

Promise and Challenges of Co-Clinical Imaging

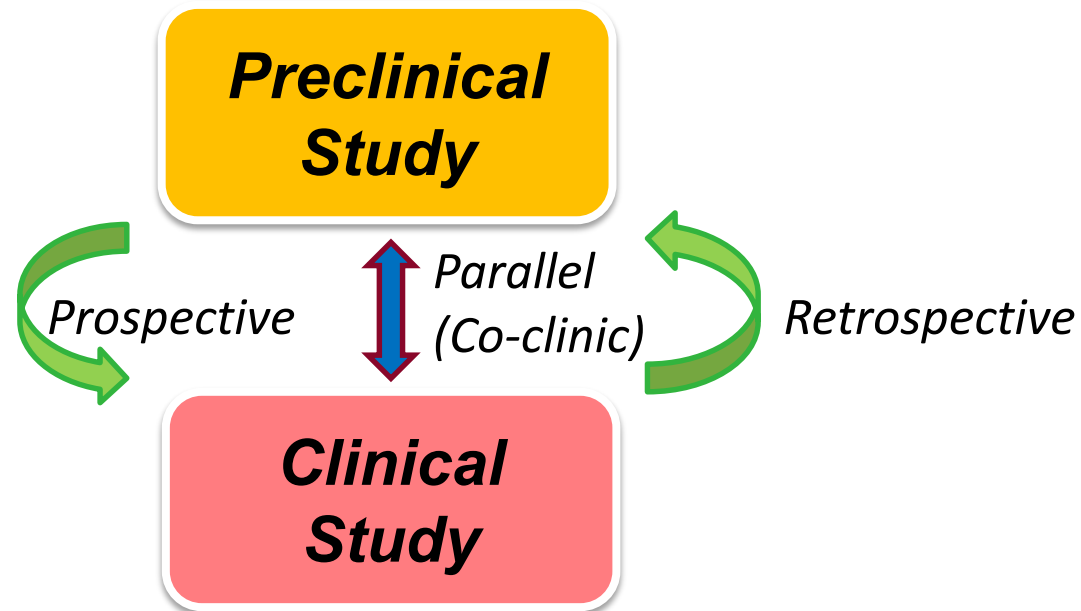
NCI Co-Clinical Imaging Research Resources Program (CIRP)

