MEMORIAL SLOAN KETTERING CANCER CENTER
DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

B.E.A.C.H.

DEPARTMENTAL NEWSLETTER
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BIOSTATISTICS SEMINARS
Streaming online

- ❖Sept 1st, 2021 — **Wesley Tansey & Haoran Zhang**, MSK / Univ of Texas
- ❖Sept 8th, 2021 — **Jeffrey Morris**, UPenn
- ❖Sept 22, 2021 — **Bin Zhu**, NCI
- ❖Sept 29, 2021 — **Karen Messer**, UCSD
- ❖October 6, 2021 — **Theodore Karrison**, University of Chicago

COMPUTATIONAL ONCOLOGY SEMINARS
Streaming online

- ❖Sept 21, 2021 — **Simon Tavare**, Columbia University
- ❖October 10, 2021 — **Catherine Wu**, Dana Farber

EPIDEMIOLOGY SERVICE MEETINGS
Streaming online

- ❖Sept 13, 2021 — **Melinda Irwin**, Yale
- ❖Sept 27, 2021 — **Robert Klein**, Mt. Sinai

POPULATION SCIENCES RESEARCH PROGRAM SEMINAR SERIES
Streaming online

- ❖Sept 21, 2021 — **Olveen Carrasquillo**, University of Miami
- ❖October 19, 2021 — **Jim Hu**, Weill Cornell Medicine

HEALTH OUTCOMES RESEARCH GROUP SEMINARS
Streaming online

- ❖Sept 24, 2021 — **Talya Salz**, MSK
- ❖October 8, 2021 — **Aaron Mitchell**, MSK

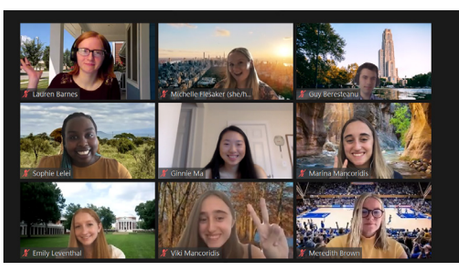
CULTURE COMMITTEE JOURNAL CLUB
Streaming online

- ❖October 21, 2021 — **TBD**

FAREWELL TO ANNA KALTENBOECK

After 5 years of serving as a senior health economist and the program director of the Center for Health Policy & Outcomes (CHPO), **Anna Kaltenboeck** left MSK in May to join the Senate Finance Committee as Senior Health Advisor for the Majority Staff where she focuses on drug pricing and outpatient prescription drug coverage under Medicare Part D. Anna was an integral part of growing CHPO into a cohesive research center that features collaboration between clinicians, health services researchers, biostatisticians, and research support staff working together to develop evidence-based policy approaches that promote high-quality care and improve patient outcomes. She was instrumental in transforming the structure of CHPO from a vertical to project-based team structure where all staff and faculty work together for the sake of a common research agenda. Anna's research within the Drug Pricing Lab explored the intricacies of pricing policies such as balancing innovation with profit, government programs and regulations, and supply chain economics. She also focused on equitable access to healthcare, for example, through a project looking at prescription medication formulary placement and access to beneficiaries. Anna was responsible for the renewal of the Laura & John Arnold Foundation and Kaiser Permanente grants which fund the center and the related Drug Pricing Lab. In addition to her influence as program director, Anna drove her own research agenda, writing seminal papers on value pricing, analysis of the quality-adjusted life-year (QALY) measure, and discussions on the FDA's Accelerated Approval program. While successfully growing the center and her many contributions to the health policy and drug pricing literature, Anna received her MBA from Yale University in the spring of 2021. It is safe to say that the success of CHPO would not have been possible without Anna. She was never afraid to take on a daunting project and always encouraged the team to dive headfirst into new challenges and think in innovative ways. We would like to congratulate Anna on this next step in her career and thank her for the great public service she is undertaking on behalf of all of us.

