Emory Transplant Center
Biorepository and Integrated Research Support Service

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Research Resources 101
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Outline

• Background
• Sample Acquisition
• Sample Tracking and Phenotyping
• Data Integration
• Current Status
Emory and Georgia Research Alliance Establish Biorepository for Transplant Research

Extraordinary advances in organ and tissue transplantation have saved thousands of lives over the past few decades, yet researchers continue their quest to learn more about the causes of organ failure and to overcome toxicity in the drugs used to maintain transplants. A new facility at Emory University, supported by the Georgia Research Alliance (GRA), will help researchers better link their discoveries in the laboratory to patient care in organ transplantation. The facility is named the Georgia Research Alliance-Emory Transplant Center Biorepository for Translational Science.
Overview of ETC Biorepository

• Developed as a resource to further investigations in the consequences of immunosuppression and the mechanisms of transplant rejection

• A bank of blood, urine and tissues samples associated with clinical phenotypes from transplant donors and recipients, and healthy volunteer

• Ability to collect, process, store and distribute samples reliably

• Prepare samples for downstream assays to be performed at Emory or with other collaborators
How do we build it?
Immune Monitoring Protocol

- **Immune Monitoring and Assay Development in Organ Transplant Recipients**
  - Purpose: “...collect samples of your blood, urine, biopsy and/or lymph node tissue to develop and validate new tests of the immune system at the Emory Transplant Center. These tests are designed to see how the immune system works and to see how medicines can change the immune system.”
  - “No experimental procedures, investigational medicines or other interventions will be done to you for the purposes of this study.”

- Adult and pediatric transplant recipients and donors
- Normal controls enrolled for a comparator group as needed
Immune Monitoring Protocol

• Broad applicability
  • Specific language in the consent for exploratory use of the samples and “genetic testing”

• All investigators on one protocol
  • Consent storage is centralized
  • Consenting process is disbursed
  • One IRB interface

• No procedures specifically for research
  • Sample draws during normal clinical visits

• Robust means of tracking samples
  • Sample of interested pulled for research
  • Destroyed upon request
Data can only be as good as the samples stored

Standardization and Testing
Example of different storage methods affecting results

- Thawed PBMCs that were stored by different freezing protocols
- Stimulated with mitogen
- Analyzed by flow cytometry for functionality by intracellular cytokine production

<table>
<thead>
<tr>
<th>Resting cells</th>
<th>Freezing media of 90% FCS and 10% DMSO</th>
<th>Freezing media (20% FCS, 7.5% DMSO, 72.5% RPMI-1640)</th>
</tr>
</thead>
</table>

Xu alone_Tube_002.fcs...Q3: CD45RA+, CD197—
Xu#1 vs Enn_Tube_002.fcs...Q3: CD45RA+, CD197—
Xu#2 vs Enn_Tube_002.fcs...Q3: CD45RA+, CD197—

[Flow cytometry graphs]
Standardization of methods

- All PBMCs stored by standard SOP
- Significantly improved cell viability and consistency

### % Viability of Cryopreserved PBMCs

<table>
<thead>
<tr>
<th>Years</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
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<tbody>
<tr>
<td>Number of values</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>7</td>
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<tr>
<td>Minimum</td>
<td>55</td>
<td>76.3</td>
<td>74.8</td>
<td>73.77</td>
<td>78.9</td>
<td>84.6</td>
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<tr>
<td>25% Percentile</td>
<td>75.13</td>
<td>77.01</td>
<td>82.7</td>
<td>82.49</td>
<td>84.2</td>
<td>86.2</td>
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<tr>
<td>Median</td>
<td>77</td>
<td>84.42</td>
<td>90.45</td>
<td>92.55</td>
<td>88</td>
<td>90.9</td>
</tr>
<tr>
<td>75% Percentile</td>
<td>90.43</td>
<td>88.75</td>
<td>92.1</td>
<td>94.85</td>
<td>94.1</td>
<td>93.3</td>
</tr>
<tr>
<td>Maximum</td>
<td>90.9</td>
<td>90.1</td>
<td>95.1</td>
<td>95</td>
<td>97.41</td>
<td>93.8</td>
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<tr>
<td>Mean</td>
<td>79.18</td>
<td>83.46</td>
<td>87.87</td>
<td>89.01</td>
<td>88.7</td>
<td>90.02</td>
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<tr>
<td>Std. Deviation</td>
<td>12.69</td>
<td>5.677</td>
<td>7.129</td>
<td>8.294</td>
<td>6.248</td>
<td>3.683</td>
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<tr>
<td>Std. Error of Mean</td>
<td>4.797</td>
<td>2.317</td>
<td>2.911</td>
<td>3.386</td>
<td>2.361</td>
<td>1.392</td>
</tr>
<tr>
<td>Lower 95% CI of mean</td>
<td>67.44</td>
<td>77.5</td>
<td>80.39</td>
<td>80.31</td>
<td>82.92</td>
<td>86.62</td>
</tr>
<tr>
<td>Upper 95% CI of mean</td>
<td>90.92</td>
<td>89.42</td>
<td>95.35</td>
<td>97.72</td>
<td>94.48</td>
<td>93.43</td>
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<tr>
<td>Coefficient of variation</td>
<td>16.03%</td>
<td>6.80%</td>
<td>8.11%</td>
<td>9.32%</td>
<td>7.04%</td>
<td>4.09%</td>
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</tbody>
</table>
Standardization of methods

