Welcome
### Scientific Experts

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adi Diab, M.D.</td>
<td>MD Anderson Cancer Center</td>
</tr>
<tr>
<td>Jianjun, M.D., Ph.D.</td>
<td>MD Anderson Cancer Center</td>
</tr>
<tr>
<td>Valentina Hoyos Velez, M.D.</td>
<td>Baylor College of Medicine</td>
</tr>
<tr>
<td>Andrew Sikora, M.D., Ph.D.</td>
<td>Baylor College of Medicine</td>
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### Patient Experts

<table>
<thead>
<tr>
<th>Name</th>
<th>Disease</th>
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<tr>
<td>Isolde Artz</td>
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<td>Mesothelioma</td>
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Our Sponsors

This event is made possible with generous support from:

- Bristol-Myers Squibb
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- gsk
- Lilly Oncology
- Immunotherapy Foundation
- REGENERON
- SANOFI GENZYME
- NOVARTIS
- Pfizer
Our Educational Partners

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- LUNGevity
- MyCancerConnection MD Anderson
- National Ovarian Cancer Coalition Texas
- Pancreatic Cancer Action Network
- Patient Empowerment Network
- SHARE
- Us TOO
- Young Survival Coalition
Clinical Trial Navigator Appointments are available from 9:00 AM to 4:00 PM. Please stop by the check-in desk near registration to learn more.

<table>
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<th>Summit Program</th>
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<tr>
<td>Morning Session</td>
<td>10:00 AM – 12:00 PM</td>
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<td>Lunch</td>
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<td>Afternoon Session</td>
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<tr>
<td>Breakout Sessions</td>
<td>2:30 PM – 3:15 PM</td>
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</tbody>
</table>
You will receive two emails after the summit:

1. **A survey** to share your feedback on the summit as well as insights into future programming.

2. **Information** from the summit day, including this presentation and instructions on how to use our [Clinical Trial Finder service](#).
Pioneering Immunotherapy

William B. Coley, M.D.
Father of Cancer Immunotherapy
1862 - 1936

Helen Coley Nauts, D.Sc. (Hon.)
Co-Founder, Cancer Research Institute
1907 - 2001
SAVE MORE LIVES
by fueling the discovery and development of powerful immunotherapies for all types of cancer.

Sharon Belvin
Melanoma Survivor & Mom
FUNDED 3,300 scientists worldwide
INVESTED $420+ million
TRUSTED Platinum, A+ charity

#CRIsummit
Immunotherapy 101

Adi Diab, M.D.
Associate Professor, Department of Melanoma Medical Oncology, Division of Cancer Medicine, MD Anderson Cancer Center
Origin & Revival of Immunotherapy

1890s: William B. Coley

1900s: Paul Ehrlich

1960s: Lloyd J. Old

1980s-present: Jim Allison
Immunotherapy: A Potential Cure?

- **Standard therapy**: Pts take longer to progress, but succumb at the same rate.
- **Immunotherapy**: Increased survival.

Room for improvement.
The Immune System at a Glance: Our Natural Defense System

**Nose**
- Hairs and mucus trap foreign particles and prevent them from entering the body.

**Thymus**
- Small organ located just behind the breastbone where T cells mature (the “T” is for thymus).

**Bone Marrow**
- Tissue in the center of bones that is responsible for making blood cells, including white blood cells.

**White blood cells**
- White blood cells—including macrophages, dendritic cells, and lymphocytes—are the cellular actors of immunity.

**Tonsils**
- Structures at the back of the throat that sample bacteria and viruses that enter the body through the mouth or nose.

**Lymph nodes**
- Small, bean-shaped structures located throughout the body that filter lymph fluid: where immune cells are alerted to the presence of pathogens or cancer.

**Spleen**
- Fist-sized organ located in the upper-left part of the abdomen, containing white blood cells that fight infection and cancer.

