San Francisco June 30, 2018
Brian Brewer
Cancer Research Institute

WELCOME
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This event is made possible with generous support from:

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- Alta Bates Summit Comprehensive Cancer Center (Sutter Health)
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- Mark M. Davis Lab at Stanford Medicine
- Parker Institute of Cancer Immunotherapy
- ThyCa Support Group of Fresno, California
- Women’s Cancer Resource Center
- UCSF Helen Diller Family Comprehensive Cancer Center
Speakers

Scientific Experts

Lewis Lanier, Ph.D.
University of San Francisco, California

Kara Davis, D.O.
Stanford University Medical Center

Terence Friedlander, M.D.
University of San Francisco, California

David Miklos, M.D., Ph.D.
Stanford University Medical Center

Katy Tsai, M.D.
University of San Francisco, California

Patient Experts

Sharon Birzer
Diffuse Large B Cell Lymphoma (DLBCL)

Kelly Brooks
Melanoma

Kristin Kleinhofer
Acute Lymphoblastic Leukemia (ALL)

Caregiver Perspective

Benny Juarez
Caregiver
## Schedule of Events

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 am</td>
<td>Registration and networking</td>
</tr>
<tr>
<td>10:00 am</td>
<td>Program commences</td>
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<tr>
<td></td>
<td><strong>WELCOME</strong></td>
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<tr>
<td></td>
<td>Brian Brewer</td>
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<tr>
<td>10:15 am</td>
<td><strong>HEAR FROM THE EXPERTS</strong></td>
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<tr>
<td></td>
<td>Immunotherapy Basics</td>
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<tr>
<td></td>
<td>Lewis Lanier, Ph.D.</td>
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<tr>
<td>10:30 am</td>
<td><strong>PANEL: RESEARCH UPDATES</strong></td>
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<td>Moderator</td>
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<td>Lewis Lanier, Ph.D.</td>
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<td>Panelists</td>
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<td>Katy Tsai, M.D.</td>
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<tr>
<td>11:30 am</td>
<td><strong>PATIENT PERSPECTIVE</strong></td>
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<tr>
<td></td>
<td>Choose Hope, a message from</td>
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<tr>
<td></td>
<td>Kristin Kleinhofer, leukemia survivor</td>
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<tr>
<td>12:00 pm</td>
<td>Lunch and networking</td>
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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>10:00 pm</td>
<td><strong>LEARN ABOUT CLINICAL TRIALS</strong></td>
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<tr>
<td></td>
<td>Brian Brewer</td>
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<tr>
<td>11:15 pm</td>
<td><strong>IMMUNOTHERAPY PATIENT PANEL</strong></td>
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<td>Kelly Brooks</td>
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<td>Morey W.</td>
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<td>2:15 pm</td>
<td><strong>BREAKOUT SESSIONS</strong></td>
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<td>Your choice of a deeper dive Q&amp;A with our experts</td>
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<td><strong>General Immunotherapy</strong></td>
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<td>Terence Friedlander, M.D.</td>
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<tr>
<td>3:45 pm</td>
<td>Program closes</td>
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<tr>
<td>9:00 am -</td>
<td><strong>CLINICAL TRIAL NAVIGATOR APPOINTMENTS</strong></td>
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<tr>
<td>4:00 pm</td>
<td>Appointments will be available all day. If you didn’t register for an</td>
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<td>appointment, but you’re interested in speaking with a navigator,</td>
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<td>please check with the registration desk.</td>
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</table>
Fundamentals of Cancer Immunotherapy

Lewis L. Lanier, Ph.D.
American Cancer Society Professor and Chair, Department of Microbiology and Immunology, UCSF
Leader, Cancer Immunology Program, UCSF Helen Diller Family Comprehensive Cancer Center
J. Michael Bishop, MD, Distinguished Professor in Microbiology and Immunology, UCSF
Director, Parker Institute for Cancer Immunotherapy, UCSF
Scientific Advisory Council Member, Cancer Research Institute
Immunotherapy: The New Darling of Oncology

*Science’s 2013 Breakthrough of the Year*

*ASCO’s Top Advance of 2016, 2017, and 2018 (cancer immunotherapy, CAR T cell therapy, and adoptive cell immunotherapy)*

*The New York Times*

*Patient’s Cells Deployed to Attack Aggressive Cancer*

*The Washington Post*

*New therapies raise hope for a breakthrough in tackling cancer*
William B. Coley, M.D.

