An Overview from the Biospecimen Research Network Scientific Steering Committee

Jennifer L. Hunt, MD, MEd
Associate Chief of Anatomic & Molecular Pathology
Subcontractor, SAIC-Frederick, Inc., Frederick, Maryland
Massachusetts General Hospital and Harvard Medical School

SAIC | Frederick

DISCLAIMER

DISCLAIMER: This project has been funded in whole or in part with federal funds from the National Cancer Institute, National Institutes of Health, under Contract No. HHSN261200800001E. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

Agenda

- Background
- The Biospecimen Research Network Research initiative
- The Scientific Steering Committee
- Experimental design
- Summary

Biospecimen Research: Fundamental to OBBR

- **BEST PRACTICES** *to produce state-of-the-science guidance in biobanking for collection, processing, storage and distribution*
  - The NCI Best Practices for Biospecimen Resources

- **RESEARCH** *to better understand how pre-analytical variables affect the biospecimen molecular integrity*
  - The NCI Biospecimen Research Network

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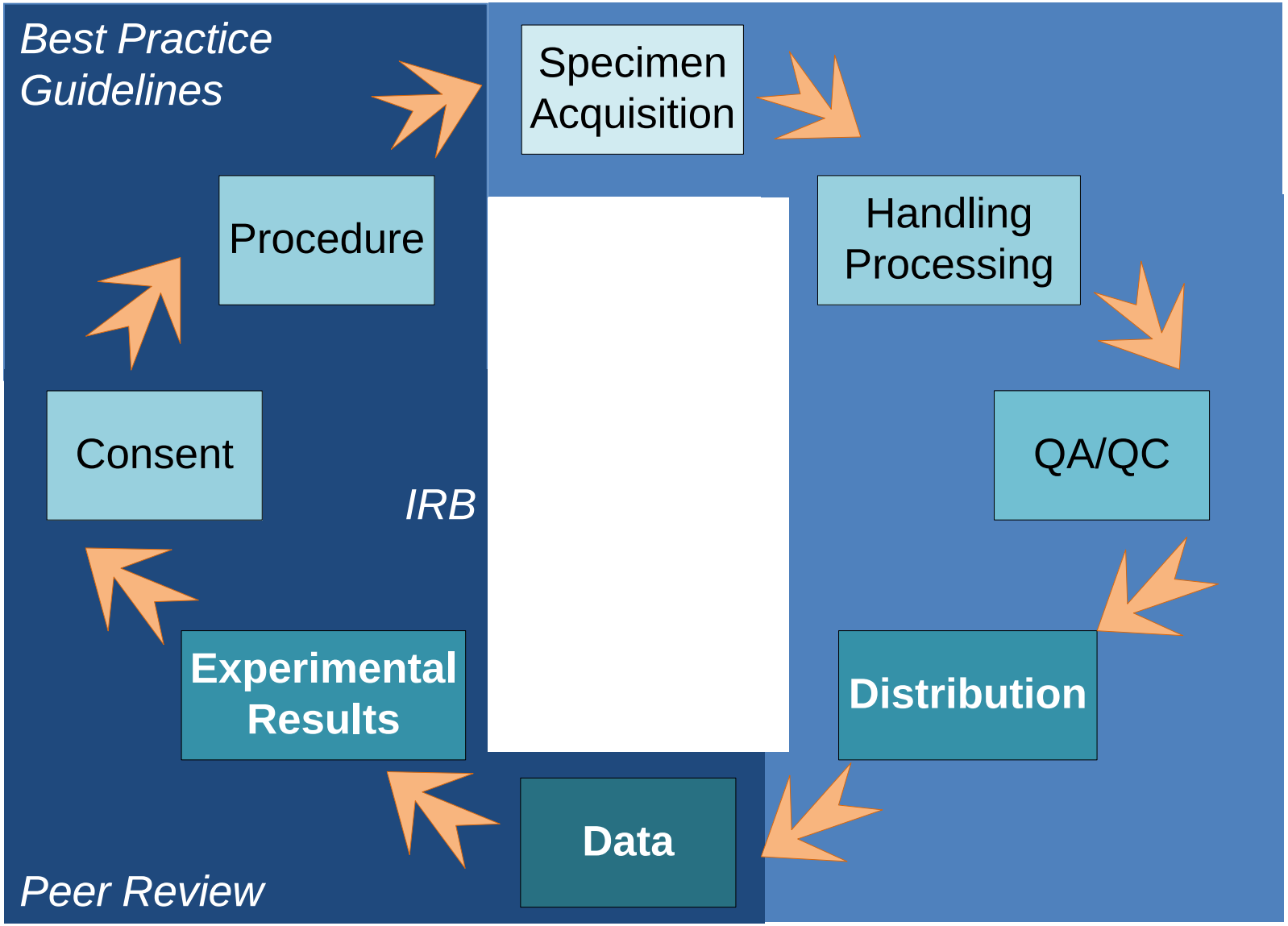
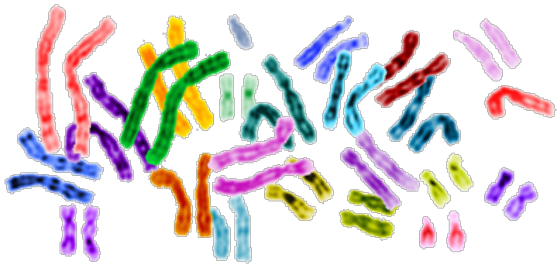
Lifecycle of a Biospecimen