<https://nciphub.org/groups/cirphub>

Huiming Zhang, Ph.D., Cancer Imaging Program, DCTD, NCI

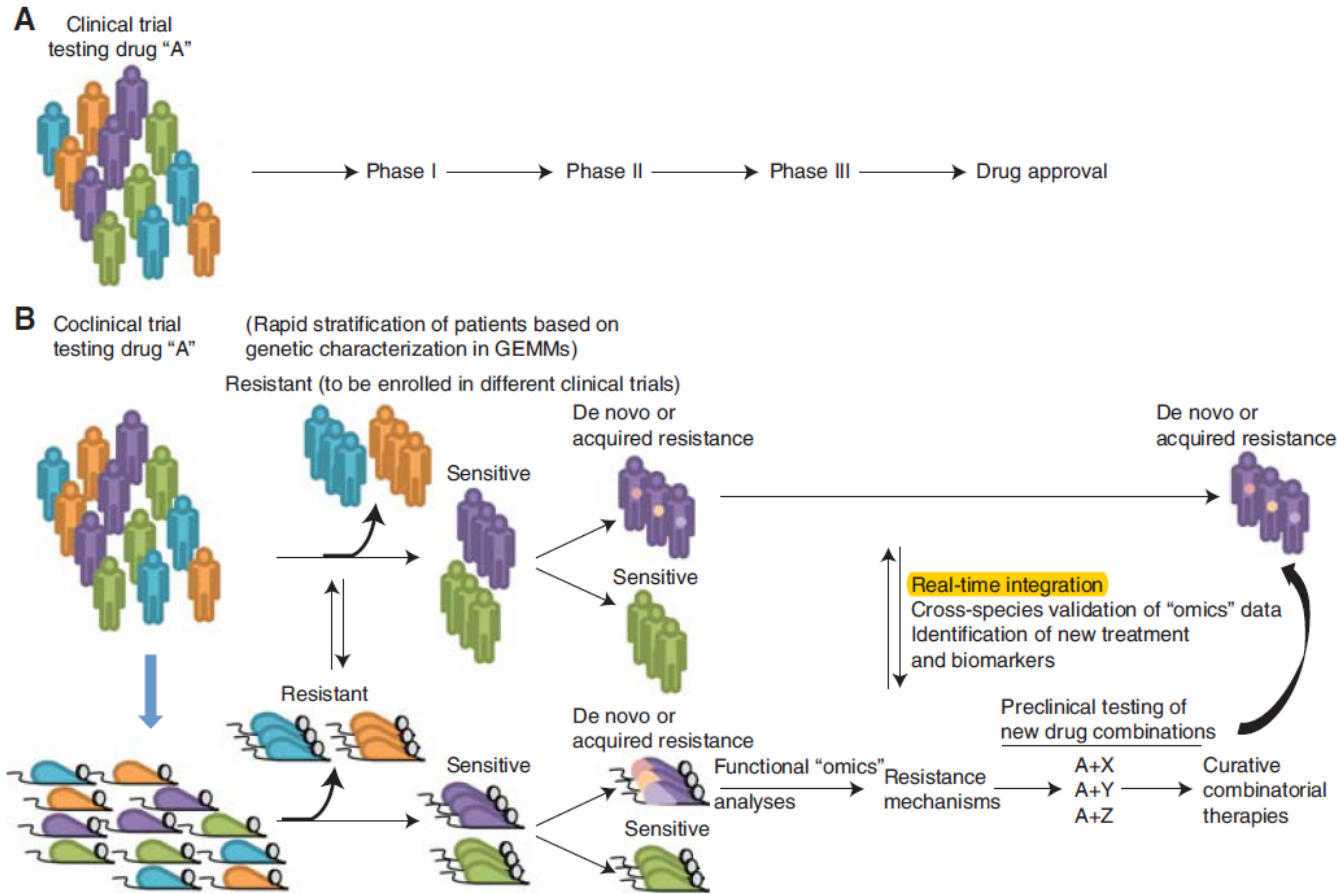
Rationale

- ❑ Precision medicine requires better animal models & novel research,
- ❑ Preclinical study is linked to clinic study via multiple pathways,
- ❑ Quantitative imaging (QI) as a non-invasive tool.



Collins FS, and Varmus H, *A new initiative on precision medicine*, NEJM, 372:793 (2015)

GEMMs-Based Co-Clinical Trial Platform



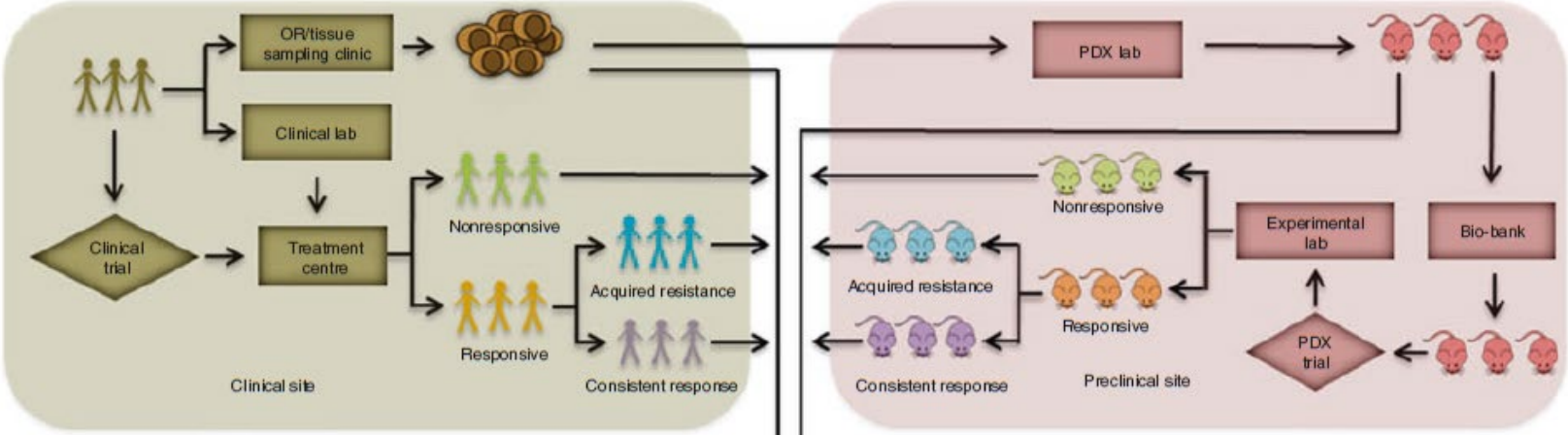
Co-Clinical trials:

Investigations in patients and in parallel (or sequential) in mouse or human-in-mouse models, such as GEMMs or PDXs.

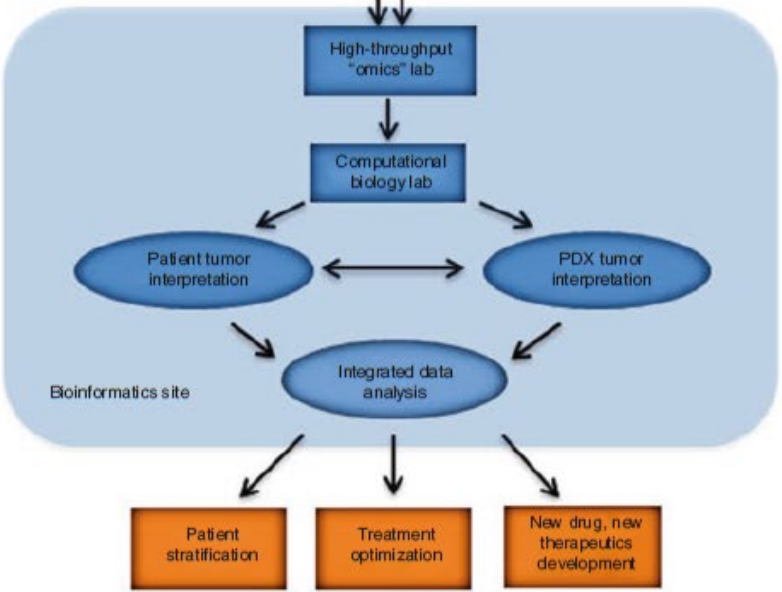
Applications:

