BIOGRAPHICAL SKETCH

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NAME: Diehn, Maximilian

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

POSITION TITLE: Professor, Vice Chair of Research, and Division Chief of Radiation and Cancer Biology

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
Harvard College – Cambridge, MA	A.B.	06/97	Biochemical Sciences
Stanford University, Stanford, CA	M.D.	06/04	Medicine
Stanford University, Stanford, CA	Ph.D.	06/04	Biophysics
Stanford University, Stanford, CA	Internship	06/05	Internal Medicine
Stanford University, Stanford, CA	Residency	06/09	Radiation Oncology
Stanford University, Stanford, CA	Postdoc	06/09	Stem Cell Biol & Regenerative Medicine

A. Personal Statement

I am a thoracic radiation oncologist and physician scientist who focuses on the development of novel strategies for treatment personalization of lung cancers. My training prepared me well for this research focus: I completed my PhD under Patrick Brown at Stanford where I focused on gene expression profiling of cancers and immune cells. During my postdoctoral training I worked with Drs. Michael Clarke and Irving Weissman at Stanford on radiation resistance of cancer stem cells and murine models of cancer. In my own laboratory, I have leveraged this diverse background by pursuing work in three main areas: 1) development of genomics-based biomarkers for personalized medicine; 2) understanding and overcoming treatment resistance in lung cancers; and 3) leading clinical trials that translate laboratory findings into the clinic.

Among our most impactful research contributions, my group developed ultra-sensitive and specific methods for detection of circulating tumor DNA (e.g. CAPP-Seq [1] and PhasED-Seq [2]) and we have applied these tools to advance approaches for cancer screening and detection of minimal residual disease [3]. We have also worked to develop novel approaches for predicting clinical benefit from immune checkpoint inhibitors [4]. Of relevance to this application, we have developed a optimized method for detection of bladder cancer DNA in urine called urine tumor DNA CAPP-Seq (uCAPP-Seq). Our cancer biology research efforts are focused on improving our understanding of tumor development and overcoming treatment resistance. In this area, we have made contributions by identifying *KEAP1/NFE2L2* mutations as key drivers of clinical radiation resistance and used liquid biopsies to study resistance to targeted therapies. My clinical research is focused on improving outcomes for lung cancer patients, including by leading investigator-initiated therapeutic studies and contributing to cooperative group trials.

In terms of leadership, I am Vice Chair of Research and Division Chief of Radiation and Cancer Biology in the Department of Radiation Oncology at Stanford. I am also the co-leader of the Stanford Cancer Institute's Radiation Biology Program. Furthermore, I have national leadership experience through roles such as being a member of ASCO's Cancer Research Committee and having been a Conference Co-chair of an AACR Special Conference entitled "Advances in Liquid Biopsies". I also serve on NCI's Thoracic Malignancies Steering Committee and am a member of NCI's Molecular Cancer Diagnosis and Classification Study Section. In recognition of my contributions, I was elected to the National Academy of Medicine in 2021. Therefore I have the appropriate expertise to contribute to this project.

Ongoing projects that I would like to highlight include:

R01 CA257655, NIH / NCI
Alizadeh/Diehn (MPI)
03/01/21-02/28/26
Circulating Genomic Determinants of Treatment Failure in Hodgkin Lymphoma

R01 CA254179, NIH / NCI
Diehn/Alizadeh (MPI)
08/01/20–07/31/25
Molecularly-based outcome and toxicity prediction after radiotherapy for lung cancer

R01 CA244526, NIH / NCI
Diehn/Alizadeh/Liao (MPI)
07/01/20–06/30/25
Analysis of urine tumor nucleic acids for detection and personalized surveillance of bladder cancer

R01 CA233975, NIH / NCI
Alizadeh/Diehn (MPI)
08/01/19–07/31/24
A Genomic Framework for Molecular Risk Prediction & Individualized Lymphoma Therapy

Citations:

1. Newman AM, Bratman SV, To J, Wynne JF, Eclov NC, Modlin LA, Liu CL, Neal JW, Wakelee HA, Merritt RE, Shrager JB, Loo BW, Jr., Alizadeh AA*, **Diehn M*.** An ultrasensitive method for quantitating circulating tumor DNA with broad patient coverage. ***Nat Med*** 2014;20(5):548-54. PMID: 24705333; PMCID: PMC4016134
2. Kurtz DM, Soo J, Co Ting Keh L, Alig S, Chabon JJ, Sworder BJ, Schultz A, Jin MC, Scherer F, Garofalo A, Macaulay CW, Hamilton EG, Chen B, Olsen M, Schroers-Martin JG, Craig AFM, Moding EJ, Esfahani MS, Liu CL, Dührsen U, Hüttmann A, Casasnovas RO, Westin JR, Roschewski M, Wilson WH, Gaidano G, Rossi D, **Diehn M*,** Alizadeh AA*. Enhanced detection of minimal residual disease by targeted sequencing of phased variants in circulating tumor DNA. ***Nat Biotechnol*** 39(12):1537-1547, 2021. PMID: 34294911; PMCID: PMC8678141.
3. Chaudhuri AA, Chabon JJ, Lovejoy AF, Newman AM, Stehr H, Azad TD, Khodadoust MS, Esfahani MS, Liu CL, Zhou L, Scherer F, Kurtz DM, Say C, Carter JN, Merriott DJ, Dudley JC, Binkley MS, Modlin L, Padda SK, Gensheimer MF, West RB, Shrager JB, Neal JW, Wakelee HA, Loo BW, Jr., Alizadeh AA*, **Diehn M*.** Early Detection of Molecular Residual Disease in Localized Lung Cancer by Circulating Tumor DNA Profiling. ***Cancer Discov.*** 2017;7(12):1394-1403. PMID: 28899864
4. Nabet BY, Esfahani MS, Moding EJ, Hamilton EG, Chabon JJ, Rizvi H, Steen CB, Chaudhuri AA, Liu CL, Hui AB, Almanza D, … Hellmann MD*, Alizadeh AA*, **Diehn M*.** Noninvasive Early Identification of Therapeutic Benefit from Immune Checkpoint Inhibition. *Cell* 2020;183(2):363-376. PMID: 33007267

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022–	Jack, Lulu, and Sam Willson Professor (with tenure), Dept. of Radiation Oncology, Cancer Institute, and Institute for Stem Cell Biology & Regenerative Medicine, Stanford University
2022–	Molecular Cancer Diagnosis and Classification Study Section (MCDC), NCI
2021–2022	Cancer Biomarker Study Section (CBSS), NCI
2021–	Thoracic Malignancies Steering Committee (TMSC), NCI
2021–	ASCO Cancer Research Committee
2020–	Division Chief of Radiation and Cancer Biology, Dept of Radiation Oncology, Stanford University
2020–	Vice Chair of Research, Dept. of Radiation Oncology, Stanford University
2019–	Scientific Editor for *Cancer Discovery*
2018–	Associate Professor (with tenure), Dept. of Radiation Oncology, Cancer Institute, and Institute for Stem Cell Biology & Regenerative Medicine, Stanford University School of Medicine

2018–2021 ASCO Annual Meeting Scientific Program Committee
2017– Member, AACR Annual Meeting Scientific Program Committee
2017– Scientific Editor for *JCO Precision Oncology*
2017–2019 AACR Exhibits Committee
2016–2017 ASCO-CAP Liquid Biopsies Working Group
2015–2018 RSNA Radiation Oncology & Radiobiology Subcommittee of the Scientific Program Committee
2014–2019 Scientific Advisory Board, Annual Next Generation Diagnostics Summit
2013– Member, Stem Cell Biology and Regenerative Medicine Graduate Program Admissions Committee, Stanford University
2012–2018 Member, Cancer Biology Graduate Program Steering Committee, Stanford University
2010–2018 Assistant Professor, Dept. of Radiation Oncology, Cancer Institute, and Institute for Stem Cell Biology & Regenerative Medicine, Stanford University School of Medicine
2010–2016 Member, Radiological Society of North America (RSNA) Research Development Committee
2009–2010 Acting Assistant Professor, Dept. of Radiation Oncology, Cancer Institute, and Institute for Stem Cell Biology & Regenerative Medicine, Stanford University School of Medicine
2006–2009 Postdoctoral Fellow, Stanford University. Mentors: Michael Clarke, MD & Irving Weissman, MD

