Welcome to USC’s Institute and Department of Translational Genomics

Where our team strives to make healthcare smarter, based on a vision that future advances in personalized medicine will build from, benefit, and ultimately serve an incredibly diverse set of individuals.

Medicine is undergoing one of its biggest transitions in recent history. For the first time, we can treat patients based not on what works best for an average person in the population, but based on what will work best for each individual patient.

Personalized medicine, also known as precision medicine, has been enabled by game-changing discoveries in genomics. Our deep understanding of DNA and how it varies from person to person is powering a new golden age of diagnostics and treatment, as well as predictive and preventive medicine. In areas like cancer and rare disease, however, it is just the starting point as we utilize high-throughput technology to integrate information from the molecular and systems level to ultimately improve patient outcomes.

To realize the promise of precision medicine, we need to understand the molecular and genetic diversity across all individuals. We believe that precision medicine doesn’t build or benefit from focusing on one population, but instead requires studies involving diverse populations.

The diversity of Los Angeles in many ways mirrors the future diversity of healthcare across America, highlighting its challenges and opportunities. We launched USC Translational Genomics to serve as a catalyst for precision medicine — a home for scientific and medical experts dedicated to challenging the status quo in healthcare by implementing and advancing precision medicine across all populations.

With a foundation of cutting-edge scientific facilities at the USC Keck School of Medicine, our renowned team of researchers and physicians is collaborating to realize the potential of genome-based medicine with the understanding that these

“We are deeply committed to excellence in translational genomics research, bringing to bear vast experience and expertise in molecular genetics, genome science, biomedical informatics, translational science, and molecular medicine.”

John D. Carpten, Ph.D.
Director, Institute of Translational Genomics
advances will be made from and serve the diverse clinical populations that will make up the future of healthcare.

We also believe that advancing precision medicine to affect a diverse set of populations requires diversity in leadership. Our faculty span diverse backgrounds and experience, and collectively we are committed to integrating these together to improve lives by combining the best genome science with the best clinical care.

“By developing new tools for integrative analysis of genomic, epigenetic, proteomic, and clinical data and assimilating them into the clinic, we can enhance treatment decisions and make a real impact on the future of medicine.”

David W. Craig, Ph.D.
Co-Director, Institute of Translational Genomics
What is translational genomics?

The story of each person is a saga, comprised of the tales of ancestors, the history of the species, and the collection of vignettes that makes everyone unique. Encoded in our DNA is a manual with 46 chapters called chromosomes that hold about 20,000 genetic instructions in sequences of four letters — A-T-C-G. Written out, each DNA strand would be 30 million letters long. These instructions are read by RNA, which in turn tells proteins to carry out all the essential functions of our bodies. How do we translate such an immense source of data into something useful?

At USC Translational Genomics, our researchers speak the language of DNA, RNA, and proteins. As pioneers of precision medicine, we have dedicated our careers to deciphering the genetic code, harnessing the latest technology to comb through the deluge of data, and interpret the results to create breakthroughs in medicine.

We are now poised to translate those discoveries in ways that will directly benefit patients. By studying each patient’s unique genetic signature and interpreting the biological and environmental events that have shaped their stories, we can more precisely diagnose disease, predict risk, and tailor therapies to improve outcomes.

“The future of medicine requires groundbreaking research, with rapid translation to the operating room and the clinic. USC Translational Genomics and the USC Institute of Urology epitomize this synergy. Together, we are unlocking the secrets of cancer at the genome level and developing new, cutting-edge treatments personalized to each patient.”

Inderbir Singh Gill, M.D.
Chair and Distinguished Professor of Urology
Shirley and Donald Skinner Chair in Urologic Cancer Surgery
Executive Director, USC Institute of Urology
Associate Dean For Clinical Innovation
USC Translational Genomics was founded in January 2016 under the leadership of John Carpten, Ph.D., and David W. Craig, Ph.D., who both came to Keck School of Medicine from TGen in Arizona.

USC Translational Genomics includes a truly transdisciplinary team of biologists, geneticists, and data scientists working hand in hand with engineers, chemists, and clinicians across USC departments, campuses, and hospitals.

Together, we work in the lab and behind the computer to advance our understanding of a range of diseases and disorders — from neurological diseases and rare genetic syndromes to adult and pediatric cancers — and in the clinic to produce practical applications. We are also committed to understanding why certain diseases and disorders are more prevalent among different populations.

