For CTAC Meeting, July 10, 2018

The CIMAC-CIDC Network

(Cancer Immune Monitoring and Analysis Centers & Cancer Immunologic Data Commons)

Helen Chen and Magdalena Thurin

NCI-DCTD

CIMAC centers:
- MD Anderson Cancer Centers
- Stanford University
- Dana Farber Cancer Institute
- Icahn School of Medicine at Mount Saini

CIDC Site
- Dana Farber Institute

DCTD: Jeff Abrams
CDP: Magdalena Thurin (**Program Director**)
CTEP: Helen Chen,
Elad Sharon
Howard Streicher ,
Minkyung Song
Bill Merritt

CBIIT: David Patton
BRP: Yingdong Zhao
Laura Yee,
TRP: Andrew Hruszkewycz
Administrative: Rebecca Enos;
Melissa Bowman

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CIMAC-CIDC
Immuno-Oncology
Biomarkers Network

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**
  - 20+ Phase 3 trials (metastatic or adjuvant)
  - 20+ Randomized phase 2 trials (advanced or neoadjuvant)
  - Novel combinations
  - 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**

CIMAC-CIDC
Immuno-Oncology
Biomarkers Network

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

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

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- 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)*.

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**

FNIH
Foundation for the National Institutes of Health

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

(Status as of March 2018)
- Blue text = Tier 1 assays
- Black text = Tier 2 assays

