

FACILITIES & OTHER RESOURCES

CHILDREN'S HOSPITAL LOS ANGELES (CHLA)

Established in 1901, Children's Hospital Los Angeles, located in the heart of metropolitan Los Angeles, is one of the nation's largest pediatric hospitals. It is ranked by U.S. News and World Report as among the top 10 pediatric hospitals for clinical excellence in the nation. With an established track record of high-quality, patient-centered research, it is currently eighth in funding by the National Institutes of Health among children's hospitals. CHLA is also one of America's premier teaching hospitals through its affiliation since 1932 with Keck School of Medicine of the University of Southern California (USC). It is also an active partner in USC's Southern California Clinical and Translational Science Institute.



A private, non-profit hospital, CHLA provides care to a large and highly diverse pediatric population, treating more than 107,000 individual patients annually, with nearly 14,600 inpatient admissions and 72,000 Emergency Department visits every year. Over 16,000 pediatric surgeries are performed annually, including heart and lung transplants, cardiac catheterizations, cancer and neurosurgeries, and orthopaedic procedures. The institution is designated as a Level I Pediatric Trauma Center, and has a 365-bed capacity, including 106 pediatric critical-care beds – more than any other hospital in the Western United States.

One of CHLA's overarching aims is to foster innovative research to improve the health and wellness of children, as well as ensuring the delivery of culturally competent care for diverse pediatric populations. This is achieved through a combination of basic, clinical and translational research studies focused on developing and improving diagnostics and therapeutics – research conducted under the auspices of The Saban Research Institute, one of the largest and most productive pediatric research facilities in the United States.

THE SABAN RESEARCH INSTITUTE

The Saban Research Institute is one of the few freestanding research centers in the U.S. where scientific inquiry is combined with clinical care and is devoted exclusively to children. Our goal is to improve the health and wellness of children through a combination of basic, clinical and translational studies. Research is performed at the lab bench, in the clinic and in the community. The Saban Research Institute maintains strong scientific and strategic affiliations with the University of Southern California (USC) and, in particular, the Keck School of Medicine of USC. All of the Institute's principal investigators (clinical investigators, physician-scientists and PhD scientists) are USC faculty, and many have collaborative projects with scientists at the Keck School of Medicine and other departments at USC. The Institute's researchers also are involved in collaborative projects with academic institutions throughout the U.S. and abroad. CHLA is currently ranked 7th in NIH funding among freestanding children's hospitals.

TSRI is responsible for providing administrative support for all research activities at CHLA. This facility occupies a total of 198,000 net sq. ft. of research space on the CHLA campus including a 10 story Smith Research Tower, a 5 story Saban Research Building, an 8,000 sq. ft. Clinical Investigation Center, and a 10,000 sq. ft. Community Health, Outcomes and Intervention Research Unit. The Research Institute is home to a centralized Sponsored Projects Office, which is responsible for proposal and award administration as well as financial management. The Institute also supports a series of core facilities fully equipped with state of the art instrumentation to facilitate research at CHLA and USC.

A central initiative of TSRI seeks to understand the childhood and developmental origins of health and disease across the lifespan. The Institute's interdisciplinary research is organized around three synergistic areas of focus that together fully explore the developmental origins of health and disease while addressing the most pressing issues of children's health. These three areas are: The Institute for the Developing Mind; Metabolism, Immunity, Infection and Inflammation; Regenerative Medicine and Cellular Therapies. Research Programs also include 1) Cancer and Blood Diseases, 2) Community, Health Outcomes and Intervention Research, 3)

Developmental Biology and Regenerative Medicine, 4) Developmental Neuroscience, 5) Diabetes and Obesity, 6) Human Physiology and Imaging, and 7) Immunology, Infectious Disease and Pathogens. Additionally, TSRI has committed resources to the following strategies in pursuit of our goal of becoming a top 5 nationally ranked stand-alone children's academic health center: 1) recruiting and retaining outstanding junior and senior faculty from all groups; 2) expanding the scientific infrastructure and research facilities to promote synergy and interaction and to enhance translational research; 3) training and mentoring the next generation of pediatric scientists; and 4) promoting innovative and interactive research.

The Institute for the Developing Mind: The Institute for the Developing Mind (IDM) capitalizes on the unique strengths of CHLA and TSRI, and is dedicated to achieving a new understanding of what fundamentally underlies mental health and mental illness—an understanding that will allow us to translate scientific knowledge into effective treatments for children, adolescents, and young adults. Its mission aligns with priority initiatives at USC including The Zilkha Neurogenetics Institute, The Brain and Creativity Institute, and The Institute for Neuroimaging and Informatics. The IDM's unique, team-based approach to science sets it apart from other institutions. Here, investigators from diverse disciplines—including geneticists, molecular biologists, system neuroscientists, clinical and behavioral experts, and clinicians—work together in a dynamic, collaborative environment to address very focused questions across multiple levels of study.

