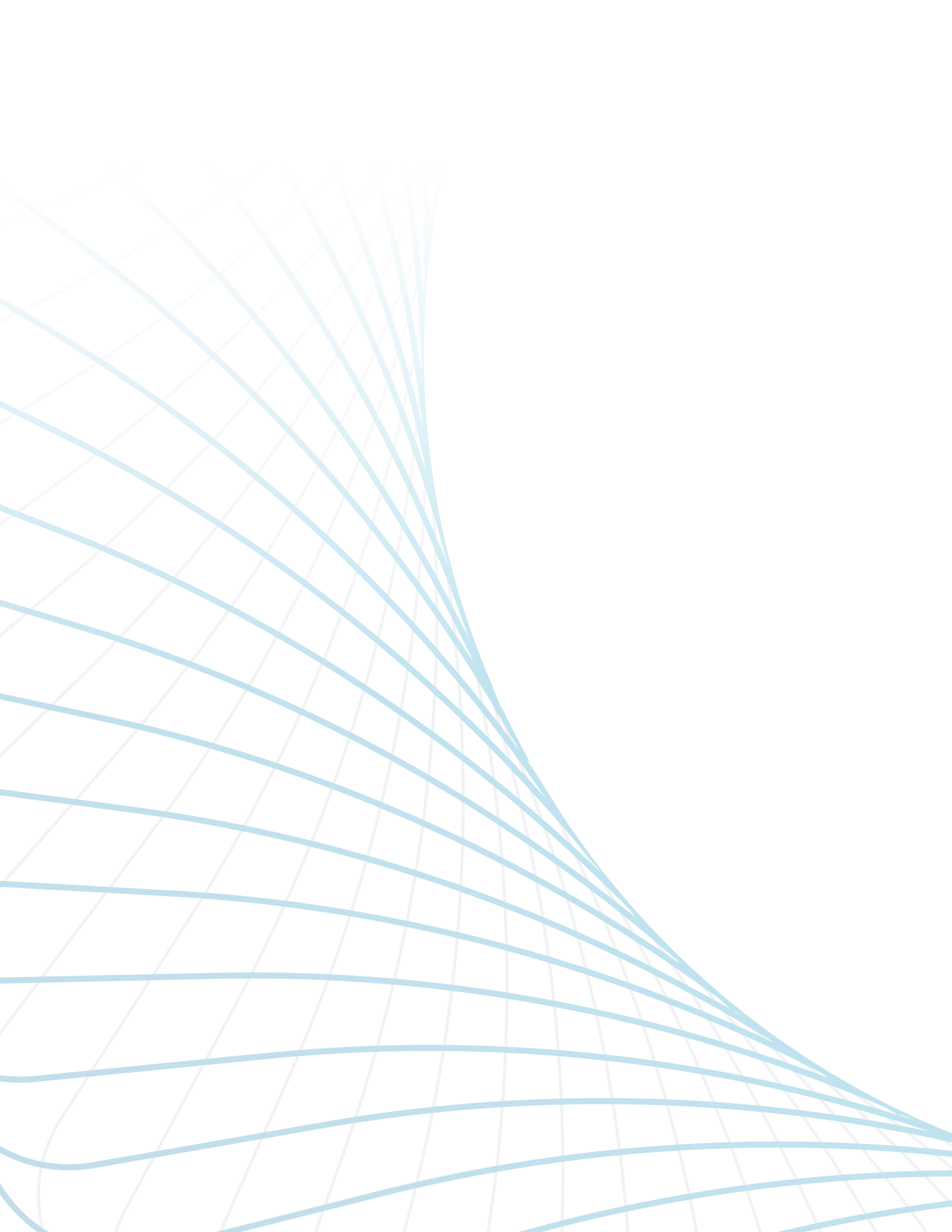




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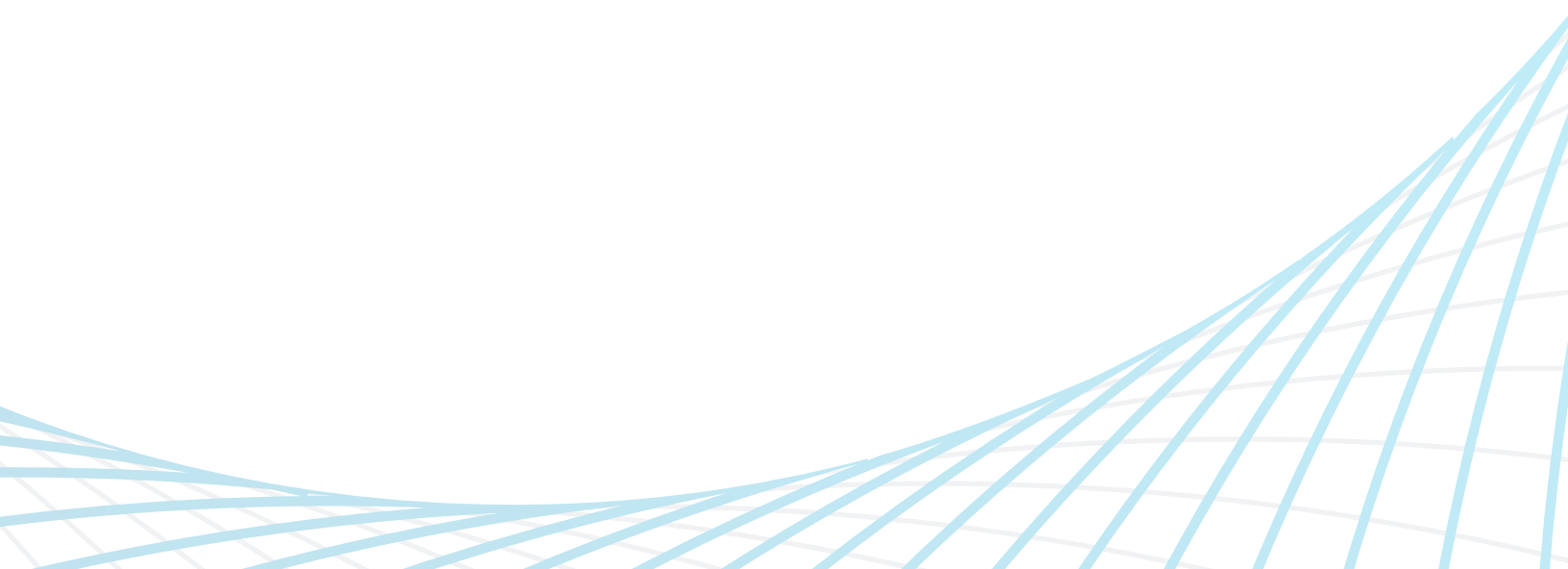
# Translating Science to Accelerate Cancer Prevention, Early Detection and New Therapies

**City of Hope Comprehensive Cancer Center  
2022-2027 Strategic Plan**



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# About City of Hope's Comprehensive Cancer Center

City of Hope Comprehensive Cancer Center (COHCCC) is ideally poised to address cancer disparities and burdens, enhance cancer prevention, improve early detection and advance new therapies within our catchment area. The center's 2022-2027 Strategic Plan identifies — and presents goals and action plans for — six areas of priority for COHCCC to focus over the next five years. These focus areas include four strategic initiatives and two cross-cutting themes:

## Strategic Initiative

1. Precision Medicine
2. Cellular Therapeutics
3. Health Equity
4. Clinical Network

## Cross-Cutting Themes

1. Cancer and Aging
2. Survivorship



As of calendar year 2021, City of Hope’s CCC has 175 Members, five Research Programs, 11 established Shared Resources (SRs) and one developing SR, a robust cancer-focused research funding base that achieved tremendous growth over the last five years, and an impactful research effort spanning basic, translational, clinical, and population-focused research (see Tables 1-3).

Table 1. Research Programs

Program Name (No. of Members)	Acronym
Molecular and Cellular Biology of Cancer (31)	MCBC
Developmental Cancer Therapeutics (40)	DCT
Cancer Immunotherapeutics (27)	CI
Hematologic Malignancies (40)	HM
Cancer Control and Population Sciences (37)	CCPS

Table 2. Shared Resources (SR)

SR Name	Acronym
Analytical Cytometry	AC-SR
Analytical Pharmacology	AP-SR
Biostatistics and Mathematical Oncology	BMO-SR
Drug Discovery & Structural Biology	DDSB-SR
GMP Manufacturing	GMP-SR
Integrative Genomics	IG-SR
Integrated Mass Spectrometry	IMS-SR
Light Microscopy Digital Imaging	LMDI-SR
Population-Facing Research	PFR-SR
Research Pathology	RP-SR
Small Animal Studies	SAS-SR
Clinical Microbiome (Developing)	CMB-SR

Table 3. Cancer — Focused Research Metrics

Metric	2017	2021	% Change
Total Peer Reviewed	\$32.5M	\$50.2M	55% Increase
National Cancer Institute (NCI) Funding	\$16.6M	\$29.2M	76% Increase
Other National Institutes of Health (NIH) Funding	\$7.7M	\$8.5M	10% Increase
NCI Team Science Awards (U, P, MPI R-type)	12	45	275% Increase
Total Publications	1,378	2,896	110% Increase
Intra-Programmatic Publications	343	746	118% Increase
Inter-Programmatic Publications	492	512	4% Increase
Interventional Trial Accurals	7,273	8,427	16% Increase

Research conducted at COHCCC has led to significant advances in cancer treatment, including the technology behind the widely used monoclonal antibody cancer therapeutics Herceptin, Rituxan, and Avastin. COHCCC is also a leader in clinical and translational research, particularly in chimeric antigen receptor (CAR) T cell therapy and hematopoietic cell transplant (HCT) approaches. Another notable strength of COHCCC is population-based research that covers the span of diagnosis through long-term survivorship. COHCCC studies have facilitated the personalization of cancer treatment at the time of diagnosis and have informed national clinical care guidelines to improve health and quality of life outcomes in survivors of HCT.



COHCCC strives to speed cures through innovative research by fostering basic discoveries to better understand the cellular and systemic perturbations associated with the development of cancer, by employing strategies to prevent and identify patients at high risk for the development of cancer, by creating and advancing state of the art therapeutics, and by implementing strategies to reduce human suffering and promote survivorship. These initiatives will address the needs of individuals in the COHCCC Catchment Area while benefiting men and women around the globe. Toward these goals, COHCCC has aligned a diverse cohort of talented basic, clinical and population-focused investigators into five Research Programs that span a continuum from basic studies through early-phase clinical trials and, ultimately, to community-engaged survivorship studies (Table 1). Knowledge gained from outcomes research, cancer risk, and prevention studies feeds back to inform and promote basic science studies. These Research Programs are supported by strengths in informatics, a spectrum of state-of-the-art Shared Resources including in-house good manufacturing practice (GMP) facilities, culturally sensitive community outreach and engagement, and a well-developed administrative infrastructure. COHCCC provides, through the director, a cohesive vision that drives Catchment Area-responsive cancer research, education, and training.