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

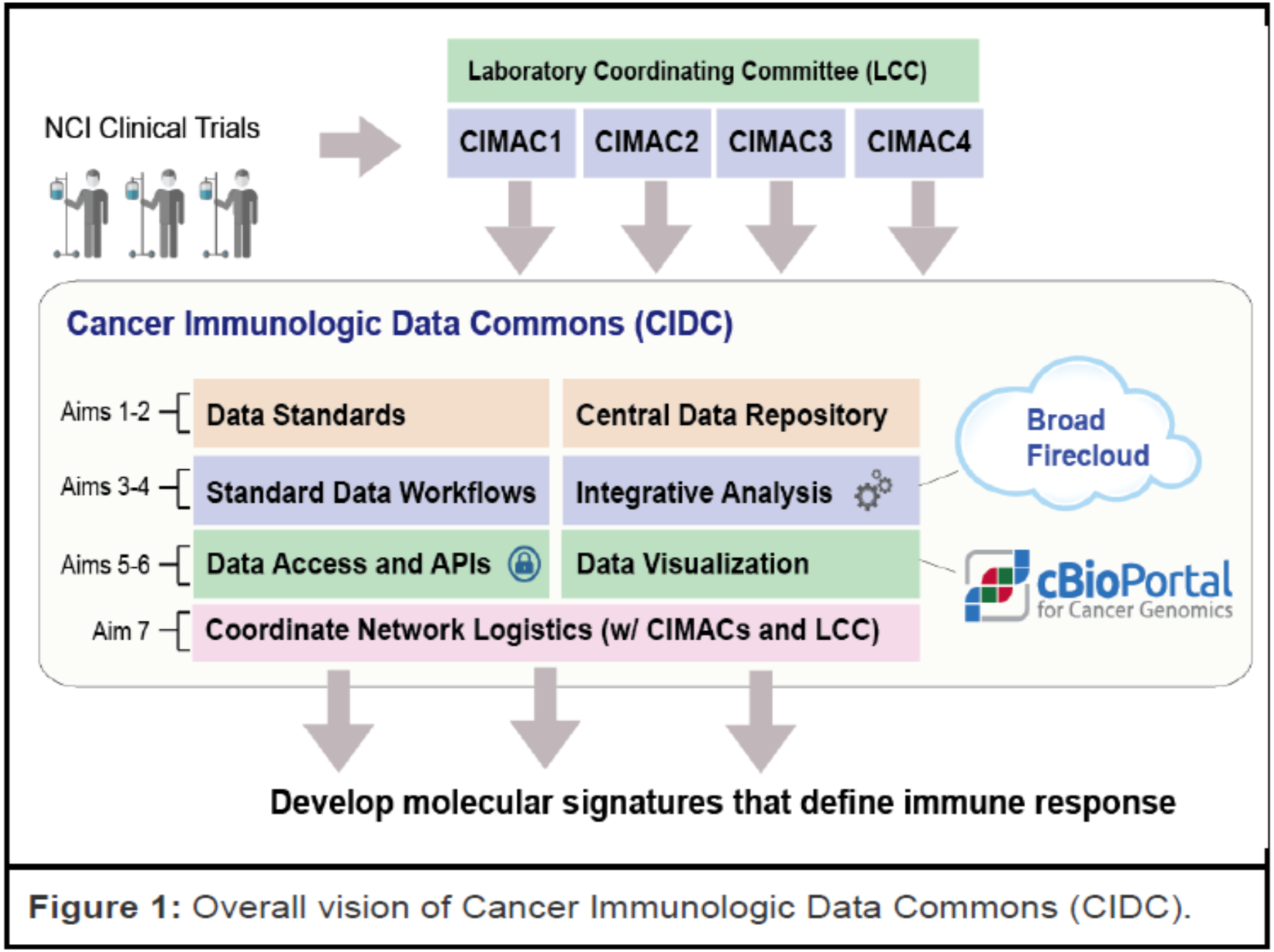
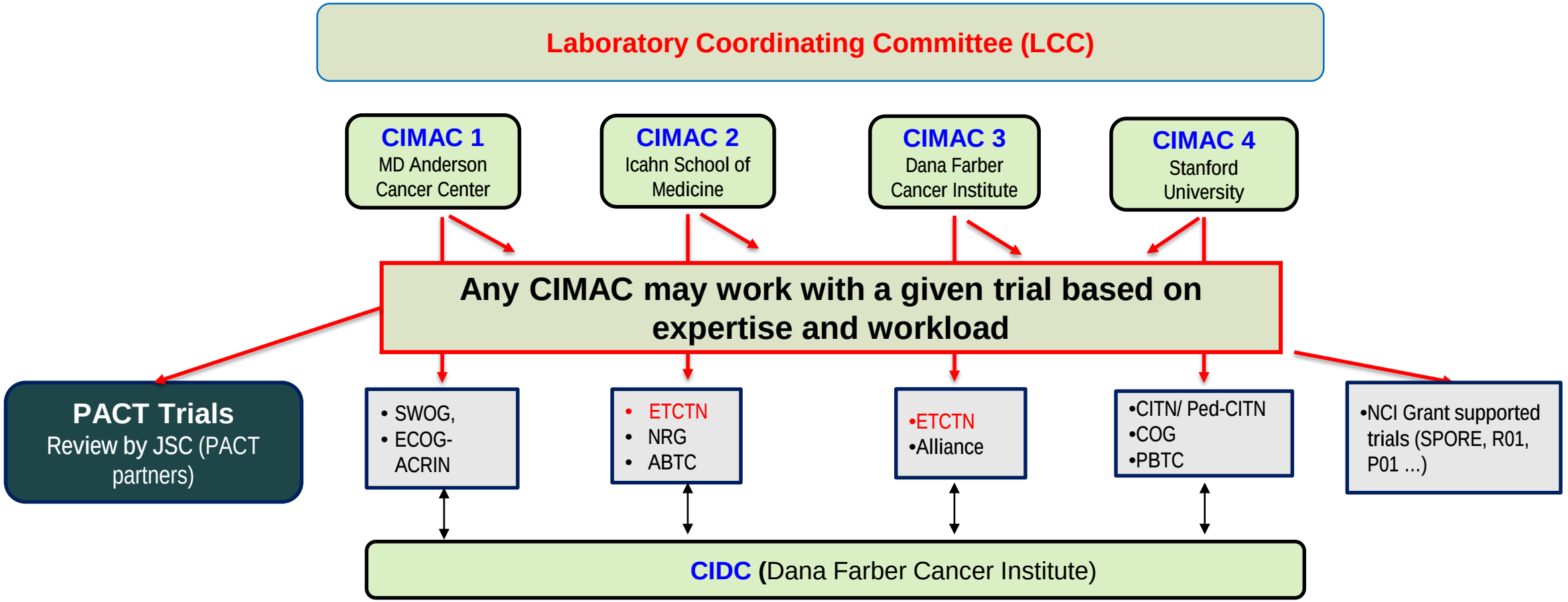


Figure 1: Overall vision of Cancer Immunologic Data Commons (CIDC).