Cancer -omics
Patient stratification
Response
Drug resistance
Combined therapy

PDX-Based Co-Clinical Trial Platform

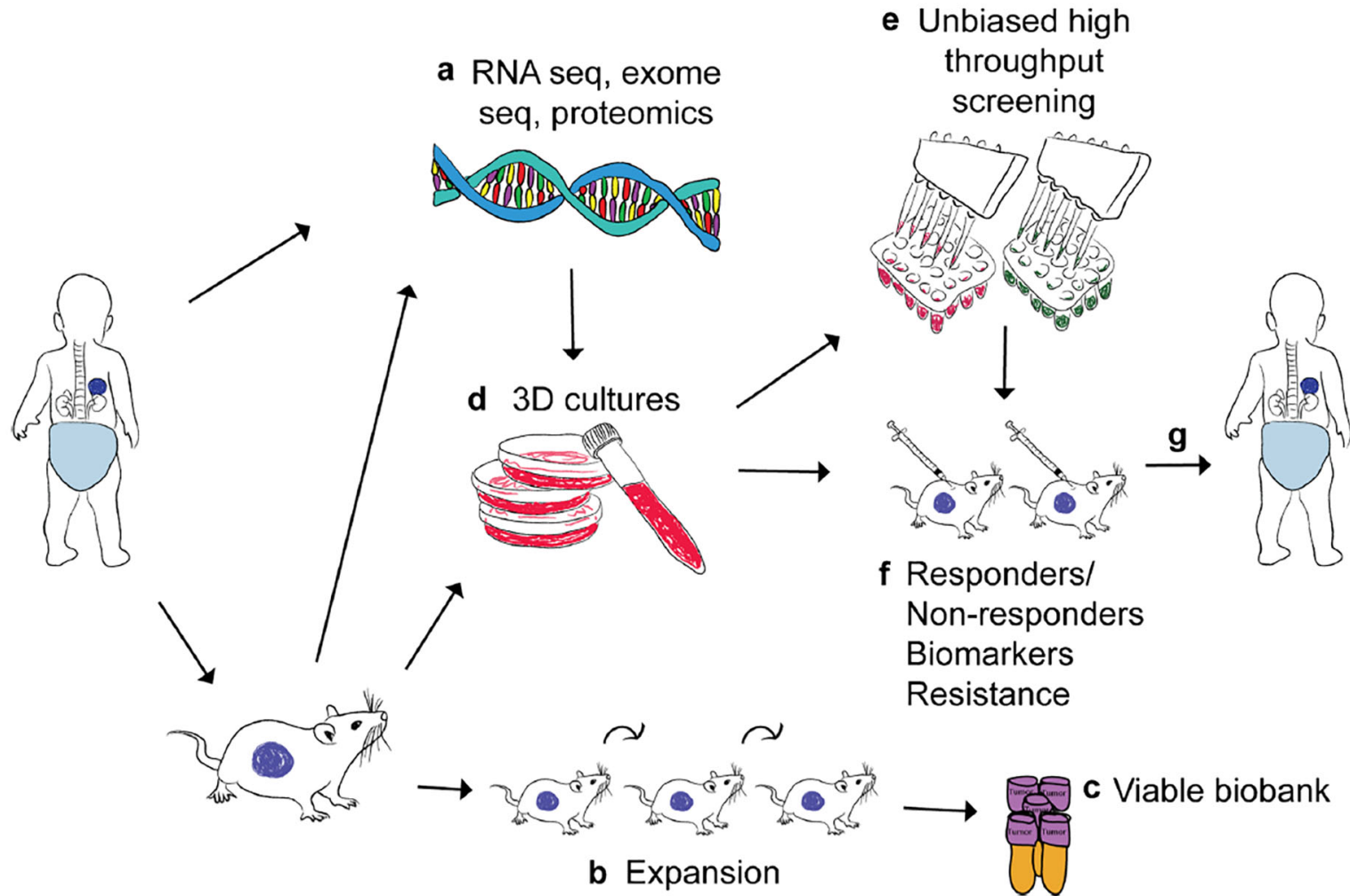


Applications:
Cancer -omics
Patient stratification
Response
Drug resistance
Combined therapy



Cheng H, et al, 2017

PDXs in Pediatric Cancers



History & Progress Timeline

2009: NCI U01s: *Integration of Mouse Models into Human Cancer Research*,

2012: first co-clinical trial report on NSCLC,

2015: NCI U24s: Co-clinical Imaging research resources, [PAR-15-266](#), [PAR-16-385](#),

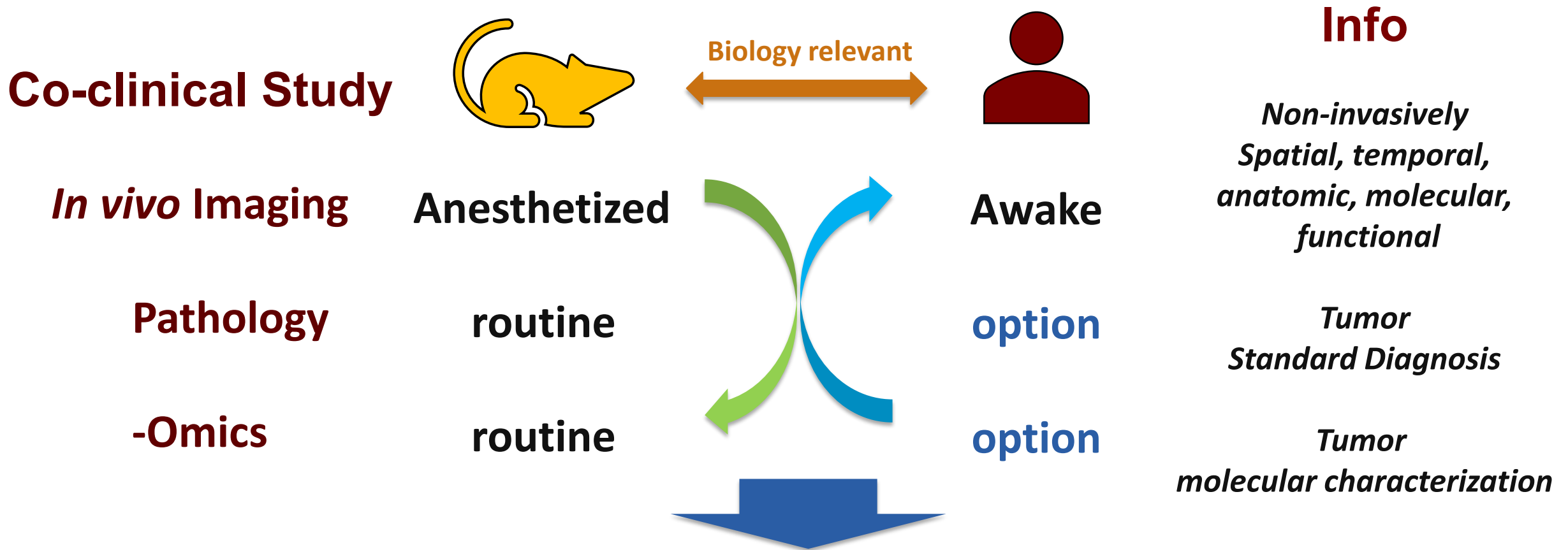
2018: NCI U24s reissued: [PAR-18-841](#)