**Lymphatic vessels**
- Thin-walled tubes that collect and transport lymph fluid throughout the body.
The Cells of the Immune System: The “Soldiers” in our Army

- Dendritic Cell
- Monocyte
- Neutrophil
- B Cell
- Natural Killer Cell
- T Cell
- Macrophage
Adaptive Immune Responses Against Cancer

Cancer Cell (being engulfed)

Antigen-Presenting Cell (e.g., Dendritic Cell)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)

Tumor Antigens
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)

Tumor Antigen (bound by MHC1)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)

Tumor Antigen (bound by MHC1)

T Cell Receptor (TCR)
Adaptive Immune Responses Against Cancer

Antigen-Presenting Cell (e.g., Dendritic Cell)
Antigen-Presenting Cell (e.g., Dendritic Cell)
Adaptive Immune Responses Against Cancer

Cancer Cell

Activated “killer” T Cell
Adaptive Immune Responses Against Cancer
Adaptive Immune Responses Against Cancer

Cancer Cell

Activated “killer” T Cell

CANCER CELL ELIMINATED!
Activated "killer" T Cell

Cancer Cell

PDL1 - PD1

Immune Checkpoints Can Suppress Immune Responses
Immune Checkpoints Can Suppress Immune Responses

Cancer Cell

Activated “killer” T Cell

PDL1 - PD1
Normally, **PDL1-PD1** leads to T cell “exhaustion”
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated "killer" T Cell

PD-1/PD-L1 Checkpoint Inhibitors
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

- Cancer Cell
- Activated “killer” T Cell
Activated “killer” T Cell Can Promote Anti-Cancer Activity
Activated “killer” T Cell

Cancer Cell

PD-1/PD-L1 Pathway Blocked!

Checkpoint Immunotherapy Can Promote Anti-Cancer Activity
Checkpoint Immunotherapy Can Promote Anti-Cancer Activity

Cancer Cell

Activated “killer” T Cell

CANCER CELL ELIMINATED!
Adoptive T Cell Immunotherapy

1. Isolation

2. Activation

3. Expansion

4. Re-infusion
Adoptive T Cells In Action (Against Melanoma)
Equip T cells with new, cancer-targeting TCR
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

CARs enable MHC-independent targeting & killing!
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

CARs enable MHC-independent targeting & killing!
CAR T Cell Immunotherapy (Chimeric Antigen Receptor)

CARs enable MHC-independent targeting & killing!
• Viruses can alter our cells’ DNA, by inserting their own genetic material
• Impaired defenses make tumor cells more susceptible to infection
AFTER INJECTION:
1) Viruses cause tumor cells to “burst” & release antigens
2) Immune cells uptake & present tumor antigens
3) Stimulates adaptive, and potentially systemic, immune responses
Reprogramming Oncolytic Viruses To Enhance Anti-Tumor Activity

(+) INSERT Immune-stimulating genes

(—) REMOVE Disease-causing genes (selective targeting of tumors)
Cancer Vaccines

Tumor Antigens
(provided by vaccine)
Cancer Vaccines

Dendritic cell

Tumor Antigens (provided by vaccine)
Cancer Vaccines

Dendritic cell
Cancer Vaccines

Activated "Killer" T Cell

Dendritic cell
Vaccine-Induced Elimination of Cancer Cells

Cancer Cell

Activated “killer” T Cell
Activated “killer” T Cell Vaccine-Induced Elimination of Cancer Cells
Personalized Neoantigen Vaccine Trial
Challenges in Cancer Immunotherapy

• Discovering and validating new biomarkers to help doctors predict which patients will respond to which immunotherapies

• Determining the best way to combine immunotherapies with each other as well other treatments to extend immunotherapy’s benefits for more patients

• Learning how to decouple side effects of immunotherapy from benefit
Why have most responses been modest and why are some cancers refractory to immunotherapy?

