BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Sanders, Keith L

eRA COMMONS USER NAME (credential, e.g., agency login): KEITHLSANDERS

POSITION TITLE: Graduate Research Assistant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Houston; Houston, TX	B.A.	05/16	Biotechnology / Bioinformatics focused
UTHealth McWilliams School of Biomedical Informatics Houston, TX	Ph.D.	05/27 (Expected)	Bioinformatics and Systems Medicine

A. Personal Statement

My passion for science is driven by two guiding principles: “Make the world a better place” and “Never stop growing”. These values have shaped my journey in translational bioinformatics, where I seek to harness the power of big data to improve human health. Through both successes and challenges, research has reinforced my commitment to leveraging artificial intelligence for meaningful clinical advancements. During my Ph.D. studies in biomedical informatics, my work focuses on AI-driven computational phenotyping—integrating multi-omics, electronic health records, and deep learning to uncover clinically relevant disease phenotypes and their associated genetic markers. My research aims to bridge computational modeling with real-world clinical applications, particularly in complex diseases, to advance precision medicine. My research experience has

Beyond research, I have taken on key roles in interdisciplinary health studies and NIH-funded projects. I have also held leadership positions, mentoring trainees on navigating scientific literature and organizing national conferences to foster collaboration and knowledge exchange. I remain steadfast in my mission to utilize artificial intelligence and big data to drive innovations in precision medicine and improve health outcomes.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2022- Graduate Research Assistant, Dept. Bioinformatics & Systems Medicine, MSBMI, Houston, TX
2019-2022 Graduate Research Assistant, Quantitative Science, MD Anderson Cancer Center, Houston, TX
2016-2019 Research Assistant, Dept. of Radiation Oncology, MD Anderson Cancer Center, Houston, TX

Scholarship Awards

2024 D. Bradley McWilliams Scholars Award
2023 Travel Award (International Conference on Intelligent Biology and Medicine (ICIBM))
2022 Eugene H. Vaughan Endowed Scholarship (SBMI)

Honors

2024 AMIA Year-in-Review Leader
Genomic and Translational Bioinformatics Working Group
2024 Awardee, 1st Place Winner
UTHealth Healthcare Innovation Challenge Competition
2023 Chair of the Trainee Committee,
International Conference on Intelligent Biology and Medicine
2021 Awardee, Best Seminar Award for Quantitative Science Seminar.
MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences
2019 Awardee, NIDCR Diversity Supplement
MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences

C. Contributions to Science

1. Multi-omic Data Integration and Network Analysis

By integrating multi-omic data through a network-based approach, this project aimed to uncover fundamental gene interactions associated with Alzheimer's Disease (AD), advancing our understanding of its mechanisms and identifying potential targets for drug repurposing. Initially, genetic data was extracted from a large-scale AD Genome-Wide Association Study (GWAS) alongside epigenetic data from a biomedical repository. Utilizing the dense-module searching capabilities of the GWAS (dmGWAS) tool, densely connected gene subnetworks were identified, offering a holistic view of AD's molecular landscape. Further analysis provided genetic and epigenetic risk assessments, facilitating the identification of potential therapeutic targets and functional enrichment. This project marks a pivotal step in my career journey within translational bioinformatics.

1. **Sanders KL**, Manuel AM, Liu A, Leng B, Chen X, Zhao Z. Unveiling Gene Interactions in Alzheimer's Disease by Integrating Genetic and Epigenetic Data with a Network-Based Approach. *Epigenomes*. 2024; 8(2):14. https://doi.org/10.3390/epigenomes8020014

2. Utilizing Imaging Biomarkers in Head and Neck Cancer to Improve Human Health

Each year, it is estimated that 650,000 new cases of head and neck cancer (HNC) are diagnosed, making it the 6th leading cancer by incidence worldwide. Due to the prevalence of the disease, there is much interest in investigating applications to improve our understanding and response to HNC. Contributions I have provided to this area include investigating methods to improve predictions of radiation-induced xerostomia. Xerostomia is a dry mouth condition that may drastically hinder the quality of life of those afflicted. My work sought to improve the predictive performance of normal tissue complication probability (NTCP) models through radiomics, the high throughput process of mining quantitative data from medical images. Furthermore, since medical imaging is already a standard of care in HNC treatment, utilizing this quantitative data to characterize imaging biomarkers (IBMs) can potentially provide decision-support tools for optimizing patient treatment planning.

