BIOGRAPHICAL SKETCH

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NAME: Makohon-Moore, Alvin Patterson

eRA COMMONS USER NAME (credential, e.g., agency login): amakoho1

POSITION TITLE: Assistant Member, Center for Discovery and Innovation, Hackensack Meridian Health

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
Michigan State University East Lansing, Michigan, USA	BS	05/2010	Zoology
Johns Hopkins University Baltimore, Maryland, USA	PhD	05/2015	Pathobiology
Memorial Sloan Kettering Cancer Center New York, New York, USA	Postdoctoral	04/2022	Cancer evolution

A. Personal Statement

My research focuses on the evolution of cancer to quantify the extent of heterogeneity in tumors and to define molecular factors that impact cancer evolutionary processes. Towards these goals, I have acquired expertise in pathology, multi-region sequencing and phylogenetics of human tumor samples. I have also developed and implemented genetic analyses and quantitative measurements of evolutionary dynamics across spatially distinct tumors to quantify the evolution of aggressive tumor types, including pancreatic cancer and melanoma. My training in evolutionary analysis, genomics and pathology has provided me with a unique skillset to build an innovative and independent research program to systematically define tumor evolution, the factors that impact tumor evolution, and the dynamics that ensue. I will pursue two quantitative strategies: 1) identify cellular and environmental factors that shape tumor evolution, and 2) measure evolutionary dynamics in real-time using experimental evolution of cancer. Ultimately, my goal is to benefit patients and enhance treatments by manipulating evolutionary determinants to derail tumor evolution.

Ongoing and recently completed projects I would like to highlight include:

K99 CA229979 Makohon-Moore (PI) 9/01/2019-5/01/2022
Experimental evolution of pancreatic cancer
The goal of this grant is to develop novel approaches and quantitative metrics of pancreatic cancer evolutionary dynamics.
Role: PI

T32 CA160001-06 Sawyers (PI) 10/1/2016-9/30/2017
Memorial Sloan Kettering Translational Research Oncology Training program
This grant aimed to train postdoctoral fellows in the MSK Human Oncology and Pathogenesis program.
Role: Research Fellow

F31 CA180682 Makohon-Moore (PI) 9/20/2013-3/27/2015
Subclonal Evolution in Metastatic Pancreatic Cancer
The goal of this grant was to ascertain the extent to which pancreatic cancer evolves by subclonal diversification among metastases.
Role: PI

T32 CA067751-13 Gabrielson (PI) 7/27/2010-7/26/2011
Training Program in the Pathobiology of Cancer
The goal of this grant was to train graduate students in the Johns Hopkins Pathobiology program.
Role: Graduate Student

Citations:

1. **Makohon-Moore, A.***, Zhang, M.*, Reiter, J.G.*, Bozic, I., Allen, B., Kundu, D., Chatterjee, K., Wong, F., Jiao, Y., Kohutek, Z.A., Hong, J., Attiyeh, M., Javier, B., Wood, L.D., Hruban, R.H., Nowak, M.A., Papadopoulos, N., Kinzler, K.W., Vogelstein, B. and Iacobuzio-Donahue, C.A. Limited heterogeneity of known driver gene mutations among the metastases of individual pancreatic cancer patients. *Nat. Genet.* **49,** 358–366 (2017). PMID: 28092682 PMCID: PMC5663439 ***co-first authorship**
2. **Makohon-Moore A.P.***, Matsukuma K.*, Zhang M.*, Reiter J.G.*, Gerold J.M.*, Jiao Y., Sikkema L., Attiyeh M.A., Yachida S., Sandone C., Hruban R.H., Klimstra D.S., Papadopoulos N., Nowak M.A., Kinzler K.W., Vogelstein B., and Iacobuzio-Donahue C.A. Precancerous neoplastic cells can move through the pancreatic ductal system. *Nature* **561**, 201-205 (2018). PMID: 30177826 PMCID: PMC6342205 ***co-first authorship**
3. **Makohon-Moore, A**. and Iacobuzio-Donahue, C. A. Pancreatic cancer biology and genetics from an evolutionary perspective. *Nature Reviews Cancer* **16**, 553–65 (2016). PMID: 27444064 PMCID: PMC5739515

