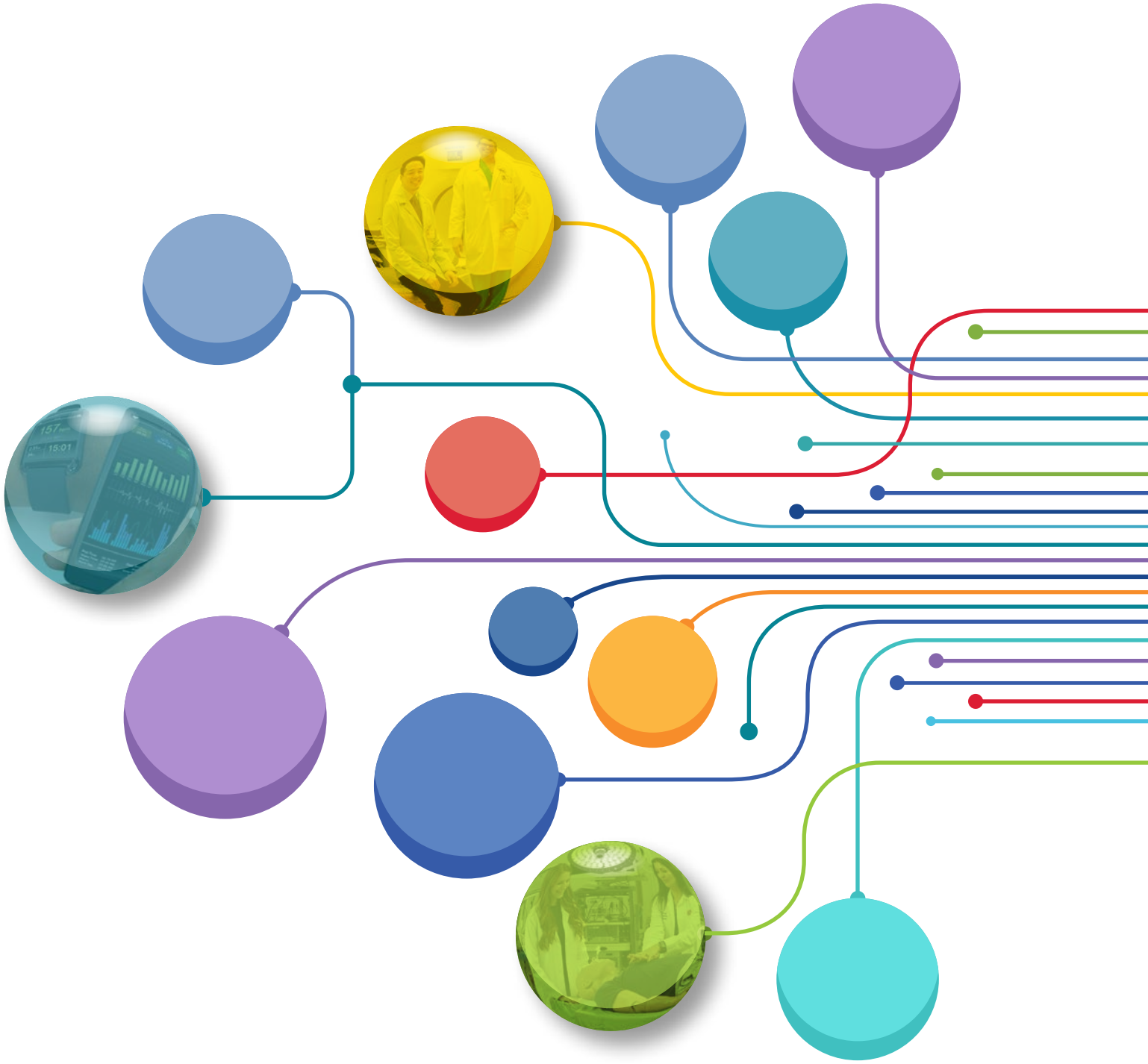
2023 ANNUAL REPORT

CANCER

Cedars Sinai



The Power and Promise of Convergent Science to Transform Cancer Research and Care

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Professor of Urology, Pathology and Laboratory Medicine

Numerous disciplines—from basic science to electronics to engineering to mathematics, including artificial intelligence (AI)/machine learning—can look at a single problem from myriad angles. Operating separately, these disciplines make slow, hard-won progress. When we work together through truly integrated, side-by-side collaboration, we have the opportunity for paradigm-shifting advances by virtue of their synergism with each other.

