Development of Sample Biorepository for the TRIBE-AKI Consortium

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Objective

- Overview of the TRIBE-AKI consortium
- Informatics and Design of Sample Biorepository Database
- Processes for Sample Storage
TRIBE-AKI Consortium

TRANSLATIONAL RESEARCH
INVESTIGATING BIOMARKER ENDPOINTS- ACUTE KIDNEY INJURY

• Created in 2005
• Cardiac surgery, Transplant, HIV, Aging, Cirrhosis
• www.yale.edu\tribeaki
Acute Kidney Injury

- AKI is common and complicates 5% of hospital admissions and 25% of ICU admissions
- AKI contributes to increased length of stay and mortality
- The annual cost of AKI in US is over $8 billion
TOP PRIORITY RESEARCH QUESTION IN AKI

Acute Kidney Injury

Serum Kidney "Troponin"

Urine Kidney Injury "Troponin"
Biomarkers in Relation to Site of Injury in Nephron

**Proximal Tubule Injury**
- Urine IL-18
- Urine KIM-1
- Urine L-FABP

**Glomerular Filtration and Proximal Tubule Function**
- Serum Creatinine
- Serum Cystatin C
- Urine Cystatin C

**Glomerular Injury**
- Urine albumin excretion

**Loop of Henle Injury**
- Uromodulin

**Distal Tubule**
- Urine NGAL

**Interstitial Fibrosis**
- Urine TGF-β₁
Urine Based Biomarkers
Biomarkers of AKI in Cardiac Surgery

- NIH funded multi-center, prospective, Phase 4 translational research study
- Yale is the data and sample coordinating center
- Multidisciplinary consortium: nephrologists, epidemiologists, basic scientists and cardiac surgeons
- >2,500 patients enrolled; >20,000 samples of urine, serum and DNA collected
Eligible Patients:
Cardiac surgery patients at risk for developing Acute Kidney Injury (AKI)

One pre-op blood sample (10mL)
One pre-op urine sample (10mL)

Post-OP Blood Collection
Day 1: 10mL sample
Day 2: 10mL sample
Day 3: 10mL sample
Day 4: 10mL sample
Day 5: 10mL sample

Post-OP Urine Collection
Day 1: 10mL samples X 4
Day 2: 1 10mL sample
Day 3: 1 10mL sample
Day 4: 1 10mL sample
Day 5: 1 10mL sample
TRIBE-AKI STUDY SITES

Adults
- London, Canada 44%
- Yale 29%
- Danbury 9%
- Duke 8%
- Chicago 6%
- Colorado 4%

Children
- Cincinnati 69%
- Montreal 20%
- Yale 11%
Need For a Biorepository

- Support multisite study
- Research all phases of biomarker development
- Allow linkage with the clinical database as well as biomarker laboratories
- Track inventory and freezer space
- Track the location and movement of individual aliquots at all times
Key Question
Leveraging a clinical research information system to assist biospecimen data and workflow management: a hybrid approach

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Types of Information Captured

- Study Protocol Definition
- Specimen Characteristics
- Inventory Information
Protocol Definition

- Collection time-points
- Specimen types collected at each time point
- # of Aliquots / specimen type / time point
- List of Patient IDs for a given Study
Specimen Characteristics

- **Sample Identification**
  - Barcode, Surrogate Patient ID, Protocol #, Site (for Multi-site studies), Specimen Collection Time (with respect to Protocol), Aliquot #

- **Biological Tissue used**
  - (e.g., Blood, Urine, DNA)

- **Status**
  - Not received, processed and stored, consumed

- **Timestamps**
  - Collection date, Processing Date, Consumption/Shipping Date
Inventory

- Master List of Locations
  - Freezers with Rack and Slot/Box Locations
- Location of individual Aliquots
  - Freezer, Rack, Slot/Box, Row, Column level
- Tracking history of location changes
- Aliquot Consumption
- Aliquot Trans-shipment
Feature Set

- *Scanning Received Specimens*
  - Error Recovery for damaged Barcode Labels
- *Barcode Label printing*
- *Inter-operation with Clinical Research System (TrialDB)*
  - Real-time bulk data import and export
- *Variety of Reports*
Patient Consent