Training, Education, Career Planning and Development: The TSRI Office of Training, Education, Career Planning and Development (TECPAD) serves the Children's Hospital Los Angeles/University of Southern California community of pediatric residents, clinical fellows, postdoctoral fellows and students collaborating with the 140-plus Principal Investigators at TSRI. The Institute aims to recruit the most talented and dedicated research trainees from diverse backgrounds, providing them with the optimal resources, support and setting to investigate new breakthroughs and build successful and fulfilling independent research careers. The mission of TECPAD is to provide state-of-the-art training, education, career planning and development to research trainees across career stages and at different academic levels.

Intramural Funding Program. TSRI supports a broad intramural funding program designed to support the research training and career development of trainees at all career stages, including Cores Utilization Grants (\$5K), Research Career Development Awards (\$50K) for junior faculty, Innovative Pilot Projects (\$100K), Pre-Doctoral Support (\$30K), Research Career Development Fellowships (\$40K) for postdoctoral fellows, Innovative Pilot Project Planning Grants (10K), and 2nd R01 Pilot Projects (\$50K) designed for assistant and associate professors with one R01 to open a new line of research to submit a second R01.

Merit Awards Program. TSRI is committed to the recruitment and retention of transformative faculty and supports a program that recognizes external funding success through annual distribution of unrestricted funds calculated at a percentage of external funding. These funds are designed to further a faculty members research efforts.

Donnell Society. CHLA and TSRI support *The Donnell Society*, which is dedicated to improving the health of children by training pediatric scientists to perform innovative and high quality research. The Society includes pediatric residents, subspecialty fellows, graduate students, research post-doctoral fellows and faculty who are interested in performing pediatric research. The Society provides mentorship, infrastructure and a community for pediatric scientists in training. Activities include invited physician scientist speakers, chalk talks, educational activities, mixers, social events, offsite educational opportunities and administrative support including, grant preparation, manuscript submission, society memberships, license renewal and certifications.

Weekly Research Seminar Series. The Saban Research Institute hosts a weekly research seminar series, with lunch provided. The Research Seminar series is intended for our scientists to learn about exciting new scientific developments important to our research community. Graduate students, research and clinical fellows as well as faculty members (MD's and PhD's) regularly attend our seminars, which makes the event very unique. The topics are generally broad in scope in order to accommodate the heterogeneous research minded community at our Institution.

Annual Open House and Poster Session. Every June, TSRI holds an open house and poster session to showcase the broad range of research being done at Children's Hospital Los Angeles. The day provides a networking opportunity for basic, clinical and community health researchers to come together and celebrate their accomplishments. Junior faculty and trainees perform much of the hands-on work involved in research and the poster session provides them a forum to share their progress. With so much research occurring at The Saban Research Institute, this annual event provides a way for researchers at all levels to keep up with what

the other research labs are doing. Additionally, TSRI supports journal clubs, chalk talks, and special career development seminars and workshops. Faculty also have access to all of the resources offered through USC.

RESEARCH CORES, FACILITIES AND EQUIPMENT

The Saban Research Institute provides scientific direction and the critical space to support a wide array of research activities at CHLA. The Institute supports a number of core facilities fully equipped with state of the art instrumentation to facilitate research at CHLA. The list of these core facilities and equipment follows.

Animal Core: The Animal Core consists of an Animal Care Facility (ACF) as well as an Acute Animal Care Facility (AACF). The ACF provides state-of-the-art housing for research animals and support to investigators performing research on animals, and is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care and maintains a facility where animal research is performed with the highest standards. Services include animal purchasing and housing, quarantine facilities, training of investigators in the performance of animal research, and assistance in performing minor and surgical procedures with animals.

Capacity—The 10,940 square foot ACF has 19 animal housing rooms, 5 procedure rooms, 2 BSL2 rooms, 1 quarantine room, and several storage rooms. Also, there is office space, restrooms/lockers, and a lounge area to support numerous staff members.

Equipment

- HEPA-filtered air distribution system
- Automated RO water supply system
- Static micro isolator cages
- Steris 36 inch belt tunnel washer and dryer
- Automatic bedding dispenser unit
- Pass-through washer and bulk autoclave
- Heat sensitive tape for cage sanitation
- Automatic watering valves
- Freezer/24 hour refrigerator
- Additional state of the art equipment includes an irradiator, caging, and security equipment.

The Acute Animal Care Facility (AACF) provides housing for animals with special care requirements. The facility provides short-term or acute housing for laboratory animals; it is not intended for long-term housing of breeding colonies. Both facilities are monitored by the Animal Facility Usage Committee, which establishes policies related to the use of the facilities, and the Animal Care and Use Committee, which reviews and approves protocols involving animal research.

Biostatistics Core: The Biostatistical Core is designed to provide statistical consultation, data analysis and data management services to research staff and faculty throughout CHLA. The Biostatistical Core has been built to reflect the institution's growing research portfolio in the areas of basic, translational, clinical, health services, and community health research. Members of the Biostatistics Core offer assistance with:

- Formulating a research question
- Selecting an appropriate study design
- Calculating sample size and power
- Developing data forms and databases
- Formulating an analysis plan
- Performing statistical analysis
- Developing graphs and tables
- Answering critiques from reviewers
- Database management
- Statistical analyses
- Manuscript preparation

Clinical Imaging Research Core: The new, state-of-the-art Philips Achieva 3.0T MRI system has been in operation since Spring 2011. Offering Children's Hospital physicians and scientists unique access to a 3.0T MR system dedicated to research (CHLA is one of only 3 free-standing Children's Hospitals in the US with a dedicated research MR scanner), the Philips scanner is the nucleus of a mounting imaging research program here at CHLA. The research dedicated 3.0 T system provides an opportunity to develop, refine, test and implement novel MR protocols and greatly accelerate the implementation of these advanced protocols to the clinical care of patients here at CHLA. In addition, the research agreement with Philips gives the accessibility to research protocols for development and advancement of imaging protocols.