"Convergent science" is the concept that recognizes the power and promise of developing these deep synergisms and harmonizes them to tackle seemingly unsurmountable problems by addressing them with a thoughtful, sophisticated, multifaceted solution. In cancer, use of convergent science principles and this cross-pollination also cultivates connections faster than ever before, speeding up and simplifying the evolution of cancer care.

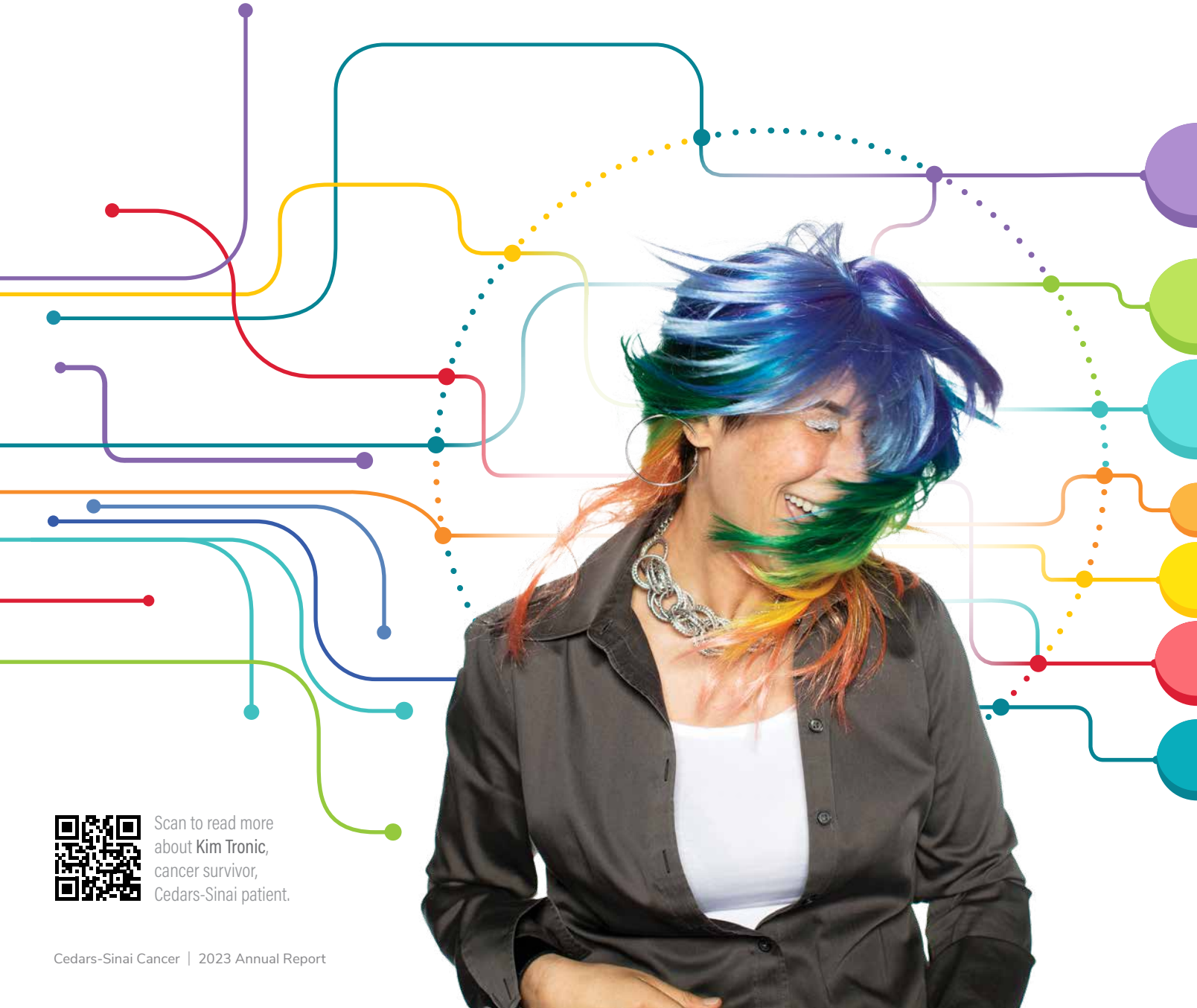
Best of all, convergent science is inextricably patient-focused. Patient needs, coupled with feedback and engagement of our Community Advisory Board, define the tracks of research on which investigators train their efforts.

