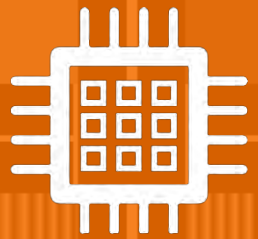
Bristol-Myers Squibb is actively conducting translational medicine research to further our understanding of cancer biology and to identify which patient populations may be more likely to derive benefit from Immuno-Oncology (I-O) agents.

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



Bioinformatics and Integrated Sciences

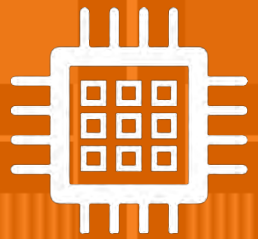
Clinical Pharmacology and Pharmacometrics

Exploratory Translational Research

Collaboration

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



Bioinformatics and Integrated Sciences

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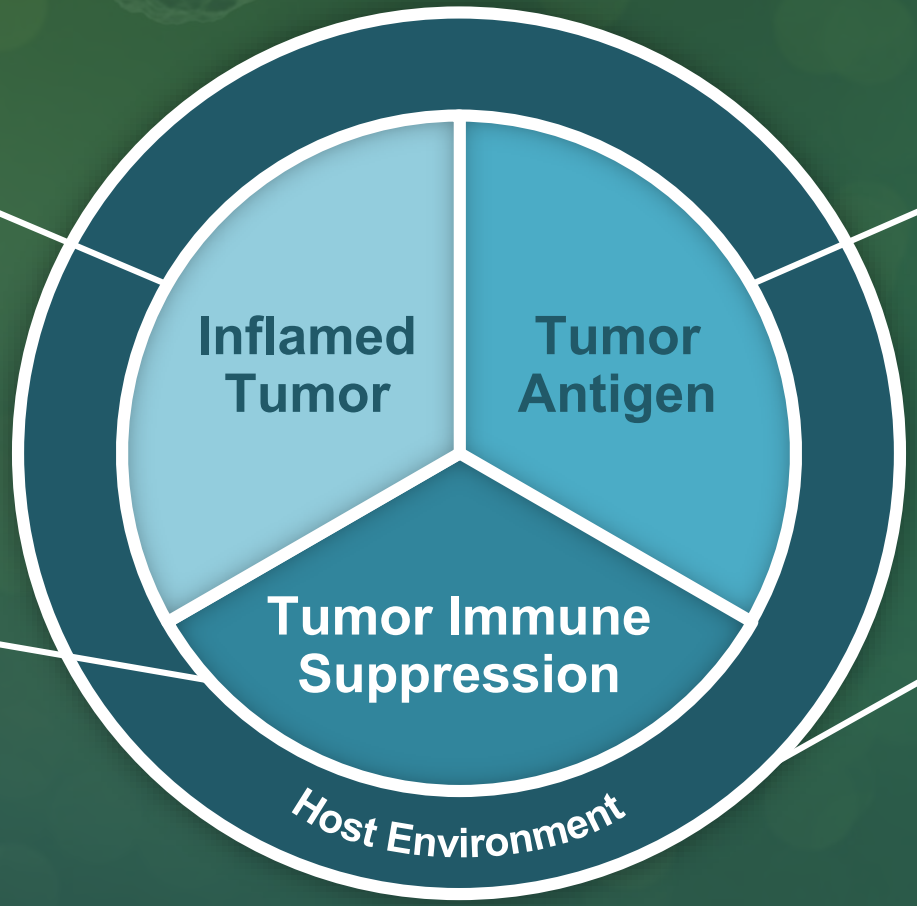
Areas of Focus in Biomarker Research

Inflamed Tumor Microenvironment:
Biomarkers within the tumor, T cells or microenvironment that may predict response

Tumor Immune Suppression:
Biomarkers related to mechanisms of resistance via specific immune pathways that may be addressed with I-O treatment



Tumor Antigens:
Biomarkers to identify hypermutation and neo-antigens that may predict response to I-O

Host Environment:
Biomarkers to characterize the host environment, beyond the tumor microenvironment, which may reveal immune-related mechanisms predictive of response

