The CIMAC-CIDC Network
(Cancer Immune Monitoring and Analysis Centers & Cancer Immunologic Data Commons)

Helen Chen and Magdalena Thurin

NCI-DCTD

<table>
<thead>
<tr>
<th>CIMAC centers:</th>
<th>DCTD:</th>
<th>CBIIT:</th>
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<tbody>
<tr>
<td>• MD Anderson Cancer Centers</td>
<td>Jeff Abrams</td>
<td>David Patton</td>
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<td>• Stanford University</td>
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<td>• Dana Farber Cancer Institute</td>
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<td>• Icahn School of Medicine at Mount Saini</td>
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<td>CIDC Site</td>
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<td>• Dana Farber Institute</td>
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CTEP: Helen Chen, Elad Sharon, Howard Streicher, Minkyung Song, Bill Merritt

CDP: Magdalena Thurin (Program Director)

BRP: Yingdong Zhao, Laura Yee

TRP: Andrew Hruszkewycz

Administrative: Rebecca Enos; Melissa Bowman

NIH NATIONAL CANCER INSTITUTE
What is needed to accelerate further development of immunotherapy?

• Basic science discovery

• Biomarker strategies suitable for the complexity of immunotherapy

• Databases and Data Commons for clinically annotated tumor and immune profiling data to enable analysis across trials and organizations
DCTD-supported trial Networks represent a rich public resource to address important clinical and biomarker questions

• > 100 new immunotherapy trials since 2010
  o 20+ Phase 3 trials (metastatic or adjuvant)
  o 20+ Randomized phase 2 trials (advanced or neoadjuvant)
  o Novel combinations
  o Rare tumors and special populations (Pediatric, HIV+ patients)

• > 20 I-O agents under CTEP IND, and targeted agents relevant to combinations

• Established infrastructure for clinical data collection AND biorepository

However, a systematic approach to correlative studies is needed to maximize the translational outcome of individual trials and enhance the collective power of analysis across trials
A standing network of assay laboratories and a data commons to provide tumor-immune profiling using standardized or compatible platforms

- **Immediate goal** – Supporting NCI-funded immunotherapy trials
- **Longer term goal** - Building a framework that will evolve into a sustainable I-O data resource serving the larger research community

- A Cancer Moonshot Initiative, funded through the **NCI Cooperative Agreements (U24)** (Awarded in September 2017)

- Partnership with 12 pharmaceutical companies through the **FNIH PACT Initiative** (Partnership for Accelerating Cancer Therapies) ([Press release October 2017](https://www.cancer.gov/news-events/press-releases/2017/nci-partnership-accelerating-cancer-therapies)).
Partnership for Accelerating Cancer Therapies (PACT)

Press release - October 12, 2017. NIH partners with 11 leading biopharmaceutical companies to accelerate the development of new cancer immunotherapy strategies for more patients
The CIMAC-CIDC Network (Launched September 2017)

**CIMACs**

1. **The University of Texas MD Anderson Cancer Center**  
   PIs: Ignacio Wistuba* and Chantale Bernatchez

2. **Icahn School of Medicine at Mount Sinai**  
   PI: Sacha Gnjatic

3. **Dana-Farber Cancer Institute**  
   PIs: Catherine Wu and F. Stephen Hodi

4. **Stanford University**  
   PIs: Holden Maecker and Sean Bendall

**CIDC**

- **Dana-Farber Cancer Institute**  
  PIs: Xiaole Shirley Liu and Ethan Cerami
Scope of work under the NCI funding
(~$55M over 5 years)

• Each CIMAC is a multidisciplinary team (clinical, IO, technical, statistical and informatics expertise)
  • In conjunction with CIDC, will work on correlative studies from study design to bioassays and data analysis.