In addition to our research and clinical efforts, USC Translational Genomics began to offer degree programs in innovative areas of biomedical research in 2017. We are dedicated to training the field’s next generation of leaders in genomics, biotechnology, and biomedical informatics.
What we do

The USC Translational Genomics faculty have helped write the book of precision medicine. Not only have we penned hundreds of defining publications, but we have also created many of the technological tools that have enabled the field to progress. Today, our discoveries continue to move precision medicine forward.

Clinical and genomics data integration

- Clinical protocol, consenting, enrollment
- Following patient outcomes and adverse events
- Therapy selection and patient treatment
- Molecular characterization in CLIA environment (pathology)
- Molecular grand round examination
- Access to prior data
- Clinical & genomic data integration (Knowledge mapping)
- Security, regulation, and integration of clinical & genomic things
- Library prep/sequencing
  Genome-wide RNA/DNA
- DNA mapping
  Raw data to variants in under 24 hours

Data management platform supporting complex regulatory environment

- Regulation by CMS, FDA, and IRBs
- Clinical utility requires turnaround in days not months
- Utilizing a rapidly updated, growing body of knowledge
Omics

Our scientists are utilizing next-generation genomic (DNA), transcriptomic (RNA), and proteomic (protein) sequencing technologies to shed light on a variety of diseases, and were among the first to prospectively apply these to improving patient care and treatment. For example, David W. Craig and John Carpten helped lead one of the first studies of whole-genome and transcriptome sequencing for the treatment of triple negative breast cancer. This foundational work led to other studies in late-stage metastatic oncology including melanoma, pediatric oncology, pancreatic cancer, glioblastoma, and colorectal cancer.

As part of their efforts, they helped establish standards and frameworks by which groups across the world apply clinical medicine. They led the development of one of the first CAP/CLIA certified laboratories focused on integrated analysis of whole-genome and transcriptome data, working with the FDA and others on establishing best practices for applying these approaches in clinical studies. They have helped lead the establishment of standards and references for other laboratories to implement similar approaches, partnering with researchers at healthcare systems across the country.

As part of the new department and institute, they are building and expanding such efforts to tackle integration across multiple scales and systems. They are using the latest methods and technology, and integrating these directly within the Keck healthcare system from the ground up.

Precision diagnostics

These technologies can treat, and they can also diagnose from a molecular and genetic level. Bodour Salhia, Ph.D., has developed a way to test for the presence of gene modifications via circulating tumor DNA taken from blood samples. The hope is that these could be used as biomarkers to find previously undetectable evidence of breast cancer that is likely to return or spread to other parts of the body. This could be transformative for the 234,000 Americans who develop breast cancer annually, 41,000 of whom die from the disease, usually due to metastasis that is detected too late for effective treatment.

David W. Craig has utilized integrated analysis of DNA and RNA to improve diagnosis in children with rare neurological conditions. He helped to establish a research clinic enrolling thousands of individuals across hundreds of families, developing approaches that improved diagnosing children at a genetic level from 5% to nearly 50%. He is now partnering with Keck leaders in cardiothoracic surgery to apply these methods in new populations and conditions.

Data integration

Advancing precision medicine means building and creating the informatics systems to gather, integrate, and analyze patient data at massive scales, across multiple dimensions and time points in decision making, for clinical value and utility. The scale of data our scientists sift through on each patient is massive and requires integration of bioinformatics, statistics, genetics, epidemiology, clinical medicine and public and global health reports. Working with David W. Craig, Enrique I. Velazquez-Villarreal, M.D., Ph.D., M.P.H., M.S., is integrating clinical and genomic data from a variety of technologies to assemble a more complete reference library in hopes of developing machine-learning tools that more rapidly help physicians access the critical decision-making datapoints they need.

We are building transformative data-driven discovery platforms where researchers can collaborate daily and make discoveries that would not otherwise be possible under the current paradigm of fragmented research groups working in isolation. These platforms are mission-driven around principles of linked data, integrative analysis, structured curation, inherent sharing, and data harmonization across researchers and environments.
There is a skills gap in trained individuals within biotechnology, genomics, and bioinformatics that is significant and cannot be overstated. Within laboratories across academia, healthcare and industry, researchers are finding themselves lacking the ability to analyze or understand the next generation of genomics technology, its data, and how it can be interpreted. This is affecting the field’s ability to make new biomedical discoveries and translate these from bench to bedside. In many cases, the tools exist — it is the expertise to use and apply them to a specific biomedical problem that does not. Bridging the gap will require interdisciplinary training that explores business as well as biology, and fosters collaboration at the bench, the bedside, and the boardroom. We are committed to addressing these problems by training biomedical students, technicians, and other healthcare scientists in the application of bioinformatics and biotechnology tools and translational research focused on moving biomedical research from bench to bedside.

