Massachusetts General Hospital
Founding Member, Mass General Brigham

An Impact Report for Jon and Patricia Baker

July 2025

Give hope. Build health.

Dear Pat and Jon,

In our inaugural year, we received 62 exceptional applications for funding from the Baker Family Fund for Transforming Patient Experience and Outcomes. These requests came from a wide variety of departments and programs, and the selection committee faced a challenging task selecting only nine to receive funding.

The winners represent countless physicians, researchers, nurses and staff at Mass General and across the MGB system who are dedicated not only to ensuring our hospitals deliver exceptional patient care now, but pushing the envelope to make sure they set the standard for the future. I know they share my gratitude to you for these awards that help drive and support that innovative spirit at Mass General.

I am pleased to share an overview of the projects selected this year. Their methods are diverse, but whether overcoming language barriers, improving patient-care team messaging, improving access to resources or easing the surgical experience, they all integrate technology in ways that solve important problems, transform how we deliver patient care and improve patient outcomes.

I hope you agree they embody our shared mission of ensuring positive outcomes through exceptional care and continuous improvement of the patient experience. I look forward to talking through how we celebrate and measure their success in the coming weeks.

Warmly,

Will Curry, MD
Chief Medical Officer
Academic Medical Centers
Mass General Brigham

EmpowerCare+

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Chantal Barksdale, MD, MSc
Internal Medicine PGY3,
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Kathy May Tran, MD
Internal Medicine Attending,
Massachusetts General Hospital

Chris Kirwan, PhD
Director, Interpretation Services,
Massachusetts General Hospital

Research consistently demonstrates that patients with limited English proficiency (LEP) experience higher rates of adverse events, longer hospital stays and increased readmission rates compared to English-speaking patients. Studies also show that proactive, patient-initiated language services improve clinical outcomes and patient satisfaction.

At Mass General, at least 157,649 patients required interpretation services in 2024. The hospital's approach to interpretation remains reactive: physicians, nurses or other members of the care team must connect patients with interpreters rather than allowing patients to initiate interpreter services themselves. This results in avoidable delays and disempowered patients who must rely entirely on the care team to facilitate clinical communication. Further, patients cannot rely on interpretation for nonclinical communication, like ordering meals, requesting assistance for toileting or adjusting their bed — which are all simple dignities that every patient should be afforded.

EmpowerCare+ is a bold, patient-driven solution that eliminates clinician bottlenecks, allowing patients with limited English proficiency (LEP) to independently access video interpreters from Mass General interpretation services via secured iPads. This simple yet critical and innovative patient-initiated model will result in better communication and stronger therapeutic relationships between patients and those who care for them.

Aligned with the mission of the Baker Family Fund for Transforming Patient Experience and Outcomes, *EmpowerCare+* will:

- Redesign patients' access to interpreter services with a simple, innovative, patient-initiated model.
- Leverage technology to create an accessible, seamless, real-time language access system using existing infrastructure.
- Strengthen patient-clinician connectedness.

This program will implement a phased launch on Mass General's inpatient floors, enhancing patient autonomy, reducing interpretation delays and improving clinician workflow efficiency. Success will be gauged by measurable outcomes, including higher patient trust scores, increased interpreter utilization and reduced lengths of stay and readmission rates for patients with LEP.

Backed by generous support from the Baker Family Fund, *EmpowerCare+* will ensure that every patient — regardless of English proficiency — has the tools to engage in their care with confidence and dignity and transform language access at Mass General.

Quiet at Night

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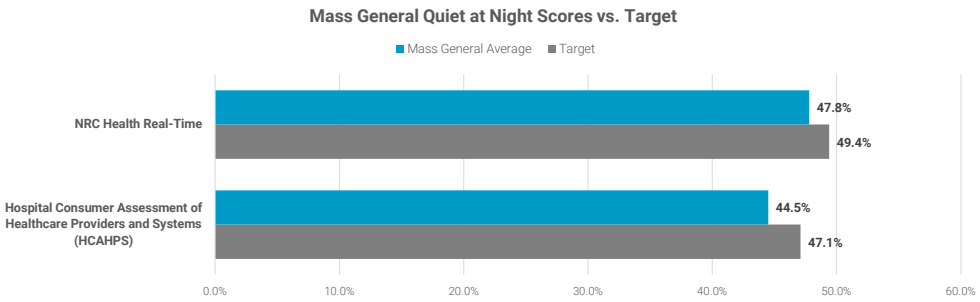
Sleep disturbances among hospitalized patients can lead to several adverse outcomes, including delirium, increased fall risk, mood disturbances, heightened pain sensitivity, cardiovascular issues, metabolic imbalances and disrupted circadian rhythms. Addressing sleep deprivation with improved sleep hygiene and by minimizing disruptions is essential for promoting recovery and overall health.