EPI BIO SUMMER STUDENTS



The Department had another very busy summer in 2021! In total, there were 38 students that interned in the department this summer, spanning HORG, Biostatistics, Epidemiology and Computational Oncology. The QSURE program, now in its fourth year, hosted nine undergraduate students who presented to the department at the end of July. Notably, our Bridge to Biostats (B2B) committee partnered with MSK's Summer Exposure Program (SEP) to offer a virtual biostatistics program for three students from under-resourced public high schools in New York City. In addition to the college preparatory training and exposure to clinical cancer care that all SEP students receive, our students attended introductory statistics lectures, R coding labs, statistical thinking sessions, and a speaker series. Our students also used publicly available NCI data to explore a research question, and then presented their work to the entire SEP group at the end of the five-week program.
Thank you to all the mentors - and the department as a whole - for helping make this summer a great one for so many students!

Click here for a list of the 2021 students and their mentors.

BIG BROTHERS BIG SISTERS

The Big Brothers Big Sisters Workplace Mentoring Program at MSK, sponsored by Work/Life, has successfully completed its 17th year! Two members of the department, **Renee Gennarelli** & **Andrew McPherson**, served as Bigs for this past program year. This was Renee's fourth year in the program and Andrew's first. The Workplace Mentoring Program is an educational, vocational, and cultural activity program that matches volunteers from a workplace with youth from a local school in grades 10-12. The program builds leadership skills and enhances students' academic performance and career readiness through individualized guidance, virtual workshops, career development and social engagement. Every two weeks, students from nearby Talent Unlimited High School visit MSK after school. Currently, the program is held virtually as we continue to practice social distancing guidelines. The program is open to both exempt and non-exempt staff. If you are interested in joining and/or want to learn more about the program, please contact Luba Trost at **Trostl@mskcc.org**.

STAFF PROMOTIONS

Mia Austria promoted to Research Project Associate

Geula Cunin promoted to Data Analyst II

Mike Curry promoted to Research Biostatistician II

Sean Devlin promoted to Associate Attending

Keimya Sadeghi promoted to Research Assistant

Talya Salz promoted to Associate Attending

STAFF FAREWELLS

After 10 years, our esteemed colleague **Narre Heon** will be moving to Columbia University to serve as a program manager and evaluator in the Department of Faculty Development with a focus on equality, diversity and inclusion. Over the past 10 years, Narre has been a core member of the Health Outcomes Research Group focusing her work on the validation and feasibility of the PRO-CTCAE and most recently on our U01 Moonshot Tolerability Consortium. She has also been working on the OBCD project with Elizabeth Kantor as a project coordinator. Notably, for the past year, Narre has been the chair of our departmental culture committee, helping to create and lead ED&I initiatives throughout our department.

After 8 years in the Biostatistics service and 11 years at MSK, **Debra Goldman** will be pursuing a new opportunity at Regeneron. We wish her the best in her new endeavor and know it will offer new challenges for her to develop her enormous potential.

We bid farewell to **Megan Fiasconaro**, Assistant Research Biostatistician in the Biostatistics Service, who will be pursuing new opportunities at Flatiron Health. We wish her luck in her new position and in all her future endeavors.

CULTURE COMMITTEE

Please check out the departmental Teams page for updates from the Culture Committee! You can find slides from previous Journal Club meetings, resources, and links to events of interest. Please also feel free to post items you would like to share as well. Link to the channel is **here**.

MSK SUPPORT FOR STAFF

These are challenging times, which is all the more reason to take care of yourself. The **MSK Info Hub** has a **dedicated page with resources** available to support you. This page includes information on Staff Relaxation Zones, resources for managing stress and anxiety, sign-ups for live weekly group meditation Zoom classes, and more!

GRANTS

Xiang Shu received a supplement award to his R00 study "Uncovering Roles of Metabolites in Colorectal Cancer Etiology."

Sigrid Carlsson received a Prevent Cancer Foundation award titled "Improving prostate cancer screening using innovative Technology."

Margaret Callahan, **Katherine Panageas** and **Ronglai Shen** were awarded an MSK MIND award for their project titled "Defining immunologic factors associated with response or toxicity after checkpoint blockade."