We are crafting a new era of oncology care and research by applying convergent science disciplines to discovery-centric programs. AI applications lead to boundary-free exploration of the most promising avenues for improved diagnostics and therapeutics.

We hope that you will recognize our push toward convergence and join us for new collaborations that have the power to accelerate improvements in care for cancer patients everywhere.

Cedars-Sinai Cancer: Many Routes, Many Destinations, One Infrastructure

Imagine a network of clinicians and researchers from numerous fields—biology, chemistry, physics, pharmacology, mathematics, computer science, engineering, technology and more—working together on shared problems in the realm of cancer treatment. Projects proceed without silos. Research efficiency increases. Before you know it, the results meaningfully impact patients' lives.

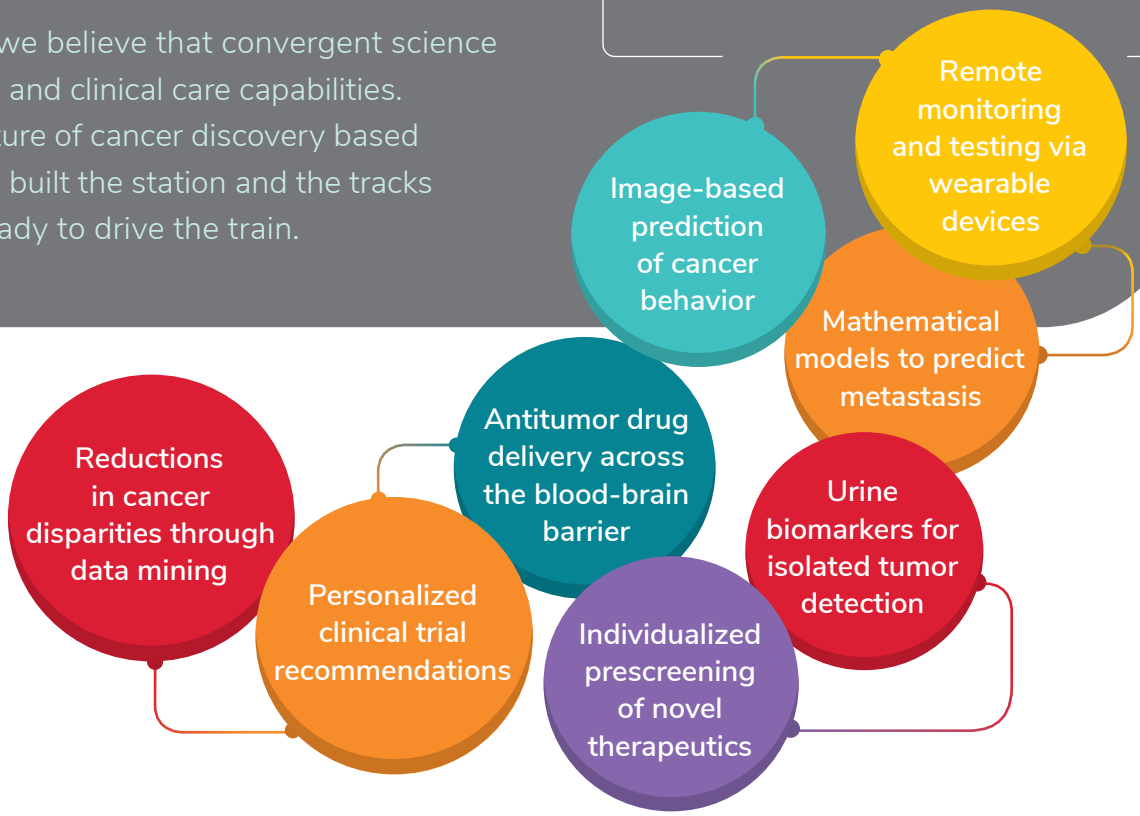


Scan to read more about **Kim Tronic**, cancer survivor, Cedars-Sinai patient.

This is the future of medical science: a convergence of disciplines, ideas and efforts to enable progress on the field's toughest challenges. It is centered on patient needs in every possible way, from individuals here and now to large communities in the future.

At Cedars-Sinai Cancer, we believe that convergent science will enhance our research and clinical care capabilities. We are embracing the future of cancer discovery based on this principle and have built the station and the tracks to proceed. Now we're ready to drive the train.

Convergent science makes solutions not just possible, but probable, for the most intractable problems in cancer medicine.