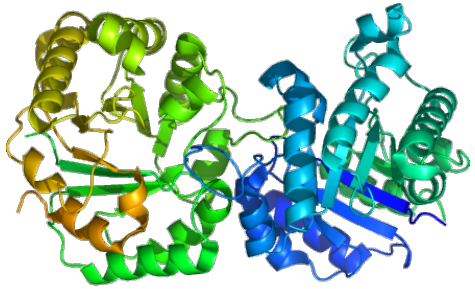
Changes in Molecular Integrity of Biospecimens Affect Molecular Readout

Genomics



Changes in specific transcript levels based on ischemic time

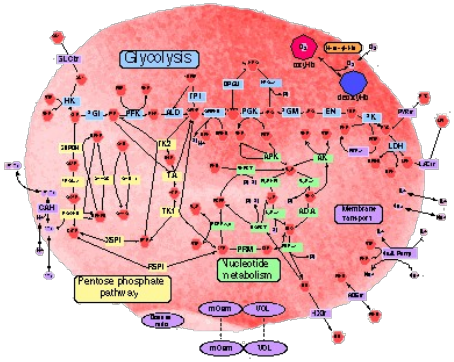
Proteomics



Lack of reproducibility of protein biomarkers in discovery research

Inconsistent IHC results in Research & Clinical Labs

Metabolomics



Inconsistencies in small molecule readouts, yielding results that point to the wrong pathway

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American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Human Epidermal Growth Factor Receptor 2

Optimal tissue handling requirements	Time from tissue acquisition to fixation should be as short as possible. Samples for ER and PgR testing are fixed in 10% NBF for 6 to 72 hours. Samples should be sliced at 5-mm intervals after appropriate gross inspection and margins designation and placed in sufficient volume of NBF to allow adequate tissue penetration. If tumor comes from remote location, it should be bisected through the tumor on removal and sent to the laboratory immersed in a sufficient volume of NBF. Cold ischemia time, fixative type, and time the sample was placed in NBF must be recorded. As in the ASCO/CAP HER2 guideline, storage of slides for more than 6 weeks before analysis is not recommended. Time tissue is removed from patient, time tissue is placed in fixative, duration of fixation, and fixative type must be recorded and noted on accession slip or in report.