The MRI Scanner is equipped with multichannel head and torso coils allowing for faster acquisition and higher resolution examinations of both the head (brain) and body. Additionally, we have just acquired a multichannel head-and-spine coil specifically designed for neonatal imaging. In addition, the MRI suite is equipped with the

Visuastim a MR-compatible video-goggle system which may be used to present stimuli during functional imaging studies or child-friendly videos during structural scans, thereby reducing anxiety and boredom and allowing children as young as 4 years of age to participate in MR studies. A video camera has also been installed in the scanner room to monitor patient movement and enhance the safety of our pediatric patients during their MR scans. A Biopac physiological monitoring system is available as well (ECG, pulse-ox, respirations) that may be used to monitor patients and to carry out advanced imaging acquisitions that time the MR scans to the patient's physiology (thereby removing artifacts generated by breathing or blood pulsing through arteries).

Dixon Cellular Imaging Core: The Congressman Julian Dixon Cellular Imaging Core provides access to state-of-the-art equipment in microscopy and digital imaging to investigators at CHLA. The primary focus of the Core is technology transfer and provision of facilities for acquisition and analysis of histological and cytological preparations. An important aspect of this technology transfer is to provide training in the use of digital imaging devices, as well as in the application of image analysis procedures for generation of quantitative data.

Equipment

- Zeiss Wide-field Fluorescence Imaging Workstation
- Zeiss Axioplan Microscope
- SPOT QE Color Digital Camera
- 3x5 Large Format Film Camera
- MetaMorph Image Analysis Workstation
- PC (Software: MetaMorph, Photoshop, Office)
- Leica Fluorescence Upright Microscope
- Differential interference contrast (DIC) optics
- SKY Spectral Imager
- Zeiss 710 Laser Scanning Confocal Imaging System
- Lasers provide excitation at 405, 458, 488, 514, 561, and 633 nm.
- 34 Spectral detection channels
- Axio Observer Z1 Inverted microscope with 3-axis motorized stage
- Leica Stereozoom Fluorescence Microscope
- Hamamatsu CCD Camera
- Slide scanner, flatbed scanner

Embryonic Stem Cell Core: The purpose of this Core is to provide investigators with the knowledge, training, resources, and support required to initiate human embryonic stem cell (hESC) research in their laboratories. There are many barriers to the widespread study of hESC, including the need for a high degree of expertise and training for investigators and the labor-intensive nature of the development, maintenance, and testing of good quality undifferentiated hESC stocks. Access to the hESC Core facility at CHLA decreases the technical development time for investigators without previous hESC experience and increases the productivity of hESC studies. Staffed by a number of specialists, the following services are offered:

- Technical training for establishing and maintaining human embryonic cells.
- Development of high quality hESC frozen stocks for investigators.
- Provision of high quality, tested working stocks of hESC for trained investigators.
- Performance of standard tests for stem cell pluripotency and differentiation.

Equipment—TaqMan ABI 7900 HT FAST Real-Time PCR system, a dissecting microscope, a fluorescent microscope with inverted advance software, and an Amnis ImageStream excitation laser (405nm) with workstation software; located in 1,700 square feet of space.

Fluorescent Activated (FACS) Core: The FACS Core provides technical expertise and access to equipment for CHLA investigators who use analytical and sorting flow cytometry. Data acquisition is achieved with specialized computer software directly interfaced with the cytometer. The following applications are supported by instrumentation at CHLA: Absolute Counts, Apoptosis, Calcium Flux, Protein Co-localization, Cytometric Bead Assay (CBA) for up to 30 soluble cytokines or proteins per sample, DNA Cell Cycle Analysis, Flow-FISH for telomere length, Immunophenotyping, Intracellular and Nuclear proteins analysis, Live cell sorting, PhosFlow, Rare Event Detection/Sorting, Reporter Molecules, Side Population, Single-cell Cloning, Single Color Apoptosis, Sizing, Spot Counting for viral load, Subcellular compartmentalization, Synapse activity, Translocation, and Viability.