- 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

CIMACs-CIDC Network Structure



- ALL CIMACs can work with any trial networks, depending on specific needs, expertise and work load
- 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

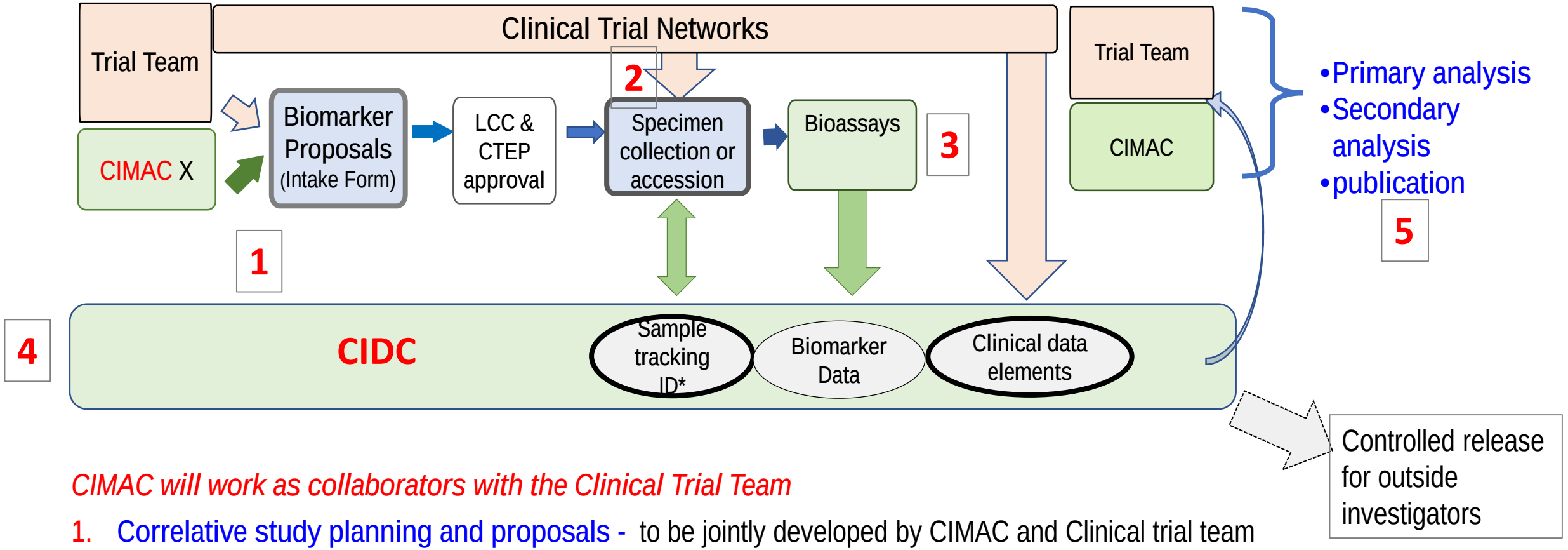
NCI Leader:
Yingdong Zhao

PACT representatives

Non-CTEP Network Trials WG

NCI Leader:
Min Song

Work flow for CIMAC-CIDC and Clinical Trial collaborations



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