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AI

Imaging Gets Boost From AI

Two very different populations are the latest to benefit from collaborations with the Biomedical Imaging Research Institute at Cedars-Sinai: children with a cancer predisposition syndrome called neurofibromatosis and men with prostate cancer.

A pilot study is using MRI of pediatric patients to screen for markers that can predict cancerous tumors as well as benign tumors capable of malignant transformation. When combined with AI/machine-learning algorithms informed by both retrospective and prospective scans, investigators believe the technique could revolutionize proactive management and preventive interventions.

> "We want to create a fundamental shift in how we manage prostate cancer with imaging. AI/machine learning will help us localize cancer more precisely to noninvasively characterize and monitor it over time and to deliver more accurate, safer therapies.
>
> – Hyung Kim, MD"

> "With predisposition syndromes, it is often difficult to get a whole-body MRI paid for by insurance. We can do precise scans in about an hour as a valuable addition to both a patient's record and the study and follow up with more detailed imaging if any masses are found."
>
> – Nicole Baca, MD

Across the Age (and Disease) Spectrum

Enhanced imaging techniques also offer hope for an improved standard of care among men with prostate cancer. Historically, prostate imaging has been an unreliable tool for detecting and tracking disease. With the recent advent of higher-resolution MRI developed at Cedars-Sinai—PSMA PET MRI—along with computer-aided AI/machine learning-based image analysis, clinicians can now pinpoint the location and characteristics of prostate tumors for consideration in focal therapy and longitudinal radiologic monitoring.

Together, these diverse applications of imaging science and AI/machine learning offer a glimpse into a future of accurate, early cancer prognostics and enhanced monitoring capabilities —no matter the diagnosis.

Pediatric patient **Victoria Coats** takes cancer in stride. Scan to read her story.

Digital Enhancement of Science and Care

Cedars-Sinai's integration of remote data from wearables, apps and home monitors began in 2015. Seeing the value that remote data held for improved disease description and prediction, clinician-investigators have now embraced it, using it to identify at-risk patients and gain reliable knowledge on how best to intervene early.

It is also useful for following patients post-treatment. For example, wearable devices have linked postoperative step count with functional outcomes in cancer patients, leading to the creation of tailored interventions such as virtual exercise programs and art tours in surgical recovery units. Ongoing research includes studies funded by the Pancreatic Cancer Action Network and the U.S. Department of Defense to determine whether wearable-reported activity predicts functional outcomes for prostate cancer patients.

"Wearables and remote monitoring devices have allowed us to break down the four walls of the clinic to measure patient activity in a moving environment, rather than a single snapshot during occasional office visits."

– Gillian Gresham, PhD

Transforming Treatment With Technology

Wearables also now complement VR technology to create an immersive, biofeedback-tailored intervention for cancer patients to reduce their physical and cognitive experience of disease. A National Cancer Institute grant allows Cedars-Sinai investigators to explore the impact of these combined technologies on pain, opioid use and activity levels among patients with gastrointestinal cancer.

Moving forward, Cedars-Sinai clinician-investigators plan to use machine learning to titrate each patient's VR sessions according to their unique biometric profile to provide the most therapeutic session possible.

AI

BIO

"By combining VR with wearable biosensors, we get a second-to-second picture of the autonomic nervous system as it experiences that immersive environment.

– Brennan Spiegel, MD"

Virtual reality has laid Descartes' theory of mind-body dualism to rest. Scan to read more.

From Cells to Chip to Clinic and Back Again

AI

TWIN

BIO

Induced pluripotent stem cells, organs-on-a-chip and an integrated network of patient-focused practices for streamlined research have launched a new era of cancer innovation at Cedars-Sinai. By bringing together experts in regenerative medicine, fluid dynamics, the tumor microenvironment, single-cell sequencing, bioinformatics and multiple subspecialties in clinical oncology, Cedars-Sinai has begun validating new methods to provide actionable information on cancer development, prevention and treatment.

