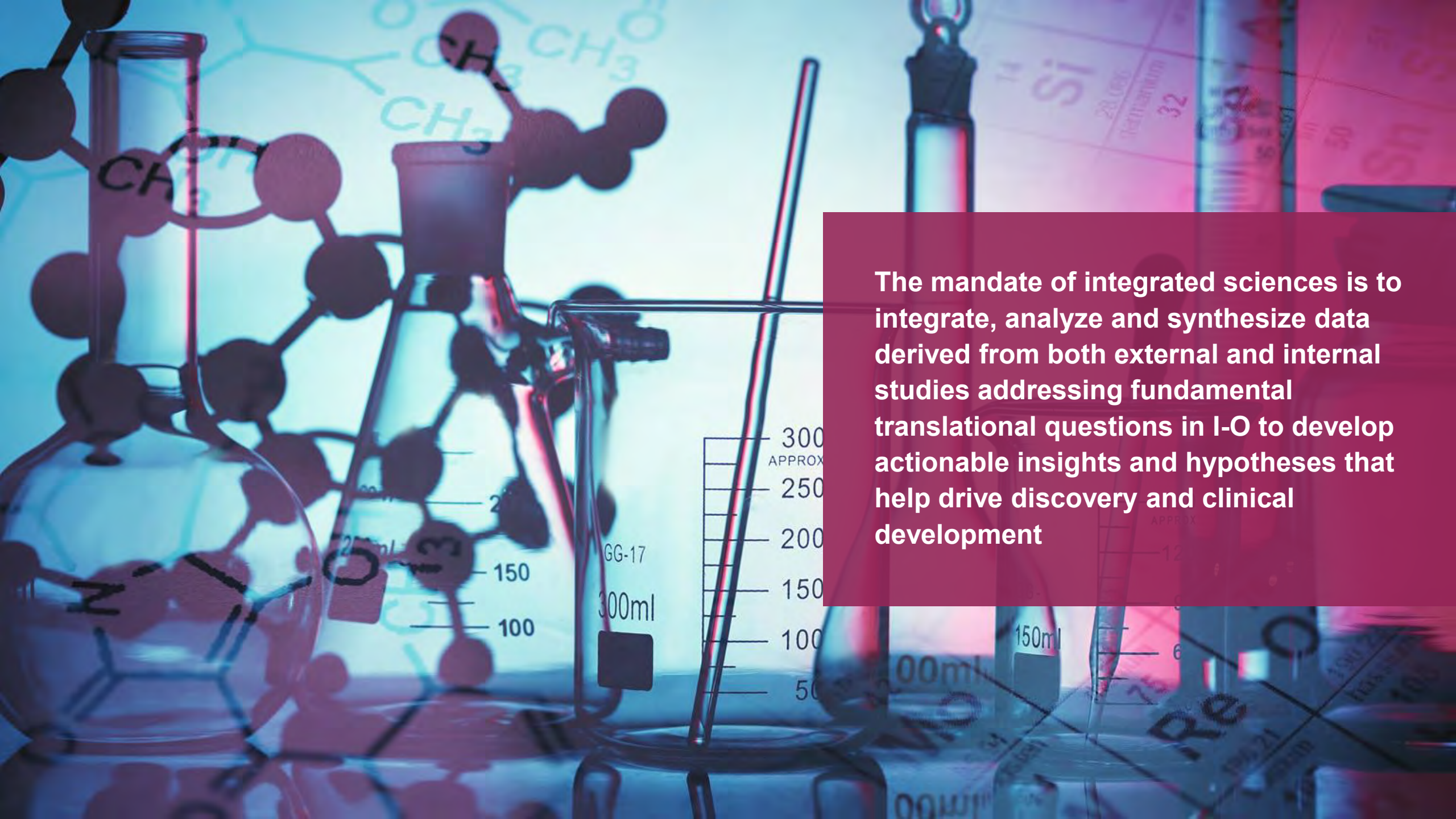
Partnerships with leading data bioinformatics companies enhance our in-house capabilities.