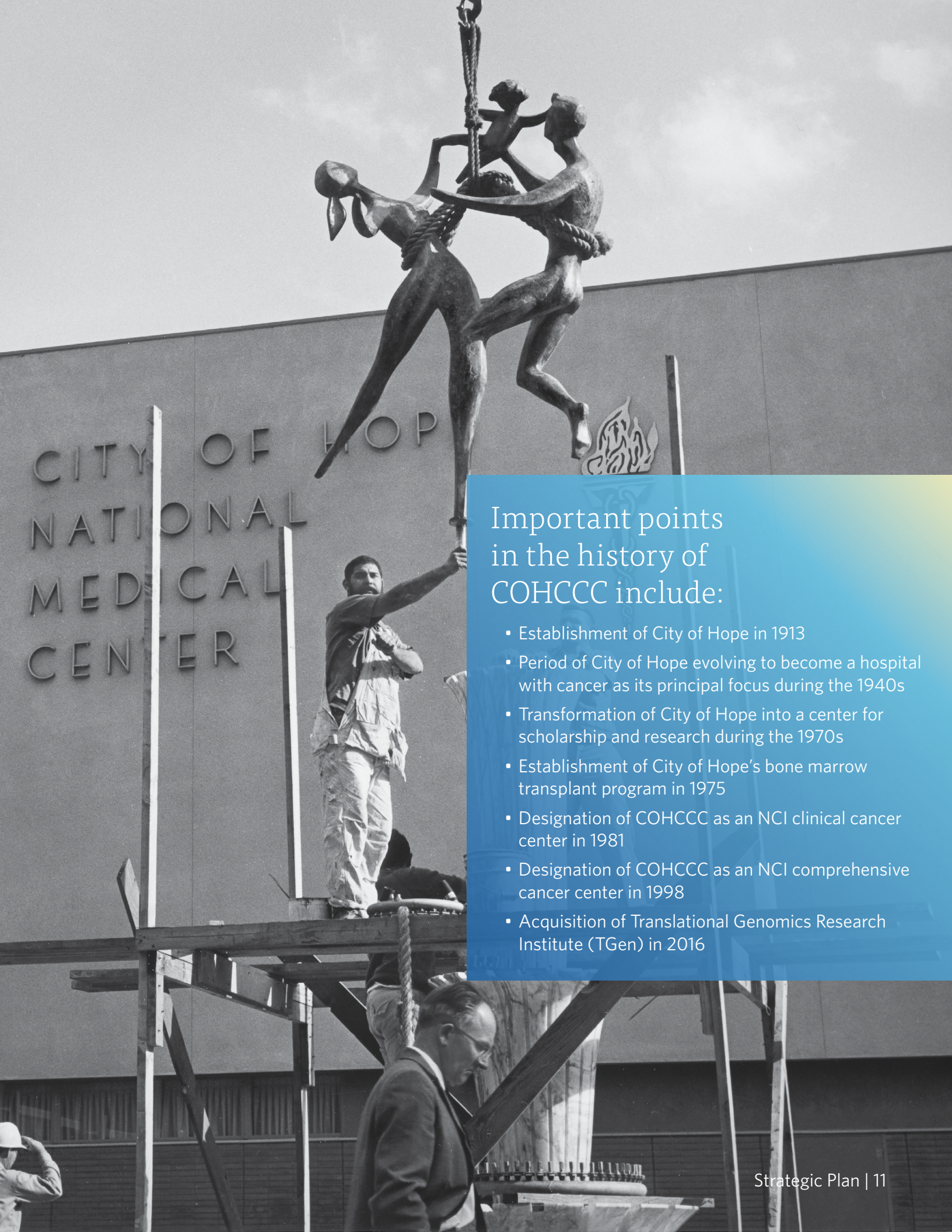
## City of Hope Comprehensive Cancer Center Mission

To reduce the burden of cancer for the patients of today through skilled, integrated and compassionate care, and to eliminate the threat of cancer for the patients of tomorrow through research and education

To support its culture of transdisciplinary collaboration, COHCCC leverages resources, structures, faculty, and staff to facilitate the rapid advancement of promising molecules or biologics into clinical evaluation (see Figure 1). This approach is founded on strong translational research collaborations among basic, clinical, and population-focused scientists to generate novel approaches. COHCCC has made a concerted effort to put into place — all within a single institution — tangible systems-level mechanisms to stimulate the movement of laboratory findings toward the clinic. These mechanisms were designed to address specific bottlenecks in developmental translational research — namely, identification of scientific observations with translation potential, a unified and better-coordinated assembly of appropriate expertise (team) around the translatable project, an understanding of the regulatory pathways for translation, controlled facilities for the manufacture of materials specifically for the clinic, and the necessary clinical expertise to guide and perform first-in-human clinical trials

Figure 1





CITY OF HOPE  
NATIONAL  
MEDICAL  
CENTER

## Important points in the history of COHCCC include:

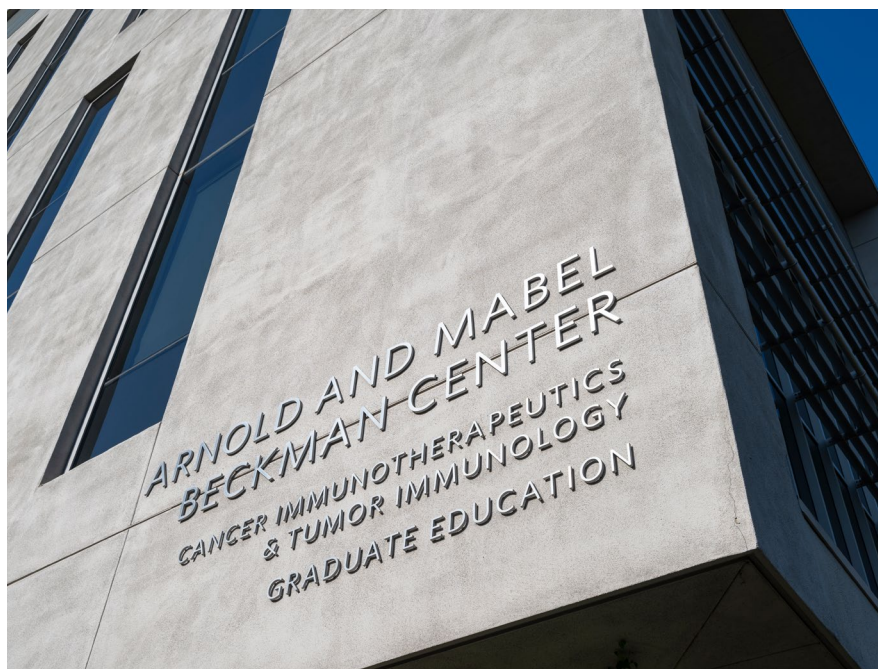
- Establishment of City of Hope in 1913
- Period of City of Hope evolving to become a hospital with cancer as its principal focus during the 1940s
- Transformation of City of Hope into a center for scholarship and research during the 1970s
- Establishment of City of Hope's bone marrow transplant program in 1975
- Designation of COHCCC as an NCI clinical cancer center in 1981
- Designation of COHCCC as an NCI comprehensive cancer center in 1998
- Acquisition of Translational Genomics Research Institute (TGen) in 2016



## Center for Biomedicine & Genetics

Opened in 2000

Lentivirus, retrovirus, adenovirus, oncolytic pox vectors, oncolytic herpes simple vectors, MVA



## Chemical GMP Synthesis Facility

Opened in 2012

Small Molecules

Oligonucleotides

Drug Discovery



## Cellular Therapy Production Center

Opened in 2010

Cellular therapies:  
CAR T, CAR-NK, TIL TCR



## Cancer Theranostics Center

Opened in 2017

CA Licensed

Radiopharmacy

# Large, Diverse Southern California Catchment Area

COHCCC is a freestanding cancer center located in Duarte, California. Patient care is delivered through hospital and outpatient facilities in Duarte as well as through 30 clinical network sites located throughout a highly diverse Catchment Area (see Figure 2). The COHCCC Catchment Area encompasses 33,109 square miles and includes the entirety of Los Angeles (LA), Orange, Riverside and San Bernardino counties, where ~84% of COHCCC patients reside. By rank order, COHCCC patients live primarily in LA (51%), San Bernardino (13%), Orange (10%), and Riverside (10%) counties. This Catchment Area includes urban population centers concentrated in LA and Orange counties and rural and frontier regions in eastern San Bernardino and Riverside counties. Remarkably, the population of the COHCCC Catchment Area (nearly 18 million people) is greater than the individual populations of 46 states. LA County alone is home to over 10 million people and is the most populous county in the U.S.

The COHCCC Catchment Area is home to a racially and ethnically diverse population, representing ~45% of all Californians. Nearly one third of this population is foreign born (30.1%). This heterogeneous majority-minority population includes 35% Non-Hispanic White (NHW), 45% Hispanic/Latinx, 13.9% Asian and Pacific Islander (API), 5.9% Non-Hispanic Black (NHB), and <1% American Indian and Alaska Native populations.