National Cancer Institute

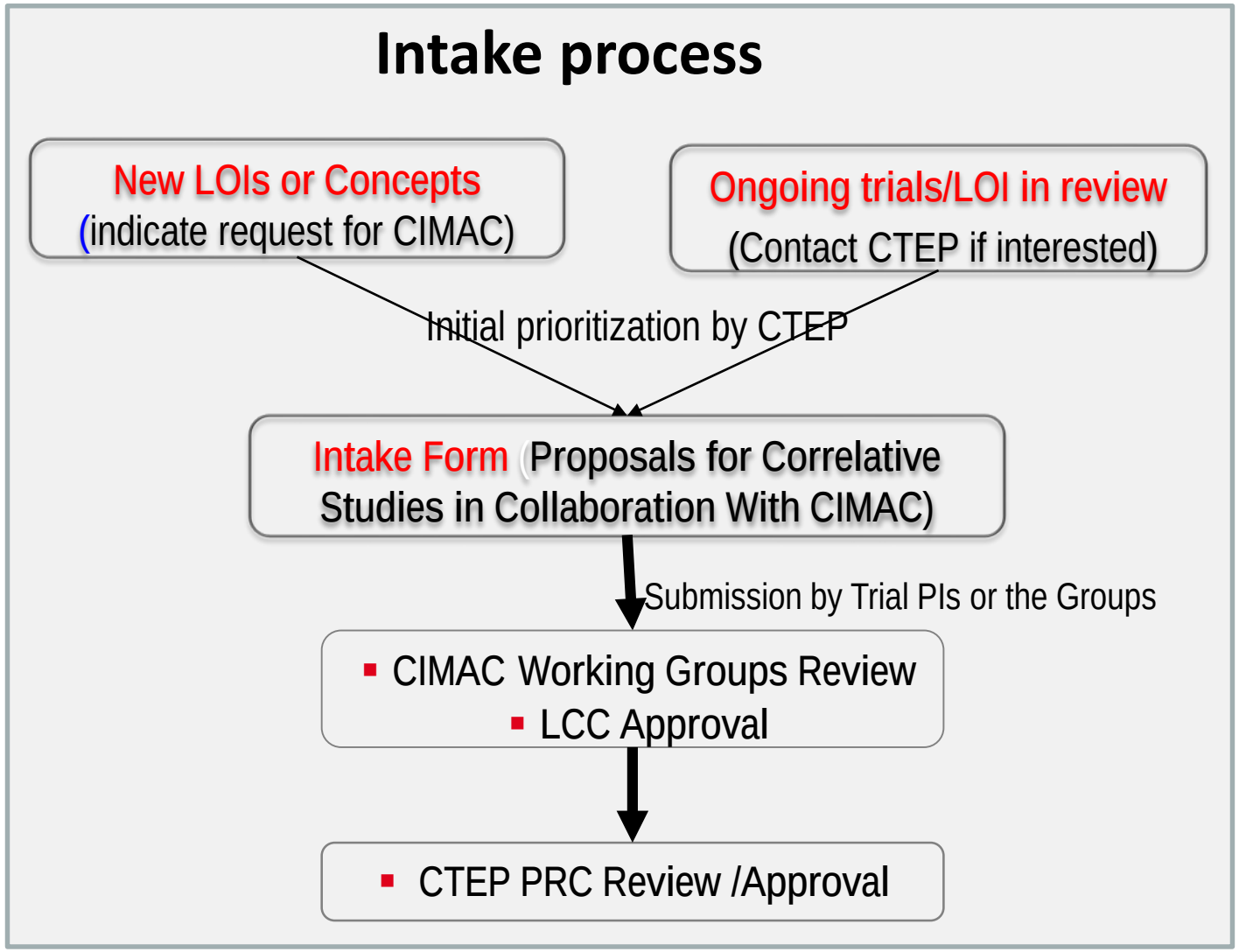
Working group progress

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



- 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

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

ASSAY & PLATFORM WORKING GROUP

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

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

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.