Our Translational Bioinformatics team uses cutting-edge methods to perform integrative data analysis. We study the interplay of tumor genomes, their regulation and the tumor microenvironment to further our understanding of response to I-O agents.

Our comprehensive analysis of The Cancer Genome Atlas (TCGA) identified networks of co-expressed genes that can be used to identify specific types of immune cells in the tumor microenvironment. In some tumors, certain genetic mutations correlate with the abundance of such cells.

Our team analyzes tumor mutation burden, RNA sequencing, serum cytokine, and other large-scale biomarker data sets generated from clinical trials.



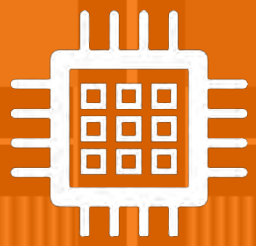


**The mandate of integrated sciences is to integrate, analyze and synthesize data derived from both external and internal studies addressing fundamental translational questions in I-O to develop actionable insights and hypotheses that help drive discovery and clinical development**

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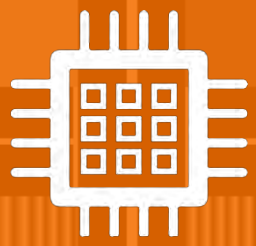
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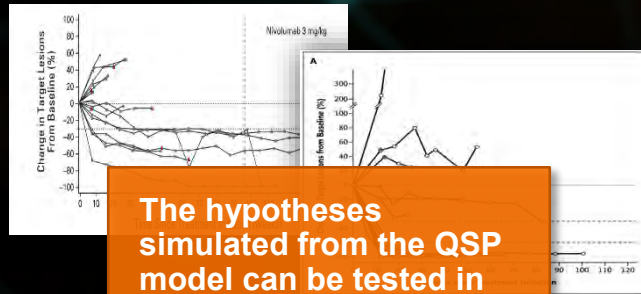
**Collaboration**





# Mechanistic Modeling (QSP) Fuels New Questions and Continued Exploration in Immuno-Oncology

## Hypothesis Testing



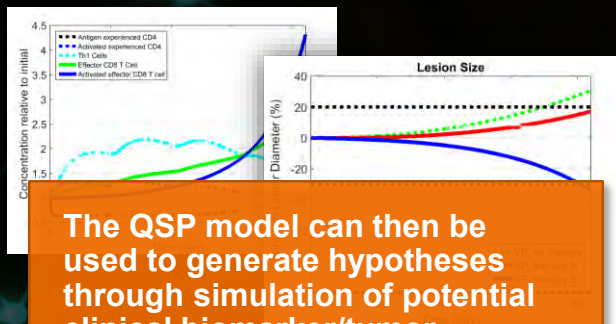
The hypotheses simulated from the QSP model can be tested in clinical studies.

## Prior Knowledge



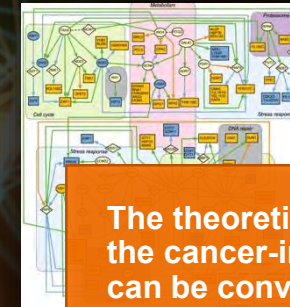
Prior knowledge can be integrated into a theoretical model of the cancer-immunity cycle.

## Model Application



The QSP model can then be used to generate hypotheses through simulation of potential clinical biomarker/tumor responses.

## Model Development



$$\frac{dx_1}{dt} = f_1(x_1, x_2, \dots, x_n)$$
$$\frac{dx_2}{dt} = f_2(x_1, x_2, \dots, x_n)$$
$$\dots$$
$$\frac{dx_n}{dt} = f_n(x_1, x_2, \dots, x_n)$$

The theoretical model of the cancer-immunity cycle can be converted into a mathematical QSP model.