One project I performed to contribute to this endeavor was to assess the performance improvements of NTCP models using pre-treatment T1 Dixon-fat magnetic resonance imaging biomarkers (MR-IBMs). The primary endpoint was patient-rated moderate-to-severe xerostomia six months after radiotherapy. I created a reference NTCP model and an NTCP model incorporating T1 Dixon-fat sequence MR-IBMs from the salivary parotid glands. After comparing the performance measures of the two models, my study concluded that MR-IBMs have the potential to improve the performance of NTCP models.

My following projects provided crucial steps in highlighting the need for standards in deriving imaging biomarkers. One project explored the importance of image acquisition parameter standardization by

highlighting inconsistency in quantitative MR imaging (MRI). Another project is used to determine the utility of low-flip angle black bone MRI for cortical mandibular bone assessment by comparing interdentium cortical measurements and inter-observer morphometric variability with computed tomography (CT).

1. Kareem A. Wahid, Renjie He, Brigid A. McDonald, Brian M. Anderson, Travis Salzillo, Sam Mulder, Jarey Wang, Christina Setareh Sharafi, Lance A. McCoy, Mohamed A. Naser, Sara Ahmed, **Keith L. Sanders**, Abdallah S.R. Mohamed, Yao Ding, Jihong Wang, Kate Hutcheson, Stephen Y. Lai, Clifton D. Fuller, Lisanne V. van Dijk. MRI Intensity Standardization Evaluation Design for Head and Neck Quantitative Imaging Applications. medRxiv 2021.02.24.21252322
2. Mulder, S. L., Heukelom, J., McDonald, B. A., Van Dijk, L., Wahid, K. A., **Sanders, K.,** Salzillo, T. C., Hemmati, M., Schaefer, A., & Fuller, C. D. (2022). MR-Guided Adaptive Radiotherapy for OAR Sparing in Head and Neck Cancers. *Cancers*, *14*(8), 1909. https://doi.org/10.3390/cancers14081909
3. **Sanders, K. L.**, Mulder, S., Wahidy, K. A., McDonald, B. A., Ahmed, S., Salzillo, T. C., He, R., Naser, M. A., Dede, C., Salama, V., Way, A., Sharafi, C. S., Mohamed, A. S. R., Rigert, J., Chambers, M., Moreno, A. C., Hutcheson, K. A., Lai, S. Y., Fuller, C. D., & van Dijk, L. V. (2022). Improved Xerostomia Prediction in Head and Neck Cancer Patients with Dixon Magnetic Resonance Imaging of Glandular Adiposity: Validation of Semi-Quantitative Parotid T1 Signal Intensity Metrics for Biomarker Pre-Qualification. MedRxiv, 2022.07.11.22277439. [In Submission]
4. Wahid KA, Kiser KJ, **Sanders KL**, Sharafi CS, McCoy LA, Ventura J, Ahmed S, Fuller CD, van Dijk LV. Chapter 10 - Radiotherapy outcome prediction with medical imaging In: Kang J, Rattay T, Rosenstein BS, editors. Machine Learning and Artificial Intelligence in Radiation Oncology. [Internet]. Academic Press; 2024 p. 239-315. DOI: 10.1016/B978-0-12-822000-9.00008-2

3. Pancreatic and Rectal Cancer Review

Pancreatic cancer currently has one of the lowest prognosis and survival outcomes at five years. My work included efforts to review the biological mechanisms of pancreatic cancer. Further, I helped investigate and record novel treatment options, including advancements in chemotherapeutic agents, radiation therapy, and immunotherapy models. This review also includes modality, radiation dose, and radiation fraction size information. I reviewed the relationship between radiation treatment and immune response, which has opened novel avenues of research. This review includes recent advances in radiation treatment for pancreatic cancer, which concentrates on preoperative chemoradiation, radiation treatment that reduces lymphopenia, dose escalation radiation treatment, and an amalgamation of radiation treatment with immunotherapy.