> "We are focused on making sure that we have a good representation of mutation carriers from other ethnic groups, specifically our Los Angeles-based Korean population, Mexican-heritage Latinx people, Ashkenazi Jewish community and Black patients, all of whom may carry unique BRCA-germline mutations."
>
> – Bobbie J. Rimel, MD

> "Innovation in the combination of organoids and single-cell sequencing allows us to pick out every individual cell within a tumor without needing a biopsy. We can pull that into a diagnostic or to test targeted therapies.
>
> – Clive Svendsen, PhD"

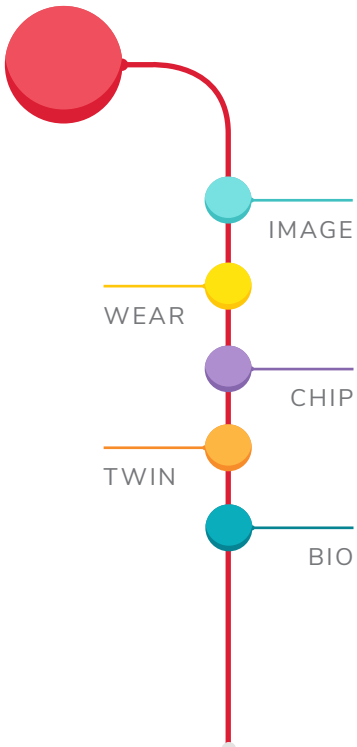
Why **diversity matters** in cancer clinical trials. Scan to read more.

A New BRCA Screening Tool

Organoids made from induced pluripotent stem cells coupled with chip techniques hold tremendous potential as a complementary risk metric and preclinical drug-screening tool for people with BRCA mutations. Mutations in the BRCA1 and BRCA2 genes predispose patients of both sexes to several cancers, such as ovarian, breast, pancreas and prostate, all of which are major areas of focus at Cedars-Sinai. They may also help illuminate the origins of sporadic cancer development.

To advance these promising technologies, Cedars-Sinai now offers multipurpose visits in programs such as the new BRCA previvor multidisciplinary clinic. In a single, coordinated visit, the clinic provides patients with personalized screening and care as well as information on opportunities for research participation—enabling research into BRCA-driven cancers. That also addresses issues driving health disparity.

Machine Learning and the Power to Outsmart Cancer



Sequencing the human genome, transitioning to electronic health records and digitizing pathology images have all contributed to advancements in data generation and analysis that have catapulted science and medicine forward. But the true synthesis of this information—and more, including social media posts, drug databases, clinical trials and even text from clinical notes—is now possible, thanks to powerful algorithms and the collaboration of computational biomedicine experts and curious clinicians. This is emblematic of the promise of convergent science.

"We created the Department of Computational Biomedicine to address disparities in health through studies that use real-world data and to bring experts that can advance the methods needed to deal with such high-volume, content-rich data."

– Graciela Gonzalez-Hernandez, PhD

"It's hard to imagine an area of cancer biology and research that could remain unaffected by the advancement of AI and machine learning.

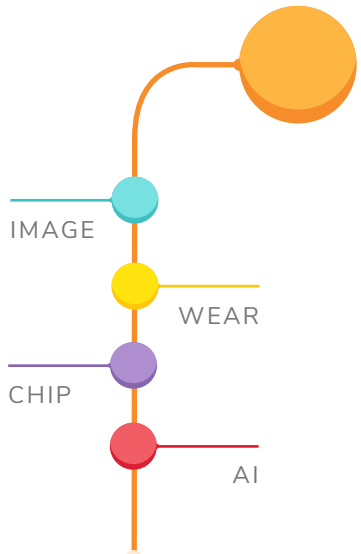
– Nicholas Tatonetti, PhD"

AI in Action

AI and machine learning can already enable identification of pancreatic cancer before it's detected on CT scans, help with early differential diagnosis of often underrecognized cardiac diseases and triage stroke patients to reduce length of stay.

Machine learning offers a huge opportunity to enhance the precision of clinical research and advance the data science infrastructure of Cedars-Sinai Cancer by supporting multimodal data processes through applications such as Molecular Twin, (see next page). AI can also be used to provide the data that helps promote cancer clinical trials enrollment and engagement of minorities and underrepresented populations, such as the local Korean and LGBTQ+ communities.

Natural language processing, or NLP, holds significant potential for the future of medical research by enabling rich, nuanced exploration of written text in patient files and online posts. This offers the ability to mine clinical notes for clues to early disease symptoms, success or failure in treatments, prevailing patterns as disease evolves, or eligibility for potential participation in clinical trials or sociological research.



Ten Analytes, Unlimited Applications

The Molecular Twin initiative brings together diverse experts in clinical, scientific and computing fields to solve oncology questions using virtual replicas of thousands of patients' biological samples and clinical information to help identify the most effective approach to each individual's disease. By creating these "molecular twins," scientists can build a database of cancer-specific genes, tumor proteins and relevant pathways to be mined by investigators around the world.