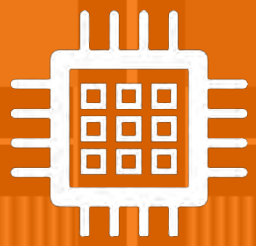
Hypothesis Testing

Hypothesis Generation

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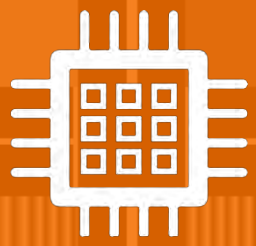
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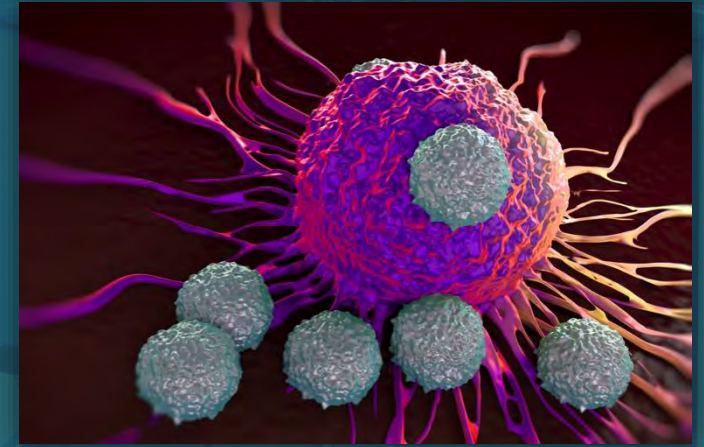
**Collaboration**



Experimentation provides the knowledge and data to form hypotheses that can be tested in the clinic



We leverage existing and advanced clinical assays to explore and test new hypotheses using biologic samples



Insights gained from this research can quickly be implemented in prospective clinical trials to enhance and accelerate our pipeline

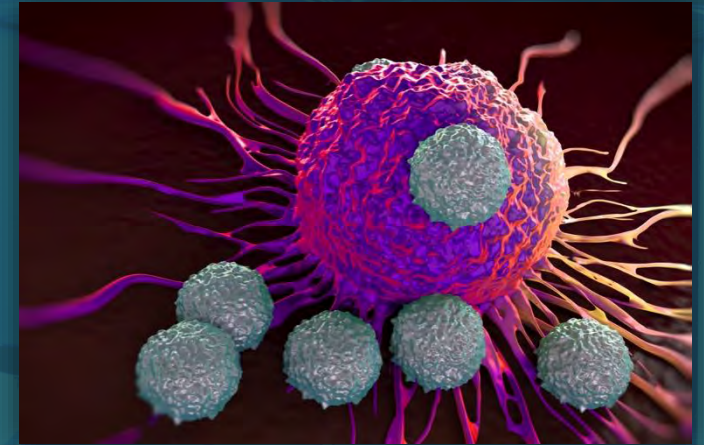




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**SINGLE CELL GENOMICS:**

Leveraging next generation technologies to examine sequence information from individual cells.

**PROTEOMICS:**

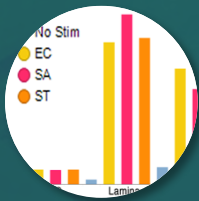
Study of proteins and how they interact within tumor microenvironment.

# Conducting Research to Understand the Immune System in Patients with Cancer

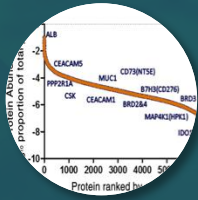
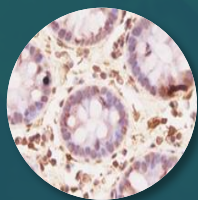
TISSUE ↔ BLOOD