IMMUNO-ONCOLOGY BIOMARKERS NETWORK

CIMAC-CIDC

HOME CIMACS ASSAYS CIDC WORKING GROUPS ABOUT CONTACT

CIMAC-CIDC
Immuno-Oncology Biomarkers Network

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,

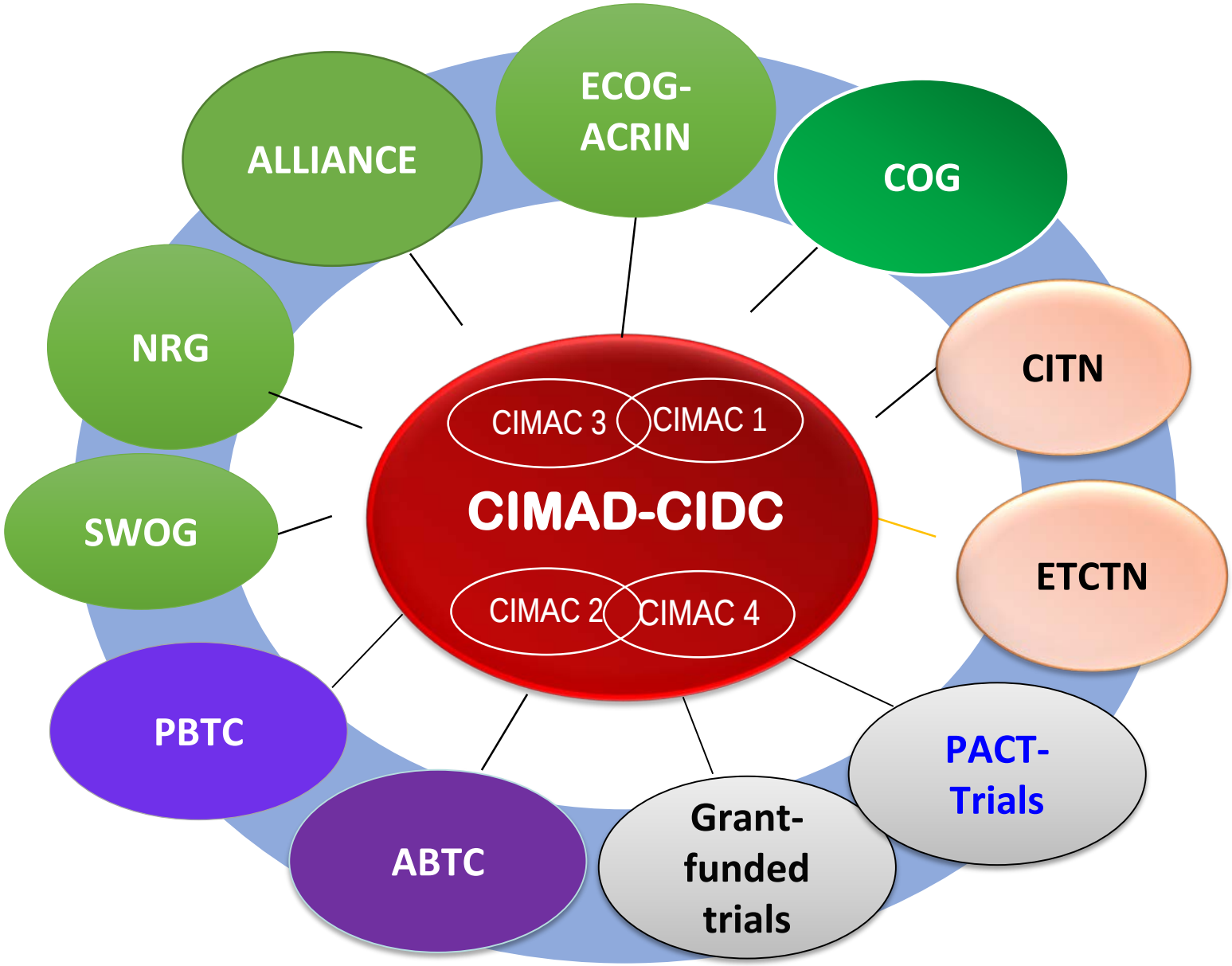
National Cancer Institute

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/standardizati**on 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, …)
  - …


ALLIANCE
ECOG-ACRIN
COG
NRG
CITN
CIMAC 3
CIMAC 1
CIMAD-CIDC
SWOG
ETCTN
CIMAC 2
CIMAC 4
PBTC
PACT-Trials
ABTC
Grant-funded trials

Questions

CIMAC Intake Forms

CIMAC Intake Form for "Clinical Trial #"

(Template Version Mar 8, 2018)