STAFF ACHIEVEMENTS

Tyler Funnell has graduated with his PhD from the Weill Cornell Medicine's Tri-Institutional PhD Program in Computational Biology and Medicine (CBM). Tyler was a student in the Shah Lab with Sohrab Shah serving as his PhD mentor, and he has recently accepted a position as a Senior Computational Biologist II at MSK working in Marcel van den Brink's lab.

Peter B. Bach, MD, MAPP, currently the Director of MSK's Center for Health Policy and Outcomes, has been named one of Crain's New York Business 2021 "Notable in Health Care" leaders. This honor is given to individuals who have distinguished themselves through their expertise and innovation, as well as shown stamina and commitment to building a healthier future. Peter is a physician, epidemiologist, researcher, and respected healthcare policy expert whose work focuses on the cost and value of anticancer drugs. He has devoted his career to improving drug pricing and affordability and is leading efforts to increase understanding of the US drug development process and to develop new models for drug pricing that include value to patients. His research concentrates on disparities in health care impacting minorities and women, the comparative effectiveness of cancer screenings, and the cost and value of anticancer drugs. He has published more than 100 peer-reviewed articles and editorials in scientific journals such as the New England Journal of Medicine and the Journal of the American Medical Association. Congratulations Peter for this achievement!

After being nominated by several colleagues, **Daniel Sjoberg** was awarded the Section for Statistical Programmers and Analysts (SSPA) Award in Innovation in Statistical Programming and Analytics (AISPAA) for his distinguished work on the {gtsummary} R package. Building off of the {gt (grammar of tables) R package, {gtsummary} contains easy to use, well-documented R functions that summarize datasets and analysis results, effectively eliminating time spent by programmers formatting output.

The R code corresponding to the {gtsummary} package is publicly available on GitHub, providing an avenue for collaboration. More than 10 members of our department as well as more than 70 programmers internationally have contributed to the source code and/or documentation for this package, underscoring its significance in the R programming community. With over 11,000 monthly downloads as of May 2021, up from 3,000 per month at this time last year, {gtsummary} has become the default R package for creating summary tables, outpacing similar packages, such as {tableone} and {table1}. The {gtsummary} package saves statistical programmers hours of time formatting results, creating more time to focus on statistical analysis and other productive professional endeavors. It cannot be overstated the extent to which such a simple yet effective package has transformed R programming for the better. Congratulations to Daniel for this well-deserved award and recognition!

Congratulations to **Axel Martin** who will be pursuing his PhD in Biostatistics at NYU this fall.

STAFF CONGRATULATIONS

Kay See and Elias welcomed baby Nora on May 6th, 2021! Congratulations to Kay See and Elias on the new addition to the family!

Melissa and Nate Assel welcomed their baby girl, Cecilia, on March 5th, 2021. Melissa, Nate and Cecilia are doing well!

EMPLOYEE SPOTLIGHT

Sophie Zimbalist joined MSK in June of 2020. Prior to joining MSK, Sophie spent three years working as an undergraduate research assistant in the Department of Pediatric Neurosurgery at St. Louis Children's Hospital and in the Biomedical Magnetic Resonance Lab at Washington University Medical School. She holds a BA from Washington University in St. Louis in anthropology with a minor in biomedical physics. At the Center for Health Policy and Outcomes (CHPO), Sophie is a Research Data Assistant who focuses on calculating cost of care and analyzing federal policy proposals for the Drug Pricing Lab (DPL). She also manages the Launch Price Tracker and is the lead analyst on the DPL Policy Tracker. She has worked on a variety of projects, including a written piece called *PhRMA Talking Points*, which focuses on contextualizing information from the pharmaceutical industry lobbying group's website and preparing a thorough review and rebuttal of their main policy talking points. Sophie has also worked closely with Peter Bach, analyzing the importance of drug packaging, as the sizing of single-dose vials can lead to drug waste and excess spending. Another major focus of her work has been a scoping review of industry conflicts of interest with Debbie Korenstein and Susan Chimonas. Outside of these research interests, she has participated in department-wide initiatives, such as leading the CHPO journal club with Renee Gennarelli and being the subcommittee leader for the Data & Research group on the Epi-Bio Culture Committee.