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

Areas of Focus in Biomarker Research

Inflamed Tumor Microenvironment:
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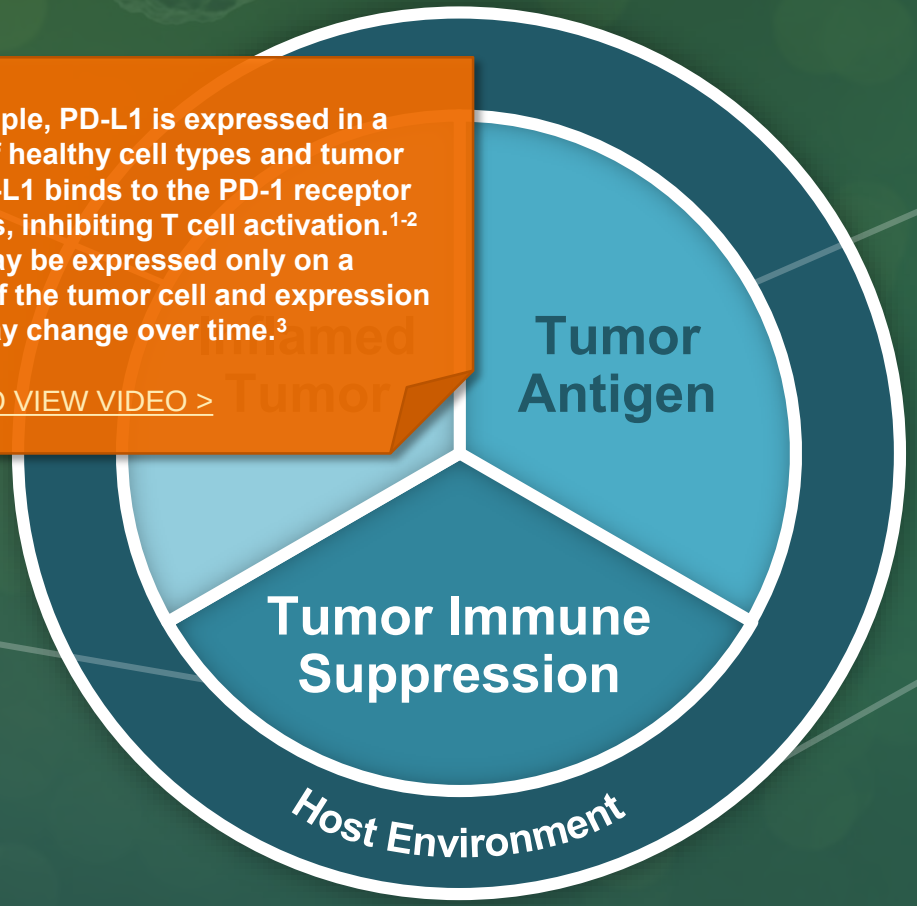
may predict response

For example, PD-L1 is expressed in a variety of healthy cell types and tumor cells. PD-L1 binds to the PD-1 receptor on T cells, inhibiting T cell activation.[1-2] PD-L1 may be expressed only on a portion of the tumor cell and expression levels may change over time.[3]

CLICK TO VIEW VIDEO >



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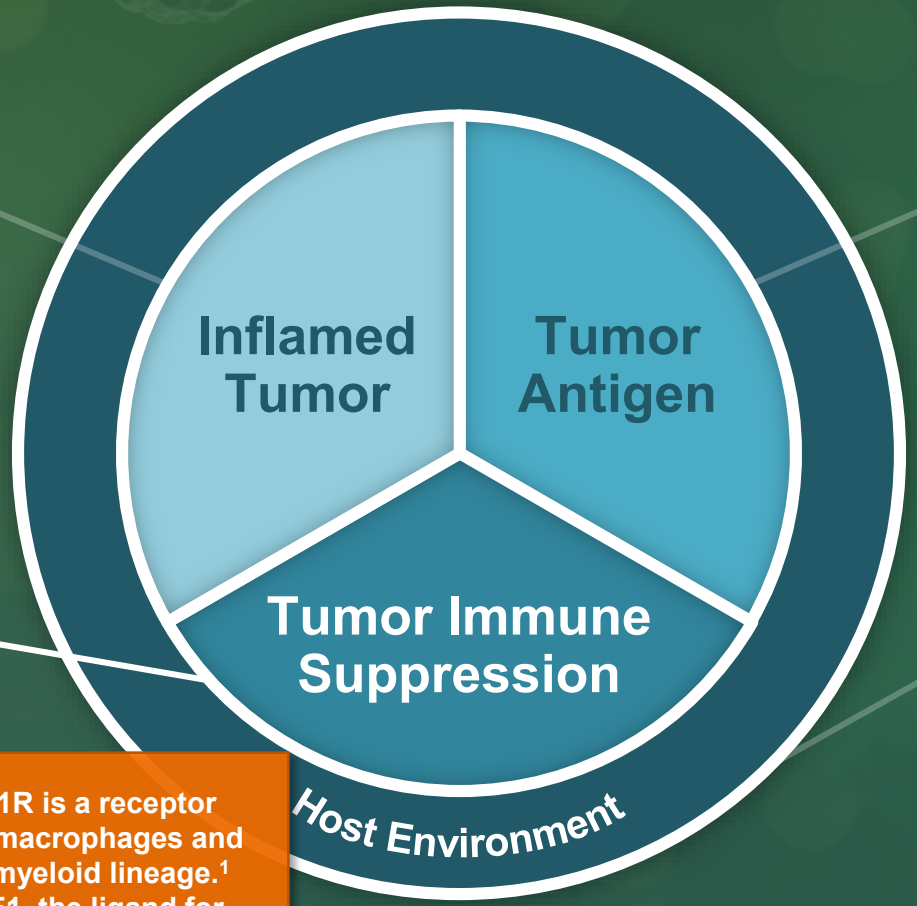

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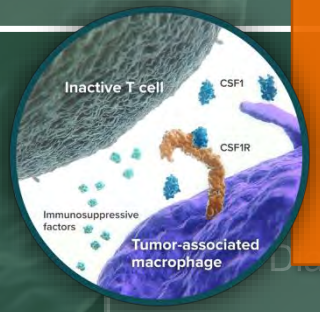