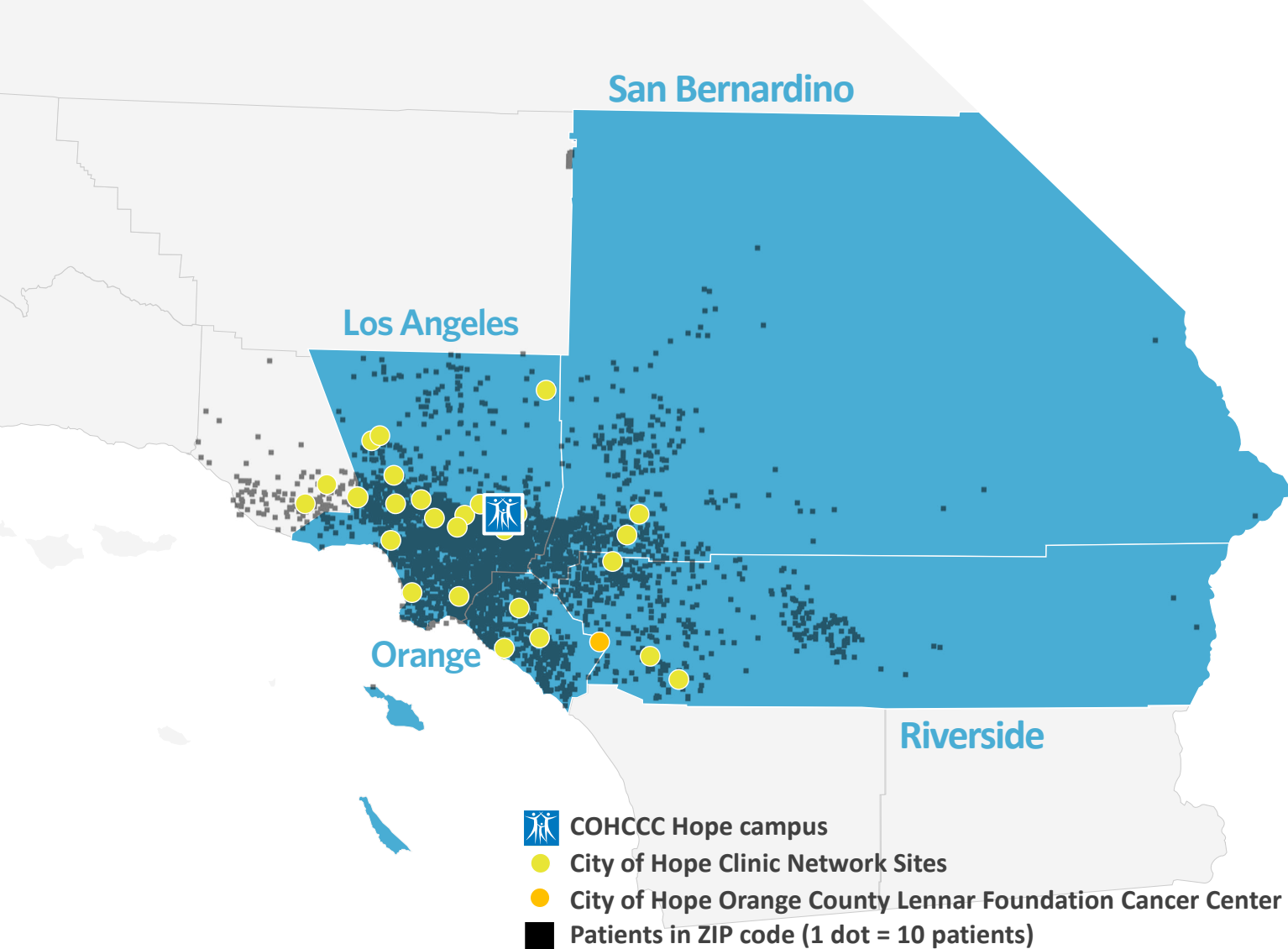


Catchment Area research priorities are informed by population-level data analyses conducted by the COHCCC Community Outreach and Engagement (COE) team and community health needs assessments, with guidance from the COE Multiethnic Community Advisory Board, COE External Advisory Board (EAB), and COHCCC EAB. The COHCCC COE team has close ties with diverse community leaders and acts upon their recommendations to ensure that the research and clinical activities of COHCCC are responsive to cancer burden and disparities present in the ethnically, racially, and socioeconomically diverse communities within our Catchment Area.

Using this process, two major Catchment Area related research priority areas have been identified:

- **Common Cancers.** Common cancers that are Catchment Area priorities include those with high incidence or mortality, such as breast, prostate, lung, colon, hematologic (e.g., non-Hodgkin lymphoma, leukemias, multiple myeloma), and pancreatic cancers, as well as those with high incidence in certain populations in the Catchment Area (e.g., liver cancer in Asian/Pacific Islander and Hispanic/Latinx populations that is due to HBV-related infection).
- **Preventable Cancers.** Preventable cancers that are Catchment Area priorities include those for which risk may be lessened through lifestyle modification (e.g., tobacco use, nutrition) or infection (e.g., viral-related cancers), as well as those associated with genetic predisposition and environmental exposures.





**4** counties 33,109 square miles.

**18** (~45% of CA) Racially and ethnically diverse population

**84%**  
of City of Hope patients reside

**30%**  
Foreign born

**45%**  
45% Hispanic/Latinx

**<1%**  
Non-Hispanic White

**6%**  
Non-Hispanic Black

**12%**  
Asian/Pacific Islander

**35%**  
Non-Hispanic White

# Strategic Plan


## 2017-2022 Strategic Plan

Progress against COHCCC's 2017 strategic plan goals are outlined in Table 4 below. Progress was considerable and has helped facilitate the groundwork that serves as the basis for the current plan.

Table 4. Strategic Plan Goals

Strategic Initiatives	Key Outcomes
Enhance established Research Programs through targeted faculty recruitment: 20 new recruits by 2022.	We exceeded this goal, with 48 recruits.
Establish collaborations with the Arthur Riggs Diabetes & Metabolism Research Institute.	Founding of first-of-its-kind Department of Diabetes and Metabolism
Grow peer-reviewed extramural funding and philanthropic support.	Considerable increases in both external peer-reviewed and philanthropic support
Develop multi-investigator programs with disease focus and discovery science.	Growth in P01 and SPORE applications and in Team Science Awards
Foster integrated cancer care delivery soon.	Dedicated centralized resources have been added to support network research
Develop culture of mentorship.	Initiation of Office of Membership
Advance supportive care and survivorship initiatives.	New cross-cutting themes of 1) cancer and aging 2) survivorship
Foster efforts to investigate and reduce cancer burden among underserved populations in the catchment area.	Grant funding targeting racial disparities; training 105 multiethnic navigators to improve community research awareness and participation (e.g., clinical studies)



 City of Hope

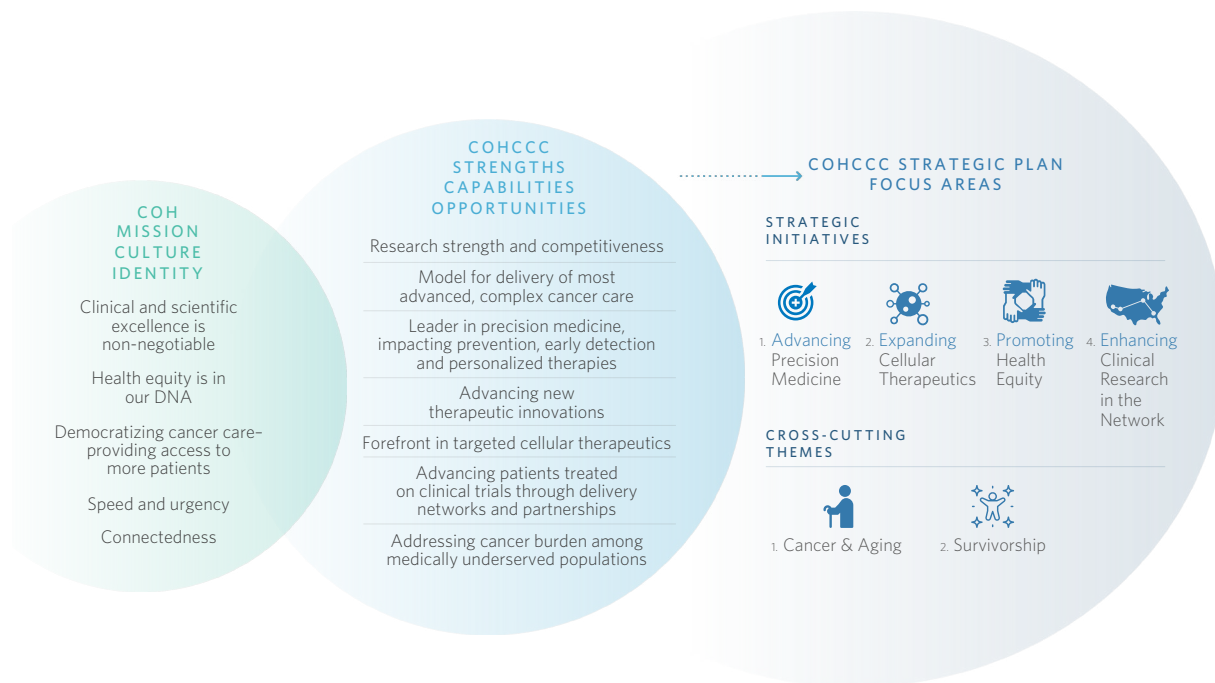
# Strategic Planning Process

Every five years, COHCCC engages in a process of developing a Cancer Center Strategic Plan. The most recent process began in 2021 and was led by COHCCC Director Steven T. Rosen, M.D., the Irell & Manella Cancer Center Director's Distinguished Chair. The director charts a vision for the direction of COHCCC based on the center's strengths, opportunities, and past performance. The deputy director (Larry Kwak, M.D., Ph.D.) oversees the development of strategic initiatives, playing a central role in addressing specific details required for successful formulation of the plan. Key COHCCC leaders, including the director, deputy director, and associate directors, meet to outline an appropriate methodology for the development of the strategic planning objectives and approach. The approach includes data collection and analysis, interviews with key COHCCC stakeholders, and an iterative review and approval process for the final deliverable.

With engagement of the Cancer Center Executive Committee (CCEC) and program members, COHCCC Administration supported development of the COHCCC Strategic Plan via a process that considered inputs, such as:

- **Needs of the COHCCC Catchment Area**
- **Current COHCCC research strengths**
- **Opportunities to further strengthen COHCCC research resources and infrastructure**
- **Alignment with strategic priority initiatives across City of Hope mission areas**
- **Future directions of COHCCC cancer research discovery and translation**
- **Responsibilities of NCI-designated comprehensive cancer centers**
- **Potential high-impact, transdisciplinary internal and external research collaborations**
- **Unique research investment opportunities**

In parallel to these inputs, Figure 3 schematically illustrates how the focus areas that emerged in the COHCCC Strategic Plan also link importantly to the mission, culture, and identity of City of Hope as well as to the strengths, capabilities, and opportunities of COHCCC.



**Figure 3. Identification of Strategic Focus Areas for the Next Five Years**

The associate director for Administration (Ashley Baker Lee) has responsibility for tracking the CCC’s Strategic Plan implementation and monitoring progress using measurable objectives during the 2022-2027 period. Performance and progress updates are shared during executive meetings and with internal and external oversight bodies for the CCC, including the Cancer Center Leadership Committee (CCLC), CCEC and EAB. Feedback from these committees enhances the CCC’s ability to drive accountability and measure progress.

## STRATEGIC INITIATIVE 1.

# Precision Medicine

The Precision Medicine Initiative aims to genetically profile the tumors of City of Hope patients, regardless of cancer type, with the goal of providing patients with effective targeted therapies or access to innovative clinical trials, while also accelerating new research discoveries. Clinical grade germline and tumor testing are provided to all patients at City of Hope who actively opt in and consent at no cost to the patient or their insurer. This agnostic approach to testing and genomic-driven care has dramatically improved access to genetic testing to patient populations that may have not had the opportunity through routine care pathways. Supporting this, the COHCCC Precision Medicine Initiative is

led by and includes national leaders in genomic analysis and its application to diagnosis and targeted therapies development. Our faculty are unique in their ability to interpret complex, comprehensive genomic data, enabling COHCCC to deliver personalized therapies that offer the best outcomes for our patients. Substantial institutional investment in precision medicine has led to a wealth of data and scientific opportunity for COHCCC members, culminating in highly impactful publications that are transforming the future of cancer care and population health. For example, this initiative has led to collaborations that have provided new insight into personalized treatment for metastatic kidney cancer and has delineated how the differentiation and signaling activities of circulating immune cells at the start of immunotherapy can inform patient response.

### **OBJECTIVE:**

#### **Strategic Initiative 1. Precision Medicine**

Harness genomic-driven insights, clinical expertise and advanced analytics to pioneer personalized prevention and treatment plans to transform the outcomes and quality of life for patients, their families, and our community.