NEW STAFF

Lauren Chakraborty, Computational Biologist I
Lauren recently graduated from the University of Chicago with a degree in biology and joins MSK as a Computational Biologist I. Lauren previously interned with the Greenbaum Lab for two summers where she researched tumor neoantigens and cross reactivity. Lauren looks forward to continuing her research with the Greenbaum Lab.

Hannah Kalvin, MSPH, Assistant Research Biostatistician
Hannah joins the Epidemiology & Biostatistics Department as an Assistant Research Biostatistician. Hannah graduated in May with her Master of Science in Public Health in Biostatistics from Emory University. During her master's program, Hannah was involved in research examining breast cancer mortality disparities on the state level. Hannah also served as a data analyst for the Biostatistics Collaboration Core and a graduate teaching assistant for Statistical Methods I. Prior to attending Emory, Hannah worked for three years at Statistics Collaborative, Inc. where she found her passion for clinical research, programming, and statistics. Hannah received her undergraduate education at The George Washington University, earning a BS in Public Health and a minor in Biological Sciences in 2016. Hannah is excited to join the department and continue learning about the application of biostatistics in the oncology field.

Armaan Kohli, Bioinformatics Software Engineer I
Armaan Kohli has joined the MSK MIND team as a Research Software Engineer. He has been at MSK since 2020 working as a student research assistant for the MIND team. He graduated from The Cooper Union with a BEng. in Electrical Engineering and is pursuing his master's degree part time.

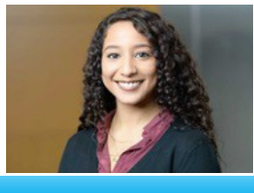
Caroline Kostrzewa, Assistant Research Biostatistician
Caroline joins the Epidemiology & Biostatistics Department as an Assistant Research Biostatistician. Caroline recently graduated from Texas A&M University with her MS in Statistics. Before attending graduate school, Caroline worked as a math teacher and she is now looking forward to working on projects with and getting to know the department!

Alexa Lamore, Administrative Assistant
Alexa joins the Computational Oncology service as an Administrative Assistant supporting Benjamin Greenbaum, Eduard Reznik, and Wesley Tansey. Previously, she worked in Radiology as the Senior Office Coordinator for the Interventional Radiology service. Alexa has been with MSK for the past three years, and is looking forward to furthering her career in Epidemiology & Biostatistics.

Sabrina Lin, Assistant Research Biostatistician
Sabrina joins the Epidemiology & Biostatistics Department as an Assistant Research Biostatistician. Sabrina recently completed her Master of Science in Biostatistician at Columbia University Mailman School of Public Health this past May. While earning her master's degree, Sabrina was a graduate research assistant in the Epidemiology department looking at the association between immunobiomarkers and pubertal outcomes.

Kristina Manzano, Facilities Coordinator
Kristina Manzano has joined the department of Epidemiology & Biostatistics Department as the new Facilities Coordinator for the Joy Building. Kristina started as a Session Assistant in 2003, working up through the ranks to Senior Care Coordinator. She has worked within several clinical departments with a wide variety of people during her tenure. In addition to her work here at MSK, Kristina is active within her church and works as part of music ministry, performing in the choir as well as singing solo.

Alexandra Rizzatti, Administrative Assistant
Alexandra joins the Epidemiology & Biostatistics Department as an Administrative Assistant to support the clerical needs of principal investigators in the Epidemiology Service. In May 2020, she completed her MPH at Hofstra University. Before coming to MSK, she participated in an internship at Northwell Health and worked on the Food as Health program, which strives to improve food security within the patient population.



Jessica Urraca, Research Assistant
Jessica Urraca is the newest research assistant to join Sohrab Shah's lab. She has been at MSK since 2016 working at the Center for Immune Cell Therapy. Jessica attended Syracuse University and Georgetown University to earn a BS in Biomedical Engineering and a MS in Physiology and Biophysics.