The effort goes far beyond "single-omics"—the extent of most institutions' forays into personalized medicine through a DNA, RNA or protein screening—into a realm of linked information comprising thousands of data points per patient. The overarching ideal of the Molecular Twin undertaking is tumor-agnostic precision medicine for everyone.

> "It is only through improved understanding—which we gain through studies such as Molecular Twin and other scientific work—that we can improve options for patients with difficult-to-treat cancers."
>
> – Cristina Ferrone, MD

From Concept to Reality

Cedars-Sinai has already expanded from collecting comprehensive samples for just pancreatic cancer to collecting samples for breast and lung cancers, too, and is working to incorporate radiomics and more comprehensive analyses of the tumor microenvironment. In the next few years, all major tumor types will be included in the Molecular Twin program. Longitudinal sampling and multi-institutional collaborations will further strengthen the platform's ability to draw accurate conclusions and patient-specific insights.

Cedars-Sinai Cancer facilitates sample collection from patients of all backgrounds by promoting one-stop-shop clinics for cancer. These enable patients to receive truly integrated, multidisciplinary evaluations and treatment plans—as well as invitations to participate in research—in a matter of hours, instead of over the course of a half-dozen separate appointments.

74 patients with pancreatic cancer participated in the original Molecular Twin pilot study.

6,363 data points per patient considered by the model.

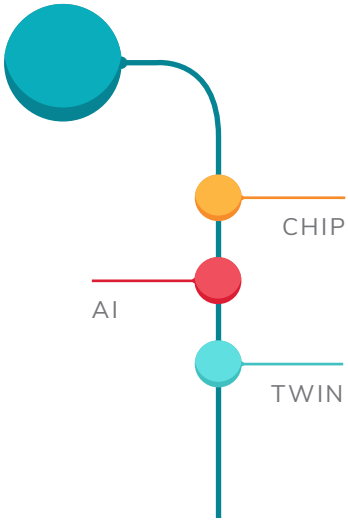
500 points identified as useful in prognostics.

10 analyte sources for data.

1 cell pathway quickly identified for intervention in pancreatic cancer.

> "The platform enables the discovery of parsimonious biomarker panels with similar predictive performance to that of larger and resource-intensive panels, and thereby has a significant potential to democratize precision cancer medicine worldwide."
>
> – Arsen Osipov, MD

A Collaborative Effort to Cross the Blood-Brain Barrier



From designing novel proteins to isolating natural compounds for antitumorigenic effects, bioengineering and pharmacological innovation occurs on a daily basis in the Department of Biomedical Sciences and Cedars-Sinai Cancer. But the magic really happens when experts in these fields routinely engage with colleagues in bioinformatics, cell biology, molecular biology, nanotechnology, chemistry, clinical therapeutics and even art.

> "When we systemically deliver the engineered bioparticle loaded with Dr. Turkson's tumor-toxic molecules, it can enter the brain and target resistant and metastatic tumors."
>
> – Lali Medina-Kauwe, PhD

Computer design is helping scientists speed up improvements in **protein design**, work that could enhance our ability to reach breast cancer that has metastasized to the brain. Scan to read more.

Early Success Stories

The cross-pollination of ideas has already resulted in a virus-based drug-delivery vector that crosses the blood-brain barrier, making the targeted treatment of triple-negative breast cancer that has metastasized to the brain (and other hard-to-treat brain tumors) a real possibility.

The novel nanoparticle can be customized to carry a wide range of drug substances, including those recently designed to attack HER cancers. Add to that the identification of a natural therapeutic that triggers apoptosis by targeting abnormal cells with cancer's characteristic metabolic changes and oxidative stress signals, and consultations with experimental therapeutics and trial design experts are growing exponentially.

> "Our compound shows a strong selectivity for targeting cancer cells and suppresses their ability to cope and survive under high oxidative stress."
>
> – James Turkson, PhD

AI

TWIN

Nurturing the Next Generation of Convergent Science Thinkers

Cedars-Sinai Cancer clinicians and investigators have embraced the world of convergent science to such an extent that our efforts now extend outward to training emerging researchers well beyond our campus. This education-focused work has the potential to transform the concept of convergence into something more holistic and powerful than previously envisioned, transcending the disciplines of medicine, engineering and computer sciences to reach into the realms of policy, socioeconomics and, above all, population health.