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Glenn Francis; N
a McShane;
Keith Miller;
Fred C. G. Sweep; Sheila Taube; Emina Emilia Torlakovic; Paul Valenstein; Giuseppe Viale; Daniel Visscher; Thomas Wheeler; R. Bruce Williams; James L. Wittliff; Antonio C. Wolff

(*Arch Pathol Lab Med.* 2010;134:e48–e72)

Pre-analytical variables affect the integrity of the biospecimen

Time 0

Variables (examples):

- **Antibiotics**
- **Other drugs**
- **Type of anesthesia**
- **Duration of anesthesia**
- **Arterial clamp time**

Variables (examples):

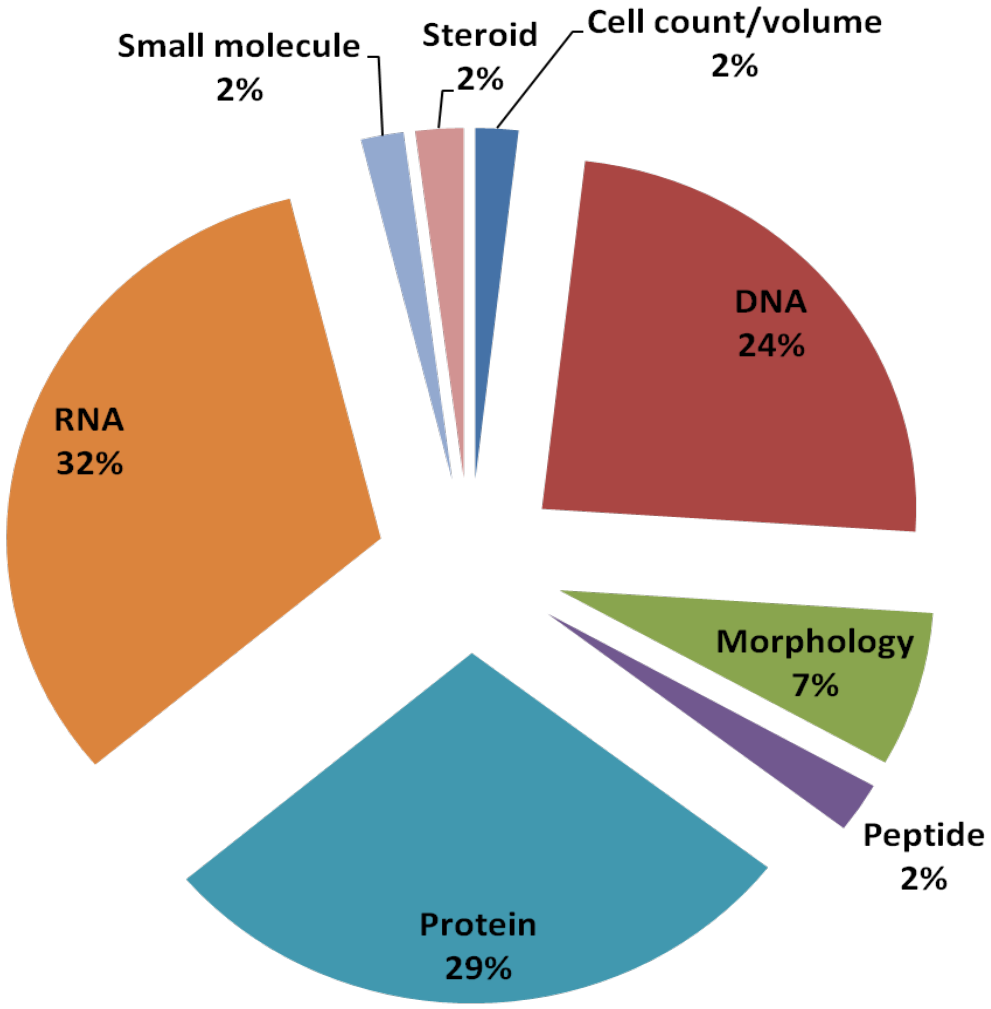
- **Time at room temperature**
- **Temperature of room**
- **Type of fixative**
- **Time in fixative**
- **Rate of freezing**
- **Size of aliquots**