Honors

2021 Elected to the National Academy of Medicine
2017–2018 ASCO Leadership Development Program
2017 Inducted into American Society for Clinical Investigation
2013 NIH New Innovator Award
2012 Henry S. Kaplan Memorial Prize for Teaching
2011 Baxter Foundation Faculty Scholar Award
2010 Sidney Kimmel Scholar Award
2010 Doris Duke Clinical Scientist Development Award
2009 Malcolm A. Bagshaw Award
2008 RSNA Roentgen Resident/Fellow Research Award
2006–2009 ABR Holman Research Pathway
2006 ASTRO Annual Meeting Basic Science Travel Grant Award
2005 Franklin G. Ebaugh, Jr. Award for Research, Department of Medicine, Stanford University
1997–2004 Medical Scientist Training Program, Stanford University School of Medicine
1997 Thomas Temple Hoopes Prize for outstanding senior thesis, Harvard College
1997 College & Departmental Honors (*summa cum laude*), Harvard College

C. Contributions to Science

1. The main focus of my research program is developing and evaluating methods for detection of circulating tumor DNA (ctDNA). As tumors grow, a subset of cancer cells die and release some of their genetic material into the blood where it can be non-invasively sampled. Our group developed a deep sequencing-based method for detecting ctDNA called Cancer Personalized Profiling by deep Sequencing (CAPP-Seq). CAPP-Seq is extremely sensitive and specific and was designed to apply to the vast majority of patients with a given cancer type, without the requirement for patient-specific optimization. In ongoing work we are further improving CAPP-Seq and developing novel approaches for integrating ctDNA with other biomarkers.

    a. Kurtz DM, Esfahani MS, Scherer F, Soo J, Jin MC, Liu CL, Newman AM, Dührsen U, Hüttmann A, Casasnovas O, Westin JR, Ritgen M, Böttcher S, Langerak AW, Roschewski M, Wilson WH, Gaidano G, Rossi D, Bahlo J, Hallek M, Tibshirani R, **Diehn M*(co-corresponding),** Alizadeh AA*. Dynamic Risk Profiling Using Serial Tumor Biomarkers for Personalized Outcome Prediction. ***Cell***. 2019;178(3):699-713. PMID: 31280963.
    b. Dudley JC, Schroers-Martin J, Lazzareschi DV, Shi WY, Chen SB, Esfahani MS, Trivedi D, Chabon JJ, Chaudhuri AA, Stehr H, Liu CL, Lim H, Costa HA, Nabet BY, Sin MLY, Liao JC, Alizadeh AA*, **Diehn M***. Detection and surveillance of bladder cancer using urine tumor DNA. ***Cancer Discov***. 2018; 9(4):500-509. PMID: 30578357; PMCID: PMC6467650.
    c. Newman AM, Lovejoy AF, Klass DM, Kurtz DM, Chabon JJ, Scherer F, Stehr H, Liu CL, Bratman SV, Say C, Zhou L, Carter JN, West RB, Sledge GW, Shrager JB, Loo Jr. BW, Neal JW, Wakelee HA, **Diehn M*(co-corresponding),** Alizadeh AA*. "Integrated digital error suppression for ultrasensitive

detection of circulating tumor DNA." ***Nature Biotechnol***. 2016;34(5):547-55. PMID: 27018799; PMCID: PMC4907374.

d. Newman AM, Bratman SV, To J, Wynne JF, Eclov NC, Modlin LA, Liu CL, Neal JW, Wakelee HA, Merritt RE, Shrager JB, Loo BW, Jr., Alizadeh AA*, **Diehn M***. An ultrasensitive method for quantitating circulating tumor DNA with broad patient coverage. ***Nat Med***. 2014;20(5):548-54. PMID: 24705333; PMCID: PMC4016134.