1. Cancers upregulate molecules to turn off immune cells
Why have most responses been modest and why are some cancers refractory to immunotherapy?

1. Cancers upregulate molecules to turn off immune cells

2. Cancers secrete chemicals to turn off the immune system
1. Cancers upregulate molecules to turn off immune cells
2. Cancers secrete chemicals to turn off the immune system
3. Cancers recruit suppressive cells to inactivate/block the immune response

Why have most responses been modest and why are some cancers refractory to immunotherapy?

- CD3 (T cell)
- CD8 (cytotoxic T cell)
- CD68 (macrophage/microglia)
- DAPI (nuclear)
Panel Discussion

LATEST RESEARCH UPDATES

Panelist
Jianjun Gao, M.D., Ph.D.
Genitourinary cancer

Panelist
Valentina Hoyos Velez, M.D.
Breast cancer

Panelist
Andrew Sikora, M.D., Ph.D.
Head and neck cancer

Moderator
Adi Diab, M.D.
Melanoma
Immunotherapy Patient Perspective

Dale Biggs
Skin Cancer Veteran

#CRIsummit
Lunch and Networking
Brian Brewer
Cancer Research Institute

LEARN ABOUT CLINICAL TRIALS
What Are Clinical Trials?

• Research studies that involve people

• Designed to answer specific questions about new and existing treatments

• Aim to improve treatments and the quality of life for people with disease
Getting from Discovery to Approval

Pre-Discovery
- ~5,000–10,000 Compounds
- 3–6 Years

Drug Discovery
- 250

Preclinical
- 5

Clinical Trials
- Phase 1
- Phase 2
- Phase 3
- Number of Volunteers: 20–100, 100–500, 1,000–5,000
- 6–7 Years

FDA Review
- NDA Submitted
- 0.5–2 Years

Scale-Up to Mfg.

Post-Marketing Surveillance
- INDEFINITE

Source: AppliedClinicalTrials.com
What Are Clinical Trial Phases?

**Phase 1**

Is the treatment safe?

- Purpose:
  - First study in humans
  - Find best dose, delivery method, and schedule
  - Monitor for side effects
  - Determine safety

- Number of people: 20-100

**Phase 2**

Does it work?

- Purpose:
  - Look for effect on specific type(s) of cancer
  - Continue monitoring for side effects and safety

- Number of people: 100-500

**Phase 3**

Does it work better?

- Purpose:
  - Compare new treatment (or new use of a treatment) with current standard treatment
  - Determine risk vs. benefit

- Number of people: 1,000-5k+

### Pros and Cons of Clinical Trials

<table>
<thead>
<tr>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
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<tbody>
<tr>
<td>Access to best possible care</td>
<td>Unknown side effects or risks</td>
</tr>
<tr>
<td>Receiving new drugs before they’re widely available</td>
<td>Unknown benefits—drugs may not work as intended</td>
</tr>
<tr>
<td>Close monitoring by medical team</td>
<td>Not all patients may benefit</td>
</tr>
<tr>
<td>Chance to play active role in healthcare and research</td>
<td>Frequent tests and clinic visits</td>
</tr>
<tr>
<td>Help future generations</td>
<td>Possible need to travel to trial sites</td>
</tr>
</tbody>
</table>

*Patient Resource*, “Understanding Clinical Trials: A Guide for Patients and Their Families”
Questions to Ask Before Volunteering

• Why is this trial being done?
• Why is it believed that the treatment being studied may be better than the standard treatment?
• What are my other options (standard treatments, other trials)?
• How did patients do in any previous studies of this treatment?
• How will the doctor know if treatment is working?
• How long will the trial last?

Questions to Ask Before Volunteering

• Can I continue to receive this treatment after the trial ends?
• What kinds of procedures or tests are involved?
• What impact will the trial have on my daily life?
• Will I have to travel for treatment? Will I be compensated?
• How often will I need to travel to receive treatment?
• Will I be hospitalized as part of the trial?
• What costs (if any) will be my responsibility to pay?