Equipment

- The three-color FACScan (BD) analyzer is a one-laser instrument, capable of collecting a maximum of seven parameters: two scatter, three colors (green, yellow-orange, and red), plus two derived parameters. CellQuest Pro software drives this instrument.
- The four-color FACSCalibur (BD) analyzer is a two-laser instrument, capable of collecting a maximum of eight parameters: two scatter, four colors (green, yellow-orange, red, and a second red), plus two derived parameters. CellQuest Pro software drives this instrument.
- The seventeen-color LSR-II (BD) analyzer incorporates four solid-state lasers (blue, red, and violet, UV). It is suitable for the CBA assay. DiVa software drives the LSR-II.
- The FACS Aria-I (BD) instrument is equipped with three lasers capable of detecting up to thirteen colors and are high-speed cell sorters. It delivers four populations simultaneously to purity frequently in excess of 99%. The Aria-I laser bench holds solid-state lasers—488nm, 633nm, and 405nm—that are delivered to the flow cell via fiber optic cabling. DiVa software drives the instrument.
- The DiVa FACS Vantage SE (BD) has three lasers—a 488 nm Laser, a 635 nm, and the Innova I-302 tunable krypton laser—with UV, Violet, Green, Yellow, or Red line capability. The Vantage collects up to eight colors: four parameters (laser 1), two parameters (laser 2), and two parameters (laser 3). This is in addition to two scatter parameters as well as derived parameters. Specialized assays available include Calcium Flux and side population. Recently upgraded with a stand-alone air compressor, the DiVa FACS Vantage is capable of ultra-slow speed to high-speed cell sorting. DiVa software drives the instrument.
- The ImageStream 100 (Amnis) is a first imaging flow cytometer. Loaded with three lasers—488nm, 633nm, and 405nm—it will capture six digital images (spatial resolution: 0.75NA, 0.5µm pixel size) of each cell, measuring morphology, brightfield, and up to four parameters of fluorescence. The spectral decomposition element splits the cell imagery into six spectral bands, one for each CCD camera. The unique time-delay integration tracks the motion of the cells and increases the signal 1,000 fold before an image is recorded. Inspire software is used for data acquisition and IDEAS software is used for data analysis.

Analysis Stations—Upon data acquisition, stations are available for free-of-charge data analysis. Software packages currently available include Cell Quest, FlowJo-Mac, Flow Jo-PC, VenturiOne, and Modfit.

Mouse Genome And Pathology Core: The purpose of the Mouse Genome and Pathology Core is to provide genetically manipulated mice for biomedical studies. Services offered by this Core include transgenics, knockins and conditional/tissue specific knockouts, and centralized support for the performance of murine tissue preparation for histological analysis. Other services include tissue paraffin embedding and sectioning, routine H & E staining, and genotyping of tail DNA.

Equipment

- NIKON Eclipse E6000 Microscope
- NARISHIGE IM5B Microinjection x2
- NARISHIGE MO202 Micromanipulator x2
- LEICA Microscope MZ95
- LEICA Light Source KL 1500 LCD x2
- LEICA Microtome RM 2135
- LEICA Embedding Station EG 1160
- LEICA Microscope ZOOM 100
- LEICA Vibrotome VT 1000 S
- LEICA Microscope DMI 3000 B
- HERA Cell Incubator CELL 150 x3
- Fisher Scientific Microscope M# 12-560-45
- PRECISION Water Bath 183
- SterilGARD 3 Advance Class 2 Biosafety Cabinet from Baker
- Frigidaire Refrigerator Model # GLRT13TEW1
- LEICA Water Bath HI 1210
- LEICA Power Source NCL 150
- Thermo Forma Liquid Nitrogen Tank M# 740
- NAPCO CO2 incubator 5400

Proteomics Core: The Proteomics Core is designed to further research by providing mass spectrometric consultation, analysis, and database processing to research staff and faculty at CHLA and USC. Consultation services: Experimental design, Choosing an analysis method, Publication methods, Publication figures. Analysis: Sample clean-up, Chromatography, Mass spectrometry. Database Processing: Protein identification, Protein quantification, Identification of post.

Small Animal Imaging Core: The Small Animal Imaging Core provides investigators with access to state-of-the-art imaging equipment for research that involves small animals, primarily mice and rats. Staffed with a number of research specialists and research assistants, this Core provides images to investigators and facilitates image processing and interpretation via collaboration with the Radiology Department. *Equipment* — Bioluminescence/Fluorescence imaging, Micro-CT, 7 Tesla small bore MRI, High-Res plain film X-ray, Micro-Spect-CT, and real-time Doppler ultrasound.

Translational Biomedical Imaging Laboratory: Using imaging technologies to observe the natural course of biology in action, within living organisms, will help accelerate development of new diagnostics and treatments. The Translational Biomedical Imaging Laboratory (TBIL) provides dynamic imaging equipment and technical expertise to accelerate the trajectory of scientific discovery from bench to bedside, and is currently collaborating on studies that include intestinal stem cell propagation, neuroblastoma and heart regeneration. TBIL is designed as a research accelerator that brings clinicians together with researchers who are defining the basic mechanisms that build organs, so that they can design better therapies.

Bioimaging includes powerful, innovative tools for the study of biological processes—such as confocal microscopes that can image virtually any specimen on a slide or culture dish, live-cell imaging and in-vivo fluorescence imaging. Additionally, confocal laser scanning microscopy allows investigators to acquire in-focus images from selected depths, a process known as optical sectioning. Images are then acquired point by point and reconstructed with a computer, allowing three-dimensional reconstructions of topologically complex structures. All of these methods hold enormous potential for a wide variety of diagnostic and therapeutic applications.