> "Our programs help students harness the value of wearables and other digital technologies to reduce cancer incidence and improve cancer outcomes across the diverse populations in our community."
>
> – Patricia Thompson, PhD

Training Ground for Future Convergent Scientists

An essential part of this mission involves formal training and funding of scientists to think across disciplines, collaborate effectively and imagine solutions without barriers. The 10-student pilot class of the Undergraduates Gaining Research Opportunities for the Cancer Workforce (U-GROW) Internship Program, a partnership between Cedars-Sinai and seven California State University campuses, aims to train undergraduate students from historically underserved populations in conducting cancer prevention and control research.

For clinical and research professionals, the Convergent Science Virtual Cancer Center (CSVCC, csvcc.org) exists to mentor and support early-career investigators at leading institutions across the country. The goal is to rapidly achieve measurable progress through multidisciplinary, solution-oriented projects. CSVCC scholars have already published numerous studies, presented at national events and filed patents.

Cedars-Sinai Cancer is reaching out to talented undergraduates from diverse backgrounds to introduce them to **convergent science concepts** and the wide range of cancer research careers available to them. Scan to read more.

Scan to visit csvcc.org Convergent Science Virtual Cancer Center

Metrics

Grant Funding:
$25.976M*
(up 4% from FY2021)
*Excludes industry funding.

Philanthropy:
2,446
Donors to Cancer Program

Publications
289

18,203
Community outreach and engagement participants

Community Outreach

	Science-based cancer information dissemination (outreach)	Behavior-change intervention (workshops)	Screening or prevention interventions (breast, colorectal, cervical and lung cancers; HPV vaccinations; smoking cessation)
Total individuals reached in Korean, Latinx, Black, Filipino and LGBTQ+ communities	20,173	1,438	7,635

Clinical Volume

	Cedars-Sinai Medical Center + Medical Network	Torrance Memorial Medical Center, a Cedars-Sinai Affiliate	Providence Cedars-Sinai Tarzana Medical Center
Inpatient volume	6,401	951	349
Outpatient volume	205,604	31,913	1,011
Office visits	150,102	22,833	
Infusions	55,502	9,080	
Total	**212,005**	**32,864**	**1,360**

Total Inpatient Volume
7,701

Total Outpatient Volume
238,528

Clinical Trials FY2022

Investigational-initiated trials opened to accrual (interventional and noninterventional)	77
Investigational-initiated trials opened to accrual (interventional only)	49
Open to accrual Phase I trials	62
Active Phase I trial accruals	126
Interventional treatment trial accruals	466
Interventional (nontreatment) trial accruals	275

Report Contributors and Recent Faculty Recruits

Nicole Baca, MD
Pediatric Hematologist-Oncologist, Cedars-Sinai Guerin Children's and Cedars-Sinai Cancer
Page 1

Dolores Di Vizio, MD, PhD
Co-Leader, Cancer Biology Program, Cedars-Sinai Cancer

Cristina Ferrone, MD*
Chair, Department of Surgery
Page 5

Graciela Gonzalez-Hernandez, PhD*
Vice Chair of Research and Education, Department of Computational Biomedicine
Page 4

Gillian Gresham, PhD
Research Scientist, Cedars-Sinai Samuel Oschin Comprehensive Cancer Institute
Page 2

Hyung Kim, MD
Director, Academic Urology Program; Homer and Gloria Harvey Family Chair in Urologic Oncology in honor of Stuart Friedman, MD
Page 1

Xue (Sean) Li, PhD
Co-Leader, Cancer Biology Program, Cedars-Sinai Cancer

Lali Medina-Kauwe, PhD
Associate Director for Basic Research, Cedars-Sinai Cancer
Page 6

Arsen Osipov, MD
Medical Oncologist and Clinical-Translational Investigator in the Pancreas Cancer Research Group
Page 5

Bobbie J. Rimel, MD
Gynecological Oncologist and Medical Director, Clinical Trials Office, Cedars-Sinai Cancer
Page 3

Brennan Spiegel, MD
Director, Health Services Research for Cedars-Sinai; Director, Cedars-Sinai Center for Outcomes Research and Education
Page 2

Clive Svendsen, PhD
Executive Director, Board of Governors Regenerative Medicine Institute; Kerry and Simone Vickar Family Foundation Distinguished Chair in Regenerative Medicine
Page 3

Nicholas Tatonetti, PhD*
Vice Chair of Operations, Department of Computational Biomedicine; Associate Director for Computational Oncology, Cedars-Sinai Cancer
Page 4

Patricia Thompson, PhD
Co-Leader, Cancer Prevention and Control Program, Cedars-Sinai Cancer
Page 7

James Turkson, PhD
Associate Director for Diversity, Equity and Inclusion, Cedars-Sinai Cancer
Page 6

*New Faculty Since January 2022.

