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Summary

I am a scientist with over 15 years of experience, principally with a focus on cancer genetics and computational biology. In most of my research positions I was responsible for both the wet-lab and the computational aspects of my projects. I have worked extensively on detecting rare somatic mutations of the hematopoietic system and used these mutations to model and understand the steps involved in the process of oncogenesis. I also have spent time translating my research to the clinic to inform physician decision making during cancer treatment. Additionally, I have worked to understand the role of mutation accumulation in the first human gene therapy clinical trials. In my most recent research I have been pursuing a population genetics approach to understand the evolution of somatic mutation rates in humans. Currently I am working as a Senior Scientist in Computational Biology at a small startup that leverages mitochondrial mutations for lineage tracing of the hematopoietic tissue.

Research and Professional Experience

Branch Biosciences **Jan. 2024 - Jun. 2024**

Senior Scientist

Branch Biosciences was a startup oncology diagnostics company focused on using cutting edge multi-omics single cell sequencing to improve patient outcomes.

- Worked as part of a small team using mitochondrial mutations for lineage tracing of the hematopoietic system.
- Ran sample on AWS and Code Ocean and modified existing code to incorporate new sample types, and improved code runtimes.
- Incorporated CITE-seq data into existing codebase in an effort to refactor the internal code to handle CAR-T cell tracking.
- Began converting full codebase into an automated pipeline to limit required manual effort when analyzing samples.

Harvard Medical School, The Broad Institute, Boston Children's Hospital **Aug. 2019 - Jan. 2024**

Postdoctoral Fellow

Laboratory of Dr. Vijay Sankaran

- Described the genetic basis for somatic mutation rates within the human population and provided some of the first human evidence for evolved mutation rates. Utilized a Genome Wide Association study approach to understanding mutation rate differences throughout the human population. I used a number of large data banks to run GWAS, mendelian randomization, and polygenic risk scoring analyses to assess the genetic basis for hematopoietic mutation rates.
- Described the relationship between clonal hematopoiesis and Acute Myeloid Leukemia especially with regards to the first gene therapy clinical trials. I used somatic mutation data from people with sickle cell disease to computationally describe and model the risks of clonal hematopoiesis and AML risk.
- Used gene editing to functionally characterize drivers of clonal hematopoiesis in-vitro and in-vivo.

University of Colorado School of Medicine **Jul. 2012 - Aug. 2019**

Graduate Student

Laboratory of Dr. James DeGregori

- Created one of the most sensitive targeted deep sequencing methods, capable of reliably detecting mutations as rare as 1:20,000 variant allele frequency. I designed a UMI barcoded amplicon sequencing

approach to targeting oncogenic hotspots to sequence somatic mutations from small blood biopsies. I designed and ran all aspects of the wet-lab side of the project and then wrote the full computational pipeline to analyze amplicon samples on the University compute cluster, as well as all subsequent analyses.

- Described the role of Down Syndrome in promoting the development of leukemias. I designed and ran in-vitro models of leukemia development by transducing trisomic cells with oncogenic mutations. Transduced cells were also introduced into mouse models of Down Syndrome to track and model leukemia development. I also computationally analyzed biobank data to develop insights into rates of leukemia development.
- Described the mutagenic effects of general aneuploidy in the absence of supernumerary gene copies.

Education

2024	Research Fellow	Hematology/Oncology (Vijay Sankaran)	Harvard Medical School, The Broad Institute of MIT and Harvard, Boston Children's
2019	PhD	Cell, Stem Cell, and Developmental Biology (James DeGregori)	University of Colorado School of Medicine
2012	MS	Biology	Case Western Reserve University
2009	BS	Biomedical Engineering	Case Western Reserve University

Technical Skills

Fields: Cancer Biology, Cancer Genetics, Population Genetics, Bioinformatics

Coding Languages: Python, R, Bash, HTML/CSS, Javascript, Go

Computational Methods: Sequencing Analysis, Rare Variant Detection, GWAS, Sequence Alignment, Variant Calling, Mendelian Randomization, Polygenic Risk Scoring

Computational Tools: Scikit-learn, Numpy, Matplotlib, Pandas, SciPy, GATK, samtools, Seurat, Git/Github, Cluster Computing, Linux, Google Cloud Computing, AWS, Code Ocean, Random Forest, Deep Learning, K-Nearest Neighbor, Regression, Clustering, UKB, TOPMed, AllofUs, EHR

Wetlab Technologies: Amplicon Sequencing, Liquid Biopsies, NGS, sc-DNASeq, ddPCR, scRNA-Seq, CRISPR-Cas, System, Genome Editing, Cell Culture, ctDNA