### **New Methods and Platforms for Clinical Care**

Genomics-informed clinical care within the COHCCC Precision Medicine program is achieved by capturing and integrating genomic knowledge that incorporates both CAP/CLIA tumor/normal whole-exome-sequencing and deep germline DNA interrogation to guide therapeutic decision making. A key element of the Precision Medicine Initiative is a commitment to interrogate and, where possible, implement a range of new technologies in genomics and proteomics that are evolving at an unparalleled pace. Specifically, new “omic” methods and platforms are being regularly released that increase accuracy, precision, breadth of available information, and reduce costs. Importantly, research and development across the COHCCC is focused on how these novel approaches can be used meet unmet medical needs for patients at City of Hope and beyond. For example, to support cases where a patient’s tumor biopsy sample has a low percentage of tumor cells, we are evaluating new technologies, such as sequencing by binding from PacBio, which provides a 100X improvement in sensitivity of detecting minor variants. This enables detection of low frequency variants that cannot be accessed confidently with current technologies and will enable improvements in genomic profiling. An additional opportunity to expand the quality as well as quantity of information returned to patients is through whole genome sequencing (WGS). The Precision Medicine team is implementing workflows for rapid (<48 hour) CAP/CLIA clinical WGS and is working with companies, such as Ultima, to deploy analytic tools and technologies for interrogation of WGS data. Work is also underway to test and validate rapid analytics pipelines, driven by collaborative research and development efforts with leaders in this field, including Nvidia and Illumina.

### **New Multiomics Tools and Technologies for Discovery**

Beyond advances in genomics into the care stream, the integration of multiomic data has the potential to transform cancer research by providing a suite of new tools and technologies for discovery. Investigators across COHCCC are leading in the use of these approaches in their research. This includes technologies for sequencing RNA and DNA at the single cell level to enable deep understanding of the tumor microenvironment and clonality. In addition, through the use of high throughput imaging-based technologies coupled with artificial intelligence, investigators are developing the ability to translate the deep understanding of cell-specific transcriptomics into phenotype-based screening detection methods. Finally, spatial sequencing has become truly multiomic with the ability to assess thousands of RNA transcripts and hundreds of proteins from the same section of tissue, allowing for the first time a high throughput multiomics technology. COHCCC investments in single molecule proteomics techniques (such as Nautilus) that are complementary to mass spectrometry promise to enable high throughput discovery of how genomics knowledge directly translates into function by probing the proteome, including post-translational modifications.

Beyond the rapid growth of new discovery tools, COHCCC Program members are engaged in rapid innovation in non-invasive detection methods for screening and monitoring cancer, such as liquid biopsies. The first phase of DNA-based liquid biopsy assays has demonstrated the power of tumor-informed assays to detect tumor fractions as low as 0.001%. Future generations of these assays are driving the cost and turn-around-time down as new biomarkers and patient agnostic methods are developed. Innovation in non-invasive approaches includes investigation of the clinical utility of new types of biomarkers, including cell-free DNA methylation alterations, expression changes in various non coding RNAs, and interrogation of extracellular vesicles that can be used for early detection of cancer and for

monitoring tissue-specific cancers, as well as general health. COHCCC is working closely with technology leaders in this field (e.g., Thrive/Exact Sciences and Grail) to advance these approaches.

Through the Precision Medicine Initiative, COHCCC intends to deliver the most comprehensive application of “omics” to detect cancer early, provide precise diagnoses, identify optimal treatment(s), and offer prognoses through detection of minimal residual disease and other insights that support survivorship. This includes an emphasis on access to precision medicine for diverse populations and partnering with Community Outreach and Engagement to address cancer burden and disparities within the Catchment Area and improve inclusion of individuals from racial and ethnic minority groups for genetic and genomic testing. The Precision Medicine Initiative will also accelerate discoveries by generating, aggregating and abstracting genomic data. In turn, these data can be integrated and deployed into COHCCC’s clinical and research enterprise. The future goals described below build on accomplishments to date and will strengthen COHCCC’s reputation and standing as a leader in precision medicine.

Additional details about this initiative’s research and clinical excellence, impact (over the prior period: 2017-2022), and aspirations over the next five years are presented below, alongside a list of the initiative’s leaders at COHCCC.



## OVERVIEW

### STRATEGIC INITIATIVE 1: **Precision Medicine**

#### **Research and Clinical Excellence**

- National leader in genomic analysis and its application to diagnosis and development of targeted therapies. Faculty unique in ability to interpret very complex, comprehensive genomic data, enabling delivery of personalized therapies
- Unique program offers genomic germline and tumor testing to all patients at no cost — this testing and genomic-driven care has dramatically improved access of genetic testing to patient populations that may not have had such opportunity through routine care pathways.
- Works with City of Hope clinical cancer genomics program to provide risk assessment and follow-up care
- Partners with Community Outreach and Engagement to address cancer burden and disparities within the Catchment Area and improve inclusion of racial and ethnic minorities for genetic and genomic testing

#### **Impact** (2017-2021)

- High-impact publications in cancer care and population health
- Collaborations that have provided new insight into personalized treatment for metastatic cancers, including lung, colon, and kidney cancers
- Defining how differentiation and signaling activities of circulating immune cells at the start of immunotherapy can inform patient response

#### **Aspirations** (2022-2027)

- To genetically profile tumors of all patients, regardless of cancer type, with goal of providing patients with effective targeted therapies or access to innovative clinical trials
- To deliver comprehensive application of “omics” technologies to detect cancer early, provide precise diagnoses, identify optimal treatments, and offer prognoses through detection of minimal residual disease and other insights that support survivorship

#### **Leaders**

- Ajay Goel, Ph.D., M.S.
- Stephen Gruber, M.D., Ph.D., M.P.H
- Stacy Gray, M.D.
- Jeffrey Trent, Ph.D.
- Mark Hulse, Chief Digital Officer of City of Hope

## GOALS AND ACTION PLAN

### STRATEGIC INITIATIVE 1: Precision Medicine

#### GOALS

1. Transform clinical outcomes through genomic profiling — with longitudinal follow-up across the enterprise, precision-guided therapy for patients and tailored prevention for families — delivered at-scale and embedded within the community.

#### ACTION PLAN

- a. Provide state-of-the-art, precision-informed cancer treatment, clinical trials, and cancer prevention for every City of Hope patient by offering patients a precision diagnostic and management evaluation, conducting genomic profiling with longitudinal follow-up to ensure each patient has the right treatment at the right time, and leveraging real world evidence to strategically build clinical trial portfolios and develop novel biomarker studies.
- b. Enable lifesaving cancer prevention and early detection for hundreds of families at risk for inherited cancers by providing germline genetic testing for all high-risk families and implementing innovative genetics services to fully support patients and family members who have hereditary cancer and treatable noncancer conditions.
- c. Expand outreach to underserved populations within the Catchment Area through the provision of tailored precision-medicine services to meet the population-specific care needs, improve patient access, and enhance outcomes for diverse patient populations.
- d. Empower providers with the expertise needed to deliver precision medicine to patients within the Catchment Area through innovative provider education, point-of-care learning, and precision medicine decision support that uses performance feedback to transform clinical practice.

## GOALS AND ACTION PLAN

### STRATEGIC INITIATIVE 1: **Precision Medicine**

2. Lead diagnostic and research innovations that leverage ongoing collection of treatment/outcome data and help researchers learn the kinds of mutations that differing tumors have and how those mutations affect tumor response to treatments.
  - a. Deliver “best-in-market” liquid tumor technologies to fundamentally change treatment decisions by transforming post-treatment monitoring to identify recurrent disease and enabling early intervention and monitoring of the evolution of tumor biology to optimize treatment selection, as well as dramatically increase cure rates by proactively screening asymptomatic individuals with non-invasive blood-based testing.
  - b. Reimagine the reach of COHCCC care by remotely monitoring patients and intervening when early warning signals are detected, such as by using patient-derived data from wearable technologies to rapidly optimize remote clinical management. Iteratively evaluate digital tools to ensure they positively impact care efficiency, service delivery, patient and provider communication, and cancer outcomes.
  - c. Continually assess emerging technologies to ensure rapid translation of promising innovations into clinical care by enhancing existing laboratory services to provide competitive biological profiling for precision cancer care and disrupting strategic prioritization of emerging technologies through ongoing market dynamic assessment and expert stakeholder input.
  
3. Unlock the power of precision medicine through data and analytics by leveraging a continuous flow of data to optimize patient care and drive discovery.
  - a. Develop state-of-the-art informatics platforms to enable enterprise-wide precision medicine by transforming clinical trial matching to ensure that all patients have greater access to new diagnostics and therapies and rapidly disseminating best practices throughout COHCCC and beyond through “omic” enhanced clinical decision support.
  - b. Enable and empower scientists to use previously siloed clinical and “omic” data to accelerate discovery by scaling a best-in-class data solution to democratize data access and foster new interdisciplinary collaborations, and use data and insights to support development of clinical decision support both at COHCCC and externally.
  - c. Unlock the power of clinical data contained within the electronic health record and across health systems by using natural language processing and informatics solutions to capture essential but unstructured data.
  - d. Capitalize on advances in artificial intelligence and machine learning to transform diagnosis, patient management, prognosis, and outcomes by building City of Hope data science capabilities through investment and partnerships, and creating, validating, and tracking the performance of novel predictive algorithms to improve patient care and outcomes.

## STRATEGIC INITIATIVE 2.

# Cellular Therapeutics

COHCCC is a center of research and clinical excellence for cellular therapies, including hematopoietic stem cell transplantation (HCT) and immune effector cell (IEC) therapies. COHCCC continues to pioneer the next generation of cellular therapies for cancer by rapidly translating new scientific discoveries into the clinical care setting. This unique ability relies on our exceptional clinician scientists and researchers, a robust cell therapy pipeline, state-of-the-art manufacturing infrastructure and expertise, and extensive cell therapy clinical trial experience.

### **Hematopoietic Cell Transplantation Program**

The COHCCC HCT program, established by Dr. Karl Blume in 1976, is one of the largest and most successful programs in the nation. Since its inception through 2021, a total of 17,433 patients have received transplants at COHCCC, averaging over 750 HCTs per year since 2018. Our transplant program has been fully accredited since 2005 by the Foundation for the Accreditation of Cellular Therapy, the standard of excellence for blood and bone marrow transplant programs in the United States. The Center for International Blood & Marrow Transplant Research recognized COHCCC as the only institution in the nation performing above expectations in terms of one-year overall survival for 16/17 consecutive reporting years (2005-21). This success is attributable not only to our clinical prowess, but also to our robust, highly integrated quality management program.

As a key treatment modality in the management of hematologic malignancies, the HCT program works closely with investigators in the COHCCC Research Programs and aligns with the cross-cutting initiatives of Survivorship and Cancer and Aging. During the current CCSG funding period (2017-2021), 1,283 patients were enrolled onto HCT clinical protocols, including prevention (492), supportive care (97), and treatment studies (450) to address knowledge gaps and unmet needs in HCT. In addition to clinical trial efforts, HCT research has been funded by multiple NIH/NCI grants (P50, P01, U01, R01s, R21s) and other grant

### **STRATEGIC INITIATIVE 2.**

#### **Cellular Therapeutics**

Transform the future of cellular therapies by promoting innovative science, growing exceptional talent, enhancing manufacturing capabilities and expanding patient clinical trial accessibility.

mechanisms (The Leukemia & Lymphoma Foundation, American Cancer Society). Notably, three of the current COHCCC Lymphoma SPORE projects involve HCT. This work has been represented in over 200 publications over the last five years.