For example, CSF1R is a receptor on the surface of macrophages and other cells of the myeloid lineage.[1] High levels of CSF1, the ligand for CSF1R, may indicate that tumors are using CSF1R pathway to drive immunosuppression.[2-4]

rmacodiagnostics (PDx):
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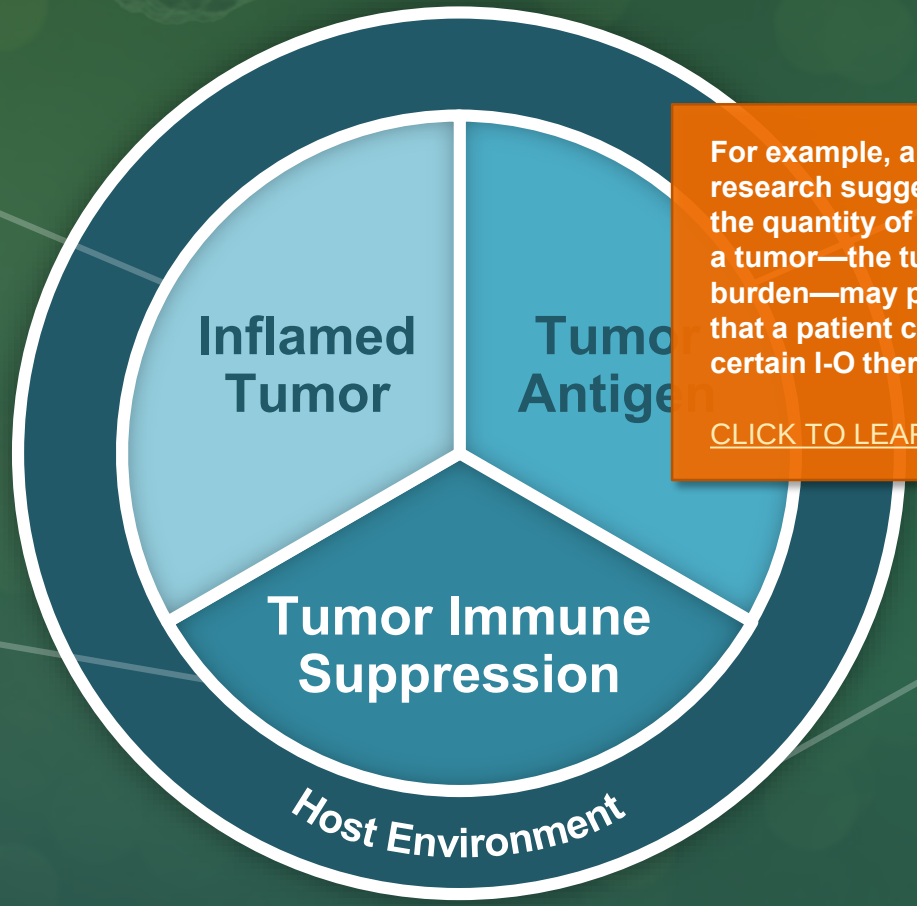

For example, a growing body of research suggests that assessing the quantity of mutations carried by a tumor—the tumor mutation burden—may predict the likelihood that a patient could benefit from certain I-O therapies.[1-3]

CLICK TO LEARN MORE >

Tumor Immune Suppression:
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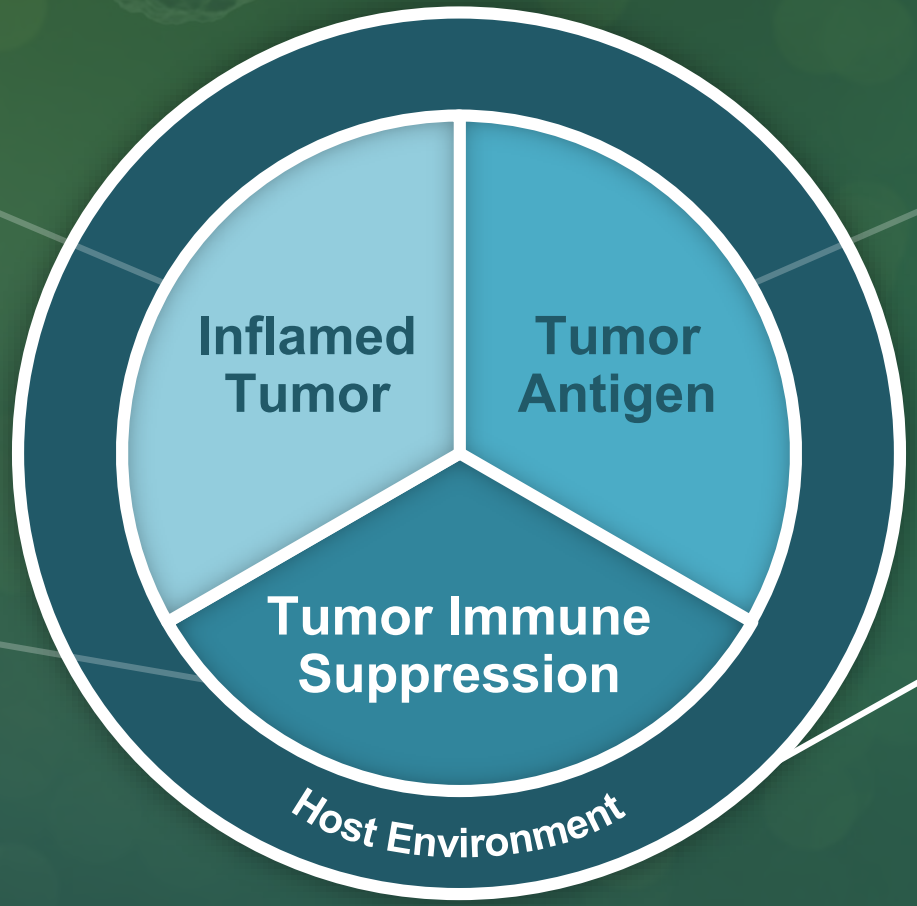