Patient | Medical/ Surgical Procedures | Acquisitio | Handling/ Processing | Storage | Distribution | Scientific Analysis | Restocking Unused Sample

Pre-acquisition **Post-acquisition**

OBBR

Biospecimen Research Database: 625 curated papers



Analytes Studied in < 2% of Papers	%
Carbohydrate	0.7%
Electrolyte/Metal	1.0%
Gas	0.0%
Glycoprotein	1.7%
Lipid	0.7%
Lipoprotein	0.3%

Prepared by: Kelly Engel

What We Do Know…

- Biomarkers are variably labile and are impacted by biopsecimen workflow

What We Don't Know…

- What pre-analytical factors lead to what alterations and how significant they are

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BRN Research Funding Program: "Biospecimen Research for Molecular Medicine“

- Approved for Contract Research
- Program aims:

(1) Investigator-driven Contract Research

Develop innovative approaches to the control, monitoring and assessment of biospecimen quality

(2) Program-directed Research

Systematically define the impact of key pre-analytical variables in human biospecimens on specific downstream data generated from different analysis platforms

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Common Biospecimens Questions

- How do I know if this biospecimen is adequate?
- What data do I need about how biospecimen collection, processing, and storage?
- How will biospecimen collection, processing, and storage affect the reproducibility of my results?
- Will this biospecimen collection allow for future advanced molecular testing?
- What is the scientific basis of a good biospecimen SOP?

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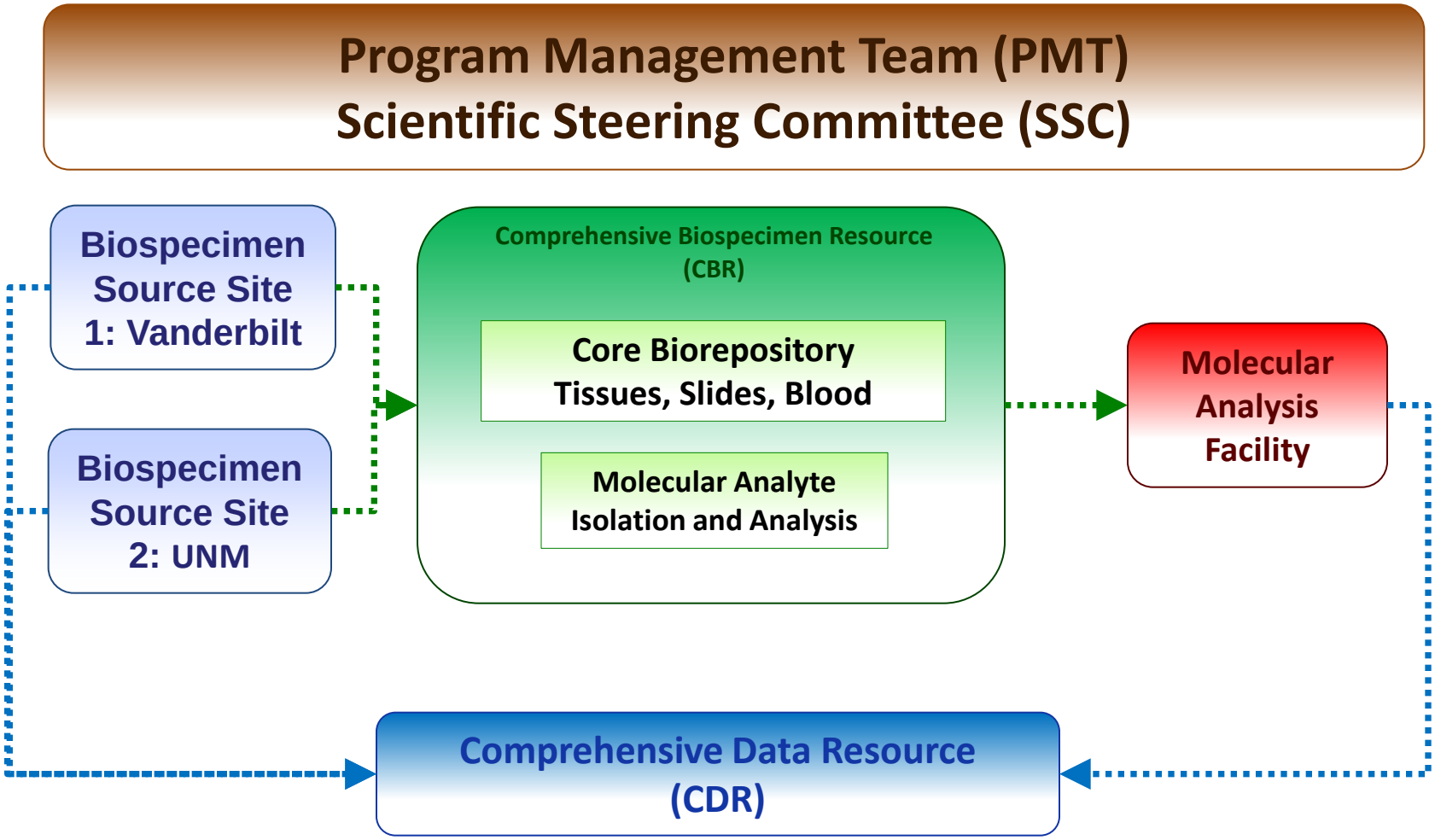
Program Management Team (PMT)
Scientific Steering Committee (SSC)
Biospecimen Source Site 1: Vanderbilt
Biospecimen Source Site 2: UNM
Comprehensive Biospecimen Resource (CBR)
Core Biorepository Tissues, Slides, Blood
Molecular Analyte Isolation and Analysis
Molecular Analysis Facility
Comprehensive Data Resource (CDR)