2. A second major research focus is application of CAPP-Seq to develop evidence for the clinical utility of ctDNA detection in diverse clinical contexts within lung cancer. Due to my clinical expertise and interest in lung cancer, we initially implemented CAPP-Seq for non-small cell lung cancer but have since extended it to a variety of other tumor types. We are exploring the use of ctDNA at all stages of a patient's cancer history, from early detection, to detection of minimal residual disease after curative treatment, through treatment resistance in advanced disease.

a. Chabon JJ, Hamilton EG, Kurtz DM, Esfahani MS, Moding EJ, Stehr H, Schroers-Martin J, Nabet BY, Chen B, Chaudhuri AA, Liu CL, Hui AB, Jin MC, Azad TD, Almanza D, Jeon Y, Nesselbush MC, Keh LC, Bonilla RF, Yoo CH, Ko RB, Chen EL, Merriott DJ, Massion PP, Mansfield AS, Jen J, Ren HZ, Lin SH, Costantino CL, Burr R, Tibshirani R, Gambhir SS, Berry GJ, Jensen KC, West RB, Neal JW, Wakelee HA, Loo BW, Kunder CA, Leung AN, Lui NS, Berry MF, Shrager JB, Nair VS, Haber DA, Sequist LV, Alizadeh AA*, **Diehn M***. Integrating genomic features for noninvasive early lung cancer detection. ***Nature.*** 2020 Apr;580(7802):245-251. doi: 10.1038/s41586-020-2140-0. PMID: 32269342; PMCID: PMC8230734.

b. Moding E, Liu Y, Nabet BY, Chabon JJ, Chaudhuri AA, Hui AB, Bonilla RF, Ko RB, Yoo CH, Gojenola L, Jones CD, He J, Qiao Y, Xu T, Heymach JV, Tsao A, Liao Z, Gomez DR, Das M, Padda SK, Ramchandran KJ, Neal JW, Wakelee HA, Loo BW, Lin SH*, Alizadeh AA*, **Diehn M***. Circulating Tumor DNA Dynamics Predict Benefit from Consolidation Immunotherapy in Locally Advanced Non-Small Cell Lung Cancer. ***Nat Cancer***. 2020 Feb;1(2):176-183. doi: 10.1038/s43018-019-0011-0. PMID: 34505064; PMCID: PMC8425388.

c. Chaudhuri AA, Chabon JJ, Lovejoy AF, Newman AM, Stehr H, Azad TD, Khodadoust MS, Esfahani MS, Liu CL, Zhou L, Scherer F, Kurtz DM, Say C, Carter JN, Merriott DJ, Dudley JC, Binkley MS, Modlin L, Padda SK, Gensheimer MF, West RB, Shrager JB, Neal JW, Wakelee HA, Loo BW, Jr., Alizadeh AA*, **Diehn M***. Early Detection of Molecular Residual Disease in Localized Lung Cancer by Circulating Tumor DNA Profiling. ***Cancer Discov***. 2017;7(12):1394-1403. PMID: 28899864; PMCID: PMC5895851.

d. Chabon JJ, Simmons AD, Lovejoy AF, Esfahani MS, Newman AM, Haringsma HJ, Kurtz DM, Stehr H, Scherer F, Karlovich CA, Harding TC, Durkin KA, Otterson GA, Purcell WT, Camidge DR, Goldman JW, Sequist LV, Piotrowska Z, Wakelee HA, Neal JW, Alizadeh AA*, **Diehn M***. "Circulating tumor DNA profiling reveals heterogeneity of EGFR inhibitor resistance mechanisms in lung cancer patients" ***Nat Commun***. 2016; doi: 10.1038/ncomms11815. PMID: 27283993; PMCID: PMC4906406.

