Scripps Health/Scripps Clinic Bio-Repository and Bio-Informatics Core Monthly Report

10/2024

Specimen Collection

Total Aliquots: **57,110 (in physical inventory)**
Aliquots added in October: **804**

Total Samples: **24,543 (in physical inventory)**
Samples added in October: **162**

Specimens (aliquots) Released for Research in October: **149**
Total Specimens Released for Research: **10,845**

New Contributing Sources: **0**
Total Contributing MD Sources/locations: **25**

Participants

BR Consented: **3,118**
New Consents in October: **44**
Non-Consented Contributors (inherited studies/remnant specimens): **11,010**

Remnant Samples

COVID-19: **2,065**
FLU A: **1,227**
FLU B: **22**
RSV: **19**
Normals: **463**
Others: **25**

Normal Samples

Apparently Healthy Donors (Consented): **166**
Participants added in October: **0**

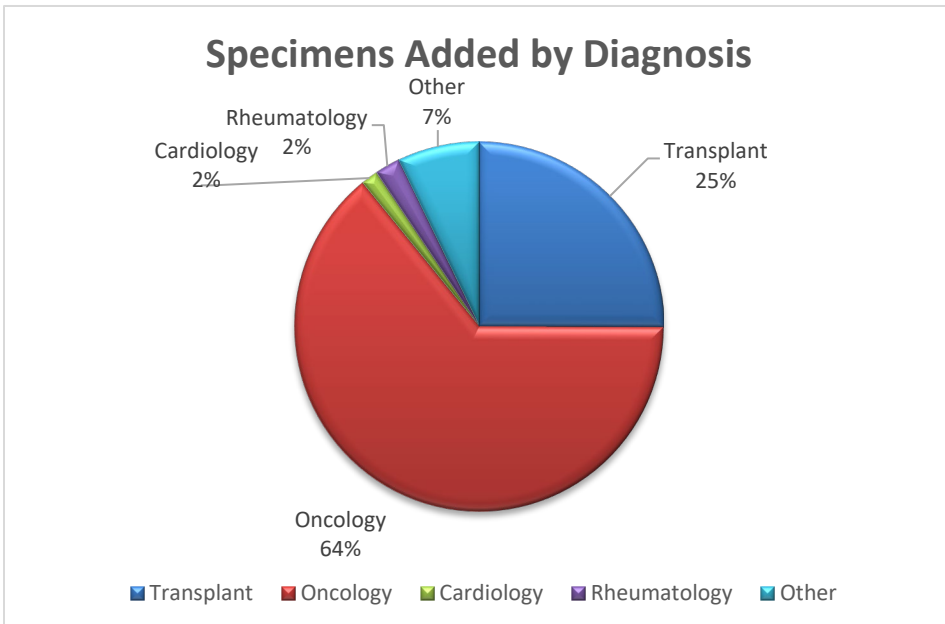## *Primary Diagnosis Breakdown*

Specimens added to Inventory
Transplant: **203**
Oncology: **519**
Cardiology: **12**
Rheumatology: **18**
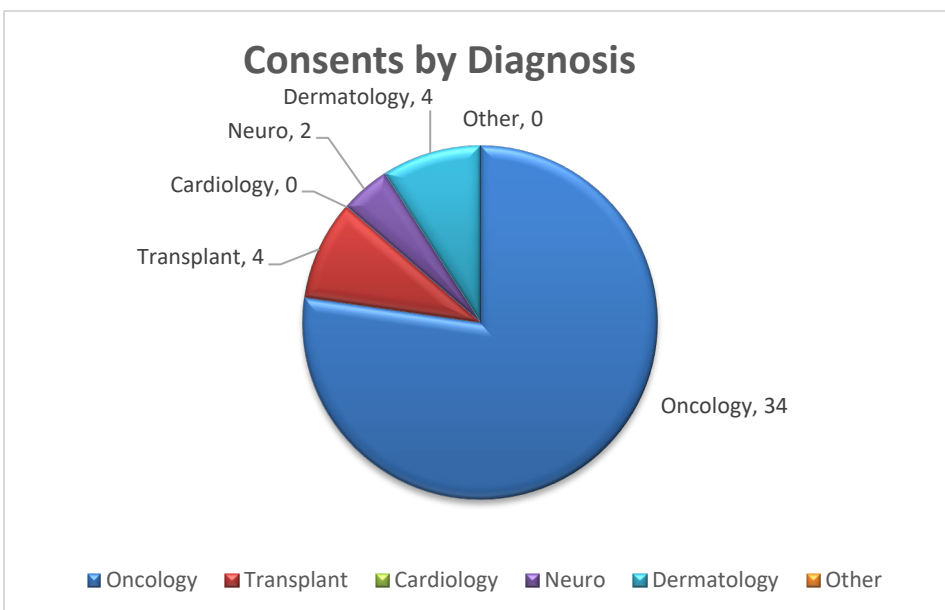Other: **58**