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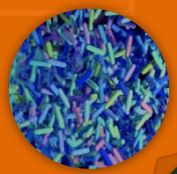
For example, markers in microorganisms (i.e., microbiome) may play a role in developing resistance to I-O treatment[1]



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Pharmacodiagnostics

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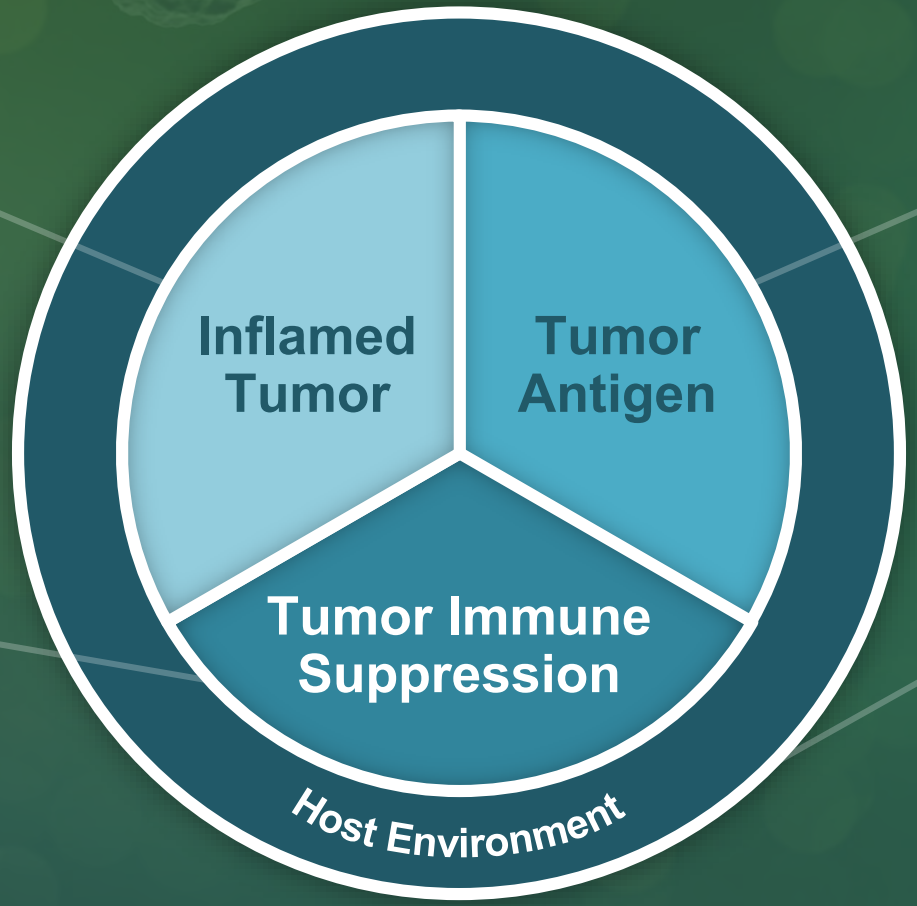

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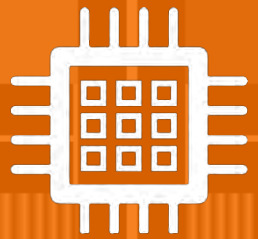
PD-L1 assays are in vitro diagnostic tests used to detect PD-L1 in certain types of cancer. This test can help determine appropriate treatment. [1]

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

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



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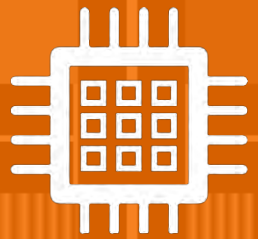

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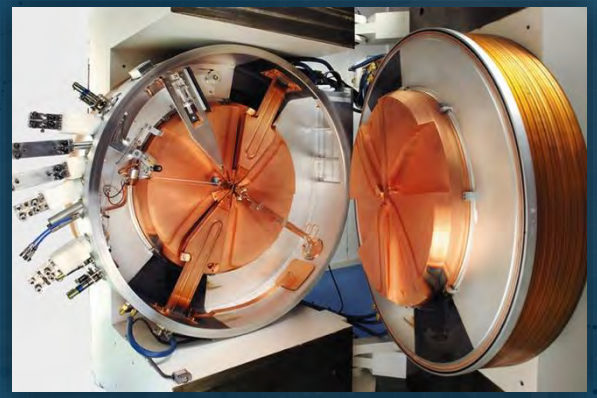
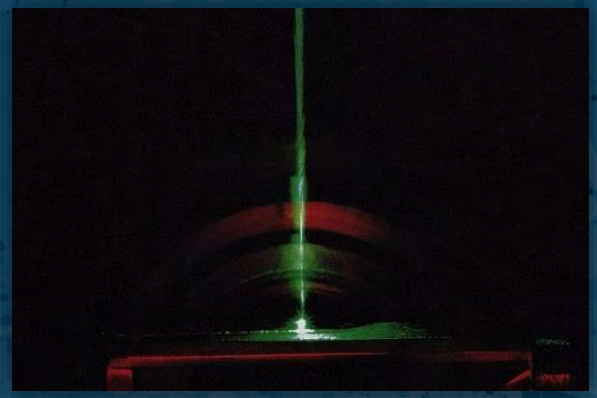