Instrumentation Capabilities

- Live Imaging Lab – with a multi-spectral, multi-photon microscope for high-resolution imaging of living specimens
- High-Speed Microscopy Lab – offering high-speed, volumetric imaging
- Extended Volume Imaging Lab – providing an integrated microtome and laser-scanning microscope for imaging large specimens
- Quantitative Image Analysis and Visualization Suite – providing high resolution workstations for image processing and image analysis The “Collaboratory” –interaction space with high resolution video and video conferencing capabilities

Vector Core: The Vector Core provides assistance in the design and construct of retroviral or lentiviral vectors, and in the production of retrovirion or lentivirion for gene-modified *in vitro* as well as *in vivo* animal studies. The core provides consultation to determine gene transfer needs and the best way to produce gene-modified cells, and to analyze and use vectors. Services include:

- 1) Design and engineer custom lentiviral, retroviral, and adenoviral vectors for gene delivery.
- 2) Package lentiviral, retroviral, and adenoviral particles.
- 3) Provide ready-made lentiviral particles containing eGFP, luciferase, and RFPs
- 4) Package lentiviral particles that encode shRNA for gene-knockdown.
- 5) Package lentiviral genes responsible for induced pluripotent stem cells (iPS).

Incorporating new technologies with the services

- a) Virus-based nanoparticles (VNPs), which are used as platform technologies for diagnostic imaging.
- b) Pantropic ViraSafe Universal Lentiviral Expression System developed at CHLA and licensed to Cell Biolabs, Inc (Cat# VPK-211-PAN). This system provides increased safety measures to prevent the generation of replication competent lentiviral particles, and includes several features that boost viral production and viral titer.
- c) Retroviral-based forward somatic cell genetic platform technology, SILENCE. This system uses retrovirus particles to deliver a *cis*-acting gene silencing element in a quasi-random fashion throughout the genome of tissue culture cells to identify unknown genes responsible for a phenotype of interest. Presently, this system works in hypodiploid cells such as CHO-K1 cells and in the mammalian cell line KBM7 chronic myeloid leukemia (CML) cell line with a haploid karyotype, except for chromosome 8 M.

Service description

- a) Vector design and construction
 - Basic cloning
 - Basic cloning w/sequencing

- Basic cloning w/PCR +2 primer sequencing
- Intermediate cloning (+ w/sequencing)
- Intermediate cloning w/PCR
- Custom cloning
- Endotoxin-free maxi-preps
- Packaging retroviral vector
- Packaging retroviral vector lacking selectable marker
- Production of lentiviral vector

b) Vector packaging

Equipment —The Vector Core is equipped with a TaqMan Real-time PCR instrument that provides quantitative PCR analysis. The use of the TaqMan is available to all Saban Research Institute members who have received training in the proper use of the instrument.

Washing Core: The Saban Washing Core provides centralized support for glassware washing for investigators housed in the Saban Research Building. Staffed by two full-time employees and one part-time employee Monday through Friday, services include collection of glassware from laboratories, washing, autoclaving, and return of clean glassware to laboratories. **Equipment**—3 pass-thru autoclaves, 2 pass-thru washers and dryers, all state of the art.

TSRI CLINICAL RESEARCH SUPPORT OFFICE

The Clinical Research Support Office (CRSO) of TSRI, in collaboration with the Southern California Clinical and Translational Science Institute, provides efficient and cost-effective research support to facilitate efficient, high-quality, and safe clinical research and trials throughout CHLA. CRSO staff are experts in implementing, conducting, and monitoring clinical research studies and trials from start-up to close-out, supporting both novice and experienced clinical investigators and study teams.

Research Navigation: Our Research Navigator connects investigators with the services and support needed to conduct efficient, safe and high-quality clinical research and trials at CHLA. This includes study design, feasibility assessment, regulatory and IRB approval, participant recruitment, study implementation and coordination, registration and billing, study closeout, etc.

<p>Study Start-up:</p> <ul style="list-style-type: none"> • Study design • Feasibility assessment • Identifying collaborators/community partners • Scientific review • IRB review • Regulatory documents • Recruitment and accrual planning • Source documents • Biostatistical consultation 	<p>Study Implementation:</p> <ul style="list-style-type: none"> • Research coordination • Research nursing • Neuropsychological assessment • Participant recruitment and retention • Participant registration and billing • Study documentation • Informed consent • Regulatory binders • Adverse events • Study drug accountability • Internal and external audits 	<p>Study Closeout:</p> <ul style="list-style-type: none"> • Sponsor and monitoring visits • IRB closeout • Case Report Form storage • Biostatistical analysis • Publication of study findings
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Clinical Research Coordinator Pool: Our Clinical Research Coordinator (CRC) pool supports research studies across the clinical divisions of CHLA. They are centrally managed and trained, SOCRA-certified and collectively provide a broad range of knowledge and expertise about conducting pediatric clinical research studies and trials here at the hospital. The CRCs are available on a fee-for-service basis to join your study team to help implement and conduct all aspects of a study from start-up to close-out.