### **Immune Effector Cell Program**

The COHCCC IEC program supports the research and translational development of new immune effector therapies, including native or gene-modified T lymphocyte and natural killer (NK) cells, and tumor-infiltrating lymphocytes. The IEC program consists of six independent laboratories, associated with two COHCCC Research Programs (Cancer Immunotherapeutics and Hematologic Malignancies), focused on malignant tumors of the brain; other solid tumors; hematologic malignancies, including acute lymphoblastic leukemia, myeloma, lymphoma, and HIV; B and lymphoma and acute myeloid leukemia and development of NK cell therapeutics for cancer. Clinician scientists within the COHCCC's Developmental Cancer Therapeutics Program work closely with these laboratories to develop these new therapies. COHCCC is in the process of unifying the cellular immunotherapy laboratories under one translational department in Beckman Research Institute of City of Hope to stimulate exchange of ideas, improve translation of IEC programs to the clinic, and unify faculty around a shared strategy for cell therapies.

Since 2012, COHCCC has treated 966 patients with CAR T cell therapies: 601 on research protocols and 365 with commercial products. The Cellular Immunotherapy Modality Team guides the development of phase 1 and phase 2 trials derived either from COHCCC investigator-initiated studies or through collaborations with Pharma focused on early phase studies. A snapshot of the clinical trial portfolio of the Immunotherapy Modality Team in November of 2021 included 52 clinical trials of which 10 used COHCCC-developed products and 42 were industry-sponsored trials. Since 2017, five new COHCCC-developed CAR T cell products have entered phase 1 clinical trials: PSCA for prostate cancer, chlorotoxin for glioblastoma, CS1 for multiple myeloma, TAG72 for ovarian cancer, and CMV-CD19 bispecific CAR T cells for leukemia and lymphoma post-HCT. The program's first IND for gene-modified NK cell treatment of lung cancer has been reviewed by the FDA and the clinical trial has opened.

The Cellular Therapies strategic initiative relies heavily on the state-of-the-art manufacturing infrastructure and expertise available through the COHCCC GMP Manufacturing Shared Resource (GMP-SR), in particular the Center for Biomedicine & Genetics and the Cell Therapy Production Center. The two facilities create the majority of cellular and gene therapies for COHCCC program members. Our ability to impact more patient's lives through enhanced accessibility of cellular therapies will also increase as the clinical network strategic initiative progresses and expands the geographic footprint of the clinical network. During the current funding cycle, dedicated centralized resources were built to support the expansion of COHCCC network research. These additional resources will support continued research addressing the cross-cutting themes of Cancer and Aging and Survivorship. During the last funding cycle, COHCCC also made great progress promoting health equities and targeting racial disparities. These experiences will be leveraged to further improve patient accessibility to cellular therapy trials in the larger network.

Additional details about this initiative's research and clinical excellence, impact (over the prior period: 2017-2022) and aspirations over the next five years are presented below, alongside a list of the initiative's leaders at COHCCC.

## OVERVIEW

### STRATEGIC INITIATIVE 2: Cellular Therapeutics

#### Research and Clinical Excellence

- Center of excellence for HCT and IEC therapies, including native or CAR engineered T cells, NK cells and tumor-infiltrating lymphocytes
- Biological GMP manufacturing capabilities that enable rapid, cost-effective translation of novel therapeutic agents to clinical trials — and distinguish City of Hope as a premier institution for translating therapies

#### Impact (2017-2021)

- 17,433 patients received transplants (1976 through 2021), averaging more than 750 HCTs per year since 2018
- 30% of patients enrolled onto HCT clinical protocols
- 966 patients treated with CAR T cell therapies (2012 — July 2022) (601 on research protocols and 365 with commercial products)
- Cell therapy research funded by NIH/NCI and foundation grants
- 300+ cell therapy publication
- Four new COHCCC-developed CAR T cell products entered phase 1 clinical trials, and five phase 1 (four first-in-human) clinical trials completed enrollment.

#### Aspirations (2022-2027)

- To stimulate exchange of ideas, improve translation to the clinic, and unify faculty around a shared strategy for cell therapies
- To impact more patients' lives via Southern California clinical network, Orange County expansion and partnership with CTCA
- To improve more patients' lives via Southern California clinical network; Orange County, California, expansion; and partnership with CTCA
- To transform the future of cellular therapies by promoting innovative science, growing exceptional talent, enhancing manufacturing capabilities, and expanding patient clinical trial accessibility

#### Leaders

- Stephen Forman, M.D.
- Larry Kwak, M.D., Ph.D.
- Michael A. Caligiuri, M.D.

## Goals And Action Plan

### STRATEGIC INITIATIVE 2: Cellular Therapeutics

#### GOALS

1. Develop the next generation of advances in cancer cellular therapies; rapidly translate these discoveries into the care setting.

#### ACTION PLAN

- a. Increase patient access to top-tier talent and enhance patient care by recruiting and retaining experienced cell therapy physician scientists with an emphasis on hematologic malignancies, solid tumors, and stem cell transplants. Lead the field in treating solid tumor patients with cellular therapies.
- b. Grow a strong internal pipeline for innovative IEC and stem cell-based therapies by recruiting and retaining leading basic and translational research investigators. Areas of innovation will include exploring novel methods for target identification, developing alternative delivery strategies, and creating new, off-the-shelf treatments.
- c. Diversify and grow our cell therapy portfolio by recruiting junior and mid-career faculty from academia, the pharmaceutical industry, and the biotechnology sector. Target researchers with experience in the growing areas of cancer genetics, metabolomics, proteomics, microbiome, immunology, and protein engineering
- d. Expand operational, translational research, and manufacturing capabilities by growing manufacturing, process development, quality assurance, quality control, biostatistics, regulatory, scientific writing, and other operations teams.
- e. Strengthen and grow a training program for COHCCC and clinical network physicians and staff to increase the number of clinicians and support personnel capable of leading and executing cell therapy clinical trials.
- f. Create a cell therapy post-doctoral training program (e.g., NIH T32 training grant) to mentor the next generation of cell therapy leaders.
- g. Recruit, train, and retain diverse faculty and clinicians reflective of COHCCC's multicultural catchment area to address health equity and disparities in the cancer cell therapy space.
- h. Expand and consolidate laboratory facilities supporting cell therapies. These new and renovated laboratories will be designed with flexibility in mind to allow investigators to expand and adapt their laboratories as new research develops.
- i. Establish a cellular therapy center housed in one building consisting of translational researchers and clinical manufacturing and process development experts. Centralizing these faculty and scientists will stimulate idea exchange, improve the translation of cell therapy programs to the clinic, and unify faculty around a shared strategy for cell therapy. Members of the five COHCCC Research Programs (CI, DCT, HM, CCPS, and MCBC) will be allowed to apply for secondary appointments in this new, translational department, thus fostering opportunities for new transdisciplinary collaborations.
- j. Adopt an enterprise-wide system for optimizing existing cell therapy resources by centralizing COHCCC's manufacturing assets in the GMP-SR.
- k. Increase the speed by which basic research discoveries can be translated into the clinic by growing the GMP-SR's process development and analytical testing capabilities.
- l. Prioritize the production of promising off-the-shelf cell therapies and other forward-looking immunotherapies, such as bispecific antibodies.

## Goals And Action Plan

### STRATEGIC INITIATIVE 2: Cellular Therapeutics

2. Democratize cancer care by expanding the care delivery model for cellular therapy treatments and exporting our expertise throughout the COHCCC clinical network.
  - a. Create a roadmap for growing COHCCC's cell therapy footprint in the solid tumor clinical trial space.
  - b. Grow the number of clinical network facilities that can support cell therapy administration. Invest in infrastructure (e.g., patient treatment facilities and pathology laboratories) and export COHCCC's cell therapy expertise (e.g., training initiatives) across the larger COHCCC clinical network. This expansion will enable expanded provision of cell therapies to more vulnerable populations, such as HIV patients with hematologic malignancies, an area where the COHCCC has pioneered new treatments.
  - c. Build on our experiences establishing the Judy & Bernard Briskin Center for Clinical Research by creating additional outpatient centers throughout the COHCCC clinical network. Lead the field in transitioning cell therapy treatments to the outpatient setting.
  - d. Couple the large patient pool available within the COHCCC clinical network with impactful correlative studies to strengthen clinical trials by generating new research hypotheses that benefit cell therapy patients.
  - e. Promote health equity and increase the patient accessibility of cell therapy clinical trials through the large geographic footprint of the expanding COHCCC clinical network. In particular, COHCCC will expand efforts to facilitate access to patients not considered for HCT at many institutions, namely older adults and individuals from racial/ethnic minority groups who traditionally have a lower chance of finding an HLA-matched donor.
  - f. Develop a population-based program in personalized medicine, in collaboration with the Precision Medicine Initiative, to rapidly evaluate genomic data across diverse populations and target new cellular therapies patients who will most benefit from them, thus promoting health equity.
  - g. Explore alternative production methods to increase yields and reduce costs by internalizing new cell therapy manufacturing technologies (e.g., entirely closed large-scale production systems), through capital investments and external biotechnology partnerships. Increased production efficiency and reduced costs will enhance accessibility of these therapeutics for patients
  - h. Develop the capabilities of the GMP-SR to manufacture cell therapies for phase 2 and phase 3 clinical trials by growing our GMP manufacturing reach to increase the number and scale of therapeutic products that can be generated.



## Goals And Action Plan

### STRATEGIC INITIATIVE 2: Cellular Therapeutics

3. Use our cellular therapy expertise to enhance alternative revenue streams through industry partnerships and national philanthropy.
  - a. Promote large scale commercialization of COHCCC-developed cellular therapeutics through licensing agreements with biotechnology and pharmaceutical companies
  - b. Improve ability of COHCCC to develop strategic relationships with external stakeholders by leveraging City of Hope's newly created Translational Development Center to provide biotechnology and pharmaceutical companies with access to COHCCC's cell therapy expertise and clinical trial services, such as project management, clinical protocol design, regulatory support, and clinical trial execution
  - c. Leverage enhanced partnerships with pharmaceutical and biotechnology companies created by the Translational Development Center to maximize patient access to novel and innovative cellular therapeutics and clinical trials.
  - d. Use cellular therapy expertise/experience and growing geographical footprint to enhance philanthropic fundraising activities needed to support new cell therapy research and clinical trials.

## STRATEGIC INITIATIVE 3.

# Health Equity

Since its origin in 1913, City of Hope has been dedicated to providing equitable treatment for all patients. This dedication resonates throughout COHCCC by engaging the voices and insights of physician scientists, research faculty, trainees, staff, patients, and community advocates. This commitment to diversity and inclusion creates an environment where different experiences and perspectives lead to both greater scientific innovation and better whole person care for our ethnically diverse community.