IMAGING

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

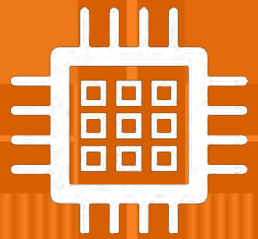
Method of single-cell analysis that allows for cell sorting, detection of disease biomarkers and a better understanding of cell biology

SAMPLE MANAGEMENT

System for storing and organizing samples for efficient future use

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



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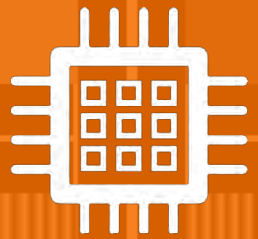

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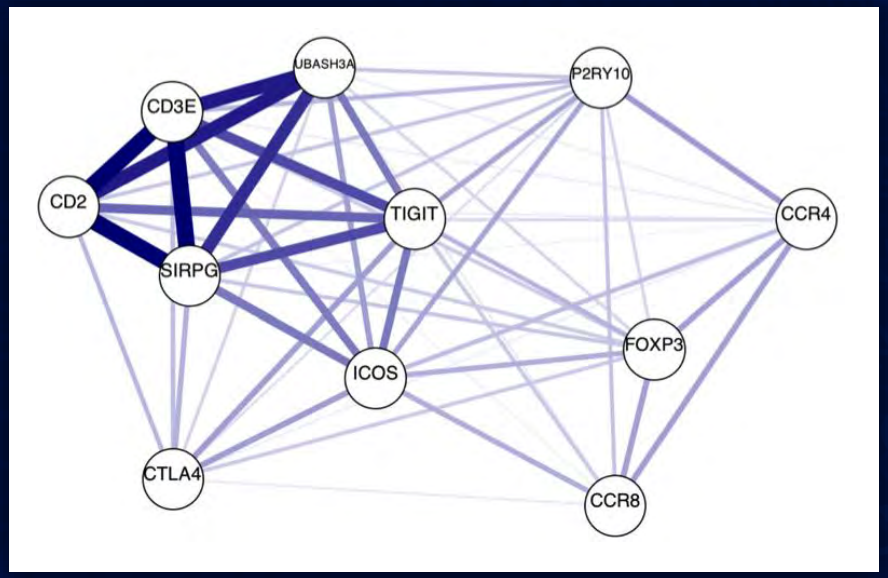
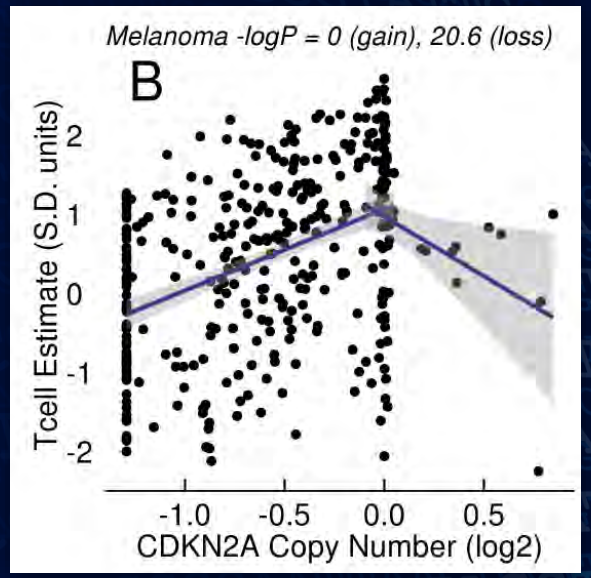


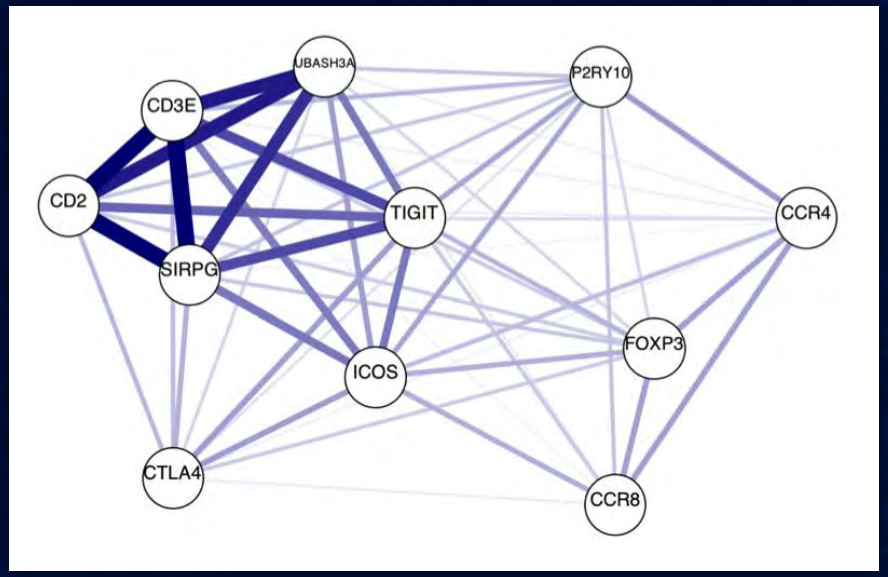
Gene expression network derived from analysis of TCGA RNA sequencing data



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.



