

Roman Reggiardo

PhD Candidate, **F99/K00 Fellow** – Daniel Kim Lab, UC Santa Cruz

Curriculum Vitae

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Summary & Highlights

- I'm finishing my PhD in Bioengineering and Bioinformatics at UC Santa Cruz under supervision of Assistant Professor Daniel Kim. I am an **NIH F99/K00** fellow supported by the NIDDK-KUH to complete my thesis work (F99) developing novel RNA liquid biopsies for the non-invasive detection and characterization of Lung and Pancreatic cancers and have an additional (K00) **4-years of funding** to develop extracellular RNA technology for non-malignant hematological applications. I expect to graduate in Winter or Spring of 2023.
- In addition to my academic training, I have also **interned with (and currently consult for) Bluestar Genomics**, a leader in commercial liquid biopsy technology.
- My **expertise is in bioinformatics and applied machine learning/statistics** – techniques I have used to help advance academic (RNA) and industrial (DNA) liquid biopsy technology development
- I am seeking a home for my **K00-Funded Post Doctoral experience** that will enable my supported research and continued growth as a scientist, mentor, and future competitive applicant to faculty positions.
- In addition to a **manuscript recently published in Cell Reports** [2], I anticipate multiple 1st-author publications from my PhD [4, more unlisted].
- I am currently **leading a UCSC Genomics Institute-sponsored Bioinformatics Short-course** for CA Community College students and writing a report on challenges to equitable diagnostics as a **Baskin Engineering Anti-Racist Research fellow**.

Education

I stayed at UCSC to pursue a dramatic shift in my expertise and research focus, transitioning from peptide engineering to bioinformatics with a focus in non-invasive, next-generation sequencing-enabled diagnostics. I dedicated myself to developing robust computational and statistical skills in addition to becoming a well-rounded scientist. I leveraged this opportunity into a productive PhD, an internship in applied AI/ML at a Biotechnology company, and an NIH F99/K00 award.

2017 - 2023	PhD Biomolecular Engineering	University of California Santa Cruz Jack Baskin School of Engineering
2012 - 2017	B.S. Biochemistry and Molecular Biology	University of California, Santa Cruz

Industry Experience

My experience with both Machine Learning and Liquid Biopsies enabled my acceptance to an internship position with **Bluestar Genomics** where I made significant contributions to a modeling approach used to diagnose Pancreatic Cancer using 5-Hydroxymethylated cytosine (5HmC) sequencing [5]. This experience afforded me the opportunity to work with large clinical data sets, interface with experienced scientists, and perform to the expectations of a fast moving startup pursuing regulatory approval.

10/21 - 08/22	Consultant Bioinformatics & AI/ML	Bluestar Genomics
07/21 - 10/21	Intern Bioinformatics & AI/ML	Bluestar Genomics

Research & Training Support

Liquid biopsies are poised to revolutionize diagnostic procedures by making them more accessible and less invasive due to the use of biofluids like blood rather than tissue samples. During my PhD I have helped develop an RNA liquid biopsy platform that the F99 will enable me to lead a validation for in patients diagnosed with lung adenocarcinoma. As an **NIDDK K00 fellow with 4 years of support**, I will develop new liquid biopsy platforms for hematological disease diagnosis and characterization through detection and analysis of cell-free nucleic acids.

2021	Cell free RNA liquid biopsies - F99DK131504 Link to RePORTER	National Institute of Diabetes and Digestive and Kidney Diseases
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Previous

- Trainee, **T32 HG008345** – National Human Genomics Research Institute

Pre-Doctoral Research Experience & Projects

09/21 - A.Y. 22	NIH F99 Pre-Doctoral Fellow National Institute of Diabetes and Digestive and Kidney Diseases	Adviser: Assistant Prof. Daniel Kim
09/18 - 09/21	Graduate Student Researcher UCSC Biomolecular Engineering PhD program	Adviser: Assistant Prof. Daniel Kim

My pre-doctoral research foci have been computational analysis, modeling, and visualization of **RNA-** and **ATAC-seq** data. Working closely with my thesis adviser **Daniel Kim**, I have taken leadership of multiple projects that range from interrogating the fundamental transcriptional dynamics of cancer and stemness to developing approaches that enable robust analysis of low-signal, cell-free RNA biopsies.