Innovative oncology research performed at COHCCC leads to improved treatment, care, and cancer prevention for ethnically, racially, and socioeconomically diverse communities within the Catchment Area. In addition, COHCCC facilitates community-scientist-clinician collaborations to understand and overcome Catchment Area cancer burden and disparities. To address population cancer burden and disparities faced by racial and ethnic minorities and vulnerable communities, COHCCC will ensure that training programs, research, and clinical care are community-responsive, taking into consideration the needs of the diverse populations within the Catchment Area. To ensure COHCCC serves diverse communities that have the highest cancer burden and worst outcomes, the center will: (1) expand ongoing efforts in health policy, partnerships, and community engagement; (2) build and foster an equitable, inclusive, and safe working environment that embraces diversity and diverse perspectives; and (3) incentivize and strengthen the science of health disparities and health equity to understand and address the intersection of biology and social determinants of health through team science, and foster greater collaboration among the five COHCCC programs and with the other strategic initiatives and themes.

### **OBJECTIVE** **STRATEGIC INITIATIVE 3.** **Health Equity**

Develop a nationally recognized health equity center of excellence that fosters team science and best practices to better serve communities with the highest cancer burden and worst outcomes.

Advancing health equity through research and conduct of research is a priority for COHCCC. This commitment is demonstrated by COHCCC program members' conduct of R01-funded studies on cancer risks in Black immigrants, metabolism, and breast cancer; clinical trials targeting Black patients with multiple myeloma, prostate cancer, and triple-negative breast cancer; a U01-funded study on breast cancer and the environment that involved the Latina community; an R35-funded clinical study on genomic test reporting; a state-funded study of tobacco-related genotoxic effects; foundation grants for research on cancer and aging, and prostate cancer; Department of Defense grants on prostate cancer in Black men; and collaborations with multiple pharmaceutical companies to advance the representation of diverse patient populations in oncology clinical trials.

Additional details about this initiative's research and clinical excellence, impact (over the prior period: 2017-2022), and aspirations over the next five years are presented below, alongside a list of the initiative's leaders at COHCCC. Strategic goals for the Health Equity initiative were developed with guidance from the COHCCC Community Outreach and Engagement-Community Advisory Board.

## OVERVIEW

### STRATEGIC INITIATIVE 3: **Health Equity**

#### **Research and Clinical Excellence**

- Provides world-class oncology research, treatment, care, and cancer prevention to ethnically, racially, and socioeconomically diverse communities in the Catchment Area
- Facilitates community-scientist-clinician collaborations to overcome Catchment Area cancer burden and disparities
- Center of Community Alliance for Research & Education implements bidirectional, community engaged work supporting community cancer screening, prevention, and education and research, including clinical studies

#### **Impact** (2017-2021)

- Research grants including:
  - R01s on risks in Black immigrants, multiple myeloma, metabolism, and breast cancer
  - Clinical trials targeting Black patients with multiple myeloma, prostate cancer, and triple-negative breast cancer
  - U01 on breast cancer and the environment
  - R35 clinical study on genomic test reporting
  - R25 health equity training program for underserved populations
  - DOD grants on prostate cancer in Black men
- Collaborations with pharma to advance representation of diverse patient populations in clinical trials

#### **Aspirations** (2022-2027)

- To address population cancer burdens and disparities faced by ethnic minorities and vulnerable communities
- To ensure that training programs, research and clinical care are community responsive, considering our diverse populations within the Catchment Area

#### **Leaders**

- Javier Gordon Ogembo, Ph.D.
- Kimlin Tam Ashing, Ph.D.
- Angela L. Talton

## GOALS AND ACTION PLAN

### STRATEGIC INITIATIVE 3: Health Equity

GOALS	ACTION PLAN
1. Expand ongoing efforts in policy, partnerships and community engagement to increase diversity in clinical care and research.	<ul style="list-style-type: none"><li>a. Establish partnerships with organizations targeting health equity to increase diversity in our patient population.</li><li>b. Expand our multisectoral, multiethnic community engagement partnership and integrate with the Community Outreach and Engagement advisory board.</li><li>c. Expand contracted payer systems to provide access and net of care for underinsured patients.</li><li>d. Partner with City of Hope's Government Relations team to impact policy and legislation that increases access to oncology care for Medi-Cal patients.</li><li>e. Increase representation of Blacks/African Americans in patient care and study representation, including via innovative applications of telehealth.</li></ul>
2. Partner across City of Hope to build and foster an equitable, inclusive and safe environment that embraces diversity and diverse perspectives.	<ul style="list-style-type: none"><li>a. Recruit and mentor talent in scientific, clinical and key leadership roles to strengthen the ability to expand disparities and Catchment Area research, care, clinical studies and policies.</li><li>b. Create interdisciplinary cluster hires of underrepresented minority faculty engaged in health equity research.</li></ul>

## GOALS AND ACTION PLAN

### STRATEGIC INITIATIVE 3: **Health Equity**

3. Strengthen the science of health disparities and health equity to understand the social determinants of health and contribute to other research programs.
  - a. Increase knowledge of the intersection of biology and social determinants of health on cancer risk, etiology, and outcomes from diverse racial/ethnic groups and communities through team science and by increasing participation of individuals from diverse groups in clinical research.
  - b. Develop a City of Hope-HBCU (Historically Black Colleges and Universities) Biomedical Research Initiative that provides pilot funding to build partnerships between COHCCC program members and investigators at HBCUs.
  - c. Provide Health Equity Community Partnership grants that support community-based organizations in establishing, extending, and strengthening collaborative research partnerships with COHCCC program members.
  - d. Launch a pilot program for a Diversity Excellence Award that incentivizes high-quality diversity, equity, and inclusion research.
  - e. Host a health equity conference or symposium on an annual or biannual basis to catalyze inter- and intra-programmatic health equity-targeted collaboration across the five COHCCC programs and with the other strategic priorities.

## STRATEGIC INITIATIVE 4.

# Clinical Network

The COHCCC clinical network is based on a unique academic and community model designed to maximize benefits to patients and bring breakthrough research and clinical care expertise to as many patients as possible. With 29 clinical locations, the COHCCC clinical network delivers the latest pioneering cancer care to patients every day.

Since 2017, City of Hope has expanded and strengthened the clinical network to increase patient accessibility to innovative care. COHCCC's growth platform has expanded significantly at the main campus in Duarte. Starting with a \$1 billion investment in 2018, the Duarte site opened a standalone outpatient imaging center, opened a 150-room hotel for patients and families, and created new office space for clinicians and leadership. Additional efforts are underway to improve outpatient facilities to make new therapies and innovative clinical trials accessible to more patients, including construction of the new Duarte Outpatient Center scheduled to open in 2021.

In addition to changes at the Duarte campus, the clinical network has significantly expanded in Southern California and now offers 30 clinical locations in Los Angeles, Orange, Ventura, San Bernardino, and Riverside counties. In particular, there has been a focus on growth in Orange County by building a dedicated cancer center in Irvine, and the county now boasts four clinical network sites to better serve the county's 3.1M community members. A 190,000 square-foot outpatient facility opened in August 2022 that facilitates both outpatient care and phase 1-3 clinical trials. In addition, an inpatient hospital is under construction that will be directly adjacent to the new outpatient center and is expected to open in 2025.

### **OBJECTIVE** **STRATEGIC INITIATIVE 4.** **Clinical Network**

Expand the COHCCC's clinical network to provide innovative therapies to more patients, families and communities with the goal of ensuring our patients are matched with the right provider and the best treatment for their disease.

In addition to its growing footprint in California, City of Hope is expanding the clinical network outside of California, having recently acquired the CTCA. This acquisition is part of a continuing strategy to expand cancer research, care, and access in community settings across three states with a goal of providing new, innovative treatments to patients. Leveraging and enhancing the existing clinical and research infrastructure of CTCA will enable clinical trials for new therapeutics, diagnostics, and technologies being developed in COHCCC to be rapidly translated to the clinic.

During the next funding period, COHCCC will leverage this expanded network to create a system that makes leading-edge research, treatment, and care accessible to more patients and communities across the country, ensuring that patients are matched with the best treatment for their disease. As part of the vision of democratizing cancer care, COHCCC seeks to combine academic medicine and community care to improve access and cancer outcomes regardless of geography; partner to ensure the organization is leveraging and building upon the expertise of others; thoughtfully advocate for cancer patients; build upon the commitment to diversity, equity and inclusion internally and externally; and bring supportive care everywhere. The expanded clinical network improves access to clinical trials for a more diverse population by conducting the research in closer geographic proximity and in the sites where a different patient demographic than our main campus demographic receives their care.

Additional details about this initiative's research and clinical excellence, impact (over the prior period: 2017-2022), and aspirations over the next five years are presented below, alongside a list of the initiative's leaders at COHCCC



## OVERVIEW

### STRATEGIC INITIATIVE 4: **Health Equity**

#### **Research and Clinical Excellence**

- The COHCCC clinical network is based on a unique academic and community model designed to maximize benefits to patients and export breakthrough research and clinical care expertise to as many patients as possible.
- With 30 clinical locations and a portfolio of clinical trials, the COHCCC clinical network delivers the latest pioneering cancer care to patients throughout the country every day.

#### **Impact** (2017-2021)

- Expanded and strengthened the COHCCC's clinical network to increase patient accessibility to innovative cancer care:
  - Created a dedicated cancer treatment center in Orange County, California, that supports phase 1-3 clinical trials
  - Integrated TGen's personalized diagnostics and precision therapeutics programs into COHCCC's clinical trials
  - Acquired the CTCA as part of City of Hope to increase our ability to bring the latest treatments to more patients across geographic regions

#### **Aspirations** (2022-2027)

- To democratize cancer care by leveraging COHCCC's expanded network to create a system that makes leading-edge research, treatment and care accessible to more patients and communities across the country

#### **Leaders**

- Marwan Fakih, M.D.
- Ed Kim, M.D., M.B.A.
- Mary Cianfrocca, D.O., M.B.A.