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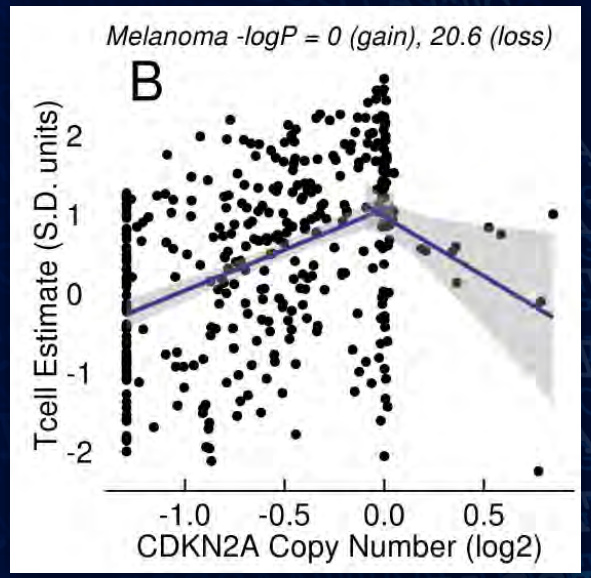

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Partnerships with leading data bioinformatics companies enhance our in-house capabilities.

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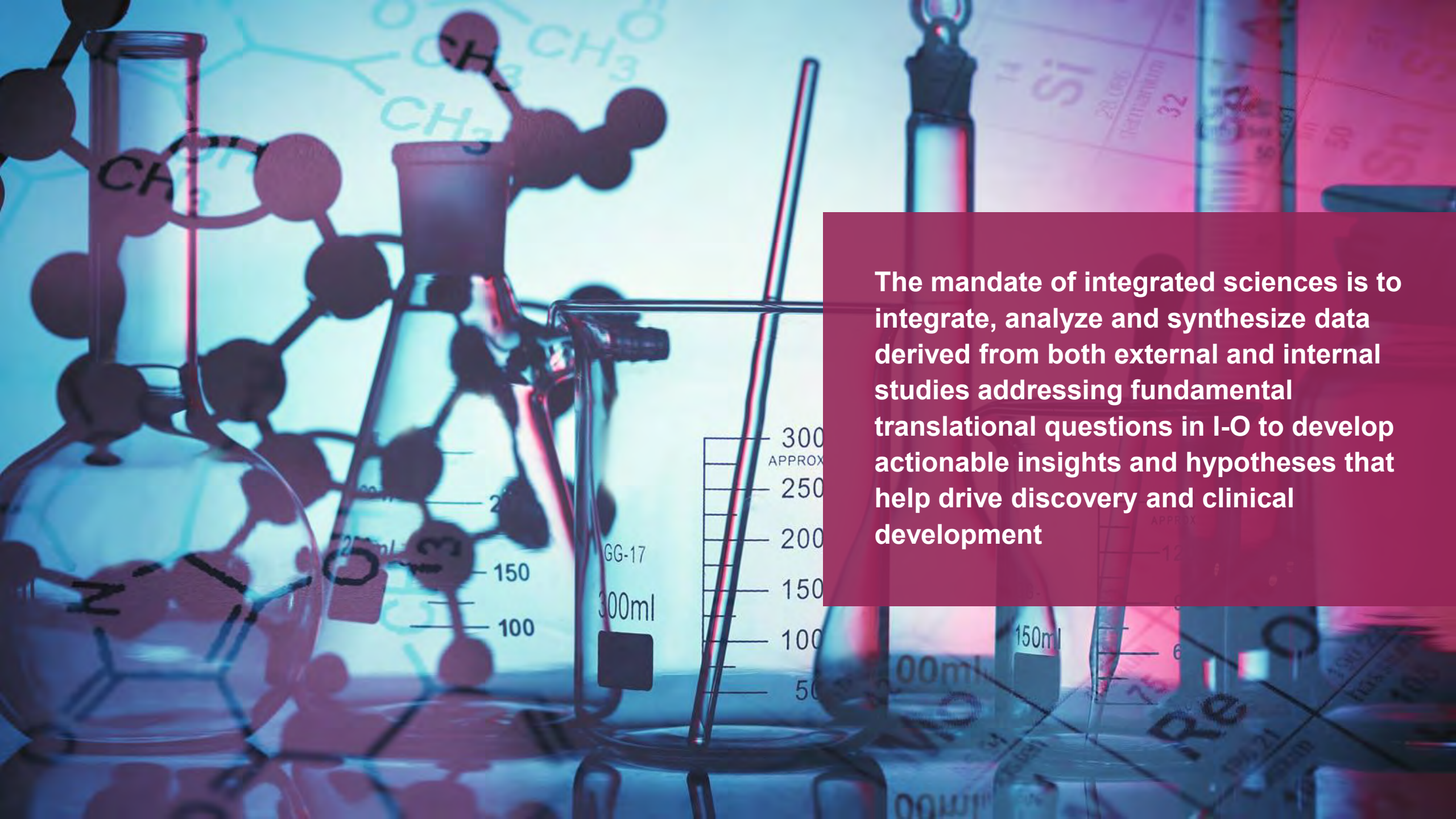
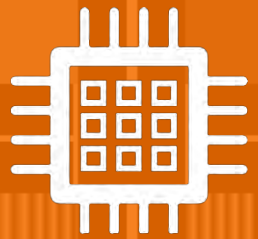
Our team analyzes tumor mutation burden, RNA sequencing, serum cytokine, and other large-scale biomarker data sets generated from clinical trials.