- Allows us to track patient consent
  - Future use for related and unrelated diseases
  - Investigators outside the institution
  - Withdrawal of consent
System Architecture

- **Client-Server Design**
  - Microsoft SQL Server Back-end Database
  - Microsoft Access Front-End - communicates with SQL Server as well as with TrialDB through Open Database Connectivity (ODBC) technology
  - We may move to a Web front-end if number of concurrent users greatly increases
Database Schema

Figure 1 Database schema.
The TRIBE Biorepository
TRIBE Biorepository

- Contains biospecimens from over eight multicenter, international translational research studies.
- Holds approximately half a million biospecimen aliquots for >5000 patients enrolled over the past six years.
Presently the repository consists of 12 freezers
- 5 contain archived samples in TAC LL99-freezer farm
- 1 is located at our Temple St laboratory
- 6 are housed in TAC S-470 (which includes a loaner for temporary storage and backup).
All units are a variety of Thermo Forma/Revco -80C freezers plugged into the emergency back-up AC power with <1min response if a standard power failure occurs.

Units are additionally connected to an analog Sensaphone 400 remote monitoring system with battery backup that is programmed to call a phone tree of four staff members if a failure occurs.
Typical Freezer

- Freezer Name
- Temperature Log
- Emergency Contact Information
- Freezer Inventory Map
Freezer Maintenance

- All units receive bi-annual preventive maintenance
  - This includes inspecting compressor operation, checking the amperage and voltage at the compressor, checking all seals, gaskets, latches and hinges, removing ice build-up from sub lids and breaker strips, inspecting all relays, checking the back-up alarm battery and cleaning the compressor compartment, condenser, fan blades and filter.
Snapshot of Samples Inventory Database
All aspects of biospecimen management are supported by the database.

Specification of biospecimen collection protocols as part of a clinical study; i.e. time points, source tissues to be sampled at each time point, and the number of aliquots for each sample.

Generation of bar coded labels that are used to tag containers sent out to collaborating institutions and used to store collected biospecimens.
<table>
<thead>
<tr>
<th>Barcode Number</th>
<th>Patient id</th>
<th>Site id</th>
<th>HIC Number</th>
<th>Time point</th>
<th>Sample Type</th>
<th>Aliquot #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barcode</td>
<td>Study Acronym (3-lettered)</td>
<td>Patient</td>
<td>Study Acronym (3-lettered)</td>
<td>Patient</td>
<td>Site id</td>
<td>HIC Number</td>
</tr>
<tr>
<td>1274570</td>
<td>CAR-001-0706 Day 1 Blood Aliquot-2</td>
<td>603001221 Day 1</td>
<td>CAR-001-0706 Day 1 Blood Aliquot-2</td>
<td>603001221 Day 1</td>
<td>1274570</td>
<td>CAR-001-0706 Day 1 Blood Aliquot-2</td>
</tr>
</tbody>
</table>
Biorepository database

- Recording of samples that are received by our laboratory with bar-code scanning (including recovery from scanning errors).
- Tracking of storage location of samples in terms of freezer and sub-locations (e.g. rack, slot).
- Tracking of samples that are shipped to external laboratories for analysis.
Snapshot of Labeled Freezer box
Top cover

Freezer, Rack & Slot Information

Patient ids

Sample Type

Study ID: CAR-005-0213
Unique ID: CAR-005-0214
Specimen type: Blood
Snapshot of Freezer Location showing contents of Saturn, Rack B, Slot 5
Snapshot showing the Freezer Location of samples for patient CAR-001-0537
Biorepository database

- Tracking of aliquot consumption, either as part of a bulk-shipping for analysis or dispatching of individual samples to research collaborators.
- Reporting on various aspects, such as aliquots consumed and aliquots available (by patient, biospecimen type, and time point)
- Reporting on the status of a freezer sub-location in terms of biospecimen content.
Snapshot showing the Number of Samples Consumed for CAR site 001 bloods
Snapshot showing the Samples Shipped in ABBOTT NGAL Box 5
Snapshot showing Empty Freezer Locations
Questions??

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