“Meeting the world’s healthcare demand will require a new workforce beyond theoretical knowledge and research skills. It must be interdisciplinary with strong training in biomedical sciences coupled with sufficient proficiency in economics, business, and law terminologies.”

Carol Lin, Ph.D.
Associate Professor of Clinical Medical Education and Biochemistry & Molecular Biology
We have created two master’s level programs to arm biomedical scientists with additional skills for analyzing, processing, and managing large-scale data, and to provide students with strong knowledge and procedural road maps of the entrepreneurial process in biotechnology from idea generation through economic viability.

**Master of Science in Translational Biomedical Informatics**

This program will take scientists’ knowledge of bioinformatics to the next level, enabling them to analyze, apply, and integrate the latest data tools in the laboratory. They will be able to extract information to better understand biomedical problems, and to design experiments to address those problems. In preparation for a spectrum of careers that span from research to the clinic, students will understand their critical role in working with data under a bevy of regulatory bodies. Graduates of the two-year program will be well suited to work as applied bioinformaticians within academic and clinical research laboratories, pharmaceutical companies, and biotechnology companies.

**Master of Science in Translational Biotechnology**

This program combines a unique curriculum of foundational learning and practical training, teaching students to translate genomic and molecular insights into the creation and application of biotechnology in the research and medical sciences industries. Bioscience-based courses are integrated with entrepreneurial elements that explore the economic and regulatory frameworks that impact the development and use of new interventions. This program is ideal for biologists, medical students, investors, industry professionals, and all those who are passionate about biomedical sciences and would like a career in biotechnology beyond laboratory research.
Sarcoma is one of the last frontiers in cancer. There aren’t too many people who have dedicated their careers to it and there have been no blockbuster drugs or modalities that have changed the landscape for sarcoma sufferers in the last few decades. We still don’t have any targeted therapies for this disease,” McEachron says. “But with the team we have here, I feel like there is a genuine opportunity to do something great for the patients and learn more about the underlying biology of this disease.”

McEachron began chasing sarcoma-causing culprits as a postdoctoral researcher at the Translational Genomics Research Institute in Arizona. “The disease appears to be driven by oncogenic fusion genes, and we know that if we inhibit them, the cancer dies. But we don’t yet know how to target them, and we have to better understand how they work,” McEachron says. “My laboratory is dedicated to developing new biological tools and approaches to investigate these mechanisms.”

Ewing sarcoma, the second most common bone cancer in children, adolescents, and young adults, is an extremely enigmatic tumor with no known viable therapeutic drug targets. Luckily, DNA detective Troy McEachron, Ph.D., is on the case, along with pathologist Timothy Triche, M.D., Ph.D., and oncologists James Hu, M.D., and Lee Helman, M.D.
McEachron has weekly meetings with his clinical counterparts at the Children’s Hospital of Los Angeles (CHLA) to understand clinically relevant issues that he might be able to incorporate into his research. He also relies on physicians to identify patients, provide samples, and eventually validate his research findings in the clinic.

“Working directly with the clinical teams helps scientists know that we are asking the right questions and doing the right experiments,” McEachron says. “It’s a critical feedback loop to make sure our results have the best chance of being meaningful for improving patient outcomes.”

“Ewing sarcoma is unique among cancers in the young for many reasons, and remains one of the most devastating cancers in that age group. This is particularly vexing, as we have known for over 30 years that the tumor is driven by a fusion gene that occurs in essentially all cases, but we don’t know how,” says Triche, co-director of CHLA’s Center for Personalized Medicine Program and one of the foremost Ewing sarcoma researchers.

“Troy brings a fresh approach to deciphering the enigma, and working with him and the new techniques he brings to bear on the problem will hopefully allow us to finally put all the pieces together into an understanding of how the fusion gene causes the cancer,” Triche adds. “Once we know that, we can also begin to craft specific therapy that blocks that mechanism, and perhaps improve the current 50% survival rate for the first time in 30 years.”

The collaboration is just one of many taking place among USC Translational Genomics faculty with researchers and clinicians around USC, in the greater Los Angeles community, across the nation, and around the world.

“As new medical approaches and technology become available, we have a unique opportunity to work with our colleagues in this diverse clinical setting to ensure they are available to everybody, including the underrepresented and underserved,” says Director John Carpten.
Caring for community, building on diversity

Truly effective personalized therapies must be based on sound science that reflects the diversity of the population it will serve. Cancer is unique to each individual. In some cases, it also presents itself differently within different populations. The blood cancer multiple myeloma, for instance, disproportionately affects African Americans and often leads to worse outcomes for those patients.