3. Another major focus of my lab is understanding and overcoming treatment resistance mechanisms to diverse therapies including radiotherapy, chemotherapy, and targeted therapy. In this area we have made important contributions to the role of the KEAP1/NFE2L2 pathway in resistance. The ultimate goal of our studies is the development of novel therapeutic strategies for improving patient outcomes.

a. Binkley MS, Jeon YJ, Nesselbush M, Moding EJ, Nabet BY, Almanza D, Kunder C, Stehr H, Yoo CH, Rhee S, Xiang M, Chabon JJ, Hamilton E, Kurtz DM, Gojenola L, Owen SG, Ko RB, Shin JH, Maxim PG, Lui NS, Backhus LM, Berry MF, Shrager JB, Ramchandran KJ, Padda SK, Das M, Neal JW, Wakelee HA, Alizadeh AA, Loo BW, **Diehn M.** KEAP1/NFE2L2 mutations predict lung cancer radiation resistance that can be targeted by glutaminase inhibition. ***Cancer Discov***. 2020;10(12):1826-1841. PMID: 33071215; PMCID: PMC7710558.

b. Jeong Y, Hellyer JA, Stehr H, Hoang NT, Niu X, Das M, Padda SK, Ramchandran K, Neal JW, Wakelee H, **Diehn M**. Role of KEAP1/NFE2L2 Mutations in the Chemotherapeutic Response of Patients with Non-Small Cell Lung Cancer. ***Clin Cancer Res***. 2020;26(1):274-281. PMID: 31548347; PMCID: PMC6942632.

c. Jeong Y, Hoang NT, Lovejoy A, Stehr H, Newman AM, Gentles AJ, Kong W, Truong D, Martin S, Chaudhuri A, Heiser D, Zhou L, Say C, Carter JN, Hiniker SM, Loo BW, West RB, Beachy P, Alizadeh

AA, **Diehn M**. Role of KEAP1/NRF2 and TP53 Mutations in Lung Squamous Cell Carcinoma Development and Radiation Resistance. ***Cancer Discov***. 2017;7(1):86-101. PMID: 27663899; PMCID: PMC5222718.

d. **Diehn M**, Cho RW, Lobo NA, Kalisky T, Dorie MJ, Kulp AN, Qian D, Lam JS, Ailles L, Wong M, Joshua B, Kaplan MJ, Wapnir I, Dirbas F, Somlo G, Garberoglio C, Paz B, Shen J, Lau SK, Quake SR, Brown JM, Weissman IL, Clarke MF. Association of reactive oxygen species levels and radioresistance in cancer stem cells. ***Nature***. 2009;458:780-783. PMID: 19194462; PMCID: PMC2778612.

4. In addition to our work on circulating tumor DNA we are developing other biomarkers that can either predict response to therapy (i.e. predictive) or patient outcome (i.e. prognostic). In this work we employ emerging technologies such as next generation sequencing and gene expression deconvolution-based cytometry.

   a. Gentles A, Bratman S, Lee L, Harris J, Feng W, Nair R, Shultz D, Nair V, Hoang C, West; R, Plevritis S, Alizadeh A*, **Diehn M***. Integrating tumor and stromal gene expression signatures with clinical indices for survival stratification of early-stage non-small cell lung cancer. ***JNCI***; 2015;107(10). PMID: 26286589.

   b. Newman AM, Liu CL, Green MR, Gentles AJ, Feng W, Xu Y, Hoang CD, **Diehn M**, Alizadeh AA. Robust enumeration of cell subsets from tissue expression profiles. ***Nat Methods***. 2015;12(5):453-7. PMID: 25822800; PMCID: PMC4739640.

   c. Gentles AJ, Newman AM, Liu CL, Bratman SV, Feng W, Kim D, Nair VS, Xu Y, Khuong A, Hoang CD, **Diehn M**, West RB, Plevritis SK, Alizadeh AA. The prognostic landscape of genes and infiltrating immune cells across human cancers. ***Nat Med***. 2015; 21(8):938-945. PMID: 26193342; PMCID: PMC4852857.

Complete List of Published Work in My Bibliography (>190):
http://www.ncbi.nlm.nih.gov/pubmed/?term=diehn+m