2019: NCI Clarify: PAR-18-841 for ***Adult and Pediatric Cancers***

Related resources: NCI patient-Derived Models Repository (PDMR), EurOPDX consortium, IMODI consortium (France), Co-clinical trials centers, mouse hospitals.

NCI initiatives: PDXnet (2017), PDMC (2016).

Co-Clinical Imaging: Promise



A platform for better informing therapeutic efficacy

Co-clinical Imaging: Biology Perspective

❑ Complexity in GEMMs & PDXs:

Fidelity, Variability, Heterogeneity,
Reliability, SOPs & GLP, etc.

❑ Design of co-clinical trials:

Animal models & patients, Dosages,
Timeline for therapy & imaging

❑ Biological validations:

Histology (H&E, Immunostaining)

Genomics (WES), Transcriptomics (RNA-Seq)

Co-Clinical Imaging: Imaging Perspective

Consensus or Standardization

Clinical Imaging

Pre-clinical Imaging

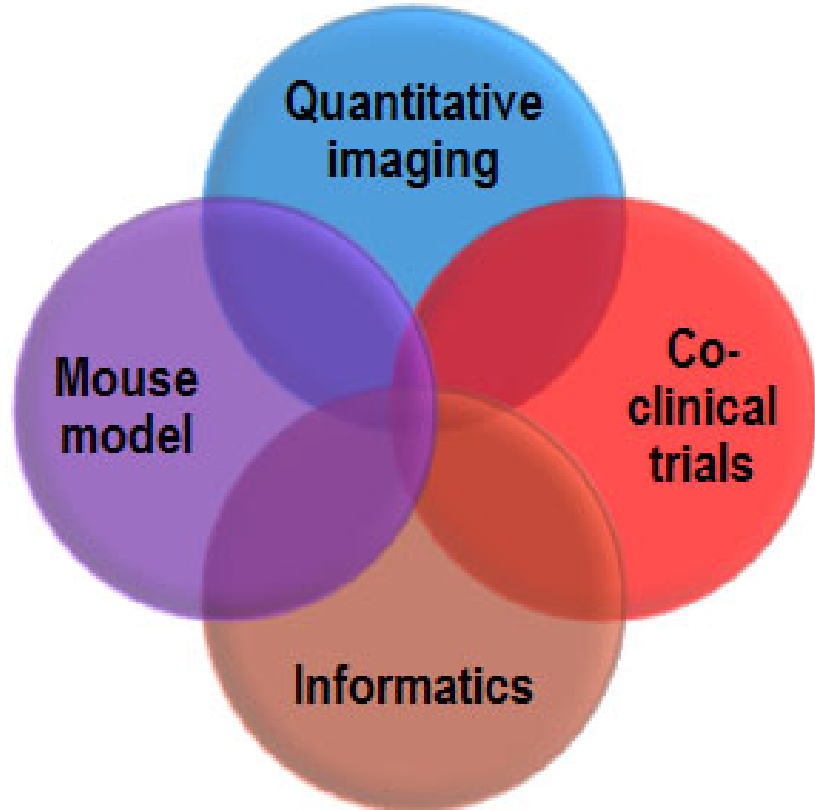
Imaging hardware	Yes	?
Imaging phantoms	MRI, PET, CT	PET (?), CT (?), MRI(?)
Imaging protocols	Quantitative	Qualitative, Semi-quantitative?
Metrology	Yes	?
Output data file formats	DICOMs	?
Data process software	Many	?
Metadata archive	Many	?
Resources	Many	?
Industry development & support	Many	?
Scientific community	SNMMI, AAPM, ISMRM, RSNA, etc.	?

PAR-18-841: Scientific Goals

Develop co-clinical imaging research resources that will encourage a consensus on how quantitative imaging (QI) methods are optimized to improve the quality of imaging results for co-clinical trials of adult and/or pediatric cancers:

- Perform optimization of pre-clinical quantitative imaging methods
- Implement optimized methods in co-clinical trials
- Populate a web-accessible research resource with all data, methods, workflow documentation, and results collected from co-clinical investigations.