Genetics/genomics experiments to tissue samples

Cell isolation for functional assays



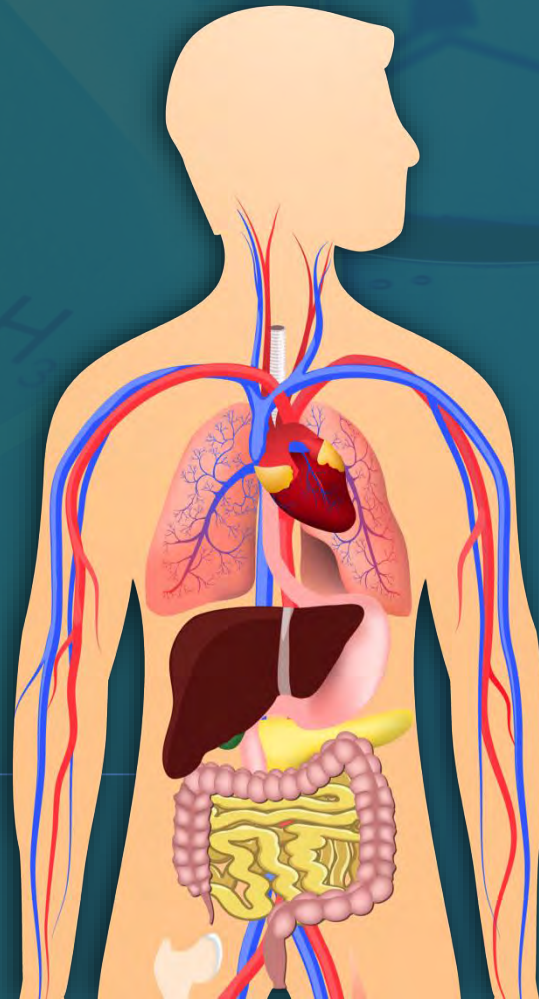
IHC/Proteomics Mass Spectrometry



Fresh tissue

FFPE

Frozen tissue



Whole Blood

PBMC

Plasma

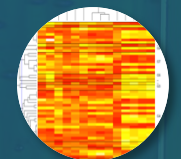
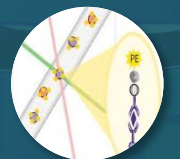
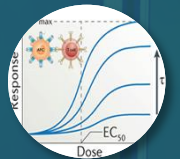
PAXgene

Comprehensive phenotyping

Functional assays: signaling, cytokine induction

Plasma analytes

Gene expression: mRNA and miRNA

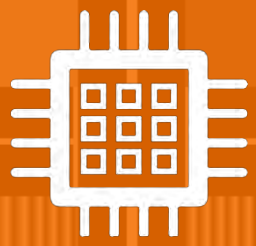




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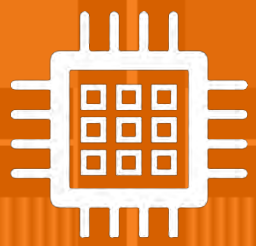


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**ACADEMIC  
COLLABORATION**

Our scientific collaborations with academic centers around the globe expand our research capabilities and accelerate our collective ability to advance the science.



**BUSINESS  
DEVELOPMENT**

We seek to partner with other I-O experts to expand our translational medicine capabilities.





## ACADEMIC COLLABORATION

Our scientific collaborations with academic centers around the globe expand our research capabilities and accelerate our collective ability to advance the science.



A global peer-to-peer collaboration between Bristol-Myers Squibb and academia that aims to advance I-O science and translational medicine to benefit patients.

[CLICK TO LEARN MORE>](#)



Research collaborations with select European research institutions to appropriately accelerate, expand and more effectively advance I-O research.



## BUSINESS DEVELOPMENT

We seek to partner with other I-O experts to expand our translational medicine capabilities.

Working with partners like Foundation Medicine and GRAIL helps to drive the identification, validation and application of predictive biomarkers.



Our robust translational medicine program informs key areas of research, including:



Disease targeting and responsive patient segmentation



Ideal treatment strategies, including combinations, for each patient



Optimal dosing, schedule and clear understanding of MOA