Specimens Added by Diagnosis

Other 7%
Rheumatology 2%
Cardiology 2%
Transplant 25%
Oncology 64%

Legend: Transplant · Oncology · Cardiology · Rheumatology · Other

New Consents:
By Diagnosis

Oncology: **34**
Transplant: **4**
Cardiology: **0**
Neuro: **2**
Dermatology: **4**
Other: **0**

Consents by Diagnosis

Dermatology, 4
Neuro, 2
Cardiology, 0
Other, 0
Transplant, 4
Oncology, 34

Legend: Oncology · Transplant · Cardiology · Neuro · Dermatology · Other

Bio-Specimen Requests

Pending Requests: **0**
Requests Approved by the Oversight Committee in October: 2
Recently Approved Requests: 2

Sangeetha Nair (Hologic): Hologic has amended their biospecimen request, increasing the total plasma samples from 50 to up to 200 for CMV diagnostic assay development.

Valeria Mas (University of Maryland): Request is for tissue, blood, and urine samples from kidney transplant patients with post-transplant acute kidney injury are requested for single-cell RNA sequencing.

Recent Publications from SCBBC Staff & Investigators Utilizing the SCBBC (2023-2024 FY)

1. Bhagar R, Gill SS, Le-Niculescu H, Yin C, Roseberry K, Mullen J, Schmitz M, Paul E, Cooke J, Tracy C, Tracy Z, Gettelfinger AS, Battles D, Yard M, Sandusky G, Shekhar A, **Kurian SM**, Bogdan P, Niculescu AB. Next-generation precision medicine for suicidality prevention. Transl Psychiatry. 2024 Sep 6;14(1):362. doi: 10.1038/s41398-024-03071-y.

2. Stephanie Almeida, William Snyder, Mita Shah, **Jonathan Fisher**, **Christopher Marsh**, Alana Hawkes, Diana Gorial, Sean DeWolf, **Dianne B. McKay**. Revolutionizing Deceased Donor Transplantation: How New Approaches to Machine Perfusion Broadens the Horizon for Organ Donation. Transplantation Reports. 2024.100160. ISSN2451-9596.https://doi.org/10.1016/j.tpr.2024.10016.

3. DeWolf SE, Hawkes AA, **Kurian SM**, Gorial DE, Hepokoski ML, Almeida SS, Posner IR, McKay DB. Human pulmonary microvascular endothelial cells respond to DAMPs from injured renal tubular cells. Pulm Circ. 2024 Jul;14(3):e12379. doi: 10.1002/pul2.12379. eCollection 2024 Jul. PubMed PMID: 38962184; PubMed Central PMCID: PMC11220341.

4. **S. Kurian**, J. Fleming, B. Barrick**, A. Martin, C. M. Marsh.** Diagnostic Performance of Peripheral Blood Gene Expression At 2 Months Post-transplant And Interim Correlation of Tests with Renal Function Over 2 Years. Abstract accepted as late breaking poster at the American Transplant Congress, Philadelphia, USA: June 1 – 5 2024.

5. **S. Kurian, A. Martin, E. Burgess, C. Marsh**. Serial Metagenomic Profiling Reveals Temporal Shifts in Microbial Composition in Kidney and Liver Transplant Recipients. Abstract accepted a poster at the American Transplant Congress, Philadelphia, USA: June 1 – 5 2024.