PAR-18-841: Required Four Elements



❑ **Co-clinical interventions:**

- Known intervention
- Therapeutic or prevention
- Prospective or retrospective

❑ **GEMMs or PDXs models:**

- Mice, available, credentialed, validated

❑ **Quantitative imaging:**

- Preclinical identical to clinic one
- New methods require IND or IDE
- User developed software tools

❑ **State-of-art informatics:**

- Encourage data integration
- Encourage use of TCIA, NCIP hub
- Encourage contribution to OMF, QIN, EDRN, etc.

PAR-18-841: Deliverable

Demonstrate the *functionality* of a web-accessible resource before the 3rd quarter of year 5 :

❑ Web-accessible functional information:

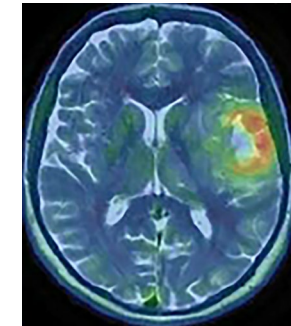
- Co-clinical imaging data
- Methods & software tools
- Workflow documentations
- Results from co-clinical investigations

❑ Demonstrating the functionality:

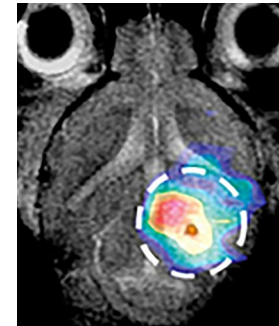
- Strategy to create the resource
- Accessibility by research community,
- Permitting research community to use and improve the proposed QI methods
- Software challenge

Available Data Expected from CIRP

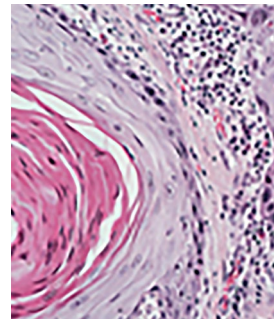
Clinical imaging



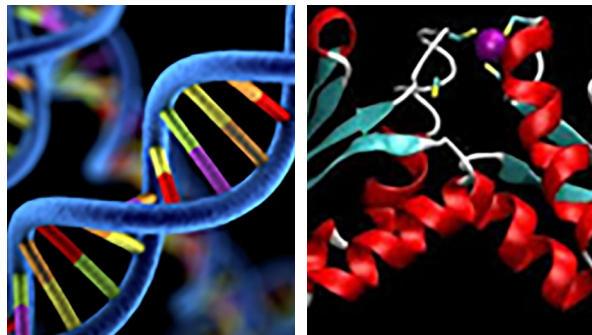
Preclinical imaging



Pathology



RNA-Seq & WES (PDXs)



Anatomical

Molecular

Correlated data sets

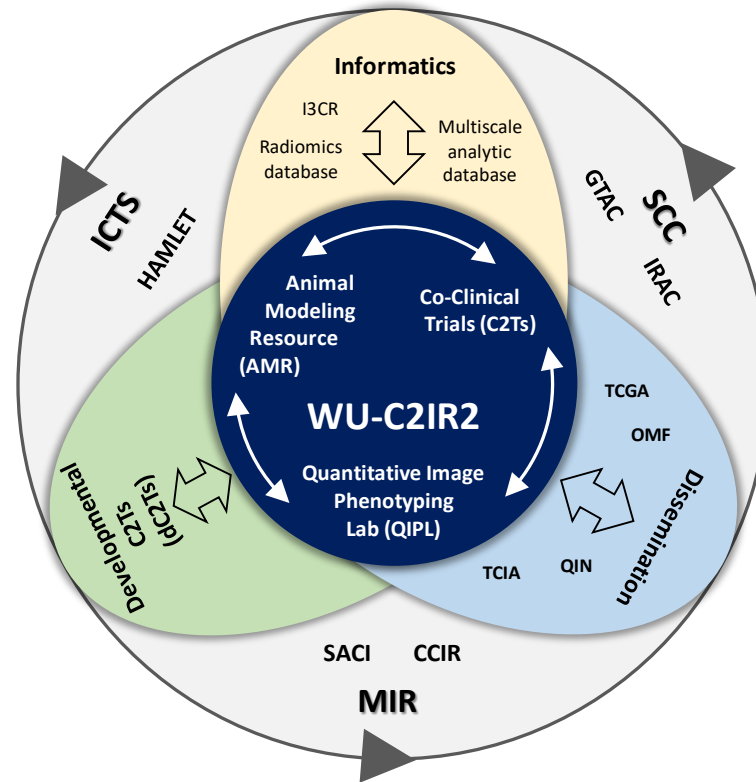
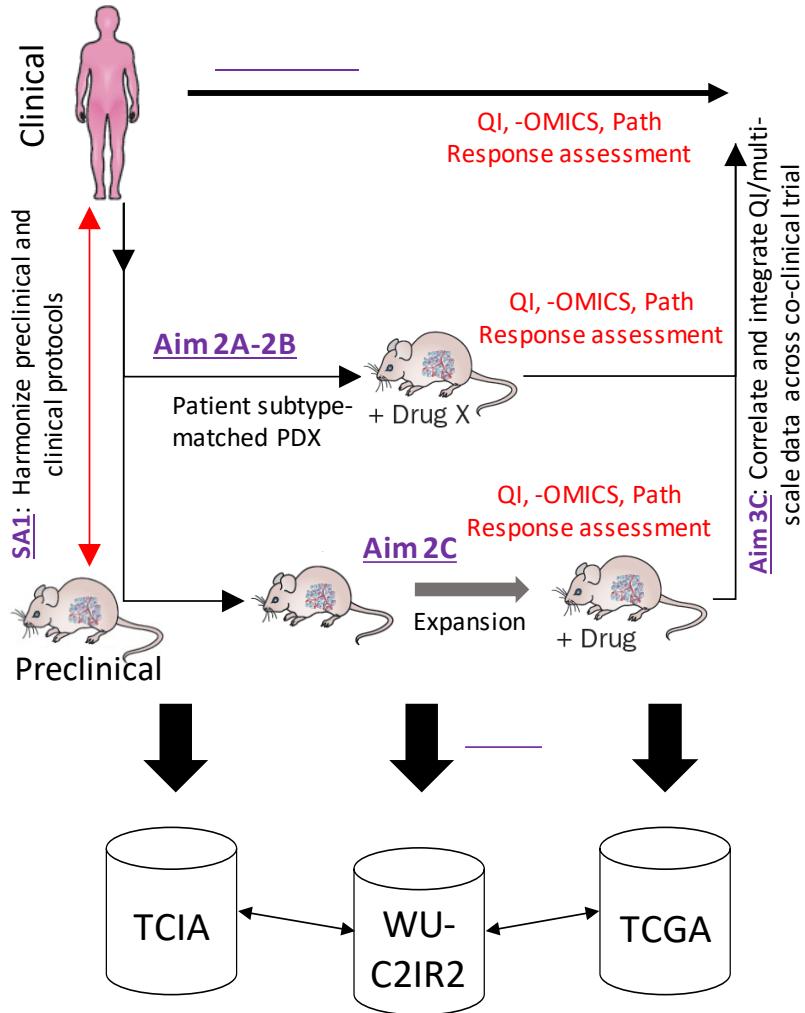
Resources provided by CIRP