Mass General Brigham's NRC Health Real-Time data indicate that there is room for improvement in this area. Average patient satisfaction scores are lackluster for key components of the inpatient experience:

- How often were you able to get the rest you needed? **MGB Avg: 41%**
- How often was the area around your room quiet at night? **MGB Avg: 49%**
- Did doctors, nurses and staff help you rest and recover? **MGB Avg: 74%**

Mass General's goal is to achieve a 10% improvement in Quiet at Night scores. Again, current scores indicate a gap to the FY2025 target:



Quiet at Night can help improve these scores and patient outcomes. The project aims to enhance the patient experience by creating a sleep-friendly environment by providing wearable LED clip flashlights to inpatient clinicians and staff. Clinicians will:

- Employ the flashlights to minimize the frequency of room lights being turned on at night, thereby enhancing patient sleep quality.
- Use a sleep-friendly red light during clinical activities.
- Use a white light for assessing patients and a blue light to promote alertness and enhanced cognitive functions when reading and preparing medications.

Generous support from the Baker Family Fund will facilitate a rollout of Quiet at Night across Mass General's inpatient floors. With clinicians and staff using wearable LED clip flashlights and adjusting lighting appropriately to task, patients will find it easier to sleep. Mass General's Quiet at Night scores will improve, along with, most importantly, overall patient outcomes.

Dermatology Videos

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Dermatology appointments have always been in high demand and, to maximize access, they are shorter than those in other specialties. The increase in administration associated with each visit is further shortening the face-to-face time available for connection and education between patients and their care teams. One effect of this is that information presented to patients during the visit is often not retained.

To ensure patients leave with the information they need, dermatologists have historically relied on educational handouts and brochures. However, these are often left behind in the patient exam room, and they are not ideal for visual and auditory learners.

Many patients are now turning to online videos and social media to learn about their conditions and connect with others who suffer from similar conditions. However, information on social media is often unvetted. This project will create introductory videos of our dermatologists and patient education videos that will augment the patients' clinical experience.

Mass General's videography team will film dermatology personnel for each video and captioning will be added to be inclusive for hearing-impaired patients. Videos will be uploaded to the Dermatology website, and links will be sent to patients depending on their circumstances.

New patients will receive links to a video introducing them to their dermatologist and videos on Mass General's chaperone policy and parking information. They might also receive a video on how best to prepare for the visit, so their dermatologist will be able to help them quickly and effectively.

If a patient is coming in for a total body skin cancer screening, for example, they will receive a video on what to expect and the steps that their care team will take to ensure that the experience is professional, comfortable and comprehensive. If they undergo a procedure, such as a skin biopsy, they will receive a video on wound care to minimize scarring and infection risk. If their physician must call them about a new skin cancer diagnosis after their skin biopsy results, in addition to the standard personalized individual phone counseling we provide about the diagnosis and treatment, the patient will receive a video on what to expect when their skin cancer is surgically removed. After the patient's skin cancer has been removed, they will receive a video on how to monitor for a surgical site infection and minimize scarring.

Success of the project will be measured through anticipated reduced no-show rates and brief patient surveys. With other specialties now facing similar access challenges and time pressures, this program, if successful, will be useful across specialties.

Presurgical Education Modules for Awake Craniotomy

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Mass General Brigham is an international leader in the use of awake craniotomy (AC) to improve and protect neurocognitive function during and after surgery. Presurgical preparation for AC for brain tumors involves numerous specialties in addition to the neurosurgeon, including nurse practitioners, physicians' assistants, anesthesiologists, neuroradiologists, neurophysiologists, speech-language pathologists (SLPs) and administrative support staff. All may be asked to address patient/family questions about AC and its rationale, and the absence of a standard set of education materials can lead to discrepancies in messaging and apprehension among patients and families.

This project brings together the expertise of multiple disciplines involved in AC to create presurgical education materials intended to enhance the patient experience. An interdisciplinary project team will develop evidence-based materials that will maximize patient and caregiver literacy around AC — enhancing patient preparation, improving patient-reported outcomes and empowering patients as they undergo treatment as well as their families.