Cedars Sinai

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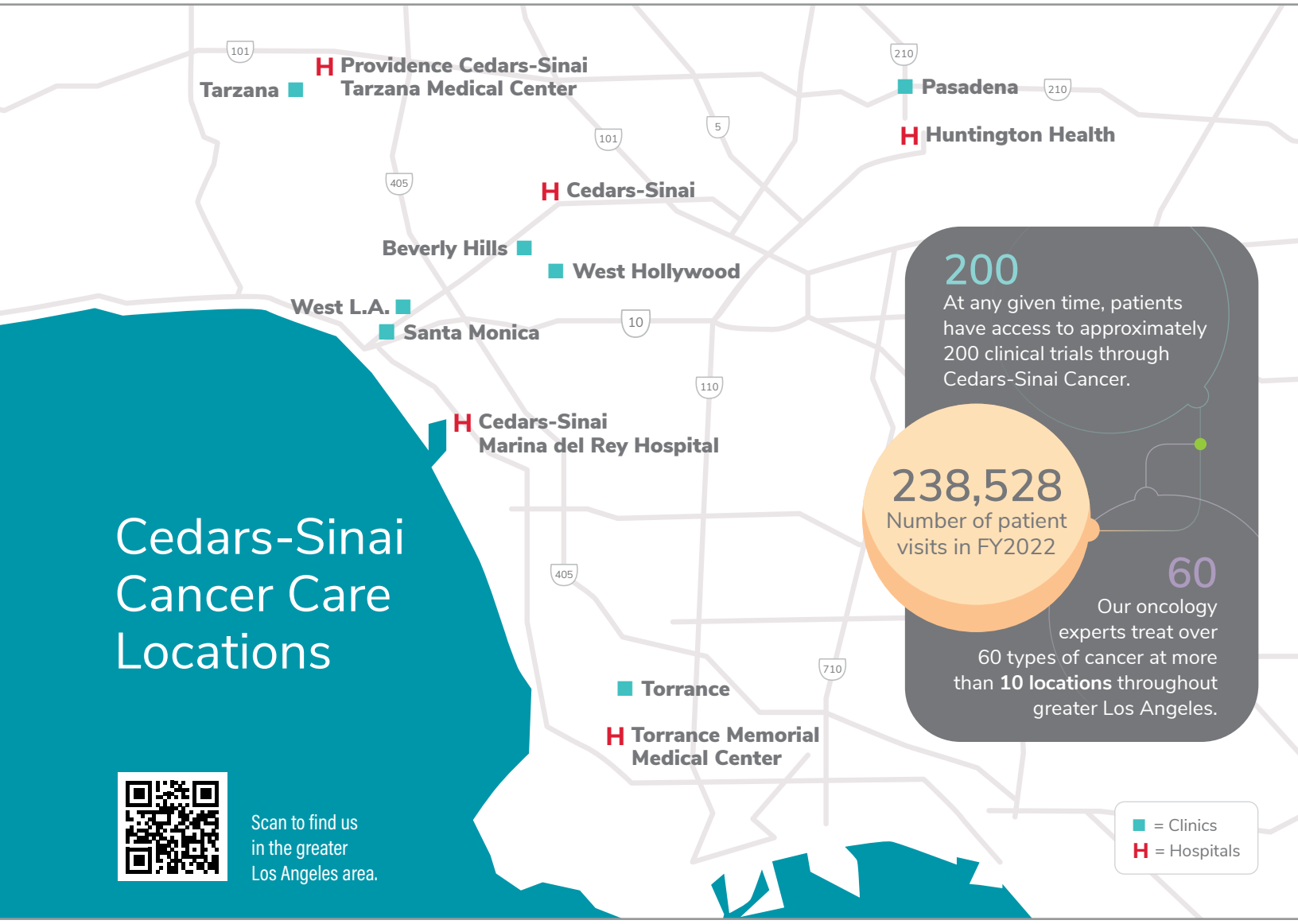
Los Angeles, CA 90048

Cedars-Sinai Cancer Care Locations



200
At any given time, patients have access to approximately 200 clinical trials through Cedars-Sinai Cancer.

238,528
Number of patient visits in FY2022

60
Our oncology experts treat over 60 types of cancer at more than **10 locations** throughout greater Los Angeles.

Scan to find us in the greater Los Angeles area.