  ▪ Eligible trials for use of the CIMAC resources – NCI funded Early trials (Phase 1 and phase 2) involving immunotherapy
    ▪ CTEP Trial Networks (NCTN, ETCTN, CITN, ABTC, PBTC)
    ▪ NCI Grant-supported trials (P01, R01, SPORE Programs etc)

  ▪ ~600 patient/timepoint/year for 5 years for comprehensive profiling (More pts if not all assays are feasible with available tissues)

* The scope is expanded with the PACT funding (infrastructure and PACT-identified trials)
Assays/Platforms in CIMACs

(Tier 1 assays) Blue text
(Tier 2 assays) Black text

Tissue based Imaging
- Multiplex immunohistochemistry –
- Conventional immunohistochemistry –
- FISH DNA –
- Multiplexed Ion-Beam Imagining (MIBI) –

Cell Profiling
- Mass Cytometry (CyTOF) –
- High-dimensional flow cytometry –
- ELISpot –

Cytokines/Serum Analytes
- O-link serum cytokine analysis -
- Luminex –
- Seromics – ELISA/Grand serology -
- MesoScale Discovery –

Sequencing
- Whole Exome Sequencing – DFCI, MDACC
- RNA-Seq – DFCI, MDACC
- NanoString – MDACC, DFCI, MSSM
- TCR/BCR clonality –,
- Single-cell TCRseq -
- HLA-Seq, Epitope prediction –
- Cell-free DNA (circulating tumor DNA) –,
- HTG-EdgeSeq (gene expression) –
- Single-cell transcriptome –

Other:
- Neoantigen Prediction –
- Mass spectrometry epitope detection [
- Epigenomics (ATAC-Seq) –
- Microbiome (16S Deep Sequencing) –Exosomes
- CRISPR []
A. Overall Vision of CIDC

- **Data Standards**

- **Central Data Repository** with censuses pipelines (Genomics, transcriptomics, proteomics, flow, IHC)

- **Data integration** with clinical data, to enable correlative analysis

- Role-based, time-controlled **data access** with web visualization by collaborating CIMAC and clinical team... and in the future, outside community

**Figure 1**: Overall vision of Cancer Immunologic Data Commons (CIDC).
CIMACs-CIDC Network Structure

**Laboratory Coordinating Committee (LCC)**

- **CIMAC 1**
  - MD Anderson Cancer Center
- **CIMAC 2**
  - Icahn School of Medicine
- **CIMAC 3**
  - Dana Farber Cancer Institute
- **CIMAC 4**
  - Stanford University

**Any CIMAC may work with a given trial based on expertise and workload**

**PACT Trials**
- Review by JSC (PACT partners)
- • SWOG, • ECOG-ACRIN

**CIDC** (Dana Farber Cancer Institute)
- • CITN/Ped-CITN
- • COG
- • PBTC
- • NCI Grant supported trials (SPORE, R01, P01 ...)

**ALL CIMACs can work with any trial networks, depending on specific needs, expertise and workload**

**Each CIMAC will be in a Primary Alignment with 1-2 trial Networks** – to facilitate scientific planning, Biobank interactions

**A given CIMAC may perform a specific assay for all trials**
Oversight of CIMAC-CIDC Functions

Laboratory Coordinating Committee (LCC)

**Leader:** Ignacio Wistuba  
**Co-leaders:** Catherine Wu, Holden Maecker, Sacha Gnjatic, Shirley Liu

**NCI Staff,** Subject experts when appropriate  
**PACT** representatives

Clinical Trials WG  
**Network Leads:** Stephen Hodi  
**NCI Leader:** Helen Chen

Biobank WG  
**Network Leads:** Ignacio Wistuba, Ethan Cerami  
**NCI Leaders:** David Patton, Irina Lubensky  
**PACT** representatives

Assays/Platforms WG  
**Network Leads:** Holden Maecker, Catherine Wu, Sacha Gnjatic  
**NCI Leader:** Magdalena Thurin  
**PACT** representatives

Software/Database WG  
**Network Leads:** Ethan Cerami  
**NCI Leader:** David Patton  
**PACT** representatives

Bioinformatics/Statistics WG  
**Network Leads:** Shirley Liu  
**NCI Leaders:** Yingdong Zhao  
**PACT** representatives

Non-CTEP Network Trails WG  
**NCI Leader:** Min Song
CIMAC will work as collaborators with the Clinical Trial Team