The project team is comprised of neurosurgeons, SLPs and nurses who have developed a unique team-based approach to ACs, which incorporates dynamic brain mapping to preserve cognitive-communication skills for patients whose tumors are situated in brain tissue crucial to speech, language or cognition. Standardized video and educational materials will educate patients and families and strengthen trust and alliance between patients and providers. Ultimately, this will enhance the neurosurgical care journey so that patients feel confident and well-prepared for surgery.

The aims of this project are to:

1. Develop and pilot high-quality, multimodal, video-based educational materials for awake craniotomy for brain tumor biopsy/resection.
2. Improve the quality of care for patients with brain tumors and their families through standardizing presurgical preparation.
3. Characterize the impact of education materials on patients and caregivers.

Thanks to the support of the Baker Family Fund for Transforming Patient Experience and Outcomes, this project shows immense potential to improve the patient's experience of AC through all phases of their journey — pre-, intra- and post-operative. In keeping with the Baker Family Fund's mission, it will redesign presurgical, patient-facing workflows, improving the patient experience; it has potential for widespread adoption across the MGB system, and adaptation to awake neurosurgical contexts beyond brain tumor (e.g., deep brain stimulation in Parkinson's disease, epilepsy surgery).

AI-Driven Patient Messaging System for Enhanced Care

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Epilepsy is one of the most common chronic neurological disorders. It is often thought of as purely a subspecialty issue, but most patients first present in an emergency room following a seizure or to a primary care provider (PCP) seeking information and evaluation. Due to the national shortage of neurologists and epileptologists, patients often wait up to 10 months for their first specialist visit, including at Mass General. As a result, PCPs play a critical role in the initial management of epilepsy, including diagnostic workup, safety counseling and seizure treatment — often without timely specialist input.

Once they receive care, patients rely on portals as a means of seeking guidance for symptom management, prescription refills and general concerns. However, neurology practices, like many subspecialties, struggle to keep pace with the increasing volume of messages. Over 60% may require clinician review, contributing to increased provider workload, inefficiencies in workflow management and burnout. It also causes delays in response time, creating patient frustration and anxiety as well as avoidable emergency visits.

The project centers on developing an AI-powered patient-messaging platform that seamlessly integrates with existing electronic health record (EHR) systems. The multidisciplinary project team aims to transform how they engage patients managing seizures by leveraging cutting-edge Artificial Intelligence (AI) to improve communication, reduce response delays and foster patient-centered connectedness.

This system will redesign the patient journey by:

1. Providing timely, contextualized responses that reduce frustrating wait times and enhance continuity of care.
2. Implement novel technology to personalize interactions through Retrieval-Augmented Generation (RAG) and Large Language Models (LLM), ensuring that patient messaging is tailored, clinically accurate and empathetic.
3. Foster a culture of connectedness by encouraging meaningful communication among patients, primary care providers and neurologists — especially vital during the lengthy intervals many patients wait for specialty consultation.

The project's goals align closely with the Baker Family Fund's pillars of improved patient experience, technological innovation and enhanced provider connectivity. The AI platform ensures patients receive clear, patient-friendly information by incorporating relevant clinical details into each message, helping them feel heard, supported and empowered throughout their care journey. For their part, providers gain an efficient, clinically validated workflow that reduces burnout and frees them to spend more meaningful time in direct patient care.

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Expected Impact:

1. Enhanced patient experience through faster, more personalized responses that support timely, accurate self-management and ease anxiety.
2. Improved outcomes and connectedness: Ongoing AI-driven communication helps providers address urgent patient needs sooner, reinforcing patient trust and fostering a more collaborative, supportive healthcare environment.
3. Scalable framework: While the initial focus is on epilepsy and seizures, it is readily adaptable to other high-burden settings, further advancing the Baker Family Fund's mission of driving broad improvements in patient care.

The interdisciplinary, multi-stakeholder team has laid the groundwork by building a secure cloud environment, curating high-quality training data and conducting preliminary validations. The Baker Family Fund's support makes possible the next phase, a rigorous evaluation and scaling this innovation to benefit a broader patient population.

Co-Designing a Digital Resource Hub to Support Pediatric Inpatient Families

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Hospitalization can be an overwhelming experience for families, especially when it involves a child. When a child is admitted, the family must adjust to the hospital environment, learn new terminology, manage logistics and absorb a vast amount of information — often while navigating emotional distress. Currently, there is no centralized or consistent way for families to access the full range of available resources and support during their inpatient stay.