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022-present	Assistant Member, Center for Discovery and Innovation, Hackensack Meridian Health, Nutley NJ
2019-2022	Research Associate, Memorial Sloan Kettering Cancer Center, New York NY
2018-2019	Research Scholar, Memorial Sloan Kettering Cancer Center, New York NY
2015-2018	Research Fellow, Memorial Sloan Kettering Cancer Center, New York NY

Honors

2021	The Memorial Sloan Kettering Postdoctoral Researcher Award
2021	The Memorial Sloan Kettering Society Scholars Prize
2020	Associate Member, Sigma Xi
2019	National Cancer Institute Pathway to Independence Award, NIH
2016	Aspen Cancer Conference Fellowship
2015-2017	MSKCC Translational Research Oncology Training (TROT)
2014	JHU Graduate Student Travel Award
2013	Predoctoral Fellowship, National Cancer Institute, NIH
2013	AACR Minority Scholar in Cancer Research Award
2010-2011	Pre-doctoral Fellowship, Johns Hopkins Training Program in the Pathobiology of Cancer
2010	MPI Research Inc., Undergraduate Research Award

C. Contributions to Science

1. Evolution of pancreatic cancer from precursors to metastases. Pancreatic cancer evolution often results in metastatic disease, yet much of this process occurs by unknown mechanisms. To define the evolution of pancreatic cancer, I quantified genetic heterogeneity using multi-region sequencing of pancreatic tumors, including precursors and metastases. These publications represent the first genome-wide quantifications of genetic heterogeneity across coexisting pancreatic lesions in the same patient. I supervised autopsies of consented patients, collected multiple tumor sections for DNA, implemented genetic sequencing, and analyzed and interpreted evolutionary dynamics. The results showed that independent precursor lesions in the pancreas are often genetically related, suggesting these cells travel via the ductal system. Among metastases, the phylogenies indicated that the samples within each patient shared many mutations in common, including unequivocal driver mutations. These findings are important because the results provide strong evidence that pancreatic cancer develops by step-wise evolution, buttressing efforts aimed at early detection when the disease is curable. Low genetic heterogeneity among pancreatic cancer metastases is also important because a targeted therapy will work more effectively if it hones in on mutations present in every cancer cell, and I found that pancreatic cancer metastases shared such driver mutations.

a. **Makohon-Moore, A.***, Zhang, M.*, Reiter, J.G.*, Bozic, I., Allen, B., Kundu, D., Chatterjee, K., Wong, F., Jiao, Y., Kohutek, Z.A., Hong, J., Attiyeh, M., Javier, B., Wood, L.D., Hruban, R.H., Nowak, M.A., Papadopoulos, N., Kinzler, K.W., Vogelstein, B. and Iacobuzio-Donahue, C.A. Limited heterogeneity of known driver gene mutations among the metastases of individual pancreatic cancer patients. *Nat. Genet.* **49,** 358–366 (2017). PMID: 28092682 PMCID: PMC5663439 ***co-first authorship**
b. **Makohon-Moore A.P.***, Matsukuma K.*, Zhang M.*, Reiter J.G.*, Gerold J.M.*, Jiao Y., Sikkema L., Attiyeh M.A., Yachida S., Sandone C., Hruban R.H., Klimstra D.S., Papadopoulos N., Nowak M.A., Kinzler K.W., Vogelstein B., and Iacobuzio-Donahue C.A. Precancerous neoplastic cells can move through the pancreatic ductal system. *Nature* **561**, 201-205 (2018). PMID: 30177826 PMCID: PMC6342205 ***co-first authorship**
c. **Makohon-Moore, A**. and Iacobuzio-Donahue, C. A. Pancreatic cancer biology and genetics from an evolutionary perspective. *Nature Reviews Cancer* **16**, 553–65 (2016). PMID: 27444064 PMCID: PMC5739515
d. **Makohon-Moore, A.**, Brosnan, J. A. & Iacobuzio-Donahue, C.A. Pancreatic cancer genomics: insights and opportunities for clinical translation. *Genome Medicine* **5**, 26 (2013). PMID: 23673020 PMCID: PMC4064313