- Noted a case of sarcoma that became cured due to a bacterial infection
- In 1891, deliberately infected sarcoma patient with *Strep. pyogenes*
- By 1893, had developed a mixture of bacterial toxins rather than live bacteria – “Coley Toxins”
- Considered the first immunologic therapy for cancer
A New Weapon Against Cancer

Cancer

Cut ‘em
Burn ‘em
Poison ‘em

We now have a new weapon against cancer
.... Your immune system
Outline

• What Are T Cells?
• Activating T Cells In Tumors
• Activating T Cells Outside of Tumors
• Combination Immunotherapy
• Biomarkers
Immune Recognition of Cancer

Cytolytic T Lymphocyte (CTL)

Class I MHC (HLA A, B) + peptide

Processing

Tumor Cell
Two General Strategies to Help the Immune System to Destroy Cancer

• Boost the offense
  – Increase the number and function of T cells capable of recognizing tumor cells

• Block the defense
  – Interfere with inhibitory pathways in the tumor site that resist T cell attack
Monoclonal antibodies that block inhibitory receptors on immune cells to enhance their function

They target the immune system – not the cancer

“Checkpoint Blockade”
Inhibitory PD-1 receptors on T Cells block their response to tumors by engaging PD-1 ligand in the tumor.

"Hot Tumor" has T cells (red) infiltrating

"Cold Tumor" No T cells

PD-1 ligand in tumors (brown) blocks action of T cells
Checkpoint Inhibitors – Antibodies to PD-1 Receptor on T cells or PD-1 Ligand in Tumor

PD-L1/PD-1 binding inhibits T cell killing of tumor cell

Blocking PD-L1 or PD-1 allows T cell killing of tumor cell
Genetic mutations

- Genetic mutations are frequent in some tumors (e.g. melanoma, lung, etc.), and rare in others.
- More mutations → more shots on goal for T cells
Clinical Activity of Anti-PD-1 in Metastatic Melanoma

- FDA approved in 2014 for melanoma
- Now in many cancer types (lung, bladder, kidney, cervical, stomach, head and neck, lymphoma, …….) and counting
New immunotherapy drug behind Jimmy Carter's cancer cure

Former president given pembrolizumab, one of the most promising new drugs in the treatment of cancer
What are Biomarkers?

**Diagnostic**
- What type does the patient have?

**Prognostic**
- What is the patient's expected outlook?

**Predictive**
- Is the patient likely to respond to immunotherapy?

**Therapeutic**
- Is the immunotherapy working?

**Safety**
- Have side effects arisen?

**Long-Term Monitoring**
- Is the cancer in the process of relapsing?
T Cell-Infiltrated Tumors Contain MULTIPLE Inhibitory Pathways

- Multiple “defense” pathways are blocked by tumors once T cells enter.

- Suggests that blocking two pathways together might be superior.

Cytotoxic CD8⁺ T cells

Suppressor FoxP3⁺ T cells

PD-L1 ligand in tumor – binds PD-1 inhibits T cells

“Hot Tumor”

“Cold Tumor”
So Many Targets, So Little Time!

Hit the Gas!

Block the Brakes!

T cell stimulation

Activating receptors
- CD28
- OX40
- GITR
- CD137
- CD27
- HVEM

Inhibitory receptors
- CTLA-4
- PD-1
- TIM-3
- BTLA
- VISTA
- LAG-3

Agonistic Abs

Blocking Abs

Nature. 2011 480:480-9
Increasing Responses By Combination Therapy

Combined PD-1 and CTLA-4 checkpoint blockade in melanoma patients

- PFS among BRAF MT patients (8.5 mo for NIVO + IPI, 2.7 mo for IPI monotherapy) was similar to that observed among BRAF WT patients

*HR = hazard ratio*
T Cell Adoptive Transfer for Cancer Therapy

- T cells are isolated from tumor site or blood
- Expanded in laboratory
- Can be engineered to recognize new targets
- T cells are re-introduced back to the patient, usually with other agents

Yee C. 2009 ASCO Educational Book
Isolate patient’s peripheral blood T cells

Lentivirus transduced with “CAR” (chimeric antigen receptor)

CAR – anti-CD19 antibody fragment fused to intracellular domains of potent T cell signaling subunits

Re-infuse “CAR”-modified T cells into patient

Successful for treating children with B cell malignancies
In Girl’s Last Hope, Altered Immune Cells Beat Leukemia

By DENISE GRADY  DEC. 9, 2012

Emma Whitehead, with her mother, Karl. Last spring, Emma was near death from acute lymphoblastic leukemia but is now in remission after an experimental treatment at the Children’s Hospital of Philadelphia.