To address this gap, a collaborative team from the Healthcare Transformation Lab (HTL), the Center for Innovation in Care Delivery (CICD), and the Mass General Brigham for Children Pediatric Patient and Family Advisory Council (PFAC) used design thinking to co-develop the concept for a centralized digital resource hub. This concept was one of the winning proposals from the inaugural Ether Dome Challenge — an open competition that crowd-sourced ideas to innovate and improve the healthcare experience from patients and families.

The primary objective of this project is to design, develop and pilot a mobile-friendly application consolidating essential hospital, local and emotional-support resources on one intuitive platform. The platform will improve the experience of pediatric inpatient families at Mass General Brigham for Children by providing them with a centralized, co-designed digital tool that eases navigation, reduces overwhelm and fosters meaningful engagement with their care team.

Anticipated outcomes include:

1. Better access to information like hospital routines, support services, local resources, and emotional wellness tools via a user-friendly, multilingual app.
2. Confidence and reduced anxiety as families navigate their child's care journey: by making clear, complete information readily available.
3. Enhanced clinician communication with families, enabling them to participate more fully in decision-making and advocacy with an accessible overview of care team roles, rounding times and patient rights.
4. An app with potential for broader implementation across the MGB system.
5. An increased patient and family voice in care design across the hospital.

The app will include practical tools such as maps, support group information and local food and childcare resources. Built with multilingual access in mind, the app aims to reduce information overload and support emotional well-being.

This initiative reflects the Baker Family Fund's mission by improving the experiences of patients and families, fostering connectedness between caregivers and clinicians and using technology to empower and personalize the care journey. The interdisciplinary team has proudly advanced the concept thus far through meaningful partnerships between families and care teams, and is grateful for the Baker Family Fund's support, which will bring this vital resource to life.

Stress Management and Resiliency Training (SMART-3RP™) for Advanced Practice Provider (APP) Well-Being

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In the past five years, advanced practice providers (APPs) in the MGB system have dealt with significant stressors including working through the COVID-19 crisis, increased patient acuity, an academic medical center merger, restructuring of reimbursement and proposed changes in clinical ladders. It is imperative to provide support for APPs to reduce stress and burnout symptoms and enhance well-being and professional fulfillment in the workplace.

One self-care, skill-building, multi-modal program intervention that significantly reduced stress among frontline clinicians during the Covid-19 and post-pandemic period was a resiliency program derived from the Benson-Henry Institute for Mind Body Medicine Stress Management and Resiliency Training Program (SMART-3RP™). The SMART-3RP program, comprised of eight 90-minute sessions, was delivered to Mass General employees and was effective in improving measures of wellness including resiliency and stress coping, and decreasing symptoms of anxiety and depression.

Support from the Baker Family Fund for Transforming Patient Experience and Outcomes makes possible a pilot pretest/post-test quality improvement cohort study to demonstrate the effectiveness of the SMART-3RP program. Mass General APPs will receive a recruitment flyer for participation in the SMART-3RP stress-management and well-being intervention program. After enrollment, participants will be invited to join an online group of approximately 15-20 APPs to engage in a multi-modal, eight-session, 90-minute stress management and resiliency training program (SMART-3RP) developed at the Benson-Henry Institute for Mind Body Medicine at MGH that includes skill-building exercises, informational components, and small group exercises.

The program features four components: eliciting the relaxation response (various meditation techniques, mini-relaxation exercises and yoga), traditional stress management techniques, healthy lifestyle behaviors, and cognitive reappraisal and adaptive coping skills (adapted from cognitive behavioral therapy and positive psychology approaches). Making lifestyle-behavior changes during challenging times is facilitated by a nurse-guided relationship focused on increasing personal awareness, intentional new choices for self-betterment and a commitment to new behavior choices.

The primary desired outcomes are a reduction in symptoms of burnout and an increase in reported well-being and provider-patient relationship connectedness among APPs who participate in SMART-3RP intervention. The effectivness of the program will be evaluated through post-program evaluation surveys and measuring changes using metrics that may include:

- The Current Experiences Scale (CES), measuring resiliency across six domains: appreciation for life, adaptive perspectives, personal strength, spiritual connectedness, relating to others and health behaviors.
- The Measure of Current Status-A (MOCS-A), measuring perceived ability to use stress-coping skills such as relaxation and adaptive perspectives.
- The Positive and Negative Affect Schedule (PNAS-PA), measuring the degree to which ten positive emotions are typically felt.
- Perceived Stress Scale (PSS-10), measuring thoughts and feelings experienced over the past month including items for anxiety and depression.
- Professional Fulfillment Index (PFI), a self-assessment of burnout (including current ability to empathize and connect with patients), professional fulfillment, self-compassion, sleep and work-life balance.
- Program post-evaluation assessing likelihood of leaving their position within the next two years, how relevant the program was to their lives and their satisfaction with the program.