1. Correlative study planning and proposals - to be jointly developed by CIMAC and Clinical trial team
2. Specimen accession – multiple biorepositories to any of the CIMACs
3. Bioassays – multiple platforms
4. Database upload and access at CIDC - for biomarker data; specimen tracking; and required clinical data elements
5. Data analysis and Publication – data analysis will be done collaboratively between the Trial Team and CIMAC
Working group progress
CLINICAL TRIAL WG

Co-Chairs: Stephen Hodi
NCI Leader: Helen Chen, with Elad Sharon and Howard Streicher

Tasks - To identify scientific opportunities and develop correlative study plans with trial investigators

- Established the trial intake process
- Selected pilot projects to “test” the network
Intake Form (Proposals for Correlative Studies in Collaboration With CIMAC)

Submission by Trial PIs or the Groups

- CIMAC Working Groups Review
  - LCC Approval
- CTEP PRC Review/Approval

Initial prioritization by CTEP

• Use of the CIMAC-CIDC resource is voluntary. However all proposals required review and approval by CIMAC and CTEP

• Prioritization will be based on strength of the hypothesis and appropriateness of the trial contexts as well as potential contribution to the field.

• If approved, CIMAC will work with the trial team as collaborators.

• Provision of clinical data (including outcome data) to CIDC is required to enable correlative analysis

Multiple proposals for CIMAC collaboration have been submitted from the trial networks (CITN, ETCTN, ECOG, SWOG, NRG, Alliance)
## Pilot Projects

... to test the CIMAC process from sample accession to assays to data analysis

5 trials from four different networks, with completed cohorts ready for biomarker studies

<table>
<thead>
<tr>
<th>Trial</th>
<th>Current Status</th>
<th>SparkNotes</th>
<th>Lead CIMAC</th>
<th>Assays</th>
<th>Scientific objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Closed to Accrual</td>
<td>Randomized IL-7 or observation after vaccine</td>
<td>Stanford</td>
<td>Blood- ATAC-Seq, CyTOF, TCR-Seq</td>
<td>Impact of IL-7 on T cell function/phenotype</td>
</tr>
<tr>
<td>2</td>
<td>Active</td>
<td>Phase I Anti-CTLA or anti-PD1 in AML after allotransplant</td>
<td>DFCI</td>
<td>Blood - CyTOF, Tumor - WES, RNASeq; IHC Singleplex, Multiplex IF TCR-Seq</td>
<td>Immune modulation on allo and host T cells, Predictive markers</td>
</tr>
<tr>
<td>3</td>
<td>Active</td>
<td>Phase 2 High or Low dose RT in combination with anti-PD1/CTLA-4 in CRC and NSCLC</td>
<td>DFCI</td>
<td>Blood - CyTOF, Olink Tissue – WES, RNASeq, IHC Singleplex, Multiplex</td>
<td>PD effects of RT/CPI on TME/blood (HD, LD), Predictive markers</td>
</tr>
<tr>
<td>4</td>
<td>Active</td>
<td>Phase I Study with an Expansion Cohort of the anti-CTLA-4 and CD30 ADC in HD</td>
<td>Mt. Sinai</td>
<td>Blood - CyTOF, Olink</td>
<td>PD effects</td>
</tr>
<tr>
<td>5</td>
<td>Active</td>
<td>Phase 2 DART: Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors</td>
<td>MDACC</td>
<td>Blood - CyTOF, Olink, Tumor - RNA-Seq, WES IHC Singleplex, Multiplex IF</td>
<td>Genomics of rare tumors, Predictive markers</td>
</tr>
</tbody>
</table>
ASSAY & PLATFORM WORKING GROUP

Co-Chairs: Holden Maecker, Stanford
Sacha Gnajatic, Mt. Sinai
NCI Leader: Magdalena Thurin

- Biospecimen collection protocol (Near completion)
- Assay harmonization for Tier 1 (Ongoing)
- Discussion on Tier 2 and 3 assays

- Many assays available in all/most CIMAC sites will be harmonized
- Many assays unique to one or two CIMACs will not be harmonized
Harmonization of Tier 1 Assays