Research Nursing Pool: Our dedicated research nurses facilitate clinical research by conducting protocol specific study activities. The nurses are able to travel to clinics or inpatients when needed to facilitate patient participation. All of our nurses are PALS certified, are trained to support specimen processing and shipping, and can assist with clinical research participant registration and CHLA hospital billing. Procedures include: detailed assessments of research participants; peripheral blood-draws; blood draws from central venous

catheters; research medication administration; oral glucose tolerance tests; and other research protocol specific clinical interventions.

Clinical Trials Unit (CTU): The Clinical Trials Unit supports outpatient and inpatient clinical trials and research studies for research teams throughout CHLA. The unit is located on the first floor in the main hospital building, in a 1625 square foot outpatient facility, alongside the Children's Health Imaging Research Program, with four dedicated patient care areas for research participant evaluations and interventions, as well as a research laboratory for specimen processing.

Research Regulatory Support: Regulatory support is critical for any clinical research involving children. Each study requires rigorous institutional and federal regulatory review and documentation, including approval of human subjects protection by the Institutional Review Board (IRB). Our Regulatory and IRB Support Specialist provides the clinical research community at CHLA with support and information, as well as fee-for-services to coordinate regulatory affairs for clinical research studies and trails. Support includes: preparation and submission of study protocol to Institutional Review Board (IRB); preparation and filing of Investigational New Drug/Investigational Device Exemption (IND/IDE) initial submissions to the Food and Drug Administration (FDA) as well as yearly reports; and completion of essential study regulatory documents.

Pediatric Neuropsychology: The Neuropsychology Research Laboratory provides assistance to study teams regarding study methodology, administration of neuropsychological measures and interpretation and distribution of neuropsychological findings. Consultations are available to discuss study methodology specific to proposed studies. The lab is staffed with a full time Neuropsychologist and research assistants. Research participant neuropsychology evaluations and testing is conducted on the 4th floor of the main hospital.

Biostatistical Support: Our Biostatisticians support clinical research across CHLA by providing expert consultation services for sample size calculation, analysis of data, and publication development, as well as educating the research community, and collaborating on active research projects.

Clinical Research Specimen Processing and Shipping. Research specimen processing and preparation services and support for both investigator-initiated and sponsor-supported clinical research studies, are provided by the Clinical Laboratory of the Department of Pathology and Laboratory Medicine. Staff support basic to complex specimen processing and shipping to central laboratories. The Clinical Laboratory ensures that clinical research specimens are processed appropriately for both outpatient and inpatient research protocols and provide 24/7 coverage when needed based on the requirements of specific study protocols. Services are provided on a fee-for-service basis.

THE SOUTHERN CALIFORNIA CLINICAL AND TRANSLATIONAL SCIENCE INSTITUTE

The Southern California Clinical and Translational Science Institute (SC CTSI) was established in 2008 to address one of the most important problems in the health sciences: the difficulty of translating basic research into real-world medical interventions. Leveraging generous institutional support from the University of Southern California (USC) and Children's Hospital Los Angeles (CHLA) and a large Clinical and Translational Science Award from the National Institutes of Health, the SC CTSI has built an organization devoted entirely to improving the success of translational science with tools and programs that support researchers and their work.

The SC CTSI has emerged as a valuable, multi-faceted resource for pre-clinical, clinical and community-partnered translational research at USC, CHLA, and throughout Southern California. The SC CTSI has created unique institutional partnerships involving USC, CHLA, the Los Angeles County Departments of Health Services, Public Health, and Mental Health, and more than 40 community organizations with special interests in improving the health of our neighbors throughout Los Angeles and Southern California. The SC CTSI has supported more than 800 investigators in their quest to create and apply new diagnostic and therapeutic advances, medical procedures, and behavioral interventions to improve clinical care and the health of individuals and the public. This work has generated \$62 million in new extramural grant funding, and has had great impact on the scientific community, as evidenced by over 350 peer-reviewed scientific publications from SC CTSI-supported projects.

Biostatistics and Bioinformatics Resources: The program offers individualized support across the lifecycle of clinical and translational research studies. Services include advice and assistance with developing study

protocols, experimental designs, and analytical strategies; preparing data analysis plans, including interim efficacy and safety monitoring; creating and reviewing data acquisition plans, including collection and coding; responding to reviewer comments; and training on study design, data collection, and data analysis.

Clinical Research Informatics: The program creates and operates the information infrastructure to support clinical trials and a broad range of clinical research, focusing on large enterprise-wide informatics tools and systems within USC, across partner institutions, and with external collaborating organizations. This includes enabling the expansion and effective use of clinical data in conjunction with information technologies, as well as the broad, safe, and compliant discovery, reuse, and sharing of data through the development of a federated clinical data warehouse for research. The program also provides training in informatics tools and methods to conduct multidisciplinary research.

Clinical Translation/Clinical Trials Unit: The program supports human mechanistic studies and early phase clinical trials by providing the appropriate clinical research infrastructure (two Clinical Trials Units [CTUs] — one at the Keck Medical Center of USC and one at Children’s Hospital Los Angeles) and assisting investigators in the development and conduct of their studies. The CTUs provide a well-equipped physical space, well-trained and dedicated clinical research staff, and a laboratory for specimen handling and processing.