My Question List

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A multidisciplinary team from Mass General's Health Decision Sciences Center (HDSC) and departments of nursing and hospital medicine, along with volunteer services, will implement My Question List on Mass General's inpatient floors. The project aims to improve the inpatient care experience by enhancing communication of patients' goals, concerns and questions to their care teams using a simple tool called a Question List.

This work builds on the Whiteboard Initiative conducted in 2023–2024 by nursing and medicine to improve the "patient input in care" metric, and an existing HDSC initiative called the Patient Support Corps (PSC). Volunteers in the PSC coach patients to prepare a detailed Question List before important medical appointments. Since 2021, project leaders have trained undergraduates and medical students in patient interview techniques to produce these high-quality Question Lists to share with their clinical teams.

As one graduate described in an article in STAT about her experience in the PSC, patients and their caregivers are frequently asked questions by a series of people as they enter the hospital and surveyed on forms, but the information collected can be fragmented and erroneous. "Question lists, on the other hand, are guided entirely by patient priority and can be used as a concise, organized tool" to structure conversation and make a sensible care plan tailored to the patient's goals and needs.

Leaders in nursing and inpatient medicine "welcome the opportunity to deepen the patient interview process using the Question Listing strategy for coaching patients and collecting detailed information about their goals and questions. We anticipate that these interviews and the Question Lists produced will enhance patients' engagement in their care plan and improve the clinical team's knowledge and understanding of patient concerns and preferences."

When My Question List is rolled out on inpatient floors, nurses and physicians will be engaged to make it an integral part of formulating each patient's daily care plan. Trained volunteers will assist patients in creating clear, organized Question Lists that are ready to share with their care teams on rounds the next morning. While My Question List will likely be a simple paper tool at first, the potential exists to develop an electronic application in the future.

The project team will study the success of My Question List by observing rounds and surveying patients, clinicians and volunteers on their experience with the tool, including measuring the impact of My Question List on patient experience-of-care surveys.

Support from the Baker Family Fund enables the team to immediately begin working with nursing and hospital medicine leadership at Mass General to make My Question List a key instrument facilitating high-quality conversations among patients and their care teams about the things that matter most at a difficult time.

Empathetics

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Empathy is often dismissed as an intangible skill that cannot be taught, but groundbreaking research at Massachusetts General Hospital has proven otherwise. A randomized controlled trial demonstrated that when Empathetics skills were taught and learned, patient experience significantly improved.

Empathy-driven programs create stronger, more engaged teams, leading to improved patient experiences, better clinician well-being, improved retention and a culture of safety and support. This, in turn, directly affects patient outcomes, workforce productivity and financial stability. Prioritizing workforce health and emotional resilience is not just a moral imperative, it's a strategic decision that drives operational excellence and long-term success.

The Massachusetts General Physicians Organization (MGPO) aims to cultivate a culture of empathy, compassion and support to improve the patient experience and alleviate burnout and frustration among its workforce of 7,000 physicians, advanced practice providers and registered nurses. Empathetics delivers evidence-based training that equips healthcare professionals with the essential skills to sustain compassionate, high-quality care. This project will implement Empathetics' evidence-based, neuroscience-driven empathy training within the 7,000-member MGPO.

The training will involve both eLearning micro-modules that are accredited for CME and CUE credits for physicians, physician assistants and nurses, respectively, and facilitator-led workshops, effectively meeting MGPO's training needs in an affordable manner. The project will:

- Empower employees with scalable, self-paced eLearning micro-modules.
- Train and certify internal facilitators to deliver workshops tailored to MGPO's culture and values of empathy.
- Establish a cost-effective, predictable pricing model.
- Achieve measurable outcomes, including improved workforce engagement, reduced turnover and enhanced patient satisfaction.
- Support the MGPO's commitment to empathy by embedding it into everyday interactions.

The implementation of Empathetics' programs within the MGPO will include self-paced elearning, facilitator-led workshops, and rigorous results analysis.

1. Empathetics Interactive eLearning

Scalable, self-paced, evidence-based courses that leverage insights from neuroscience, including three courses tailored to the MGPO's goals: Enhancing Empathy in Healthcare, Managing Difficult Medical Interactions and Communicating Bad News.