PUBLICATIONS

Chaya Moskowitz and colleagues published a paper in *Journal of Clinical Oncology* entitled "Development and Validation of a Breast Cancer Risk Prediction Model for Childhood Cancer Survivors Treated with Chest Radiation: A Report from the Childhood Cancer Survivor Study and the Dutch Hodgkin Late Effects and LATER Cohorts." Women treated with chest radiation for childhood cancer have one of the highest risks of breast cancer, yet models producing personalized breast cancer risk estimates applicable to this population do not exist. Investigators sought to develop and validate a breast cancer risk prediction model for childhood cancer survivors treated with chest radiation, incorporating treatment-related factors, family history, and reproductive factors. Analyses were based on multinational cohorts of female 5-year survivors of cancer diagnosed younger than age 21 years and treated with chest radiation; the model included current age, chest radiation field, whether chest radiation was delivered within 1 year of menarche, anthracycline exposure, age at menopause, and history of a first-degree relative with breast cancer. Results found that breast cancer risk varies among childhood cancer survivors treated with chest radiation, the highest risks among premenopausal women older than age 40 years treated with mantle field radiation within a year of menarche who had a first-degree relative with breast cancer. Accurate risk prediction may aid in refining surveillance, counseling, and preventive strategies in this population.

Sohrab Shah with BC Cancer colleague Samuel Aparicio published "Clonal fitness inferred from time-series modelling of single-cell cancer genomes" in *Nature*. Readers may also find their work featured on OneMSK. Investigators generated 42,000 genomes from multi-year time-series single-cell whole-genome sequencing of breast epithelium and primary triple-negative breast cancer (TNBC) patient-derived xenografts (PDXs), revealing the nature of CNA-defined clonal fitness dynamics induced by TP53 mutation and cisplatin chemotherapy. Investigators found that TP53 mutation alters the fitness landscape, reproducibly distributing fitness over a larger number of clones associated with distinct CNAs. Furthermore, in TNBC PDX models with mutated TP53, inferred fitness coefficients from CNA-based genotypes accurately forecast experimentally enforced clonal competition dynamics. Drug treatment in three long-term serially passaged TNBC PDXs resulted in cisplatin-resistant clones emerging from low-fitness phylogenetic lineages in the untreated setting. Conversely, high-fitness clones from treatment-naive controls were eradicated, signaling an inversion of the fitness landscape. Finally, upon release of drug, selection pressure dynamics were reversed, indicating a fitness cost of treatment resistance. These findings add to the progress in defining genomic fitness landscapes in cancer and imply that a machine-learning approach could accurately predict how human breast cancer tumors will evolve.

Aaron Mitchell, **Akriti Mishra**, and **Peter Bach** published "Use of bone modifying agents in patients with metastatic castrate-sensitive prostate cancer" in the *Journal of Clinical Oncology*. This study measured bone modifying agent (BMA) use among metastatic, castration-sensitive prostate cancer (mCSPC) patients who are unlikely to have an indication for osteoporotic fracture prevention. Authors used linked SEER-Medicare data and looked at men newly diagnosed from 2007 to 2015. Results found that in this cohort of mCSPC patients, nearly one-quarter received BMAs. The increase in BMA use which occurred during the 2007-2015 study period appears to have been driven by increased utilization of denosumab following its approval in 2010. Use of BMAs in patients with mCSPC without a need for osteoporotic fracture prevention may constitute overuse.

Aaron Mitchell, **Niti Trivedi**, **Renee Gennarelli**, **Susan Chimonas**, **Sara Tabatabai**, **Deborah Korenstein** and other MSK faculty published a systematic review, "Are Financial Payments From the Pharmaceutical Industry Associated With Physician Prescribing? A Systematic Review", in the *Annals of Internal Medicine*. Since financial payments from the drug industry to U.S. physicians are common and payments may influence physicians' clinical decision making, it is important to evaluate whether receipt of these payments is associated with physician prescribing practices. Authors searched various data sources for relevant studies up to September 2020. Results demonstrated that the association between industry payments and physician prescribing was consistent across all studies that have evaluated this association. Findings regarding a temporal association and dose-response also suggest a causal relationship.