Community Engagement: The program bridges researchers and local communities, building sustained partnerships to ensure that research initiatives meet real community needs. Researchers benefit by focusing on timely, responsive, culturally relevant targets, while community members can directly influence research choices and academia-community relations. Services include training and technical assistance workshops for community-engaged research, individual consultations for faculty, partners and community members, and matchmaking between those constituencies.

Education, Career Development, and Ethics: The program plays an essential role in the training and career development of the next generation of clinical and translational researchers and offers in-depth training and career development for selected pre-doctoral trainees and early career clinical researchers through NIH-supported programs. Access to certificate and Master of Science programs and assistance with locating mentors and improving mentoring skills are available for a wider audience throughout USC and CHLA. In addition, the Research Ethics program provides education and training as well as consultations to help researchers and clinicians anticipate, identify, and respond to ethical issues.

Electronic Home and Digital Strategies for Clinical Research: The program promotes innovation in communications and technology to develop and disseminate highly accessible, web-based research tools, services, and information resources. Areas of focus include easy access and discoverability of knowledge resources, novel ways to enable research collaborations, and promotion of clinical studies. The program also develops technical solutions that improve operational efficiencies for planning, evaluation, and tracking. The program further coordinates SC CTSI communications and develops novel, measurable communications approaches to more effectively increase the visibility of research and engage partners.

Planning, Evaluation, and Tracking: With a focus on transparency and accountability, the PET program works to create a more strategic organization with greater alignment between program and institute-wide priorities and activities. It supports the development of goals, targets, and relevant metrics of success, assesses progress, and improves overall performance and management to build a data- and metrics-driven organization. SC CTSI measures its impact in various ways including efficiency of service delivery, transformative changes in how research is conducted, and new science generated.

Pre-Clinical Translation and Regulatory Support: The program served as an accelerator for pre-clinical development of novel therapeutics, devices, and biomarkers. It catalyzed the advancement of projects towards commercial implementation and clinical practice by connecting investigators to experts and offering regulatory support services.

Research Development: The program fosters the establishment and development of interdisciplinary clinical and translational research teams, projects, and programs. It awarded ~\$1M annually in pilot grants to support

research, team building, and career development across all phases of translational research. Activities include active team-building, support for interdisciplinary project development, pilot funds for project initiation, and assistance with strategies for securing sustainable funding.

OTHER

The Children's Hospital Health Sciences Library provides resources and services to CHLA staff. In addition to its collection of 3500 print books and 170+ current print journal subscriptions, the library supplies access to over 200 electronic books and 2000 electronic journals. Online access is available anywhere in the hospital or from remote computers that connect to the USC network.

In addition to books and journals, the library also provides local and remote access to various journal article databases including: Ovid MEDLINE, Ovid CINAHL, PubMed, PsycINFO, Science Citation Index, and Journal Citation Reports. The library's book and journal catalog, as well as that of the USC Norris Medical Library (with whom the CHLA library has reciprocal borrowing agreements), is searchable online as well.

Library services include mediated literature searching (searches conducted by a librarian), interlibrary loan borrowing (for obtaining materials that the CHLA library does not own), Ovid AutoAlerts (a current awareness service that delivers weekly citations that match a researcher's predefined topic), and HouseCalls (one-one-one, time-of-need meetings where the librarian can instruct users on a variety of topics including database searching, PowerPoint, or EndNote).

The Department of Pediatrics holds a NICHD Child Health Research Career Development Award (K12) (PI, D. Brent Polk, MD) to provide supervised research training and mentoring to assist the transition into productive physician scientists in areas related to pediatrics and its subspecialties.

EQUIPMENT

FRASER, Scott: Translational Imaging Center & Advanced Light Microscopy Imaging Center Resources

Michelson Hall 1002 Childs Way, and Ray R Irani Hall, 1050 Childs Way

The Translational Imaging Center (TIC) and the Advanced Light Microscopy Imaging Center bring together advanced light and fluorescence microscopy systems, providing facilities and instruments for scientists engaged in translational research. The TIC is focused on developing new technologies for automating and providing advanced imaging technologies not yet commercially available.

Facility equipment - Commercial:

Zeiss LSM-700 inverted microscope

The LSM-700 is a four laser, point scanning, confocal microscope with 405nm, 488nm, 555nm and 633nm solid state lasers. Environment chamber and stage make it suitable for time lapse imaging of live cells. The motorized stage and autofocus device allow the imaging of large specimens through tiling together multiple imaging stacks in X,Y,Z planes.

Zeiss LSM-780 OPO Observer, inverted microscope

The LSM-780 Observer is a confocal and multi-photon microscope that offers ultimate sensitivity for demanding imaging work. Equipped with a motorized stage, an autofocus device, and a full stage-top incubator, the 780 is optimized for high-end live cell/embryo imaging. The high-sensitivity 32-channel Quasar detector allows for spectral imaging, linear unmixing, and high color count (>4) image acquisition. Frequency domain Fluorescence Lifetime Imaging (FLIM) can be performed using the FastFLIM (ISS); two hybrid detectors coupled to the non-descanned port of the microscope provides high sensitivity and penetration depth. Excitation can be performed with 6 lines of single photon lasers (405, 458, 488, 514, 561 and 633 nm), Chameleon (Coherent) 2-photon laser (range from 690nm to 1050nm), and APE Optical Parametric Oscillator (OPO) 2-Photon laser (range from 1050nm to 1300nm).