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

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



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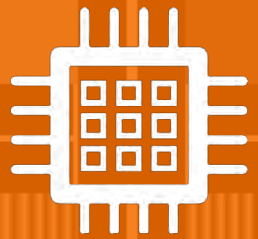

Bioinformatics and Integrated Sciences

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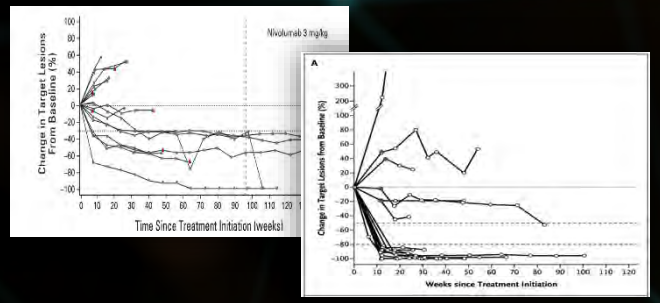
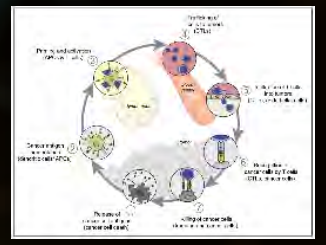
Collaboration

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

Hypothesis Testing



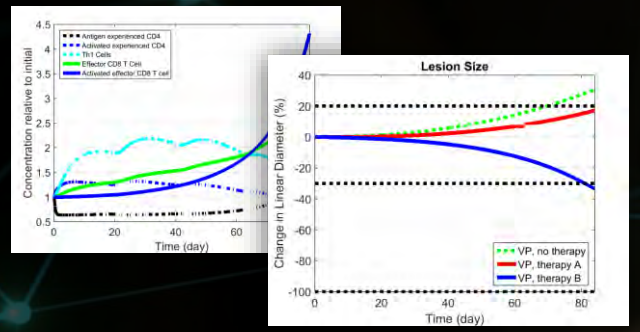
Prior Knowledge



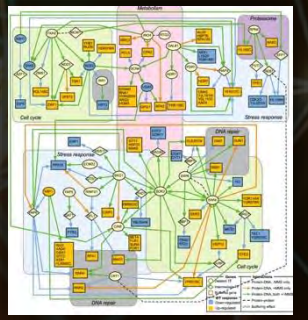
Hypothesis Testing

Hypothesis Generation

Model Application



Model Development



$$\frac{dx_1}{dt} = f_1(x_1, x_2, ..., x_n)$$

$$\frac{dx_2}{dt} = f_2(x_1, x_2, ..., x_n)$$

...

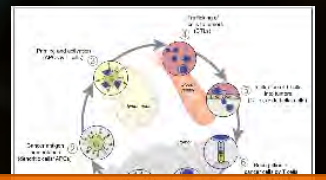
$$\frac{dx_n}{dt} = f_n(x_1, x_2, ..., x_n)$$

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.

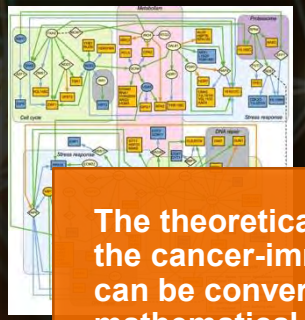
Hypothesis Testing

Hypothesis Generation

Model Application

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

Model Development



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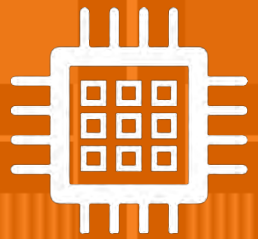
$$x_n)$$

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

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



Bioinformatics and Integrated Sciences

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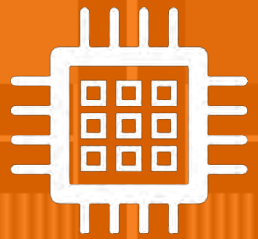

Bioinformatics and Integrated Sciences

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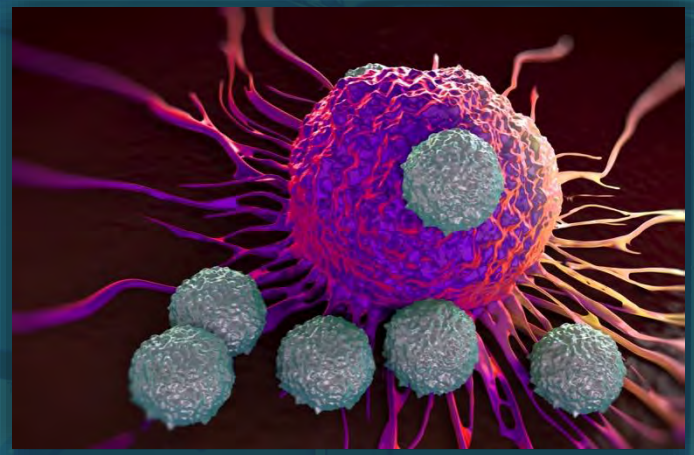
Collaboration