Susan Chimonas, **Jennifer Chen** and others recently published an article in the *American Journal of Managed Care*, titled "Value-Based Management of Specialty Drugs: Practical Considerations and Implications for Pharmacy." The purpose of this study was to evaluate how policy makers and health plans seek value-based management of specialty drugs and examine real-world factors that favor some approaches over others and their potential impact. Authors conducted a qualitative study with Blue Cross Blue Shield health plans interested in implementing value-based specialty pharmacy management. The article concluded that health plans' preferences for different forms of specialty pharmacy management may not be aligned with policy objectives, particularly those that advance innovation; policy makers should consider market and nonmarket factors that influence these preferences, including the need to mitigate spending and generate evidence to guide coverage decisions.

Aaron Mitchell, **Akriti Mishra**, **Michael Curry**, **Niti Trivedi** and **Peter Bach** recently published an article in *The Oncologist* titled "Personal Payments from Pharmaceutical Companies to Authors of Oncology Clinical Practice Guidelines." This nested case-control study evaluated the relationship between oncologists who author clinical practice guidelines and their financial relationships with the pharmaceutical industry. The sample included medical oncologists selected to join the National Comprehensive Cancer Network (NCCN) Guidelines for the 20 most common cancers from August 2013 to December 2018. Results found that medical oncologists selected to NCCN Guidelines committees had greater financial ties to industry than their peers. The potential influence of industry in oncology clinical practice guidelines may be reduced through the selection of committee members with fewer ties to industry.

Peter Bach recently published an article in *Health Affairs* titled "What A Waste! The National Academy Of Medicine's Report On Oversized Vials Of Expensive Drugs." Dr. Bach expands upon the excess spending that occurs in the U.S. health care system resulting from pharmaceutical companies packaging infusion cancer drugs in single-dose vials that are larger than they needed to be. A study from the National Academy of Science, Engineering, and Medicine on this issue had a surprising conclusion: they argued that the price of the drugs reflect what they are worth to us, not how much the drug is used, concluded that Congress should allow manufacturers to retain the billions they captured by packaging their drugs inefficiently, and that CMS should lift the JW modifier reporting requirement. Currently, the JW modifier is used on Medicare claims to track the amount of discarded, unused drug from a single-use vial or single-use package and is used by CMS to monitor how much money is spent on reimbursing for leftover drug. Peter writes a thought-provoking response to this which emphasizes why CMS must keep the JW code requirement as well as other important policy recommendations to combat drug waste.

PUBLICATIONS

Nikolaus Schultz's group, led by Ritika Kundra, published "OncoTree: A Cancer Classification System for Precision Oncology" in *JCO Clinical Cancer Informatics*. Cancer classification is foundational for patient care and oncology research. Existing systems such as International Classification of Diseases for Oncology (ICD-O) provide large sets of cancer classification terminologies but lack a dynamic modernized cancer classification platform that addresses the fast-evolving needs in clinical reporting of genomic sequencing results and associated oncology research. To meet these needs, authors have developed OncoTree, an open-source cancer classification system. It is maintained by a cross-institutional committee of oncologists, pathologists, scientists, and engineers, accessible via an open-source Web user interface and an application programming interface. OncoTree currently includes 868 tumor types across 32 organ sites. OncoTree has been adopted as the tumor classification system for American Association for Cancer Research (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE), a large genomic and clinical data-sharing consortium, and for clinical molecular testing efforts at MSK and Dana-Farber Cancer Institute. OncoTree is a dynamic and flexible community-driven cancer classification platform encompassing rare and common cancers that provides clinically relevant and appropriately granular cancer classification for clinical decision support systems and oncology research.