Scientific Steering Committee

- Jennifer Hunt, M.D., Chair
- Helen Moore, Ph.D.
- Christen Osburn, M.B.A
- Kristin Ardlie, Ph.D.
- Denise Bland-Piontek
- Peggy Devine
- Kelly Engel, Ph.D.
- Paul Fearn
- Andrea Ferreira-Gonzalez, Ph.D.
- Mitchell Gail, M.D., Ph.D.
- David Hicks, M.D.
- Dan Liebler, Ph.D.
- Elizabeth Mansfield, Ph.D.
- Boye Osunkoya, MD, Ph.D.
- Robert Peterfreund, M.D, Ph.D.
- Steven Skates, Ph.D.
- Terry Speed, Ph.D.
- Janet Warrington, Ph.D.

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Research Studies in Acquisition and Processing Variables

Aim: To define the influence of acquisition and post-acquisition variables on downstream molecular analysis

Operational Plan

•Obtain a large collection of well-annotated cancer and normal tissues under defined protocols

•Perform molecular analysis on defined platforms with strict QA/QC

•Perform iterative modification of variables in biospecimen acquisition, processing, and storage

•Analyze impact of specific variables

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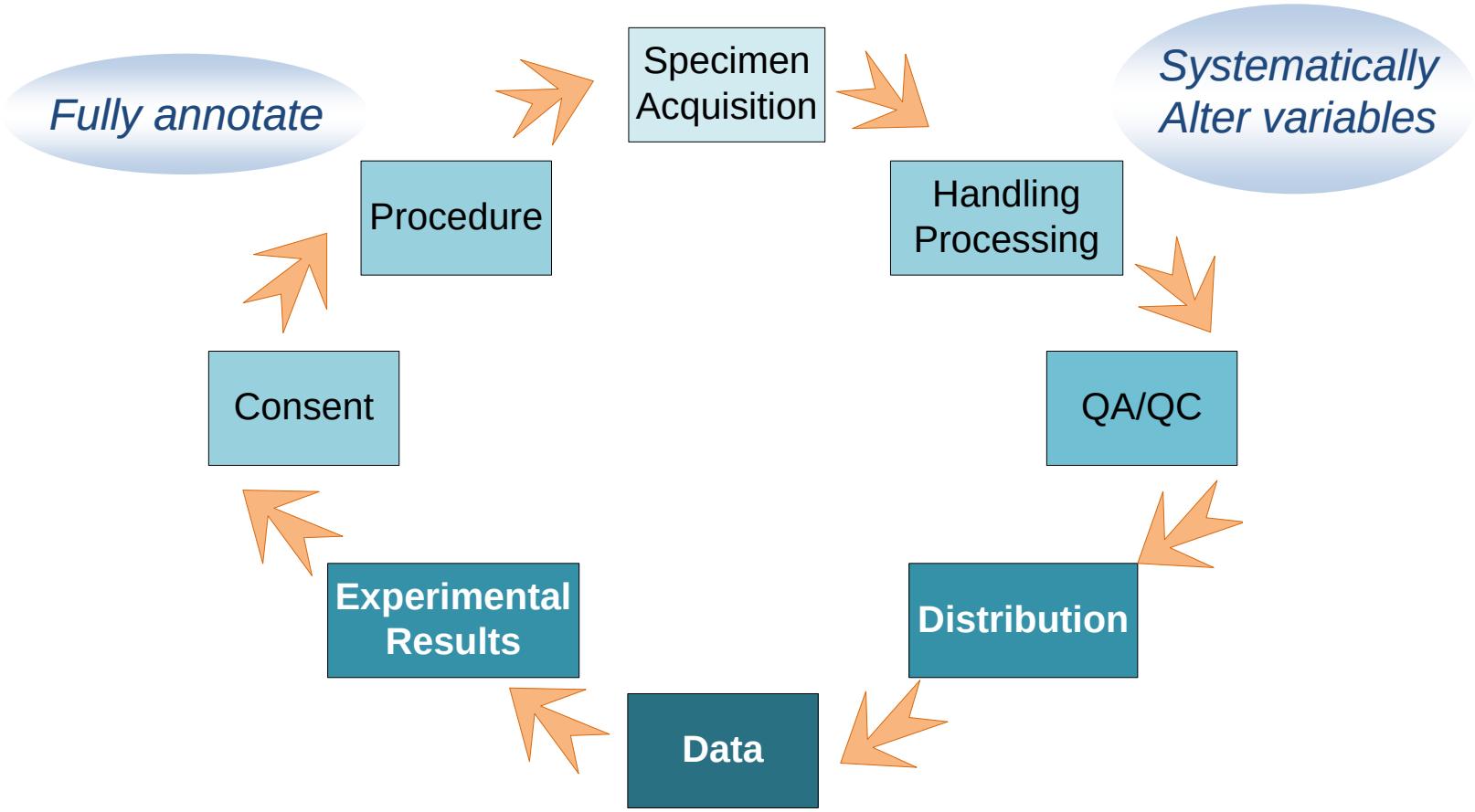
Operational Plan