Students can earn three continuing medical education (CME) credits, three risk management credits and one end-of-life–care credit, and three continuing education unit (CEU) credits (1 hour of learning per course).

2. Empathetics Workshops

Delivered by certified facilitators from Empathetics, workshops on topics like self-empathy allow participants to practice tools for self and relationship management in challenging healthcare situations. They discuss challenges through the lens of self-empathy and build a community of peer support.

3. Pre/Post Program Measurement, Reporting and Analytics

Empathetics has designed detailed pre- and post-program analytics to measure individual and organizational impact, offering actionable insights to inform ongoing cultural transformation. These target:

- Changes in climate: Perceptions of the working environment.
- Changes in communication skills: Perceived improvements in empathy-driven communication.
- Demographics: Analysis of program impact across roles, departments and the entire organization.

Dear Mr. and Mrs. Baker,

It has been a privilege to be distinguished as the Nelson Family and Jerry Younger, MD Endowed Chair in Breast Medical Oncology. This named position fuels my research and helps me push the boundaries of breast cancer care, expanding upon the strong foundation that exists here at Mass General. It is a great honor to be named the incumbent of an endowed chair, and I am grateful for your support of my work and of the Breast Medical Oncology Program at Mass General.

I have attached a report of the notable highlights from the Ellisen Lab over the past year. I hope it gives you a sense of your continued impact — enabled by your generosity and that of like-minded patients and colleagues who are dedicated to compassionate care. Thank you for everything.

Best,

Leif William Ellisen, MD, PhD
Nelson Family and Jerry Younger, MD
Endowed Chair in Breast Medical Oncology and
Program Director, Breast Medical Oncology,
Massachusetts General Hospital
Professor of Medicine,
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The Ellisen Laboratory

The Ellisen Laboratory has a broad interest in how genetic abnormalities in breast cancer and related malignancies influence tumor biology and how that biology can, in turn, be exploited to therapeutic advantage. We address these questions through basic research studies of key cancer hallmarks, including DNA repair defects through BRCA1/2 and related pathways and transcriptional reprogramming through the p53 gene family. Supporting and complementing these studies are sophisticated analyses of patient-derived precancerous and cancerous tissues. Recent innovative tissue-based studies have led to our discovery of novel cancer drivers and have provided a unique window into early cancer pathogenesis, intratumoral heterogeneity and therapeutic resistance. Our discoveries in the basic laboratory and through human tumor analysis are being applied in ongoing clinical trials that seek to identify predictive markers of response to innovative therapeutics for breast and other cancers. Our ability to work at the interface of basic tumor biology and therapeutic application is strongly supported by our network of collaborators and by the research and clinical infrastructure of the Mass General Cancer Center.

Research Highlights and Select Recent Publications from the Ellisen Laboratory and Mass General Breast Program

Novel drivers of aggressive breast cancer subtypes

Our work employing advanced tumor molecular diagnostics has revealed gene fusions as novel drivers of an aggressive breast cancer subset. In triple-negative breast cancer (TNBC), extensive differences in tumor cell populations within the same tumor are a driver that we have characterized through single-cell genomic and transcriptomic analysis, leading to our discovery of unanticipated drug resistance mechanisms with immediate therapeutic implications. Of particular interest is resistance to novel Antibody Drug Conjugates (ADCs) that are transforming cancer therapy. Unraveling the complex nature of ADC resistance is a long-term goal that touches every aspect of tumor biology and will have a major clinical impact. Our longstanding work on the biology of TNBC is supported by the institution-wide Triple-Negative Breast Cancer Program, which integrates basic research, translational and clinical studies together with human tumor propagation and high-throughput drug screening, all focused on overcoming drug resistance and improving outcomes for patients with TNBC.

The NeoSTAR Platform Trial, a collaboration between multiple Harvard Medical School affiliated institutions, was the first clinical trial of a highly effective ADC, Sacituzumab govitecan, in the pre-operative setting for primary, early-stage breast cancer. Findings from this 50-patient study were published in the Annals of Oncology in March 2024. Ongoing collaborative work between the Ellisen laboratory, computational and spatial biologists involves deep exploration of pre- and post-treatment tumor specimens from these patients. This analysis will provide unprecedented insights into mechanisms of response and resistance to this important drug.

Another pathbreaking clinical trial developed by Dr. Ellisen and colleagues employed an innovative combination of two precision therapeutics, an ADC and a PARP inhibitor, for patients with refractory TNBC. Coordinated efforts between the laboratory and clinic provided the scientific foundation for testing this promising new treatment approach using a novel dosing strategy. Findings of the trial were published in the journal Clinical Cancer Research in July 2024.