Nikolaus Schultz's group, led by Bastien Nguyen, recently published a paper in *Scientific Reports* entitled "The genomic landscape of carcinomas with mucinous differentiation." Mucinous carcinomas can arise in any organ with epithelial cells that produce mucus. While mucinous tumors from different organs are histologically similar, it remains to be elucidated whether they share molecular alterations. Authors analyzed a total of 902 patients across six cancer types by comparing mucinous and non-mucinous samples, integrating text mining of pathology reports, gene expression, methylation, mutational and copy-number profiling. They found that, in addition to genes involved in mucin processing and secretion, MUC2 up-regulation is a multi-cancer biomarker of mucinous histology and is regulated by DNA methylation in colorectal, breast and stomach cancer. Most carcinomas with mucinous differentiation had fewer DNA copy-number alterations than non-mucinous tumors. The tumor mutational burden was lower in breast and lung with mucinous differentiation compared to their non-mucinous counterparts. Authors found several differences in the frequency of oncogenic gene and pathway alterations between mucinous and non-mucinous carcinomas, including a lower frequency of p53 pathway alterations in colorectal and lung cancer, and a lower frequency of PI-3-Kinase/Akt pathway alterations in breast and stomach cancer with mucinous differentiation. This study shows that carcinomas with mucinous differentiation originating from different organs share transcriptomic and genomic similarities. These results may pave the way for a more biologically relevant taxonomy for these rare cancers.

Nikolaus Schultz, **Katherine Panageas**, and **Arshi Arora** co-authored a paper led by Alexander Shoushtari in *Clinical Cancer Research* entitled "Therapeutic Implications of Detecting MAPK-Activating Alterations in Cutaneous and Unknown Primary Melanomas." Cutaneous and unknown primary melanomas frequently harbor alterations that activate the MAPK pathway. Whether MAPK driver detection beyond BRAF V600 is clinically relevant in the checkpoint inhibitor era is unknown. Patients with melanoma were prospectively offered tumor sequencing of 341-468 genes. Oncogenic alterations in 28 RTK-RAS-MAPK pathway genes were used to construct MAPK driver groups. Time to treatment failure (TTF) was determined for patients who received first-line programmed cell death protein 1 (PD-1) monotherapy, nivolumab plus ipilimumab, or subsequent genomically matched targeted therapies. A total of 670 of 696 sequenced melanomas (96%) harbored an oncogenic RTK-RAS-MAPK pathway alteration; 33% had ≥1 driver. Nine driver groups varied by clinical presentation and mutational burden. TTF of PD-1 monotherapy (N = 181) varied by driver, with worse outcomes for NRAS Q61 and BRAF V600 versus NF1 or other alterations (median 4.2, 7.5, 22, and not reached; $P < 0.0001$). Driver group remained significant, independent of tumor mutational burden and clinical features. TTF did not vary by driver for nivolumab plus ipilimumab (N = 141). Among 172 patients with BRAF V600 wild-type melanoma who progressed on checkpoint blockade, 27 were treated with genomically matched therapy, and eight (30%) derived clinical benefit lasting ≥6 months. The study concluded that targeted capture multigene sequencing can detect oncogenic RTK-RAS-MAPK pathway alterations in almost all cutaneous and unknown primary melanomas; TTF of PD-1 monotherapy varies by mechanism of ERK activation; and finally, oncogenic kinase fusions can be successfully targeted in immune checkpoint inhibitor-refractory melanoma.

COVID-19: GET YOUR SHOT & STAY SAFE!

It is strongly recommended that MSK employees get vaccinated against COVID-19 **as soon as possible**. Real-world evidence continues to show that vaccination prevents more than 90% of severe disease caused by the highly transmissible Delta variant.

- Need a refresher on MSK's recent HICS update and COVID policies? Check out Cynthia McCollum's 8/2/21 HICS update.
- You can schedule your shots at MSK or submit your vaccination documentation if you choose to get vaccinated outside of MSK.
- Complete the COVID-19 Employee Screening Tool if you have any symptoms of possible COVID-19, regardless of vaccination status. It is also recommended to be tested 3-5 days after "close" contact with an infected person.
- You should report any positive outside tests through the COVID-19 Employee Screening Tool; this will notify multiple teams including the COVID-19 Contact Tracing team to begin an investigation. You can also contact Employee Health directly by emailing **ehws@mskcc.org** or calling **646-888-4000**.

ALL MSK STAFF MUST GET THEIR FIRST COVID-19 VACCINATION DOSE OR HAVE AN APPROVED EXEMPTION BY SEPTEMBER 27, 2021, AS A CONDITION OF CONTINUED EMPLOYMENT.