Scripps Health/Scripps Clinic Biorepository and Bioinformatics Core Monthly Report

8/2025

Specimen Collection

Total Aliquots: **63,763 (in physical inventory)**
Aliquots added in August: **526**

Total Samples: **25,975 (in physical inventory)**
Samples added in August:

Specimens (aliquots) Released for Research in August:
Total Specimens Released for Research: **12,705**

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

Participants

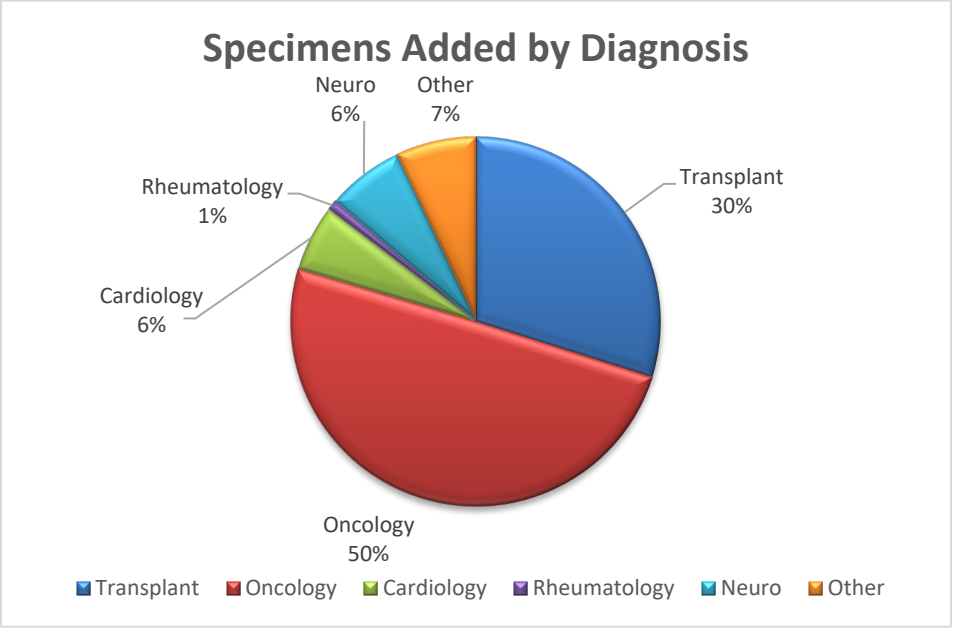
BR Consented: **3,317**
New Consents in August:
Non-Consented Contributors (inherited studies/remnant specimens): **11,832**

Normal Samples

Apparently Healthy Donors (Consented): **167**
Participants added in August:

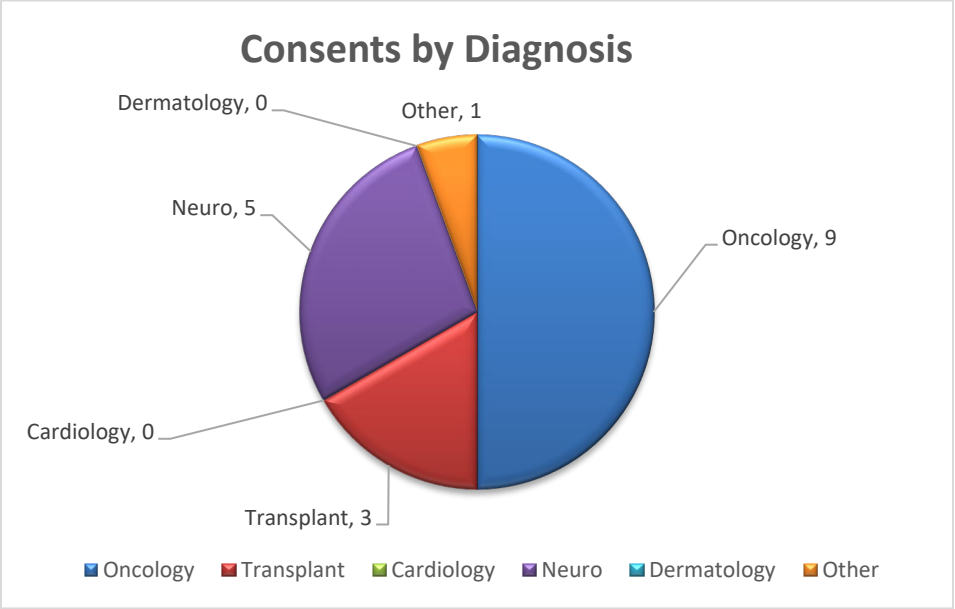
Primary Diagnosis Breakdown

Specimens added to Inventory
Transplant:
Hematology/Oncology:
Cardiology:
Rheumatology:
Neuro:
Other:



New Consents:
By Diagnosis

Oncology:
Transplant:
Cardiology:
Neuro:
Dermatology:
Other:



Bio-Specimen Requests

Pending Requests: 0
Requests Approved by the Oversight Committee in August: 0
Potential requests: **2**

Recent Publications from SCBBC Staff & Investigators Utilizing the SCBBC (2024-2025 FY)

1. Bhagar R, Le-Niculescu H, Corey SC, Gettelfinger AS, Schmitz M, Ebushi A, Matei E, Woods C, Mullen J, **Kurian SM**, Shekhar A, White FA, Niculescu AB. Next-generation precision medicine for pain. Mol Psychiatry. 2025 Aug 25;. doi: 10.1038/s41380-025-03186-8. [Epub ahead of print] PubMed PMID: 40855006.
2. Bedoya-López AF, Ahn S, Ensenyat-Mendez M, Orozco JIJ, Iñiguez-Muñoz S, Llinàs-Arias P, Thomas SM, Baker JL, Sullivan PS, Makker J, Steele JB, **Kurian SM**, Marzese DM, DiNome ML. Epigenetic determinants of an immune-evasive phenotype in HER2-low triple-negative breast cancer. NPJ Precis Oncol. 2025 Aug 16;9(1):287. doi: 10.1038/s41698-025-01023-3. PubMed PMID: 40817343; PubMed Central PMCID: PMC12356864.
3. 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.
4. 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.
5. 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.
6. **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.
7. **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.
8. 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.
9. 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.

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
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, Phlebotomy, Processing, Storage	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 poperties.
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	Retro-ART	Martin, Kurian, Burgess	Study, Pathology Requests	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
15	OCS Liver Perfusion Registry (OLP-II)	Martin, Kurian	Study, Research Coordinator	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
16	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.
17	PrRLS	Martin, Kurian	Phlebotomy, Processing, Storage		Dr. Karen Lei	

Notes:

- The biorepository had a good presence at the World Transplant Congress in San Francisco. Our booth was well received, generating a few inquiries about transplant as well as oncology samples. Our team will be following up to these requests.

- A recent study, supported by biorepository through the provision of samples to Duke University and an international team of collaborators, was published in *NPJ Precision Oncology*. In addition to supplying biospecimens, our team contributed to the project through manuscript review and writing.

npj | precision oncology

Article

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Epigenetic determinants of an immune-evasive phenotype in HER2-low triple-negative breast cancer

Andrés F. Bedoya-López[1,11], Sookyung Ahn[2,3,11], Miquel Ensenyat-Mendez[2], Javier I. J. Orozco[4], Sandra Iñiguez-Muñoz[1], Pere Llinàs-Arias[1], Samantha M. Thomas[5,6], Jennifer L. Baker[7], Peggy S. Sullivan[8], Jitin Makker[8], Julie B. Steele[9], Sunil M. Kurian[10], Diego M. Marzese[1,2,6] & Maggie L. DiNome[2,6]