2. The genetic evolution of metastasis. Metastasis represents the deadliest form of cancer because unlike many primary tumors, metastases cannot be easily excised. In addition to my research on pancreatic cancer, my work has also played a pivotal role in defining metastatic evolution across multiple tumor types, specifically by quantifying genetic heterogeneity among distinct metastases. I found that genetic homogeneity appears to be a common feature of treatment-naïve metastases across tumor types. Driver gene mutations were apparent in the trunk of each tree, while branches were mainly confined to passenger mutations. I also found that non-genetic mechanisms contribute to therapy resistance, even when responding and non-responding metastases share highly similar genomes. The results suggest that single biopsies of treatment-naïve metastases will detect targetable driver mutations, providing essential information for treatment decisions. These publications also provide hope that targeted agents of founder (truncal) alterations can yield an initial clinical benefit. My efforts generated new software tools for further research, and have detected evolutionary patterns within several major tumor types, including pancreatic, breast, colorectal, endometrial, gastric, lung, melanoma, and prostate cancers.

a. **Makohon-Moore, A.P.***, Lipson, E.*, Hooper, J., Zucker, A., Hong, J., Bielski, C.M., Hayashi, A., Tokheim, C., Baez, P., Kappgantuala, R., Kohutek, Z., Makarov, V., Riaz, N., Postow, M.A., Chapman, P.B., Karchin, R., Socci, N., Solit, D., Chan, T., Taylor, B., Topalian, S., and Iacobuzio-Donahue, C.A. The genetic evolution of treatment-resistant cutaneous, acral and uveal melanomas. ***Clinical Cancer Research*** (2020). PMID: 33323400 PMCID: PMC7925434 ***co-first authorship**
b. Reiter, J.G.*, **Makohon-Moore, A.P.***, Gerold, J.M., Heyde, A., Attiyeh, M.A., Kohutek, Z.A., Tokheim, C.J., Brown, A., DeBlasio, R.M., Niyazov, J., Zucker, A., Karchin, R., Kinzler, K.W. Iacobuzio-Donahue, C.A., Vogelstein, B., and Nowak, M.A. Minimal functional driver gene heterogeneity among untreated

metastases. *Science* **361**, 1033-1037 (2018). PMID: 30190408 PMCID: PMC6329287 ***co-first authorship**

c. Ascierto, M.L.*, **Makohon-Moore, A.***, Lipson, E.J., Taube, J.M., McMiller, T.L., Berger, A.E., Fan, J., Kaunitz, G., Cottrell, T., Kohutek, Z.A., Hruban, R.H., Pardoll, D.M., Taylor, B.S., Solit, D., Iacobuzio-Donahue, C.A., and Topalian, S. L. Transcriptional mechanisms of resistance to anti-PD-1 therapy. *Clin. Cancer Res.* **23**, 3168-3180 (2017). PMID: 28193624 PMCID: PMC5474192 ***co-first authorship**

d. Reiter, J.G., Baretti, M., Gerold, J.M., **Makohon-Moore, A.P.**, Dau, A., Iacobuzio-Donahue, C.A., Azad, N.S., Kinzler, K.W., Nowak, M.A., and Vogelstein, B. An analysis of genetic heterogeneity in cancers. *Nature Reviews Cancer* (2019). PMID: 31455892 PMCID: PMC6816333

Complete List of My Published Work in Pubmed:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Makohon-Moore+A%5BAuthor%5D