## GOALS AND ACTION PLAN

### STRATEGIC INITIATIVE 4: **Clinical Network**

#### GOALS

#### ACTION PLAN

- | GOALS  | ACTION PLAN  |
|--|--|
| 1. Expand COHCCC's clinical network into new geographic markets to provide superior access and cancer treatment options to more regional, national, and international communities.   | <ul style="list-style-type: none"><li>a. Standardize processes and patient care across clinical sites to create a national, differentiated system capable of delivering rapid and personalized care to cancer patients at the community level with speed.</li><li>b. Implement creative solutions to increase patient accessibility to clinical trials and treatments in the expanded network (e.g., telemedicine and mobile apheresis units to reach patients in minority and underserved communities without access to large centers).</li><li>c. Grow patient participation within the network by providing educational sessions led by CCC researchers and clinician-scientists to encourage community engagement.</li></ul>   |
| 2. Provide more patients and communities within the COHCCC national clinical network with access to leading edge research, personalized treatments, and patient-centric cancer care. | <ul style="list-style-type: none"><li>a. Implement creative solutions to increase patient accessibility to clinical trials and treatments in the expanded network (e.g., use mobile apheresis units to reach patients in under-represented and underserved communities who lack access to large centers).</li><li>b. Advance manufacturing technologies, establish logistical processes for bidirectional sample transport, and develop local infrastructure at clinical network sites to allow for equitable access across the entire COHCCC-national network of autologous and allogeneic innovative therapies (e.g., cellular therapeutics). Emphasize clinical trials of novel small molecule and nucleic acid therapeutics at these sites while cell therapy capabilities are developed.</li><li>c. Promote patient participation in clinical trial research studies, especially in the areas of survivorship and aging.</li><li>d. Leverage historical experiences and develop creative solutions to allow for outpatient care for patients receiving cell therapies. Establish a network-wide standardized database to collect and exchange patient demographic, clinical treatment and outcomes, and research data</li></ul> |

## GOALS AND ACTION PLAN

### STRATEGIC INITIATIVE 4: **Clinical Network**

3. Maintain and strengthen bidirectional relationships with communities and industry partners to promote patient accessibility, enrollment in clinical trials, and clinical research.
  - a. Establish regional community advisory boards to increase involvement with the lay communities served by the COHCCC network.
  - b. Encourage participation in population-based and personalized medicine programs to strengthen clinical trial design and improve patient outcomes by targeting the right treatment to the right patient.
  - c. Leverage preferred partnerships with pharmaceutical and biotechnology companies to bring the latest diagnostic technologies and cellular, viral vector, and small molecule therapeutics to patients and diverse communities within the network.
  - d. Continue to reduce barriers to enrolling patients from diverse groups on clinical trials in the network through patient navigators, documents translated from study activation, transportation reimbursement, and other measures identified as needs by the communities served.

## CROSS-CUTTING THEME 1.

# Cancer and Aging

### OVERVIEW

COHCCC is a recognized international leader in cancer and aging scholarship, training, mentorship and clinical care model implementation. The COHCCC cancer and aging efforts are led institutionally through the Center for Cancer and Aging (CCA) and internationally through the Cancer & Aging Research Group (CARG). The CCA, founded in 2008 by Arti Hurria, is led by Director William Dale, M.D., Ph.D., the Arthur M. Coppola Family Chair in Supportive Care Medicine; CARG, founded in 2006, is led by Dr. Dale and other experts across the country in the fields of geriatric oncology, clinical trial design and execution, basic and translational science, multidisciplinary care models, community-based and outcomes research, and rigorous social science. CARG is the largest group of its kind in North America, with 525 members. COHCCC efforts in cancer and aging are also supported by three research-focused multidisciplinary geriatric oncology clinics, designated by the American Hospital Association as having Age-Friendly Health System status, across the enterprise. All of this infrastructure will be increasingly integrated into COHCCC and its Research Programs over the next five years in recognition that cancer and aging are inextricably linked.

### OBJECTIVE: CROSS-CUTTING THEME 1. Cancer and Aging

Collaborate to elucidate the biological, translational, clinical and psychosocial connections between cancer and aging — focusing on eliminating toxicities from cancer and its treatments and maximizing function across the lifespan for patients, families and communities.

In two broad ways, the issues of aging and cancer effect everyone involved in cancer research and care. The first is demographic: The majority of cancer patients are over the age of 65 and the number of people over 65 is rapidly expanding. Second, as the ability to treat cancer improves, the number of people living with cancer expands, such that nearly 70% of cancer survivors are over 65. Even more concerning, the treatments provided to patients for cancer can significantly accelerate their rate of aging. To improve not only the survival rates from treatments, but the quality of that survival, treatments that minimize toxicities, maximize health span, and improve quality of life are desperately needed. Efforts addressing these needs span the research continuum from basic to clinical and population-based research, cutting across all COHCCC Research Programs.

Furthermore, older adults are under-represented in cancer research, which has led to an alarming mismatch between those most likely to have cancer and those enrolled in clinical trials setting the standard of care. COHCCC investigators have been at the forefront of addressing this evidence gap, having developed the most widely used tool for assessing toxicities in older adults, the CARG Toxicity Assessment tool. They have pioneered the use of the interventions using this tool, demonstrating in large randomized clinical trials the ability to reduce chemotherapy toxicities by 10%, 20% or more. The COHCCC CCA team has also led authorship of guidelines from major organizations that set the standard for care.

The COHCCC CCA is positioned to expand COHCCC's leadership in cancer and aging, supported by significant incoming funding (\$4.25M; Rising Tide Foundation) for expanding clinical trials across the country. Along with conducting five clinical trials based on the CARG assessment tool, this funding will support the creation of a data coordinating center for the conduct of such trials specified for older adults. This will be combined with a current R33 infrastructure grant (\$1.7M) to build the leading center for the conduct of trials at the interface of cancer and aging through COHCCC in the future.

Additional details about this theme's research and clinical excellence, impact (over the prior period: 2017-2022) and aspirations over the next five years are presented below, alongside recognition of the theme's leader.

## OVERVIEW

### CROSS-CUTTING THEME 1: Cancer and Aging

#### Research and Clinical Excellence

- Recognized international leader in cancer and aging scholarship, training, mentorship, and clinical care model implementation
- Three research-focused multidisciplinary geriatric oncology clinics designated by the American Hospital Association as having Age-Friendly Health System status

#### Impact (2017-2021)

- Leadership role in the national CARG, the largest group of its kind in North America (525 members)
- Developed most widely used assessment tool for toxicities in older adults and pioneered use of this tool to demonstrate (in large randomized clinical trials) the ability to significantly reduce chemotherapy toxicities
- Led first-of-its kind ASCO Guideline for Older Adults (2018), a Top 20 most-cited paper in Journal of Geriatric Oncology (700+ citations)
- Multiple NIH and foundation grants, including an R21/R33 infrastructure grant (NIA), a K24 mentorship grant (NIA), R03 grants (NIA), and an R25 (NIA) to conduct clinical trials for older adults

#### Aspirations (2022-2027)

- To expand current position as the leading center of its kind in the world and the leading national group (CARG)
- To further integrate cancer and aging infrastructure for research, mentorship, and clinical programs into COHCCC across its Research Programs to generate state-of-the-art, interdisciplinary science
- To take advantage of significant incoming grant funding (\$4.65M):
  - Expand clinical trials across the country based on the CARG geriatric assessment tool.
  - Create a data coordinating center for the conduct of clinical trials specified for older adults.
- To recruit basic/translational and implementation science faculty to expand our reach

#### Leaders

- William Dale, M.D, Ph.D.

## GOALS AND ACTION PLAN

### CROSS-CUTTING THEME 1: Cancer and Aging

GOALS	ACTION PLAN
1. Integrate basic science with translational biology to build a scientific foundation for understanding the impact of cancer and its treatment on aging, and vice versa.	<ol style="list-style-type: none"><li>Leverage collaborative and strategic efforts with COHCCC Research Programs to increase funding that supports pilot projects fostering transdisciplinary research, such as studying the impact of chemotherapy-induced cognition.</li><li>Recruit and assemble a team of basic and translational scientists across disciplines to collaboratively evaluate the biology of cancer and aging.</li><li>Evaluate aging-related biology and therapy-related clinical outcomes to define and measure a patient's health span and susceptibility to cancer risk across the lifespan and collaborate with Precision Medicine efforts to personalize prevention and treatment plans.</li><li>Contribute to high-impact publications that enhance understanding of the biology between cancer and aging to support clinical decision-making and an informed patient population.</li></ol>
2. Continue to build the infrastructure needed to drive innovative, team-based, and translational cancer and aging research.	<ol style="list-style-type: none"><li>Conduct activities funded by the current Rising Tide and Donaghue Foundation Grants (\$4.62M) and develop a national consortia for geriatric oncology trials.</li><li>Submit NIH program grant (P01, UG3/UH3) and PCORI grant applications to support an integrated, focused approach to study the impact of cancer on aging.</li><li>Renew R33 and K24 grants supporting Cancer &amp; Aging, including an intersection addressing Health Equity in underserved populations in the COHCCC network.</li><li>Build on the successful national and international impact of the CARG, establish the national data coordinating center at COHCCC to support multicenter, (inter)national studies focused on older adults.</li></ol>

## GOALS AND ACTION PLAN

### CROSS-CUTTING THEME 1: Cancer and Aging

3. Implement a scalable, evidence-based care delivery model — based on the COHCCC-developed geriatric assessment — into clinical settings.
  - a. Build on the success of the multidimensional geriatric assessment with interventions (GAIN), develop a scalable model to bring the assessment and corresponding multidisciplinary care teams to the clinic.
  - b. Implement a training program to educate clinicians and investigators on the role of the GAIN in their practice and clinical trial development/design to help apply developed GAIN tools in a clinical setting and via telemedicine to support treatment decision-making that reduces patients' toxicities and enhances quality of life across the COHCCC clinical network.
  - c. Introduce navigation services developed as part of an ACS grant by Cancer and Aging, Population Sciences, Health Equity, and Supportive Care Medicine researchers to the clinical setting to further enhance the COHCCC age-friendly health system across the clinical network.



## CROSS-CUTTING THEME 2.

# Survivorship

### OVERVIEW

Advances in cancer screening and early detection, improvements in therapeutics, and supportive care have all contributed to decreasing cancer mortality. As a result, there are an estimated 18 million cancer survivors in the U.S. today, and that number is expected to reach 26 million by 2040. More than two-thirds are considered long-term survivors, having survived >5 years after their initial diagnosis. These survivors are largely cared for in the community primary care setting, having transitioned away from the cancer center, and thus may not receive survivorship-focused care. Furthermore, cancer is largely a disease of older persons, and thus, the majority of cancer survivors are older than 65 years. In these individuals, survivorship often

occurs in a background setting of comorbid conditions, with a potentially greater effect on the health status of elderly cancer survivors. Efforts are needed to address the unmet needs of survivors, including developing strategies to personalize cancer treatment to account for inter-individual variability in treatment-related toxicity and for long — term surveillance for late effects of therapy. Additionally, there is a paucity of information on the long-term sequelae associated with targeted cellular therapies (CAR T cell therapy, bispecific monoclonal antibodies), which are increasingly being considered as adjunct to conventional therapies, or stand-alone in patients with resistant disease.

COHCCC has a long-standing commitment to survivorship-focused research and care that embraces the NCI Office of Cancer Survivorship definition of survivorship as starting at the time of diagnosis and lasting throughout the lifespan of the individual. This comprehensive definition encourages clinicians to think about the care of survivors as an integral part of the cancer care continuum. Included in the definition of survivors are family members, friends, and caregivers. The primary reason for including these individuals is that in most cases cancer is

### OBJECTIVE: CROSS-CUTTING THEME 2. Survivorship

Develop survivorship research and collaborations focused on the physical, mental, emotional, social and financial health and well-being of individuals with cancer from the time of diagnosis until the end of life.

not experienced alone. Examples of ongoing studies at COHCCC that embrace this approach include a self-management education intervention to prepare family caregivers and patients for lung cancer surgery and a clinical trial of a culturally tailored parent training to reduce cognitive deficits after treatment for childhood cancer. Comprehensive and well-designed survivorship research can then be translated into clinical practice through development of evidence-based clinical care guidelines and through development, testing, and implementation of intervention strategies designed to prevent or minimize the effect of treatment-related adverse outcomes.