- ❑ **Protocols for robust experimental design:** Animal models, biology, pathology, histopathology, imaging, QA/QC, etc.
- ❑ **Workflow for better study design & inform clinical outcome:** Workflow, methods
- ❑ **Data for data mining, metadata integration, software evaluation:** Biology, pathology, imaging
- ❑ **Software for robust, quantitative analysis:** Image processing, reconstruction, segmentation, data analysis & modeling, etc.

CIRP Teams

- ❑ **WUSTL (PI: Kooresh Shoghi):** TNBC, PDXs, Chemotherapy, FDG-EPT, MRI, PET/MRI
- ❑ **Duke (PI: Cristian Badea):** Sarcoma with lung metastasis, GEMMs, Immune check point inhibitors + RT, MRI, CT
- ❑ **Vanderbilt (PI: Charles Manning):** Colorectal cancer, PDXs & Humanized mice, Targeted therapy, 18F-FSPG PET, 11C-Acetate-PET
- ❑ **UPENN (PI: Rong Zhou):** Pancreatic cancer, GEMMs, Stromal targeting therapy, motion resistant MRI
- ❑ **Two new teams will join**

Example of CIRP Sites: Wu-C2IR2



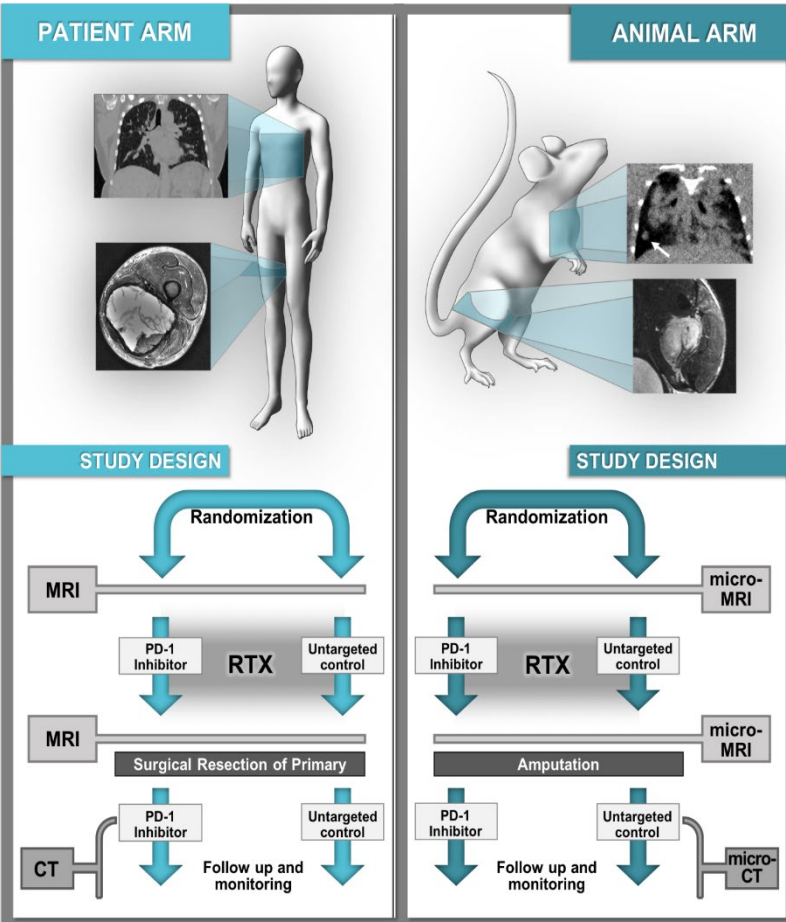
The screenshot shows the website for the Co-Clinical Imaging Research Resource (C2IR2) at Washington University School of Medicine in St. Louis. The page includes a navigation menu (HOME, ABOUT, RESEARCH, SOP DIRECTORY, DATA REPOSITORY, CONTACT US) and a main heading: "Welcome to the Co-Clinical Imaging Research Resource".