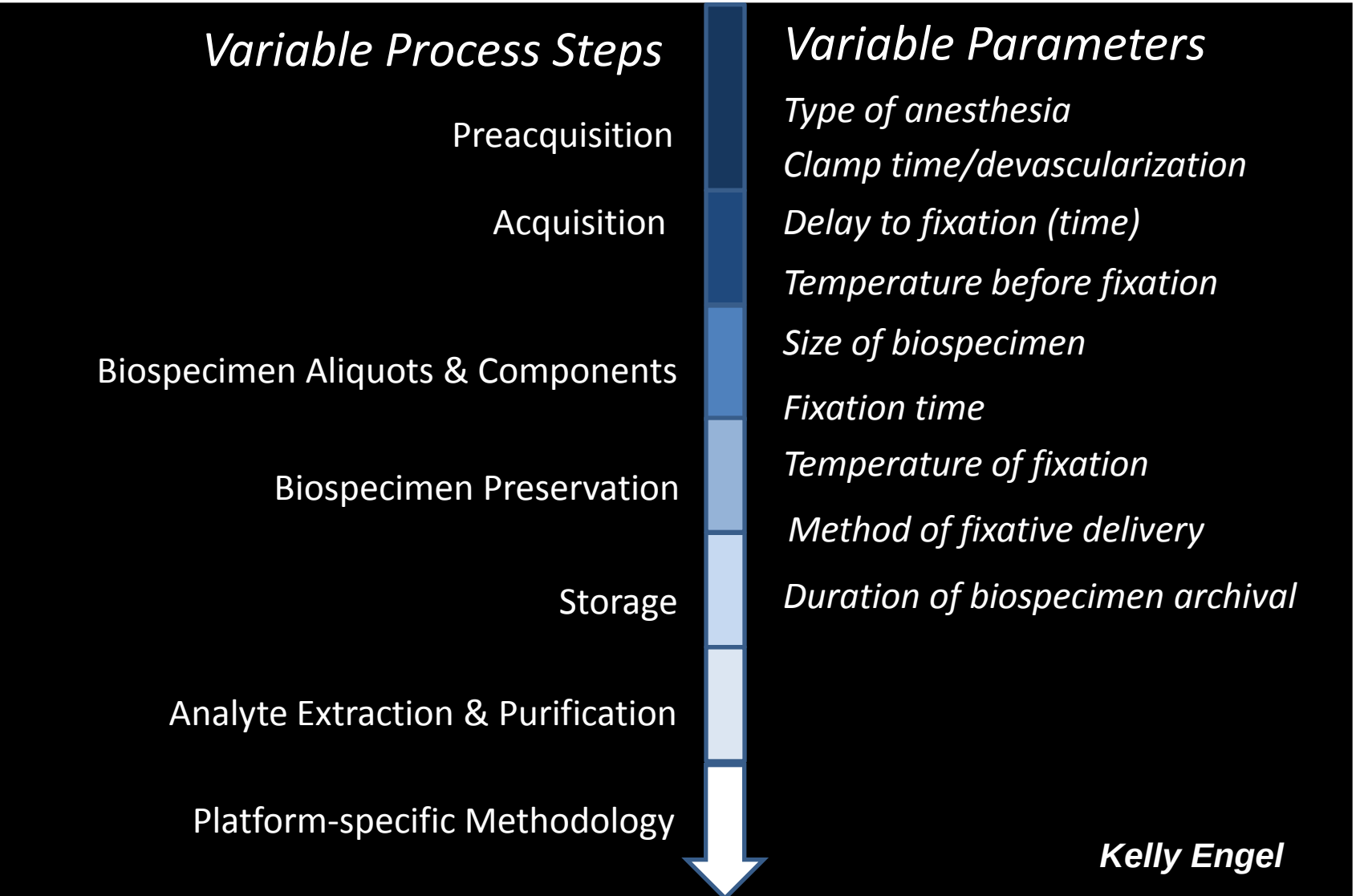
Year 1-2: Pilot experiments to test assumptions