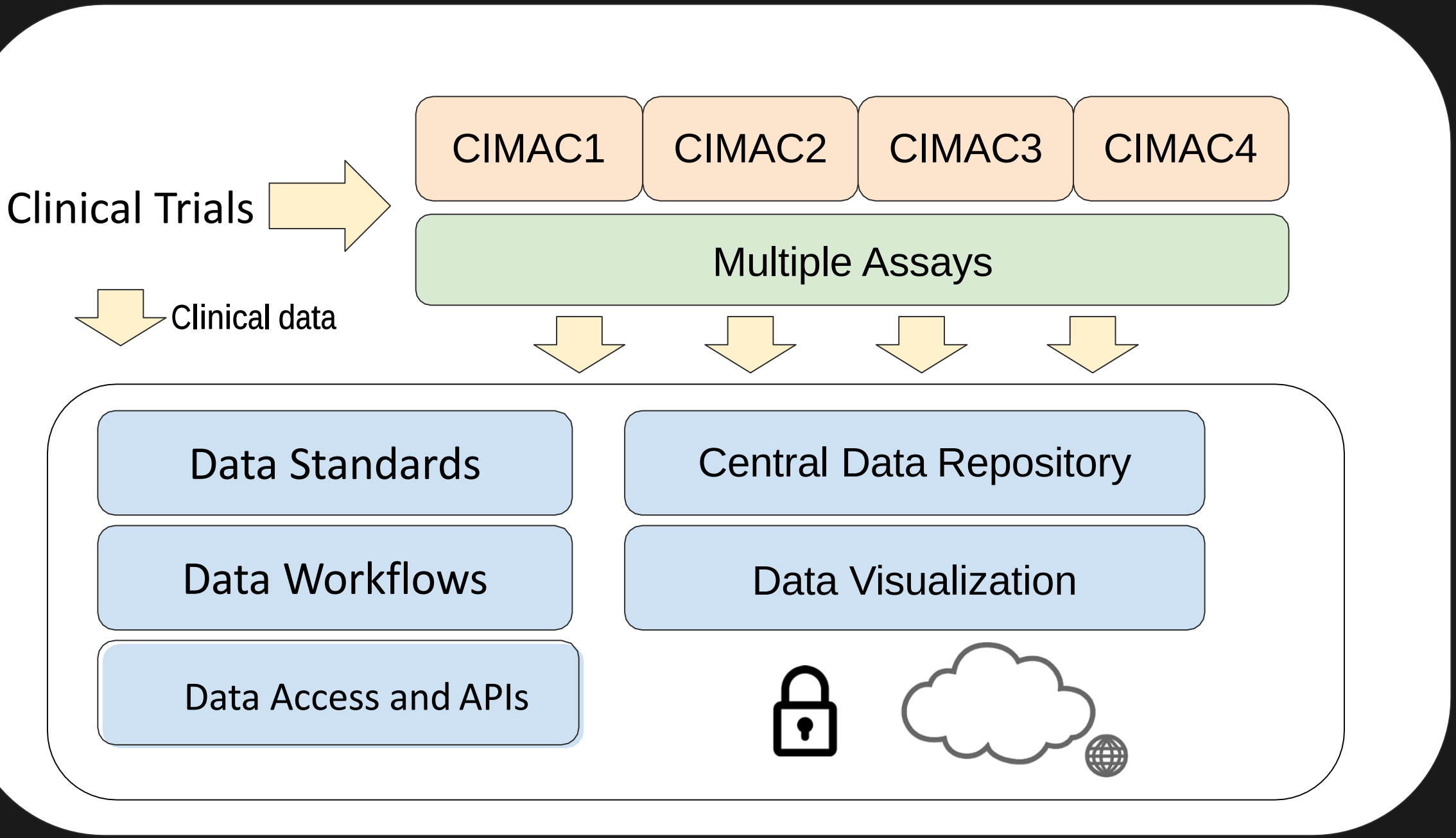
Proposal of Correlative Studies in Collaboration with the CIMACs-CIDC Network

- Cover sheet: Trial Team, CIMAC Team
- Study plan: Biomarker objectives; Hypothesis; Method of analysis, Statistics
- Biomarker table

(An example)

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

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


CIMAC1
CIMAC2
CIMAC3
CIMAC4
Clinical Trials
Multiple Assays
Clinical data
Data Standards
Central Data Repository
Data Workflows
Data Visualization
Data Access and APIs