Many late and long-term effects of cancer and its treatment may be ameliorated by early screening and intervention strategies, including consideration of cancer rehabilitation. COHCCC investigators have shown that when long-term cancer survivors transition to their primary care providers (PCPs), they no longer see their cancer physician on a regular basis and rarely visit cancer survivorship care specialists. Thus, the long-term preventive care of cancer survivors is scattered across hundreds of thousands of individual PCPs. Advances in technology, including the widespread availability of mobile phones, offer promising opportunities to improve early detection and treatment of late effects, allowing for community-based integration of survivorship-focused care. Investigators at COHCCC have fully embraced these advances to test innovative strategies for community-based survivorship care delivery.

Despite increasing awareness of survivorship issues, many challenges remain. These include a splintered health care system, clinician workforce shortages, lack of diversity in the medical workforce, knowledge gaps about the needs of cancer survivors, and lack of strong evidence-based guidelines for post-treatment care. These challenges are exacerbated by financial and other barriers to quality care, particularly for racial and ethnic minorities and low-income and rural neighborhoods, who experience substantial gaps in early detection and access to high-quality treatment. Cancer survivors are especially vulnerable to medical financial hardship, which may manifest as material (e.g., problems paying medical bills, medical debt, and bankruptcy), psychological (e.g., stress or worry about paying medical bills), or behavioral (e.g., delaying or forgoing necessary medical care because of cost) aspects. Survivors who are younger, underinsured or uninsured, and/or have lower income are more likely to experience financial hardship, as are long-term survivors of childhood cancer. To address these disparities, ongoing efforts to identify best practices for the equitable delivery of quality cancer treatment, rehabilitation, and post-treatment cancer care are needed.

COHCCC has a strong track record and established infrastructure and expertise to support cross-cutting collaborations that translate observational studies into interventions to improve the lives of cancer patients and survivors and address disparities in survivorship. During the past funding cycle, we continued to build on a robust portfolio of funded bench-to bedside research focused on cancer survivorship issues in patients with: 1) childhood, adolescent and young adult (AYA) cancers, 2) breast cancer; 3) lung cancer, 4) colorectal cancer, and 5) hematologic malignancies. There has been steadfast institutional investment in clinical and research programs to support future programmatic growth, as evidenced by the Center for Survivorship and Outcomes in the Hematologic Malignancies Research Institute and the Childhood and AYA Survivorship clinic. These are strengthened by ongoing multicenter collaborations.

Looking ahead, COHCCC aspires to become a nationally recognized center for cancer survivorship research and innovation, leveraging expertise in toxicity risk prediction, imaging/biomarker discovery, and mHealth interventions. We will establish paradigm-changing approaches to survivorship care delivery, and cultivate the next generation of interdisciplinary researchers with the skills to address survivorship-focused issues across the COHCCC strategic initiatives and Research Programs. These efforts will be facilitated by clear action plans that speak to the cross-cutting nature of our survivorship activities across the cancer care continuum (diagnosis through long-term survivorship), and are rooted by the need to integrate across the strategic initiatives (Precision Medicine, Cellular Therapeutics, Health Equity, Clinical Network) described herein.

Additional details about this theme's research and clinical excellence, impact (over the prior period: 2017-2022), and aspirations over the next five years are presented below, alongside recognition of the theme's leader.

## Overview

### CROSS-CUTTING THEME 2: Survivorship

#### Research and Clinical Excellence

- Cancer survivorship focused on the health and well-being of a person with cancer from the time of diagnosis until the end of life — including the physical, mental, emotional, social, and financial effects of cancer that begin at diagnosis and continue through treatment and beyond
- Established infrastructure and expertise to support cross-cutting collaborations that leverage advances in healthcare delivery across the continuum of cancer care
- Track record of translating observational studies into interventions to improve the lives of cancer patients and survivors

#### Impact (2017-2021)

- Developed robust portfolio of funded bench-to-bedside research in:
  - Childhood, adolescent and AYA cancer
  - Breast cancer
  - Lung cancer
  - Colorectal cancer
  - Hematology/cellular therapies
- Institutional investment in clinical and research programs to support future programmatic growth:
  - Center for Survivorship and Outcomes (Hematologic Malignancies Research Institute)
  - Childhood and AYA survivorship program
- Multicenter collaborations across the spectrum of survivorship

#### Aspirations (2022-2027)

- To become a nationally recognized center for cancer survivorship research and innovation, leveraging expertise in toxicity risk prediction, imaging/biomarker discovery and mHealth interventions
- To establish paradigm-changing approaches to survivorship care delivery
- To cultivate the next generation of interdisciplinary researchers with the skills to address survivorship-focused issues across COHCCC strategic initiatives

#### Leaders

- Saro Armenian, D.O., M.P.H.

## Goals And Action Plan

### CROSS-CUTTING THEME 2: Survivorship

GOALS	ACTION PLAN
1. Integrate patient health-related information at the time of diagnosis into treatment decisions to optimize cancer care and survivorship-related outcomes.	<ol style="list-style-type: none"><li>Expand existing longitudinal and multidimensional phenotyping research beyond individual disease groups (breast cancer, hematopoietic cell transplantation) or one patient population (older adults) to all patients.</li><li>Develop appropriate laboratory-based models (e.g., cell lines, induced pluripotent cell lines, animal) to determine the efficacy of interventions to mitigate toxicities associated with emerging targeted therapies.</li><li>Recruit investigators to lead multicenter translational biomarker-driven prevention trials in patients/survivors.</li><li>Characterize the interaction between social determinants of health (economic stability, neighborhood and physical environment, education, food, community and social context, health access) and cancer treatments on health disparities during and shortly after cancer treatment.</li></ol>
2. Develop comprehensive bench-to-bedside strategies to characterize the pathophysiology of treatment-related toxicities and translate these findings into interventions to mitigate risk during cancer treatment.	<ol style="list-style-type: none"><li>Engage researchers with expertise in advanced organ-specific imaging (e.g., magnetic resonance [spectroscopy, functional]) and biomarker discovery (multi-omics [transcriptomics, proteomics, metabolomics]) to define the mechanisms of treatment-related toxicity and to personalize monitoring during treatment.</li><li>Develop appropriate laboratory-based models (e.g., cell lines, induced pluripotent cell lines, animal) to determine the efficacy of interventions to mitigate toxicities associated with emerging targeted therapies.</li><li>Recruit investigators to lead multicenter translational biomarker-driven prevention trials in patients/survivors.</li><li>Characterize the interaction between social determinants of health (economic stability, neighborhood and physical environment, education, food, community and social context, health access) and cancer treatments on health disparities during and shortly after cancer treatment.</li></ol>

## Goals And Action Plan

### CROSS-CUTTING THEME 2: Survivorship

3. Become a national leader in cancer survivorship care delivery, leveraging advances in telemedicine, and mHealth technology to engage long-term survivors and their primary care providers in risk-based follow-up care.
  - a. In conjunction with ongoing efforts (e.g., Precision Medicine Initiative), build enterprise-wide digital health infrastructures to facilitate tele-oncology survivorship research.
  - b. Establish collaborations with community primary care networks to implement survivorship care research, with a focus on risk-stratified, shared care models post-treatment.
  - c. Recruit implementation scientists who have expertise in complex multilevel interventions to inform the development of enterprise-wide efforts to address health disparities in survivorship.
  - d. Submit competitive federal research grants, leveraging ongoing research and expertise in cancer control, cancer care delivery, and emerging cellular therapies.

## Summary of Objectives and Aspirations Across COHCCC Strategic Plan Focus Areas

Focus Areas	Objectives	Aspirations (2022-2027)
Strategic Initiative 1: <b>Precision Medicine</b>	Harness genomic-driven insights, clinical expertise and advanced analytics to pioneer personalized prevention and treatment plans to transform the outcomes and quality of life for patients, their families and our community.	<ul style="list-style-type: none"> <li>▪ To genetically profile tumors of all patients, regardless of cancer type, with goal of providing patients with effective targeted therapies or access to innovative clinical trials</li> <li>▪ To deliver comprehensive application of 'omics to detect cancer early, provide precise diagnoses, identify optimal treatments and offer prognoses through detection of minimal residual disease and other insights that support survivorship</li> </ul>
Strategic Initiative 2: <b>Cellular Therapeutics</b>	Transform the future of cellular therapies by promoting innovative science, growing exceptional talent, enhancing manufacturing capabilities, and expanding patient clinical trial accessibility.	<ul style="list-style-type: none"> <li>▪ To stimulate exchange of ideas, improve translation to the clinic and unify faculty around a shared strategy for cell therapies</li> <li>▪ To impact more patients' lives via southern California clinical network; Orange County, California, expansion; and partnership with CTCA</li> <li>▪ To transform the future of cellular therapies by promoting innovative science, growing exceptional talent, enhancing manufacturing capabilities and expanding patient clinical trial accessibility</li> </ul>
Strategic Initiative 3: <b>Health Equity</b>	Develop a nationally recognized health equity center of excellence that serves communities with the highest cancer burden and worst outcomes.	<ul style="list-style-type: none"> <li>▪ To address population cancer burdens and disparities faced by racial and ethnic minorities and vulnerable communities</li> <li>▪ To ensure that training programs, research, and clinical care are community responsive, considering our diverse populations within the COHCCC Catchment Area</li> </ul>

Strategic Initiative 4:  
**Clinical Network**

Expand COHCCC's clinical network to provide innovative therapies to more patients, families, and communities with the goal of ensuring our patients are matched with the right provider and the best treatment for their disease.

- To democratize cancer care by leveraging COHCCC's expanded network to create a system that makes leading-edge research, treatment, and care accessible to more patients and communities

Cross-Cutting  
Theme 1:  
**Cancer and Aging**

Collaborate to elucidate the biological, translational, clinical, and psychosocial connections between cancer and aging — focusing on eliminating toxicities from cancer and its treatments and maximizing function across the lifespan for patients, families, and communities.

- To expand current position as the leading center of its kind in the world and the leading national group (CARG)
- To further integrate cancer and aging infrastructure for research, mentorship and clinical programs into COHCCC across its programs to generate state-of-the-art, interdisciplinary science
- To take advantage of significant incoming grant funding (\$4.65M):
  - Expand clinical trials across the country based on the CARG geriatric assessment tool
  - Create a data coordinating center for the conduct of clinical trials specified for older adults
- To recruit basic/translational and implementation science faculty to expand our reach

Cross-Cutting  
Theme 2:  
**Survivorship**

Develop survivorship research and collaborations focused on the physical, mental, emotional, social and financial health and well-being of individuals with cancer from the time of diagnosis until the end of life.

- To become a nationally recognized center for cancer survivorship research and innovation, leveraging expertise in toxicity risk prediction, imaging/biomarker discovery and mHealth interventions
- To establish paradigm-changing approaches to survivorship care delivery
- To cultivate the next generation of interdisciplinary researchers with the skills to address survivorship-focused issues across COHCCC strategic initiatives







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