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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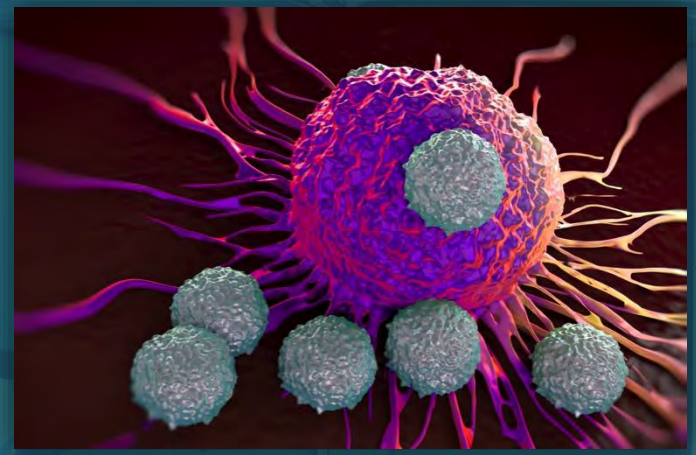


Insights gained from this research can quickly be implemented in prospective clinical trials to enhance and accelerate our pipeline

SINGLE CELL GENOMICS:
Leveraging next generation technologies to examine sequence information from individual cells.

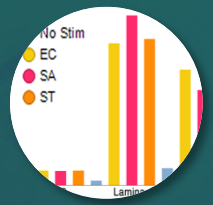
PROTEOMICS:
Study of proteins and how they interact within tumor microenvironment.

Conducting Research to Understand the Immune System in Patients with Cancer

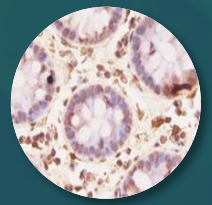
TISSUE ⟷ **BLOOD**

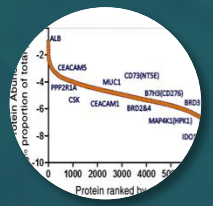
Genetics/genomics experiments to tissue samples

Cell isolation for functional assays



IHC/Proteomics Mass Spectrometry

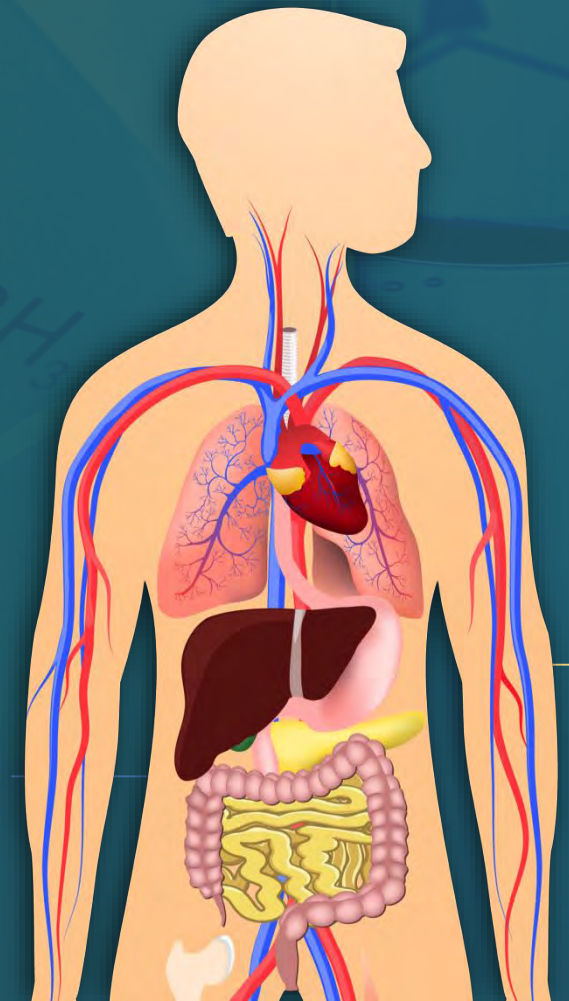




Fresh tissue

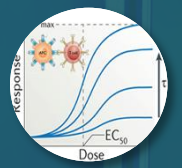
FFPE

Frozen tissue

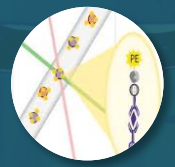


Whole Blood — Comprehensive phenotyping

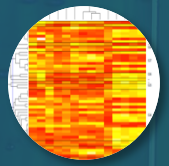
PBMC — Functional assays: signaling, cytokine induction



Plasma — Plasma analytes

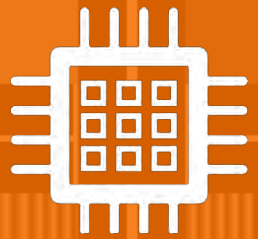


PAXgene — Gene expression: mRNA and miRNA



Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



Bioinformatics and Integrated Sciences

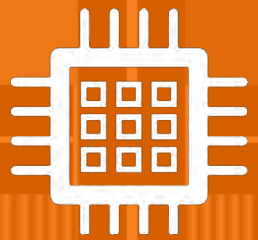
Clinical Pharmacology and Pharmacometrics

Exploratory Translational Research

Collaboration

Biomarkers and Pharmacodiagnostics (PDx)

Imaging and Technologies



Bioinformatics and Integrated Sciences

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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.

I-O International Immuno-Oncology Network

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>

GECI global expert centers initiative

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


Bristol-Myers Squibb