6. Hill MD, Gill SS, Le-Niculescu H, MacKie O, Bhagar R, Roseberry K, Murray OK, Dainton HD, Wolf SK, Shekhar A, **Kurian SM**, Niculescu AB. Precision medicine for psychotic disorders: objective assessment, risk prediction, and pharmacogenomics. **Mol Psychiatry.** 2024 Feb 8. doi: 10.1038/s41380-024-02433-8. Epub ahead of print. PMID: 38326562.

7. New J, Cham J, Smith L, Puglisi L, Huynh T, **Kurian S**, Bagsic S, Fielding R, Hong L, Reddy P, Eum KS, **Martin A, Barrick B, Marsh C**, Quigley M, Nicholson LJ, Pandey AC. Effects of antineoplastic and immunomodulating agents on postvaccination SARS-CoV-2 breakthrough infections, antibody response, and serological cytokine profile. **J Immunother Cancer.** 2024 Jan 31;12(1): e008233. doi: 10.1136/jitc-2023-008233. PMID: 38296596; PMCID: PMC10831464.

8. Long JJ, Motter JD, Jackson KR, Chen J, Orandi BJ, Montgomery RA, Stegall MD, Jordan SC, Benedetti E, Dunn TB, Ratner LE, Kapur S, Pelletier RP, Roberts JP, Melcher ML, Singh P, Sudan DL, Posner MP, El-Amm JM, Shapiro R, Cooper M, Verbesey JE, Lipkowitz GS, Rees MA, **Marsh CL**, Sankari BR, Gerber DA, Wellen JR, Bozorgzadeh A, Gaber AO, Heher EC, Weng FL, Djamali A, Helderman JH, Concepcion BP, Brayman KL, Oberholzer J, Kozlowski T, Covarrubias K, Massie AB, McAdams-DeMarco MA, Segev DL, Garonzik-Wang JM. Characterizing the risk of human leukocyte antigen-incompatible living donor kidney transplantation in older recipients. **Am J Transplant.** 2023 Sep 23: S1600-6135(23)00698-6. doi: 10.1016/j.ajt.2023.09.010. Epub ahead of print. PMID: 37748554.

9. Long JJ, Nijhar K, Jenkins RT, Yassine A, Motter JD, Jackson KR, Jerman S, Besharati S, Anders RA, Dunn TB, **Marsh CL**, Rayapati D, Lee DD, Barth RN, Woodside KJ, Philosophe B. Digital imaging software versus the "eyeball" method in quantifying steatosis in a liver biopsy. **Liver Transpl.** 2023 Mar 1;29(3):268-278. doi: 10.1097/LVT.0000000000000064. Epub 2023 Jan 19. PMID: 36651194.

10. Towards precision medicine for anxiety disorders: objective assessment, risk prediction, pharmacogenomics, and repurposed drugs. Roseberry K, Le-Niculescu H, Levey DF, Bhagar R, Soe K, Rogers J, Palkowitz S, Pina N, Anastasiadis

WA, Gill SS, **Kurian SM**, Shekhar A, Niculescu AB. **Mol Psychiatry**. 2023 Mar 7. doi: 10.1038/s41380-023-01998-0.

Active/in Startup Studies currently supported by the Biorepository.