Pancreatic cancer presents one of the most challenging prognoses and survival rates at the five-year mark. Within this context, my research endeavors focused on elucidating the biological mechanisms underlying pancreatic cancer. I contributed to exploring and documenting innovative treatment options, including advancements in chemotherapeutic agents, radiation therapy, and immunotherapy models. The comprehensive review encompasses essential details such as treatment modalities, radiation dosage, and fraction size. Notably, my investigation delved into the intricate relationship between radiation treatment and immune response, unveiling promising avenues for further research. The review also highlights recent developments in radiation treatment tailored explicitly for pancreatic cancer, with a particular emphasis on preoperative chemoradiation, lymphopenia-reducing radiation, dose escalation radiation, and the synergistic integration of radiation treatment with immunotherapy.

Neoadjuvant chemoradiotherapy (NACRT) has emerged as an established treatment for locally advanced rectal cancer (LARC). However, despite its utilization, a significant number of patients fail to achieve curative pathological responses, subsequently facing higher risks of relapse and mortality. Moreover, no established pre- or mid-treatment factors can reliably predict response to NACRT. To address this knowledge gap, our study leveraged 33 tumor samples obtained from LARC patients at pre- and mid-treatment stages, enabling the extraction of the transcriptome, exome, and high-depth targeted sequencing data. Intriguingly, our findings revealed that the genomic features of pre-treatment LARC did not yield prognostic value concerning response to NACRT. However, an RNA analysis conducted on pre-

treatment tumors unveiled a notable correlation between the abundance of Fusobacteria and poor treatment response. These outcomes suggest that while the pre-treatment NACRT genomic features may not be reliable predictors of treatment response, the pre-treatment NACRT microbiome could offer valuable prognostic insights.

1. Toomey, Sinead, Jillian Gunther, Aoife Carr, David C. Weksberg, Valentina Thomas, Manuela Salvucci, Orna Bacon, **Keith L. Sanders**, et al. 2020. "Genomic and Transcriptomic Characterisation of Response to Neoadjuvant Chemoradiotherapy in Locally Advanced Rectal Cancer." *Cancers* 12 (7). https://doi.org/10.3390/cancers12071808.
2. Bhanu Prasad Venkatesulu ,Cheng-En Hsieh , ***Keith L. Sanders****,* Sunil Krishnan. Recent advances in radiation therapy for pancreatic cancer. *F1000Research .Dec-*2018.https://f1000research.com/articles/7-1931/v1

3. Venkatesulu, B. P., B. K. Kim, C. E. Hsieh, A. Sharma, S. N. Regan, **K. L. Sanders**, P. K. Singh, and S. Krishnan. 2019. "IL-15 Rescues Lymphopenia and Adverse Tumor Control Outcomes Following Splenic Radiation in Murine Pancreatic Cancer Models." *International Journal of Radiation Oncology, Biology, Physics* 105 (1): E248–49.

4. *Venkatesulu, B. P., L. S. K. Mahadevan, B. K. Kim, **K. L. Sanders,** A. Vassantachart, P. K. Singh, and S. Krishnan. 2018. “Rescuing Lymphopenia and Adverse Tumor Control Outcomes Following Splenic Radiation in Mouse Models That Recapitulate Human Pancreatic Cancer Radiation Therapy Results.” *International Journal of Radiation Oncology, Biology, Physics* 102 (3): e167.

4. Radiation-Induced Vascular Injury

The task of this project was to create an understanding of the pathophysiological mechanisms and predictive biomarkers of radiation-induced vascular injury. Radiation treatment directly affects vascular structures by triggering endothelial apoptosis and senescence. Radiation treatment has also caused alterations in standard homeostasis. This altered environment at the endothelial surface is believed to contribute to a systemic chronic inflammatory state. This inflammation state is believed to have an overlaying effect upon the proper senescence processes, leading to atherosclerosis and chronic fibrosis. Many applications were used to investigate these effects, including radiomics, vasculature imaging, cell-component biomarkers, and applications of genomics, proteomics, and metabolomics, which can be used as possible applications for detecting vascular damage after radiation treatment.

1. Bhanu Prasad Venkatesulu, **Keith L. Sanders**, Cheng-En Hsieh, Byung Kyu Kim,Sunil Krishnan. Biomarkers of radiation-induced vascular injury.Wiley Cancer Reports.Dec-2018.