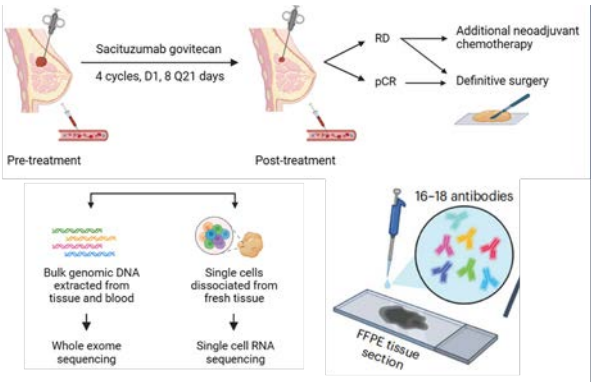

Figure: At top, the schematic shows the treatment course for the NeoSTAR clinical trial of preoperative Sacituzumab govitecan for primary TNBC. Below are shown extensive tumor specimen analyses, including RNA, DNA and spatial multi-plex profiling, that aim to understand predictors of treatment response and reveal mechanisms of resistance.

Advocating for liquid biopsy

In January 2024, Dr. Ellisen and a junior faculty colleague, Dr. Arielle Medford published an authoritative commentary in the Journal of Clinical Oncology Precision Oncology discussing the benefits of liquid biopsy — blood-based testing — for cancer patients, as well as the barriers faced by certain patient groups in accessing this type of advanced technology. In their article, recommendations were made for increasing access and mitigating disparities in order to ensure optimal cancer care for all patients.

Following that article, in April 2024, a group of colleagues within the Mass General Breast Program, including Dr. Ellisen and others,

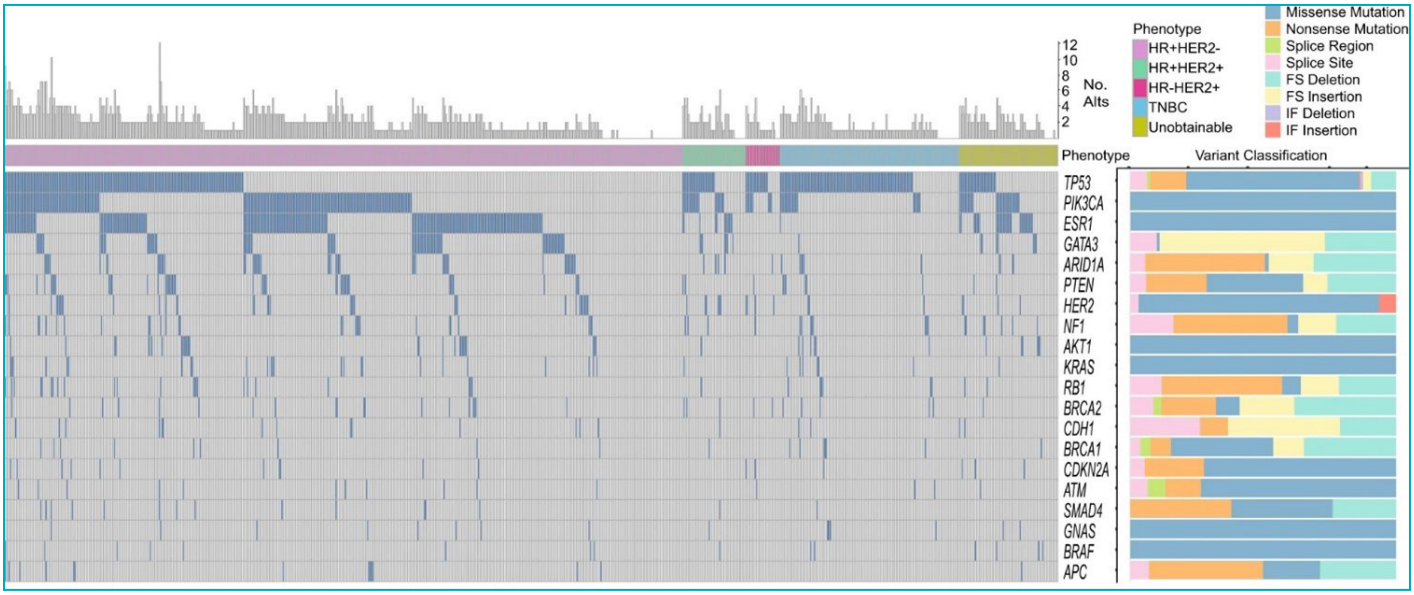

Figure: Summary of findings from nearly 500 patients with advanced breast cancer undergoing blood-based ctDNA testing at Mass General. Rows indicate individual cancer genes found to be mutated, and columns at left indicate mutations found in individual patients (blue). Breast cancer subtype is shown at top left, and the category of mutations found is shown at right. Based on the ability of this non-invasive analysis to identify tumor mutations with high-sensitivity, blood analysis for ctDNA is now becoming a standard practice to personalize therapy for breast cancer patients.