Identifying molecular drivers in triple-negative breast cancer (TNBC) is crucial. While HER2-low expression predicts response to novel antibody-drug conjugates, its biological influence on TNBC biology is unknown. We performed a comprehensive multi-omics analysis, integrating genomic, epigenomic, transcriptomic, and proteomic profiling to characterize HER2-low TNBC. We generated genome-wide DNA methylation profiles from a multi-institutional cohort and integrated our data with three independent cohorts (TCGA, SCAN-B, I-SPY2). TNBC cases were categorized as HER2-zero (IHC 0) or HER2-low TNBC (IHC 1+/2+, ISH non-amplified). Among 506 patients (HER2-low, $n = 288$; HER2-zero, $n = 218$), HER2-low TNBC exhibited significantly lower tumor mutational burden ($P = 0.02$). Epigenetic analysis identified 5287 differentially methylated sites, with consistent hypermethylation of *HLA* genes in HER2-low tumors. Transcriptomic analyses revealed significant downregulation of genes enriched in immune response pathways (e.g., leukocyte activation, T-cell signaling) in HER2-low TNBC (adjusted $P < 0.001$). Immune cell deconvolution showed reduced immune cell infiltration in the HER2-low tumor microenvironment ($P = 0.002$). Higher expression of five immune-related genes, downregulated in HER2-low, correlated with improved relapse-free (HR = 0.52; $P < 0.001$) and overall survival (HR = 0.36; $P < 0.001$). HER2-low TNBC tumors display distinct molecular features compared to HER2-zero, imparting an immune-evasive phenotype. These findings provide critical insights into the unique biology of HER2-low TNBC, warranting further clinical investigation.

- Another recent study in Molecular Psychiatry built upon a decade of work using sequencing-based gene expression analysis to identify a molecular signature for pain. The study demonstrated its potential as a tool for personalized medicine, enabling objective assessment of pain severity and guiding treatment selection with medications or nutraceuticals.

Molecular Psychiatry www.nature.com/mp

ARTICLE OPEN

Check for updates

Next-generation precision medicine for pain

R. Bhagar[1,9], H. Le-Niculescu[1,9], S. C. Corey[2], A. S. Gettelfinger[2], M. Schmitz[3], A. Ebushi[3], E. Matei[1,3], C. Woods[2], J. Mullen[4], S. M. Kurian[5], A. Shekhar[6], F. A. White[7] and AB Niculescu[1,3,8]✉

Chronic pain remains a massive problem in society in general, and in mental health patients in particular, being strongly bi-directionally connected to mental health. Lack of widespread use of objective information has hampered treatment and prevention efforts. Pain is a spectrum of severity, from transient vague discomfort to chronic excruciating incapacitation. Blood biomarkers that track pain severity can provide a window into the biology of pain, as well as could help with assessment and treatment. A previous study by us was positive. Here we describe new studies we conducted trans-diagnostically in psychiatric patients, starting with the whole genome, to expand the identification, prioritization, validation and testing of blood gene expression biomarkers for pain. We carried out two separate studies, on two different platforms, microarrays and RNA sequencing, using for each study a multiple independent cohorts design. This ensured biological and technical reproducibility. We then focused at the end on biomarkers that were convergent and reproducible between the two studies. We found new as well as previously known biomarkers that were predictive of high pain states, and of future emergency department visits related to them, using cross-sectional and longitudinal approaches. Using a polyevidence score, the overall top decreased in expression biomarker ("pain-suppressor gene") was CD55, a gene that suppresses the complement cascade and cell damage. The top increased biomarker ("algogene") was ANXA1, a gene that is an effector of glucocorticoid-mediated responses and regulator of the inflammatory processes. The top biological pathways were related to cellular response to TNF and to neuroinflammation. The top upstream regulator was TNF. Top therapeutic matches overall were the medications lithium and ketamine, as well as the nutraceuticals omega-3 fatty acids and magnesium. Drug repurposing bioinformatic analyses also identified the potential of carvedilol, sirolimus, budesonide, berbamine, and quetiapine, as well as of medications already used to treat pain such as amyleine, sulindac, sufentanil, carbamazepine, and meclofenamic acid, that serve as de facto positive controls. Additionally, we show how personalized patient reports for doctors would look like based on blood biomarkers testing, to aid with objective assessment of severity and risk, as well with individualized matching to medications and nutraceuticals. Given the fact that pain disorders are highly prevalent, can severely affect quality of life, and even lifespan, there is an urgent need for insights and tools such as the ones we have developed to be applied to and improve clinical diagnosis, treatment, and prevention options.

Molecular Psychiatry; https://doi.org/10.1038/s41380-025-03186-8