Epigenomic reprogramming of transposable element RNAs and IFN-stimulated genes by mutant KRAS

Integrated RNA- and ATAC-sequencing of human airway epithelial cells expressing mutant KRAS to identify transcriptional events with potential to indicate tumorigenesis in early-stage lung adenocarcinomas. Identified a putative regulatory network in which mutant KRAS drives de-repression of repetitive, Transposable Element (TE) RNAs that are enriched in extracellular vesicles in a KRAS-dependent manner. I found that global epigenetic silencing of KRAB Zinc Finger gene expression was a likely cause of aberrant TE expression and the co-occurring intrinsic immune response. I validated these observations with data from other cell lines and The Cancer Genome Atlas (TCGA) Lung Adenocarcinoma data set. I am lead author on a manuscript detailing these findings that is **published** at *Cell Reports* [2].

Extracellular RNA signatures of mutant KRAS(G12C) lung adenocarcinoma cells

An exploration of the potential for cell-free RNA sequencing to serve as a companion diagnostic for clinical KRAS inhibition, this study assesses multiple extracellular vesicle isolation approaches for cell-free RNA sequencing. We identify strong evidence of KRAS inhibition via extracellular signal and demonstrate its relevance to tumors sequenced in the TCGA database. I am co-lead author on this manuscript, which has been reviewed by *PNAS* and is *in-revision*.

Comprehensive characterization of full-length cell-free RNA

By utilizing expression calculated from custom annotations, cutting-edge sequencing technologies, and existing TCGA data, we demonstrate the potential for non-invasive RNA liquid biopsy to be used as both a Pancreatic Cancer diagnostic and a monitoring tool for extended COVID-19 illness. Ultra-low input RNA sequencing libraries of Human blood plasma capture disease-specific RNA expression. I am lead author on a submitted manuscript.

lncRNA Biomarkers of Inflammation and Cancer

We focus on the potential for lncRNA biomarkers to detect inflammation and cancer, highlighting key biological, technological, and analytical considerations that will help advance the development of lncRNA-based liquid biopsies in a **Published** book chapter [1].

Academic Research Collaborations

Prof. Camilla Forsberg - UC Santa Cruz

Consulted on and performed analysis for ATAC-seq libraries prepared from the murine hematopoietic lineage. Identified lineage-representative clusters via dimensionality reduction with Principal Component Analysis and Hierarchical Clustering of peaks detected across the data set. Resulted in authorship on one **published** article [3] and one manuscript *in-review*.

Assistant Prof. Ali Shariati - UC Santa Cruz

Performing data analysis of signal derived from ATAC-sequencing of naive pluripotent stem cells. Performing time-series analysis of a chromatin accessibility, clustering based on accessibility signal, and biological contextualization of the events driving results of both approaches. Manuscript *in-preparation*.

Prof. Stephen Chan - University of Pittsburgh

Sequencing cell-free RNA liquid in plasma from patients with Pulmonary Arterial Hypertension. Larger cohort including diverse pulmonary injury and pathologies underway. Manuscript(s) *in-preparation*.

Prof. Utkan Demirci - Stanford University

Key collaboration that has enabled our exploration of extracellular vesicles as carriers of cell-free RNA[1,2]. Utilizing Demirci lab technology *ExoTIC* to isolate and sequence extracellular vesicles from *in-vitro* cell culture treated with KRAS-inhibitor AMG510. Additional work underway, manuscript **published** [2], *in-review* [4], and *in-preparation*.

Internship & Consultant Role

Bluestar Genomics is a biotechnology company developing clinical liquid biopsies for cancer that utilize a proprietary assay to extract and sequence 5-hydroxymethylated cell-free DNA from human blood plasma.

Intern

I worked with the AI/ML team to introduce new feature engineering approaches that significantly improved performance of diagnostic models trained to classify pancreatic cancer. These approaches took advantage of large, detailed, clinical data sets generated in a recently CLIA-approved laboratory and were validated extensively using robust statistical assessment and simulation of performance variability. This work resulted in an authorship on a pre-printed manuscript [5].

Consultant

I've worked alongside the AI/ML team to implement new modeling approaches that improve diagnostic performance and incorporate diverse features into a powerful modeling framework. This experience has enabled my increased familiarity and comfort with common modeling libraries, implementations, and use cases for clinical diagnostics in a discovery setting.

Teaching & Outreach Support

I have leveraged my teaching and mentor-ship experience, spanning 7 quarters of TA appointments and 6 undergraduate mentees, to become the departmental 2021–22 CITL Graduate Pedagogy Fellow. **I now have support and expectations to facilitate TA-training for incoming BME PhD and Master's students** at the beginning of their graduate careers in Fall 2022. Most recently, I was selected for a **Baskin Engineering Anti-Racism research fellowship** that will enable my investigation of inequities in the development of liquid biopsies like the one I have developed during my PhD. As a member of the UCSC Genomics Institute Diversity, Equity, and inclusion committee **I am directing a free Bioinformatics Summer Short Course** for CA community college students.