Years 3-5: Systematically alter selected variables, intra-specimen comparisons

Common Data Elements
Data Annotation

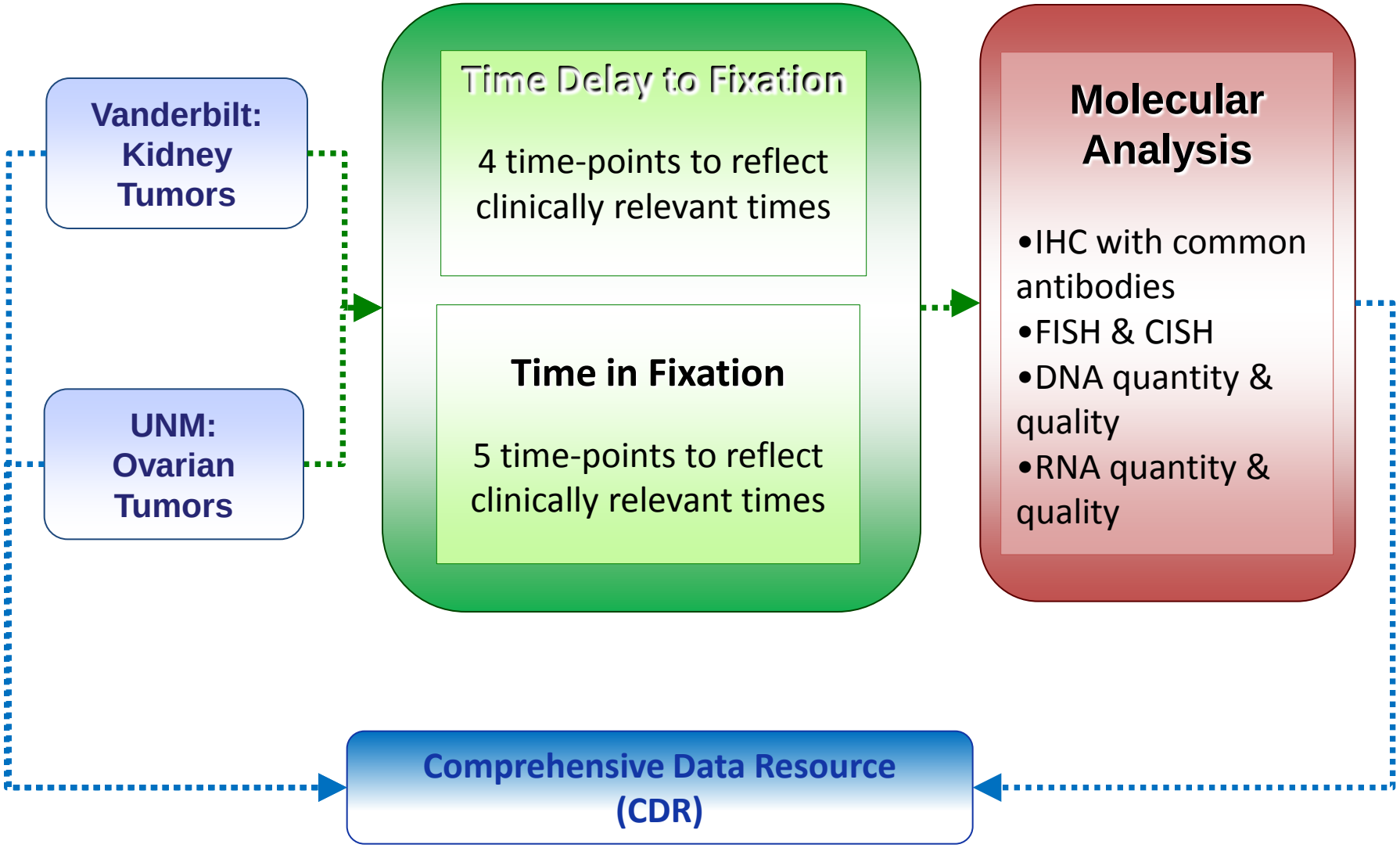
- To be discussed next: Howard Greenman

Biospecimen Research Database Variables and Parameters



Experimental Design Subcommittee

Design of Pilot Study



Considerations for Experimental Design

- Site specific SOPs
- Tumor types and numbers
- Aliquot sizes
- Collection module design
- Case requirements
- Molecular markers and analytic approaches
- Biospecimen and Clinical Data collected
- Replicate samples
- Observational and Experimental Studies

Scientific Steering Committee

- Anesthesiologist
- Pathology assistant/histotech
- Patient advocate (Medical Technologist)
- Pathologists
- Biospecimen collectors
- Molecular pathologists
- Researchers: Basic and translational
- Statisticians

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How can this project benefit R&D and cancer patients?

- Evidence-based biospecimen practices benefit the research community utilizing human biospecimens

- Evidence-based biospecimen practices benefit patients and clinical care
  - Best practices should get incorporated into clinical practice for better clinical assays
  - Tissue collections and microarrays of differentially processed FFPE tissues will serve as a resource for optimizing performance of clinical assays

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