	Research Projects - Ongoing	Lead/BR Staff	Project Type	Mechanism	Funding	Study Description
1	Genzyme Proteomics Study	Kurian, Marsh	Study	Pilot Award	Scripps RIC	Proteomic profiling of post-transplant kidney patients to look at inflammatory responses
2	TruGraf v1 Prospective Study - TRULO	Fisher, Kurian, Martin	Study/Research Coordinator	Sponsored Grant	TGI - Industry	Diagnostic monitoring of kidney transplant patients for acute rejection
3	ARIMA Genomics cfDNA	Kurian, Marsh	Study	Pilot Award	SCMG	Profiling the promoter landscape of the genome in kidney transplant patients
4	LOMR Molecular Studies	Marsh, Deising, Kurian	Study	Pilot Award	Scripps RIC	Developing a clinical and molecular predictor of liver transplant outcomes
5	Metagenomic early post-transplant clinical outcomes in kidney transplant recipients	Kurian, Martin, Burgess	Study/Research Coordinator	Pilot Award	Scripps RIC	Looking at the responses in post-transplant microbiome profiles in the tissue urine and stool
6	KW Biomarker Project	Kurian, Marsh	Study	KW Award Subcontract	Kruger-Wyeth Settlement	Creating new molecular predictors of breast cancer using genomic and proteomic profiling
7	KW REFRESH Study	Kurian, Martin	Study	KW Award Subcontract	Kruger-Wyeth Settlement	Evaluate cognitive decline and dementia indicators in women
8	KW AM-WELL Project	Kurian, Martin	Study	KW Award Subcontract	Kruger-Wyeth Settlement	Creating care across the continuum of a patient's cancer journey by implementing a Breast Cancer Survivorship Program
9	ALTA TIPS	Deising, Martin	Research Coordinator	Academic Study	Univ of Michigan	Assess contemporary patterns of use of TIPS stents and associated patient related outcomes
10	Cardiac Amyloidosis Cohort	Mohan, BR Staff	Sample Collection	_	_	Cardiac Amyloid disease

						study of risk factors and molecular correlates
11	ClearNote (previously Bluestar Genomics)	Martin	Phlebotomy, Processing, Storage	Sponsored Study	ClearNote	Liquid Biopsy colorectal cancer detection
12	aiGENE	Kurian, Martin, Burgess	Study/Research Coordinator	Sponsor	aiGene - Industry	Measure the effectiveness of any cancer therapy. The technology is based on cfDNA and ctDNA binding properties.
13	DREAM BMT	Martin, Kurian	Study	Pilot Award	SCMG	Enhance the diagnosis, management, and overall care of patients undergoing allogenic hematopoietic stem cell transplant (alloHSCT) who are at risk of developing Graft-versus-Host Disease (GVHD).
14	Surveil	Martin, Kurian, Burgess	Study	Sponsor	TGI	Registry study of biomarker guided immunosuppression in kidney transplant patients
15	Retro-ART	Martin, Kurian, Burgess	Study/Research Coordinator	Sponsor	Castle Biosciences, Inc. - Industry	To determine the efficacy of adjuvant radiation therapy (ART) in a population of subjects tested with the DecisionDx-SCC test
16	OCS Liver Perfusion Registry (OLP-II)	Martin, Kurian	Study	Sponsor	Transmedics - Industry	collect short and long-term post-transplant clinical outcomes data of donor livers preserved and assessed on OCS Liver system and to document performance of the OCS Liver device in the real-world setting
17	FETOLY Heart Study	Kurian	IRB Support	Sponsor	Diagnoly Inc	To evaluate the performance of Fetoly-Heart in automatically detecting and localizing standard fetal heart quality criteria.

## Key Insights from our Recent Conference on October 19, 2024

Alex Wiseman, MD, FAST: Advancing Transplantation with Genomics and Biomarker Discovery

- Highlights **donor-derived cell-free DNA (dd-cfDNA)** as a non-invasive biomarker for rejection.
- Discusses **HLA eplet mismatching** and gene expression profiling for risk stratification.
- Focuses on using **genomic tools** to predict transplant outcomes and tailor immunosuppression.
- Aligns with precision medicine by integrating molecular diagnostics to improve graft monitoring.

Jamil Azzi, MD, PhD, FAST: Urinary Exosome mRNA as a Diagnostic Signature for Kidney Transplant Rejection

- **Urinary exosome mRNA** as a non-invasive biomarker for detecting kidney transplant rejection.
- Reliable biomarkers using **high-throughput technologies** for transplant rejection monitoring.
- Urinary exosome RNA has a high predictive value (AUC ~ 0.90) for diagnosing all-cause rejection.
- Non-Invasive Monitoring with **urinary exosome RNA tests**, offering a faster/cost-effective diagnostic
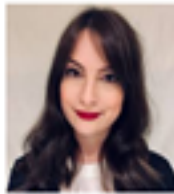
Katelynn Madill-Thomsen, PhD: The Clinical Promise of Novel Biomarkers in Liver Transplantation