01/22 - 01/23	Graduate Pedagogy Fellow University of California Santa Cruz Jack Baskin School of Engineering	Center for Innovative Teaching and Learning (CITL)
07/22 - 10/22	Anti-Racism Research Fellow University of California Santa Cruz Jack Baskin School of Engineering	School of Engineering

Teaching Positions

08/22 - 10/22	BME TA Training Facilitator BME Graduate Bootcamp	UCSC Biomolecular Engineering Dept.
05/22 - 08/22	Lead Instructor & Organizer Summer Bioinformatics Short Course	UCSC Genomics Institute
01/20 - 07/21	Graduate Teaching Assistant BME 22/23,110,167,270	UCSC Biomolecular Engineering Dept.
01/18 - 07/18	Graduate Teaching Assistant BIOC100B & 100C	UCSC Biochemistry and Molecular Biology Dept.
01/17 - 07/17	Peer Tutor CHEM 1A & 1C	UCSC Modified Supplemental Instruction

Invited Talks & Poster Presentations

07/22	Invited Speaker Gordon Research Conference: Liquid Biopsy Seminar (Cancelled)	Mt. Holyoke University
01/20	Poster Presentation Non-coding RNA: Mechanism, Function, and Therapies	Whistler, CA
05/19	Invited Speaker Bay Area Stem Cell Conference	Asilomar, Ca

References

- **PhD Adviser** — Daniel H. Kim, Assistant Professor, UC Santa Cruz Dept. of Biomolecular Engineering
— daniel.kim@ucsc.edu
- **Manager, Internship & Consultancy** — Wayne Volkmuth, SVP of Informatics and Data Discovery, Bluestar Genomics
— wvolkmuth@bluestargenomics.com
- **Undergraduate Thesis Adviser** — Glenn Millhauser, Distinguished Professor, UC Santa Cruz Dept. of Biochemistry
— glennm@ucsc.edu

Publications & Pre-prints

1. **Reggiardo, R.E.**, Maroli, S. V., & Kim, D. H. (2022). LncRNA Biomarkers of Inflammation and Cancer. In S. Carpenter (Ed.), *Long Noncoding RNA* (Vol. 1363, pp. 121–145). Springer International Publishing. https://doi.org/10.1007/978-3-030-92034-0_7
2. **Reggiardo, R.E.**, Maroli, S. V., Halasz, H., Ozen, M., Hrabeta-Robinson, E., Behera, A., Peddu, V., Carrillo, D., LaMontagne, E., Whitehead, L., Kim, E., Malik, S., Fernandes, J., Marinov, G., Collisson, E., Brooks, A., Demirci, U., & Kim, D. H. (2022). Mutant KRAS regulates transposable element RNA and innate immunity via KRAB zinc-finger genes. *Cell Reports*, 40(3), 111104. <https://doi.org/10.1016/j.celrep.2022.111104>
3. Martin, E. W., Krietsch, J., **Reggiardo, R.E.**, Sousae, R., Kim, D. H., & Forsberg, E. C. (2021). Chromatin accessibility maps provide evidence of multilineage gene priming in hematopoietic stem cells. *Epigenetics & Chromatin*, 14(1), 2. <https://doi.org/10.1186/s13072-020-00377-1>
4. Khojah, R. *, **Reggiardo, R.E.** *, Ozen, M., Maroli, S. V., Carrillo, D., Demirci, U., & Kim, D. H. (2022). *Extracellular RNA signatures of mutant KRAS(G12C) lung adenocarcinoma cells* [Preprint]. Genomics. <https://doi.org/10.1101/2022.02.23.481574>
5. Haan, D., Bergamaschi, A., Guler, G. D., Friedl, V., Ning, Y., **Reggiardo, R.E.**, Kesling, M., Collins, M., Gibb, B., Pitea, A., Hazen, K., Bates, S., Antoine, M., Fraire, C., Lopez, V., Malta, R., Nabiyouni, M., Nguyen, A., Phillips, T., ... Levy, S. (2021). *Validation of a Pancreatic Cancer Detection Test in New-Onset Diabetes Using Cell-Free DNA 5-Hydroxymethylation Signatures* [Preprint]. Genetic; Genomic Medicine. <https://doi.org/10.1101/2021.12.27.21268450>
6. Anderson, E. J. P., Ghamari-Langroudi, M., Cakir, I., Litt, M. J., Chen, V., **Reggiardo, R.E.**, Millhauser, G. L., & Cone, R. D. (2019). Late onset obesity in mice with targeted deletion of potassium inward rectifier Kir7.1 from cells expressing the melanocortin-4 receptor. *Journal of Neuroendocrinology*, 31(1), e12670. <https://doi.org/10.1111/jne.12670>