Report of Funding

2021-2023: Trans-Omics for Precision Medicine (TOPMed) Fellowship
2021-2022: Harvard Medical School Pathophysiology of Human Blood Cells T32
2019-2022: Harvard Medical School Transfusion Medicine T32
2014-2019: NIH NRSA F31
2018: Linda Crnic Institute for Down Syndrome Research Fellowship
2014: Linda Crnic Institute for Down Syndrome Research Fellowship

Thesis

Identifying Rare Somatic Mutations As A Means Of Understanding Tissue Clonal Evolution

Publications

Liggett, LA, Cato LD, Yu, F., Weinstock, J., Ma, V., NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium, Bick, A., Sankaran, V. et al. (**2024**). Heritable determinants of somatic mutations in human hematopoiesis. (In Preparation).

Yu, F., Cato, L.D., Weng, C., **Liggett, L.A.**, Jeon, S., Xu, K., Chiang, C.W.K., Wiemels, J.L., Weissman, J.S., de Smith, A.J., et al. (**2022**). Variant to function mapping at single-cell resolution through network propagation. **Nat. Biotechnol.** 1–10.

Liggett LA, Sankaran VG. Patchwork Cancer Predisposition. (**2022). *Cancer Discov***.12(4):889–891.

Liggett LA, Cato LD, Weinstock JS, et al. Clonal hematopoiesis in sickle cell disease. (**2021). JCI**.

Liggett, L.A., Galbraith, M.D., Smith, K.P., Sullivan, K.D., Granrath, R.E., Enriquez-Estrada, B., Kinning, K.T., Shaw, J.R., Rachubinski, A.L., Espinosa, J.M., et al. (**2021**). Precocious clonal hematopoiesis in Down syndrome is accompanied by immune dysregulation. **Blood Adv.** 5, 1791–1796.

Liggett, L. Alexander, and Vijay G. Sankaran. (**2020**). "Unraveling hematopoiesis through the lens of genomics." **Cell** 182.6: 1384-1400.

Alexander Liggett, L., Voit, R.A., and Sankaran, V.G. (**2020**). Sowing the Seeds of Clonal Hematopoiesis. **Cell Stem Cell** 27, 195–197.

Rozhok, A. I., Silberman, R. E., Higa, K. C., **Liggett, L. A.**, Amon, A., & DeGregori, J. (**2020**). A somatic evolutionary model of the dynamics of aneuploid cells during hematopoietic reconstitution. **Scientific reports**, 10(1), 1-10.

L. Alexander Liggett, Anchal Sharma, Subhajyoti De, James DeGregori **(2019)**. FERMI: A novel method for sensitive detection of rare mutations in somatic tissue. **Genes, Genomes, and Genetics**

Liggett, L.A., and DeGregori, J. **(2017)**. Changing mutational and adaptive landscapes and the genesis of cancer. **Biochim. Biophys. Acta**.

Aivazidis, S., Coughlan, C.M., Rauniyar, A.K., Jiang, H., **Liggett, L.A.**, Maclean, K.N., and Roede, J.R. **(2017)**. The burden of trisomy 21 disrupts the proteostasis network in Down syndrome. **PLoS One** 12, e0176307.

Sullivan, K.D., Lewis, H.C., Hill, A.A., Pandey, A., Jackson, L.P., Cabral, J.M., Smith, K.P., **Liggett, L.A.**, Gomez, E.B., Galbraith, M.D., et al. **(2016)**. Trisomy 21 consistently activates the interferon response. **Elife** 5.

Broome, A.-M., Ramamurthy, G., Lavik, K., **Liggett, A.**, Kinstlinger, I., and Basilion, J. **(2015)**. Optical imaging of targeted β-galactosidase in brain tumors to detect EGFR levels. **Bioconjug. Chem.** 26, 660–668.

Parameswaran, N., Enyindah-Asonye, G., **Liggett, L.**, Shah, N., Bagheri, N., and Gupta, N. **(2013)**. Spatial coupling of JNK activation to the B cell antigen receptor by tyrosine-phosphorylated ezrin. **J. Immunol.** 190:2017-2026.

Broome, A.-M., Lavik, K., Ramamurthy, G., **Liggett, L.A.**, Agnes, R.S., and Basilion, J.P. **(2010)**. Abstract 4341: Tumor imaging via β-galactosidase fragment complementation with a multifunctional targeted-reporter complex. **Cancer Res.** 70, 4341–4341.

Silva, F., Bederman, I., **Liggett, A.**, and Cabrera, M. **(2008)**. Effects of unloading (HS) and loading (exercise training) on overall work capacity in rats. **The FASEB Journal** 22, 121–121.