- Findings from the **INTERLIVER study**, using gene expression to explore liver transplant rejection.
- Identifies **NK cell-enriched rejection-like patterns** for diagnosing liver transplant rejection.
- Aims to improve diagnostics through non-invasive genomic profiling, reducing biopsy reliance.
- Aligns with precision diagnostics to enhance early detection of rejection and manage transplant injury

Mandy Ford, PhD: The Role of T Cell Responses in Transplantation and Immunosuppression

- Role of **memory T cells** in transplant rejection, particularly in immunosuppression resistance.
- Use of **single-cell RNA sequencing** to identify T cell signatures associated with rejection.
- Exploring **TIGIT** as a therapeutic target to enhance immune regulation in transplantation.
- Contributes to the development of targeted immunosuppressive strategies based on immune profiling.

Kiran Kaur Khush, MD: Innovations in Non-Invasive Diagnostic Approaches for Post-Transplant Monitoring

- Emphasized multi-omics approaches (genomics, transcriptomics, proteomics) for post-transplant care.
- Highlighted cell-free DNA (cfDNA) as a key non-invasive biomarker for detecting graft injury and rejection.
- Integrating gene expression profiling and miRNA analysis for precision diagnostics in heart transplants.
- Aligns with molecular diagnostics to replace traditional biopsies and improve long-term outcomes.

John Lee, MD: Translational Microbiome Research in Transplantation

- Relationship between the gut microbiome and post-transplant complications.
- Focused on bacterial metabolism of tacrolimus and mycophenolic acid, linking microbiome to drug efficacy.
- Exploring urinary cell-free DNA profiling for non-invasive infection monitoring in kidney transplant patients.
- Aligns with microbiome research trends of new diagnostic & therapeutic strategies for post-transplant care

Madhav Menon, MBBS, MD, FACP: Genomic Insights in Therapeutic Advances in CKD/Transplant Fibrosis

- Focused on **interstitial fibrosis and tubular atrophy (IFTA)** as a key cause of graft failure.
- **Shroom3 variants** and their role in CKD and allograft fibrosis.
- Development of **protein-protein interaction inhibitors (P2Is)** to target fibrosis pathways.
- Aligns with precision medicine by targeting specific molecular mechanisms to improve graft survival.

James Mathew, PhD, FAST: Decoding Indicators of Transplant Rejection with T Cell Clones

- **T cell receptor (TCR) repertoire sequencing** to study donor-reactive CD8+ T cells.
- Leverages **ImmunoSEQ technology** for non-invasive diagnostics to predict rejection.
- Offers an alternative to invasive biopsies, aligning with the trend towards blood-based diagnostics

Jorke Willemse, PhD: Organoid Technology in Graft Regeneration and Disease Modeling

- Discussed the use of **organoid technology** for liver graft regeneration and disease modeling.
- Focused on **stem-cell-derived organoids** for **biliary epithelium regeneration** and **disease modeling.**
- Highlights the potential of **organoid-based graft** repair and organ regeneration in transplantation.
- Aligns with future trends in tissue engineering and regenerative medicine to address organ shortages.

Stan Rose, PhD: A Transplant Recipient's View on the Evolution of Post-Transplant Molecular Monitoring

- **Personal Experience**: "silent rejection" underscoring the need for better monitoring tools.
- **Advocating for Genomic Tests**: genomic-based tests to detect early signs of rejection
- **Challenges in Adoption**: challenges of convincing transplant centers to adopt new molecular tests
- **Opportunities and Future Directions: AI-driven, non-invasive tests**

Dianne McKay, MD: Understanding Sex Differences in Transplant Outcomes

- **Sex and gender differences** in transplant rejection, immune responses, and access.
- Women generally have heightened immune responses, leading to different graft outcomes.
- Highlights disparities in transplant access for women, influenced by socioeconomic factors and frailty.
- Aligns with the push for sex-based personalized medicine in transplantation.

Ali Zarrinpar, MD, PhD: Personalized Immunosuppression for Liver Transplants

- Advocates for phenotypic personalized medicine (PPM) to tailor immunosuppressive regimens.
- Explores Bayesian dosing algorithms for optimizing immunosuppression, especially for tacrolimus.
- Focuses on individualized treatment based on clinical variables like genetics and pharmacokinetics.
- Supports computational tools for personalized post-transplant care, improving graft survival.