- Isolation of PBMCs
- Splenocyte isolation
- Lymphocyte isolation from tissues
- Thawing of frozen cells and cell recovery
- Cell counting and viability
- Isolation and storage of plasma and serum
- Cryopreservation of urine
- DNA processing
- Conversion of RNA to cDNA
- Determining nucleic acid concentration
Sample Tracking and Phenotyping

LIMS and REDCap
Laboratory Information Management System (LIMS)

- Emory-RWIT supported solution: Nautilus
- Track patient consent/information
  - HIPPA compliant
- Track sample types and collection events
  - Enables tracking of missed collection Events
- Patient
- Visits
- Sample
  - aliquots
- Track sample processing and required tests
- Organizes sample storage
- Tracks distributed samples
- Generates reports
In depth clinical descriptions of samples

- Using REDCap database tool from RWIT
- Eg: Biopsy specimens
  - Pathologist assessment
  - Clinician assessment
  - Acute rejection
  - Immunosuppression
  - Viral episodes
  - Other clinical events
- Can be modified for sample sets of interest
Integration
Clinical Logistics

<table>
<thead>
<tr>
<th>Time points</th>
<th>Enrollment</th>
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<tbody>
<tr>
<td></td>
<td>1</td>
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<tr>
<td></td>
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</table>

- Clinical Research Coordination
- Clinical Data
- Sample Phenotyping
- Specimens
Clinical Logistics

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Clinical Research Coordination

Clinical Data

Specimens

Sample Phenotyping
Clinical Data Collection

- OTTR
- EeMR
- EML
  - PathNet
  - Helix
  - others
- Enrollment Data, CRFs
- Outside Centers’ Data
- Clinical Data
- Specimens
- Clinical Research
Research Sample Collection

Specimens → Research

LIMS

Aliquot

Storage

Assay 1

Assay 2

Assay 3

Results record 1

Results record 2

Results record 3
Integration
Integrated Research Support Services

- Clinical research nurses and coordinators
  - Enrollment
  - Collection
  - Clinical Data

- Biorepository
  - Staff
  - Protocols
  - Processing, Processing, Processing
  - Storage
  - Shipping

- Histology Core

- Flow Cytometry Core

- Molecular Core
Current status
Current Studies

• Immune Monitoring Protocol
  • ~95% of kidney transplant patients not enrolled other trials are approached
  • ~85% enrollment
  • Expanded to liver, kidney/pancreas, lung

• > 115,000 sample aliquots stored
  • Baseline /Protocol/ for cause biopsies
  • PBMCs
  • Serum
  • Plasma
  • Whole Blood
  • Urine
Current Studies

• Immune Monitoring Protocol
  • ~95% of kidney transplant patients not enrolled other trials are approached
  • ~85% enrollment
  • Expanded to liver, kidney/pancreas, lung

• > 150,000 sample aliquots stored
  • Baseline /Protocol/ for cause biopsies
  • PBMCs
  • Serum
  • Plasma
  • Whole Blood
  • Urine

• Dedicated Web Page
  • Specimen Request
    • [http://survey.emory.edu/fs.aspx?surveyid=76a2b5509d9496183a372954fd75c57](http://survey.emory.edu/fs.aspx?surveyid=76a2b5509d9496183a372954fd75c57)
  • Study Request
    • [http://survey.emory.edu/fs.aspx?surveyid=e9e770a50784543b41ac38bd4c966c1](http://survey.emory.edu/fs.aspx?surveyid=e9e770a50784543b41ac38bd4c966c1)
Current Studies

- >40 Studies
  - 26 Multicenter
  - 25 Adult
  - 15 Pediatric
  - 12 IMP
  - 5 International
- Investigator initiated
  - Exploratory
  - Grant funded
- Clinical Trials
  - Federally Funded
  - Industry sponsored
Acknowledgments

• Biorepository
  • Rachelle Jones (manager)
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  • FDA
  • ITN