Jeff Swensen for The New York Times
Successful Preventative Vaccination Against Virus-Induced Cancers

• Vaccine to feline leukemia virus for cats
• Vaccine to herpes virus (Marek’s virus) in chickens
• Vaccine to hepatitis B in humans to prevent liver carcinoma
• Vaccination to human papillomavirus prevents cervical cancer
A decade on, vaccine has halved cervical cancer rate
Useful resources about cancer immunotherapy

What is Immunotherapy
[cancerresearch.org/patients/what-is-immunotherapy](cancerresearch.org/patients/what-is-immunotherapy)

cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html

Immunotherapy by Cancer Type
[cancerresearch.org/immunotherapy/cancer-types](cancerresearch.org/immunotherapy/cancer-types)

Local Support Services
[bcconnections.org/](bcconnections.org/)

Additional Information
Panel Discussion

LATEST RESEARCH UPDATE
<table>
<thead>
<tr>
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Kristin Kleinhofer
Leukemia Survivor

PATIENT PERSPECTIVE
My Journey of HOPE

ONCE YOU CHOOSE HOPE ANYTHING'S POSSIBLE
How did I get to Immunotherapy?
Enjoying Life.....
2014

February & March

“Once you choose hope, anything’s possible.”
~Christopher Reeve
Now, What to Do?
Now, What to Do?
2014
June - August
2014
November & December
Immunotherapy Treatment
27 out of 29 (93%) A.L.L. patients Experience Sustained Remissions
January & February
Transplant Journey Begins...
Bucket List Continues...
How to Make it Through the Dark Times?

- Choose How We Want to Live Each Day
- Take It Day by Day, Live in the Present
- Gratitude for Life’s Blessings
- Positive Attitude
- Acceptance
- Knowledge is Power
- Close Partnership with your Medical Team
- Strong Support System, Stronger Together
- Inner Strength & Resilience to Push Forward
- Faith, Spiritual Life
- Humor
- Cancer Resources
- Choosing
Immunotherapy Treatments offer HOPE

- Clinical Trials are where Revolutionary Breakthroughs Begin
- Standard Treatments Exhausted or No Longer Work
- Possible Gift of More Time
- Furthering Research to Help Future Cancer Patients
- Less Toxicity & More Targeted Therapy
- Changing the Cancer Treatment Landscape
- Profound Impact on what Cancer Care will mean in Coming Years
- Exciting time as more Discoveries are made and Perfected
Cancer will not be a Word we are afraid of. No more harsh side effects, no more relapses, just our body’s immune system being led to harness its wisdom to conquer Cancer through Immunotherapy.

Just Imagine.

“Once you Choose Hope, Anything is Possible.”
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
What Are Clinical Trial Phases?

Is the treatment safe?
Phase 1
Purpose:
- First study in humans
- Find best dose, delivery method, and schedule
- Monitor for side effects
- Determine safety
Number of people: 20-100

Does it work?
Phase 2
Purpose:
- Look for effect on specific type(s) of cancer
- Continue monitoring for side effects and safety
Number of people: 100-500

Does it work better?
Phase 3
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>
</tr>
</thead>
<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>
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<tr>
<td>Chance to play active role in healthcare and research</td>
<td>Frequent tests and clinic visits</td>
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<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
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.

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

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.

A Word About Informed Consent

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://clinicaltrials.gov/
Panel Discussion

IMMUNOTHERAPY
CLINICAL TRIALS
<table>
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<tr>
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</tr>
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<tbody>
<tr>
<td>Brian Brewer</td>
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<td>Breakout Rooms</td>
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<tr>
<td><strong>Pediatric Blood Cancers</strong></td>
<td><strong>Continental 1</strong></td>
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<td><strong>Melanoma</strong></td>
<td><strong>Continental 2</strong></td>
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<td><strong>Bladder Cancer</strong></td>
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<td><strong>General Immunotherapy</strong></td>
<td><strong>Continental 4</strong></td>
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<tr>
<td>Lewis Lanier Ph.D.</td>
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</tbody>
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**Image:**
- Breakout Rooms header
- Breakout room topics: Pediatric Blood Cancers, Melanoma, Bladder Cancer, General Immunotherapy
- Speakers: Kara Davis, D.O., Katy Tsai, M.D., Terence Friedlander, M.D., Lewis Lanier Ph.D.
- Continental rooms: 1, 2, 3, 4

**Logo:**
- Cancer Research Institute
- Immunotherapy Patient Summit

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**Note:**
- The image contains a table outlining the breakout rooms for a cancer research event.
- Each room is dedicated to a specific topic within the field of oncology.
- The speakers for each session are listed alongside their respective topics.
- The layout is designed to be clear and easy to read, with a clean, professional appearance.

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**Detailed Description:**
- The table is divided into three columns: Topic, Speaker, and Room.
- The topics cover a broad spectrum of oncology, from pediatric blood cancers to general immunotherapy.
- Each speaker's name and their designated room are clearly stated.
- The layout is simple yet informative, with a focus on readability and clarity.
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- UCSF Helen Diller Family Comprehensive Cancer Center
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 & instructions on how to use our [Clinical Trial Finder service](http://www.clinicaltrialfinder.com).
SAN FRANCISCO JUNE 30, 2018

CANCER RESEARCH INSTITUTE
IMMUNOTHERAPY PATIENT SUMMIT

SAN FRANCISCO JUNE 30, 2018