The main content area features a flowchart illustrating the process: DRUG THERAPY (MOUSE) and HUMAN (HUMAN) lead to IMAGING, RADIOMIC & GENOMIC DATA. This data is used to EXTRACT FEATURES (SHAPE, PATTERN, TEXTURE) from TUMOR MODEL, which then informs the RESPONSE TO THERAPY. A red button labeled "About the C2IR2" is visible.

Below the main content, a section titled "What Can I Find On This Site?" lists three categories: Standard Operating Procedures, Supported Co-Clinical Trial Projects, and Publications and Data.

<https://c2ir2.wustl.edu>

Example of CIRP Sites: Duke Research Resources for Preclinical Imaging in Co-Clinical Trials



Documents/Attachments

File Name
SOP - ParaVision 6.0.1 Operator and Simple Scan SOP.docx

CIVM Image Management: Tumor Growth Rate

Thumbnail	Name	Description	Stacks	ID	Scan Date
	180420-1-R20027-T2W	Scan Day 2 (one week after initial scan) of control mice be...	3	14717	2018-04-27
	180420-1-R20027-T1W	Scan Day 2 (one week after initial scan) of control mice be...	3	14716	2018-04-27

CIVM Image Management: U24 CT Lung

Thumbnail	Name	Description	Stacks	ID	Scan Date
	M-0201-0250.dcm	mouse / sarcoma	3	14725	2018-04-24
	M-0201-0250.dcm	mouse / Lung Tumors Gating	3	14724	2018-04-24

unknown sequence

The Duke Preclinical Research Resources for Quantitative Imaging Biomarkers

Duke Center for In Vivo Microscopy

HOME SPECIFIC AIMS TEAM SIGNIFICANCE MICRO-CT MRI PROTOCOLS DATA CODE

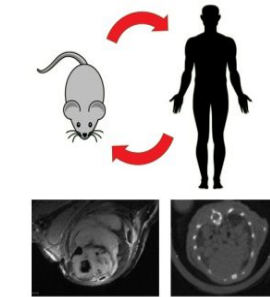
FUNDING

Our PLOS ONE paper is now published!

Posted on April 8, 2019 | [Leave a comment](#)

[Bridging the translational gap: Implementation of multimodal small animal imaging strategies for tumor burden assessment in a co-clinical trial](#)

S. J. Blocker, Y. M. Mowery, M. D. Holbrook, Y. Qi, D. G. Kirsch, G. A. Johnson, C. T. Badea, PLoS ONE 14(4): e0207555. (2019)



Posted in [Uncategorized](#) | [Leave a comment](#)

SEARCH IT!

RECENT ENTRIES

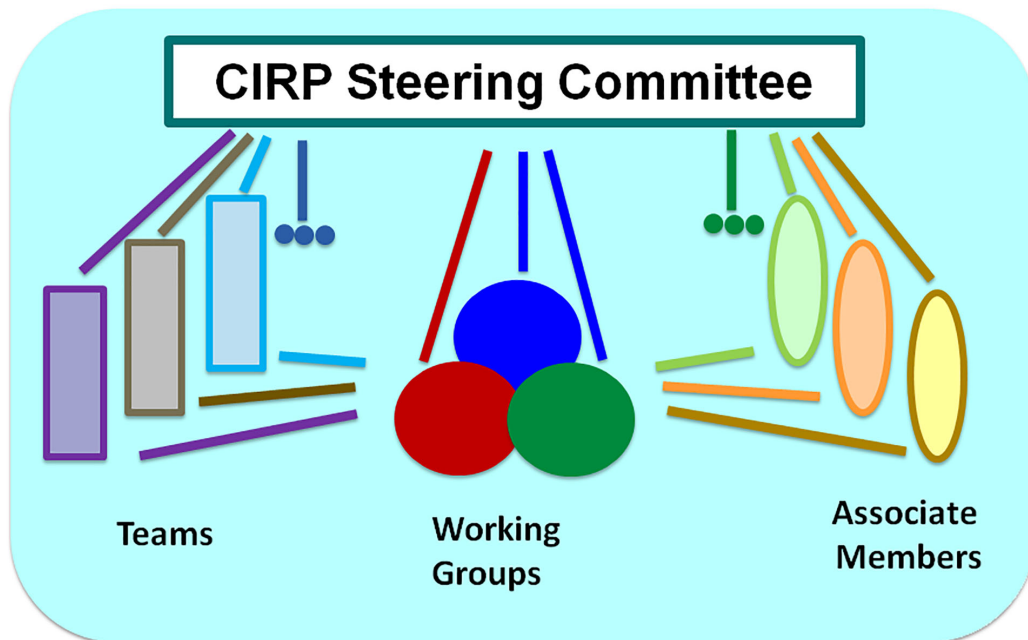
- Our PLOS ONE paper is now published!
- U24 DICOM tool
- Duke Standard Operating Procedure for MR Imaging at 7T of tumor-bearing mice using a surface coil
- SPIE manuscript on the importance of gating for preclinical CT imaging of lung nodules
- SPIE manuscript on sarcoma segmentation
- New Protocol for Tumor Segmentation using 3D Slicer
- Welcome to Duke Preclinical QIBA!