• These assays would be performed in most, if not all, CIMAC trials

• Standardization across trials is required to achieve uniformity of results
  • CyTOF [PBMC]: A core panel for all sites, uniformly labelled and lyophilized, cell preps provided across all CIMACs
  • RNA-seq and WES [tumor]: Two sites selected to lead (DFCI and MDACC)
  • Multiplex IHC [tumor]: DFCI, MSSM, MDACC
  • Immunoprofiling [serum]: Olink, MSSM
  • TCR/BCR clonality [tumor, PBMC]: all CIMACs
  • Single-cell TCR-seq [tumor]: Stanford, MSSM, DFCI
  • Gene expression profiling [tumor]: Nanostring, MDACC, DFCI

• Harmonization of some assays will not be done at all centers, unless throughput demands it

• All sites will use uniform pipelines established at CIDC for data processing
CIDC UPDATE
(SOFTWARE/DATABASE WG)

Shirley Liu
Ethan Cerami
James Lindsay
NCI Lead: David Patton
Bootstrapping the CIDC

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Phase 1: Use Public Data Sets to build the version 1.0 of CIDC infrastructure and bioinformatics platform (80% complete)

Phase 2: Enable the first DFCI Trial #10021, as concrete means to build version 1.1 of CIDC infrastructure and bioinformatics platform (currently scoping out).

Phase 3: Extend to all other pilot clinical trials with all other CIMACs.
The CIMAC-CIDC Network is an initiative of the NCI Cancer Moonshot that provides cutting-edge technology and expertise in genomic, proteomic, and functional molecular analysis to enhance clinical trials in cancer immune therapies.

CANCER IMMUNE MONITORING AND ANALYSIS CENTERS (CIMACS)

The four Cancer Immune Monitoring and Analysis Centers (CIMACS), at Dana-Farber Cancer Institute, Stanford University, MD Anderson, and Mount Sinai, will be responsible for providing a wide range of state-of-the-art analyses for genomic,
Summary

- CIMAC-CIDC Network is a standing infrastructure for cutting-edge technology and expertise in tumor/immune profiling and analysis to enhance the translational studies in immunotherapy trials.

- Pilot projects have been selected and more studies under review.

- **Work in progress**
  - Harmonization/standardization for tier 1 assays and selection tier 2-3 platforms
  - Database and informatics pipelines for key platforms and clinical data
  - Specimen tracking system across CIMACs and Biobanks and sites
  - Various agreements between CIMAC, investigators, trial networks, biobanks (data access, data sharing, MTA, Institutional Certificates, …)
  - …
Questions
**CIMAC Intake Forms**

CIMAC Intake Form for “Clinical Trial #”

(Proposal Version Mar 8, 2018)

**Proposal of Correlative Studies in Collaboration with the CIMACs-CIDC Network**

- **Cover sheet:** Trial Team, CIMAC Team
- **Study plan:** Biomarker objectives; Hypothesis; Method of analysis, Statistics
- **Biomarker table** (An example)

<table>
<thead>
<tr>
<th>Priority</th>
<th>Biomarker Name</th>
<th>Assay</th>
<th>Use (Integral or Exploratory) AND Purpose</th>
<th>Specimen Type/ Timing point</th>
<th>M/O Biopsies</th>
<th>Assay LAB</th>
<th>Funding Source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PD-L1 and TIL</td>
<td>IHC</td>
<td>• Integrated • MOA</td>
<td>• Tumor FFPE • Baseline, D8</td>
<td>M</td>
<td>CIMAC (1)</td>
<td>CIMAC</td>
</tr>
<tr>
<td>2</td>
<td>WES</td>
<td>NGS</td>
<td>• Exploratory • Correlation with response</td>
<td>• Tumor, PBL • Baseline</td>
<td>M</td>
<td>CIMAC (2)</td>
<td>CIMAC</td>
</tr>
<tr>
<td>3</td>
<td>Tumor Immune phenotyping</td>
<td>Tissue flowcytometry</td>
<td>• Exploratory • MOA</td>
<td>• Tumor Fresh • Baseline, D8</td>
<td>Optional</td>
<td>PI’s site</td>
<td>Grant xxx</td>
</tr>
</tbody>
</table>

- **Table for Specimen request and availability (If ongoing/completed trials)**