Researchers at USC Translational Genomics are committed to finding out why — and to ensuring that these populations are included in the large-scale genomic databases used for most research studies, which overwhelmingly contain samples from Caucasian patients. Out of 5,729 samples in The Cancer Genome Atlas, for instance, 660 were African-American, 173 were Asian, and 149 were Hispanic, compared with 4,389 from white patients.

“‘There is a significant paucity in our understanding of molecular factors that may be driving these cancers and leading to disparities among underrepresented populations,’ says Director John Carpten.

By creating a more diverse collection of cell lines and animal models — and contributing them to the National Cancer Institute’s database — the team hopes to improve the entire scope of cancer care for everyone.

Carpten was an early pioneer in the study of cancer disparities among underrepresented populations.

He conceived the African American Hereditary Prostate Cancer Study (AAHPC) Network, which has become a model for genetic linkage studies in underrepresented populations and led to the first genome-wide scan for prostate cancer susceptibility genes in African Americans.

“Building upon previous work done at USC, we want to draw upon our unique and diverse catchment area to ensure we include a multiethnic cohort in research and clinical care that will better benefit everyone. We want to do this in a culturally sensitive manner that will truly engage the community.”

John D. Carpten, Ph.D.
Director, Institute of Translational Genomics
All about integration

Once a week, Enrique Velazquez-Villarreal crosses the border on a mission: to bring precision medicine to Mexico. He’s starting in one clinic in Tijuana, where he delivers primary care to about a dozen patients who have had their genetic data examined and integrated into their clinical care and records.

It’s a miniature real-world implementation of work Velazquez-Villarreal does on a much larger scale. At USC, the bioinformatician interrogates and integrates huge databases and computational systems from different branches of medicine to create tools and libraries for both research and clinical applications. Earlier in his career, he worked with millions of records on the world’s largest supercomputer at Carnegie Mellon. Later, he used artificial intelligence and machine learning to predict biological processes and the effect of behavioral interventions in neurological conditions, such as autism.

A man of many hats — and five degrees — Velazquez-Villarreal uses his vast knowledge across the entire spectrum of care, discovery, and teaching.

As a teacher, he leads classes in statistics, data analytics, and bioinformatics, and as a bench scientist, he has studied neurological conditions, transplantation immunology, and basic cell biology and mechanisms.

As an epidemiologist, he’s committed to delivering precision public health, using genetic data to assess risk and inform prevention strategies for individuals and communities. The Mexican native is currently canvassing Latino neighborhoods in San Diego to collect data and educate residents about positive family dynamics as part of a project with the University of California, San Diego.

“There’s a lot of biology and behavior that you can understand by linking information,” Velazquez-Villarreal says. “I think in the future, if we can find a way to integrate clinical and genetic information, it will be a great opportunity to advance the medical field.”
The plating prowess and bioinformatic brains in the halls of Norris are available for the entire Keck academic and clinical community.

“We want to leverage our strengths to increase the research potential of departments in a variety of disciplines, and to assist patients across the disease spectrum,” says Director John D. Carpten.

One of the ways this will be achieved is through the newly launched Keck Genomics Platform. Under the direction of Zarko Manojlovic, Ph.D., the service offers a range of high-tech, high-throughput sequencing, as well as the bioinformatic backbone and support to be able to interpret the data generated. Technicians at the center also have expertise in preparing complex and fragile samples, allowing researchers and physicians to test materials that have previously been considered unusable.

“We can truly help the individual understand the sequencing of the data and the data itself, as well as the analysis,” Manojlovic says.

Manojlovic partners with physicians to bring precision medicine to the clinic in a way that’s not just a data dump. He learns from the physicians—about their needs, challenges, and the day-to-day impacts of precision medicine on their clinical practice—and educates them about what kind of data they can get from samples, how to collect and prepare them, and the relative costs.

Together with David W. Craig, his team is working to create a cradle-to-grave next-generation sequencing data management and bioinformatics platform that focuses on downstream interpretation and accelerates discovery through close collaborations between experimental and informatic groups.

“"We want to connect as many scientists and physicians as we can to bring unity and centralization. We need to play to each other's strengths to achieve the best outcomes."”

Zarko Manojlovic, Ph.D.
Assistant Professor of Research Translational Genomics,
Director of Keck Genomics Platform

Here to help: Empowering users through genomics and bioinformatics

How to get involved
To learn more about Translational Genomics @ USC research, education, and clinical services:
Visit: dtg.usc.edu    E-mail: dtg@usc.edu    Call: (323) 865-1591    Fax: (323) 442-2490