LINKS

<https://sites.duke.edu/pcqiba/>

CIRP Network: Structure

<https://nciphub.org/groups/cirphub>



- ❑ **Steering Committee (SC)**
- ❑ **Three Working Groups (WGs):**
 - Animal models and co-clinical trials (AMCT)
 - Imaging acquisition and data process (IADP)
 - Informatics and outreach (IMOR)
- ❑ **Associate Members:**
 - Join WG's T-cons
 - Contribute to consensus development
 - Participate annual meetings

CIRP Associate Membership

Qualification: Academic investigators with NCI-funded project(s):

- PDXs or GEMMs for cancers
- Quantitative imaging, investigations or cancer trials
- Informatics for cancers

Roles & Responsibility:

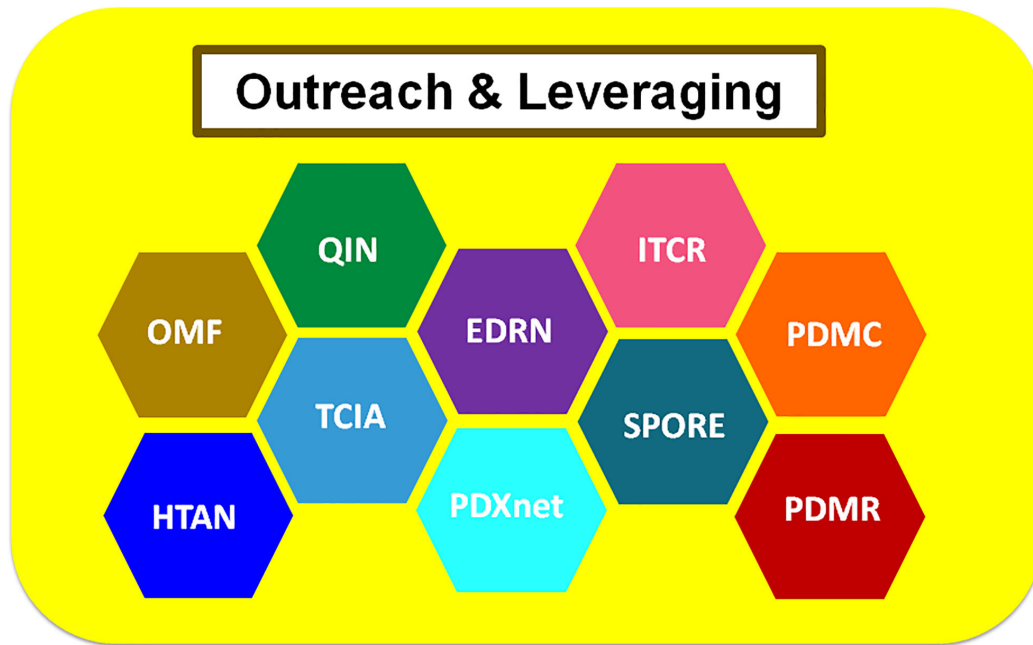
- Participate CIRP WGs quarterly teleconferences
- Attend CIRP annual meeting
- Participant all discussion and consensus-building activities
- Share network-wide publications
- More...

How to apply:

Contact NCI program director, Huiming Zhang, zhanghui@mail.nih.gov

CIRP Network: Outreach & Leveraging

<https://nciphub.org/groups/cirphub>



- Open annual meeting in 2020
June 22-23, NCI Campus
- Leverage existing resources
- Ensure best practices for every
CIRP element
- Address unmet need in cancer
community
- Provide better support to cancer
research
- More...

CIRP Hub

<https://nciphub.org/groups/cirphub>

The screenshot shows a web browser window displaying the CIRP Hub website. The browser's address bar shows the URL <https://nciphub.org/groups/cirphub>. The website header includes the text "poweredby NCIP Hub" and navigation links for "Login", "Register", and "Request Membership". The main heading is "Co-Clinical Imaging Research Resources Program Network (CIRP) [cirphub]". Below this is a teal navigation bar with links for "Overview", "Members", "Resources", "Forum", "Projects", "Calendar", "Announcements", "Collections", and "Activity". The "About CIRP" section contains a paragraph describing the program's goals and objectives. Below the text, the "Four essential elements" are listed in four colored boxes: "Animal Models" (red), "Co-Clinical Trials" (green), "Quantitative Imaging" (blue), and "Informatics" (purple). Each box contains an icon representing the element: a mouse for Animal Models, a mouse and person for Co-Clinical Trials, a microscope for Quantitative Imaging, and a computer monitor for Informatics.

poweredby NCIP Hub

Login Register Request Membership

Co-Clinical Imaging Research Resources Program Network (CIRP) [cirphub]

Overview Members Resources Forum Projects Calendar Announcements Collections Activity

About CIRP

The Co-Clinical Imaging Research Resources Program Network (CIRP) is based on the trans-NCI initiative, currently, [PAR-18-841](#). This FOA invites Cooperative Agreement applications to develop research resources that encourage a consensus on how quantitative imaging methods are optimized to improve the quality of imaging results for co-clinical trials. Projects include optimization of pre-clinical quantitative imaging methods, implementation in co-clinical trials, and creating a web-accessible research resource that contains all the data, methods, workflow documentation, and results collected from cancer therapeutic or prevention co-clinical investigations. To achieve the goals of the CIRP, applicants are encouraged to organize multi-disciplinary teams with experience in mouse models research, human investigations, imaging platforms, quantitative imaging methods, decision support software and informatics to populate the research resource. Each resource contains four essential elements: animal models, co-clinical trials, quantitative imaging, and informatics.

Four essential elements

- Animal Models
- Co-Clinical Trials
- Quantitative Imaging
- Informatics

Questions?

zhanghui@mail.nih.gov



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www.cancer.gov

www.cancer.gov/espanol