published findings from a preliminary study demonstrating the remarkable ability of blood-based testing to yield circulating tumor DNA (ctDNA) whose analysis identified key tumor mutations that could guide therapy choice for breast cancer patients. This study and others have demonstrated that liquid biopsy can be more effective and safer than tumor biopsy for identifying tumor genetic features relevant to clinical decision making. Their publication can be found here, and while they assert that more research is needed to determine various dimensions of use cases and effectiveness, this is truly a cutting-edge line of inquiry.

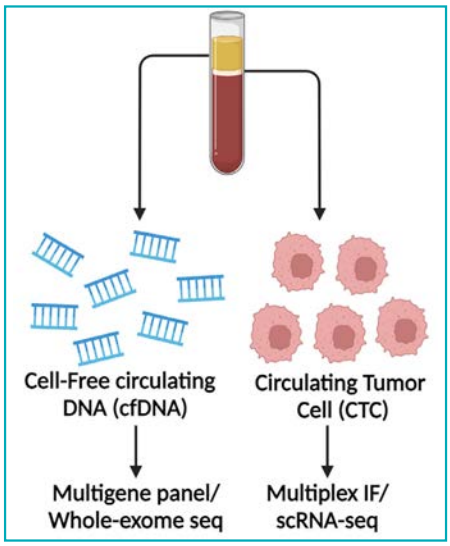

Figure: Blood-based diagnostic tumor testing, known as liquid biopsy, can involve analysis of both circulating tumor DNA (ctDNA) and Circulating Tumor Cells (CTCs). These types of analyses are now being employed in routine clinical practice for patients with breast and other cancers.

Understanding the p53 family network in cancer biology and therapy

The p53 protein is like a guardian in cells, helping them respond to stress. It controls important activities like cell growth, survival, and energy use. By studying two related proteins, p63 and p73, we and others have found that p63 has a special job in certain tissues. It helps maintain stem cells, which are like the body's raw materials that can become other types of cells. In some cancers, including breast cancer, p63 doesn't work normally. It changes how the DNA is read, preventing cells from maturing and helping the cancer avoid the immune system. This may explain why p63 is found in higher amounts in many types of cancers, especially skin and breast cancers. Collectively, this work serves as a paradigm for the analysis of transcriptional reprogramming in cancer.

BRCA1/2, hereditary cancer predisposition and prevention

Germline mutations in the DNA repair genes BRCA1 and BRCA2 confer dramatically elevated risk of cancers of the breast, ovary and pancreas, yet the precise pathogenesis of BRCA1/2-associated cancer remains to be elucidated. Together with an international team of collaborators, we are carrying out systematic studies of early events that give rise to these cancers, in part through detailed molecular analysis of normal and precancerous tissues from BRCA1/2 mutation carriers. Defining the altered signaling and early cooperating events in this context is likely to reveal new markers of breast cancer predisposition and new targets for prevention. For example, our published single-cell genome analysis has revealed extensive chromosomal damage in BRCA-mutant breast tissues that precedes any histological abnormalities. This seminal finding implies the existence of early cellular defects and associated vulnerabilities that could be exploited for cancer prevention in this setting.

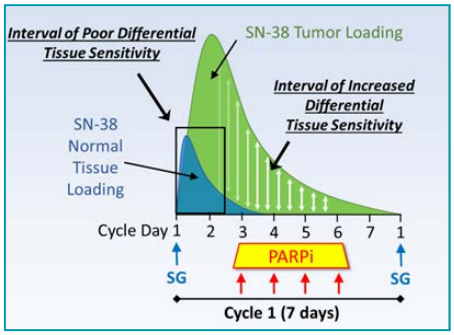

Figure: The schematic demonstrates that tumor-selective delivery of chemotherapy (SN-38) via the Antibody-Drug Conjugate Sacituzumab govitecan (SG) allows normal cells to rapidly clear the drug, while sequential PARP inhibitor (PARPi) treatment is toxic to tumor cells with residual SN-38.