Getting into a Clinical Trial Isn’t Always a Given

Trials are designed to ask specific questions, and must adhere strictly to entry criteria to ensure data is accurate and meaningful.

This also helps ensure patients who could be made worse by treatment are not exposed to the risk.

Common criteria include:

- cancer type or stage
- treatment history
- genetic factors
- age
- medical history
- current health status
Clinical Trials: Myth versus Fact

I might only get placebo ("sugar pill") instead of treatment.

Placebos are rarely used and never given in the absence of some form of treatment.

Clinical Trials: Myth versus Fact

**MYTH**
Trials are only for people who have run out of treatment options (a “last resort”).

**FACT**
Clinical trials are designed for people with cancer of all types and stages.

I need to travel to a large hospital or cancer center to participate in a clinical trial.

Trials take place at local hospitals, cancer centers, and doctors’ offices in all parts of the country, in both urban and rural areas.

Clinical Trials: Myth versus Fact

**MYTH**

My health insurance doesn’t cover the cost of care in a clinical trial.

**FACT**

Doctor visits, hospital stays, and certain testing procedures may be covered by insurance. Research costs are typically covered by the trial sponsor.

Clinical Trials: Myth versus Fact

**MYTH**

Signing a consent form “locks” me into staying in a trial.

**FACT**

Fact: You are free to change your mind for any reason about participating in a trial anytime before or during a trial.

Clinical Trials: Myth versus Fact

**MYTH**
I will be made to feel like a “guinea pig” experiment.

**FACT**
Fact: The overwhelming majority of trial participants say they were treated with dignity and respect, and report having had a positive experience in a trial.

**Clinical Trials: Myth versus Fact**

**MYTH**

Clinical trials aren’t safe.

**FACT**

Fact: Safeguards including an Institutional Review Board, Data and Safety Monitoring Board, and an ongoing informed consent process ensure patients’ rights and safety are protected.

Informed consent = having all the facts before and during a trial

- Study purpose
- Length of time of the study
- Predictable risks
- Possible benefits
- Expectations
- Patient’s rights
- Treatment alternatives
- Patient health monitoring
- Safeguards in place
- How to withdraw from study

Be bold in asking for details. It’s YOUR treatment plan.
How Can I Find a Clinical Trial?

- Ask your doctor
- Ask another doctor if necessary...
- Contact a patient advocacy organization
  - Seek assistance from a clinical trial navigator, if offered
  - CRI Clinical Trial Finder: 1 (855) 216-0127
- Search online
  - [https://www.cancerresearch.org/patients/clinical-trials](https://www.cancerresearch.org/patients/clinical-trials)
  - [https://clinicaltrials.gov/](https://clinicaltrials.gov/)
Lunch & Networking
<table>
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<tr>
<th>Moderator</th>
<th>Panel</th>
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BREAKOUT SESSIONS
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<tr>
<td><strong>General Immunotherapy</strong></td>
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<tr>
<td>Adi Diab, M.D.</td>
</tr>
<tr>
<td><strong>Room 5</strong></td>
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<tr>
<td><strong>Genitourinary Cancer</strong></td>
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<tr>
<td>Jianjun Gao, M.D., Ph.D.</td>
</tr>
<tr>
<td><strong>Room 4</strong></td>
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<tr>
<td><strong>Head and Neck cancer</strong></td>
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<tr>
<td>Andrew Sikora, M.D., Ph.D.</td>
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<tr>
<td><strong>Room 4</strong></td>
</tr>
<tr>
<td><strong>Breast cancer</strong></td>
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<tr>
<td>Valentina Hoyos Velez, M.D.</td>
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<td><strong>CPB Telehealth</strong></td>
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CANCER RESEARCH INSTITUTE
IMMUNOTHERAPY PATIENT SUMMIT

Houston October 26, 2019