5. Biomedical Applications of Radiosensitization Inducing Agents

Nanomaterials have also been studied for their potential to be used as radiosensitizers. In these in vitro studies, we used tumor-targeted gold and graphene nanoparticles to explore the radiosensitizing effects on human adenocarcinoma pancreatic and colorectal cancer cell lines. Clonogenic assays evaluated particles' effectiveness at various radiation doses and nanoparticle concentrations. In vivo studies used biodistribution analysis, time series xenograft models, and survival analysis. In vivo, study groups generally had three treatment groups: the control group, nanoparticles alone, and target nanoparticles. Many other treatment groups were created within each class to evaluate or explain other biological phenomena. The biodistribution analysis showed that targeted nanoparticles were accumulated in high numbers at the desired location (the tumor). Xenograft studies also exhibited delayed tumor growth in targeted nanoparticle groups. Survival analysis indicated better survival outcomes for the targeted nanoparticle treatment cohort.

1. *Aliru, M. L., K. Aziz, M. Bodd, **K. Sanders**, L. S. K. Mahadevan, N. Sahoo, R. C. Tailor, and S. Krishnan. 2017. "Targeted Gold Nanoparticles Enhance Radiation Effects in Pancreatic Tumor Models." *International Journal of Radiation Oncology, Biology, Physics* 99 (2): E574–75.
2. *Bodd, M., Lee, J., Mackeyev, Y., Aliru, M. L., Aziz, K., **Sanders, K**., Khoo, A., Tailor, R. C., & Krishnan, S. (2017). Radiosensitization of triple negative breast cancer with gold nanosphere conjugates targeting the folate receptor. *International Journal of Radiation Oncology, Biology, Physics*, *99*(2), E579–E580.https://doi.org/10.1016/j.ijrobp.2017.06.1995
3. *Habiba, Khaled, Kathryn Aziz, **Keith L. Sanders,** Carlene Michelle Santiago, Lakshmi Shree Kulumani Mahadevan, Vladimir Makarov, Brad R. Weiner, Gerardo Morell, and Sunil Krishnan. 2019. "Enhancing Colorectal Cancer Radiation Therapy Efficacy Using Silver Nanoprisms Decorated with Graphene as Radiosensitizers." *Scientific Reports* 9 (1): 17120.
4. *Rauta, P. R., Mackeyev, Y., **Sanders, K.**, Kim, B. K., Gonzalez, V. V., Zahra, Y., Shohayeb, M. A., Abousaida, B., Vijay, G. V., Tezcan, O., Derry, P., Liopo, A. V., Zubarev, E. R., Carter, R., Singh, P., & Krishnan, S. (2022). Pancreatic tumor microenvironmental acidosis and hypoxia transform gold nanorods into cell-penetrant particles for potent radiosensitization. *Science Advances*. https://doi.org/abm9729

In this study, we investigated the effects of active agents in the CTEP portfolio to find undiscovered radiosensitizers in pancreatic cancer. We performed a high-throughput clonogenic assay on 46 drugs in the CTEP portfolio using 96-well plates to accomplish this. Our robust and unbiased screening approach allowed us to evaluate how the combination of drug concentration and delivered radiation dose affected the propagation of two cell lines (Panc1 and HPAC). The high throughput clonogenic assay selected 14 drugs as candidates for being radiosensitizing agents. Next, a classic clonogenic assay was performed to validate the results of the high-throughput experiment. The results showed that four drugs showed consistent radiosensitizing effects. This study showed that when coupled, high-throughput and classical clonogenic assays can provide a robust and unbiased approach to assessing the potential of select agents as radiosensitizers. My responsibility in this project involved culturing, treating, irradiating, and counting the 96-well plates. During this project, I also performed many steps to optimize the treating protocol and data analysis.

1. Singh, P. K., B. P. Venkatesulu, J. Symons, L. S. K. Mahadevan, **K. L. Sanders**, B. K. Kim, and S. Krishnan. 2019. "Unbiased Drug Discovery Approaches to Identify Novel Radiosensitizers from Cancer Therapy Evaluation Program (CTEP) Portfolio of Drugs in Pancreatic Cancer." *International Journal of Radiation Oncology, Biology, Physics* 105 (1): S163.

D. Research Support

<u>Completed Research Support</u>

PA-18-906 Fuller (PI) 08/22/2018-05/29/2020
To improve the predictive performance of normal tissue complication probability (NTCP) models for radiation-induced xerostomia in head and neck cancer patients by integrating radiomics and imaging biomarkers.
Role: Awardee