Zeiss LSM-780 Explorer OPO, upright microscope

The LSM-780 Explorer is a confocal and multi-photon microscope that offers ultimate sensitivity for tissues/embryos and small animal imaging. It offers the same laser lines as the 780 Observer microscope above.

Zeiss LSM-880 Observer, inverted microscope

The LSM-880 Observer is a confocal microscope with a high-sensitivity 32-channel Quasar detector for spectral imaging, linear unmixing, and photon-counting. This microscope has the following laser lines: 405nm, 488nm, 514nm, 561nm, 594nm, and 633nm. It is equipped with an environment chamber for imaging live samples.

Zeiss Elyra Superresolution inverted microscope

The Zeiss Elyra is: a Structured Illumination (SIM), Total Internal reflection (TIRF), and Photo-activation localization (PALM) superresolution microscope capable to double the resolution of a conventional light microscope in both the lateral (XY = 50 - 120 nm) and the axial (Z = 150 - 350 nm) directions. It is equipped with environment chamber and stage, a motorized stage, and an autofocus device. The EMCCD camera achieves exceptional sensitivity and allows for imaging of bleach-sensitive and live specimens.

Leica SP8

The Leica SP8 is a highly capable microscope with dedicated 405nm, 447nm, and 1040nm lines as well as a white light laser tunable from 460-1040nm and a Spectra Physics multi-photon laser tunable from 1040-1600nm, with four GaSP hybrid (HyD) detectors, two PMTs (one for fluorescence and one for transmitted light), and a 4 channel non-descanned detector system. The SP8 has imaging modules for Fluorescence lifetime imaging as well as correlation spectroscopy. This microscope is exceptional at tiling images into large fields of view and comes equipped with environment chamber for your live-imaging needs.

M-Squared Aurora Light Sheet Microscope

The Aurora light sheet offers a unique Airy beam shape, which boosts axial (z-axis) resolution through deconvolution. The objectives have a working distance of 12 mm and have a concave lens on the front aperture. This system is capable of imaging large samples in a range of refractive indices from water (1.3) to DBE (1.5) clearing reagents, including caustic reagents i.e. BABB. 405nm, 465nm, 488nm, 561nm, and 633nm laser lines are available.

GE DeltaVision OMX Imaging System

The DeltaVision OMX Imaging System is an advanced multi-mode, super-resolution microscope system that offers super-resolution imaging using 3D structured illumination (3D-SIM) and/or localization microscopy techniques: it allows offers 120 nm resolution in XY and 300 nm in Z (resolution is wavelength and optics dependent).

Fluidigm Cytometry by Time of Flight (shared with USC's CSI-Cancer)

Cytometry by Time of Flight (CYTOF) mass spectrometry is greatly advancing the field of single cell proteomics. CYTOF enables the simultaneous analysis, in single cells, of up to 105 different proteins. We are currently helping to develop the next generation of CYTOF: Imaging Mass Cytometry. In addition, we are also working on expanding the capabilities of CYTOF beyond protein analysis to include both mRNA and DNA mutation analysis.

Facility equipment - Custom-built:

Light sheet microscope with two-photon- and one-photon-excitation

These setups consist of a fully custom-built imaging platform in both horizontal and vertical configurations to handle various tissue samples or live specimens. They can perform light sheet microscopy with not only two-photon excitation using pulsed near infrared laser light from 690 nm to 1200 nm (Chameleon Ultra II and Compact OPO, Coherent), but also one-photon excitation with a multiplexed diode/solid-state laser system (405, 458, 488, 515, 561, 633 nm, > 80 mW each line, Omicron). There are provisions to support mounting of various kinds of samples, from whole animal to culture cells on coverslips, with image recording carried out by a combination of two sCMOS cameras (Zyla 5.5/Andor, Flash 4.2/Hamamatsu) and two EM-CCDs (iXon 885, iXon Ultra, Andor), spanning the ability to image bright samples fast at 100 frames (5 megapixels) per second to image dim endogenously-labeled samples with photon-counting sensitivity. These microscopes are also capable of ultra-fast 3D imaging through selective volume light field imaging with full volume frame rates of 60 frames per second (fast enough to see red blood cells flowing through the beating heart of a zebrafish).

Custom-built microscopes in development

The TIC is currently developing other custom-built imaging platforms, including light sheet microscopes with: medium-to-high throughput sample handling capability, single objective illumination and detection, and accompanying light field capability. The TIC is developing a laser scanning microscope with adaptive optics capability. These continuing development efforts keep us exploring the latest technology and give our users access to the latest imaging capabilities.

Other microscopes available for use either with or without camera:

Zeiss Axio Observer fluorescent compound microscope with X-Cite light source and filter sets for screening or imaging DAPI, CFP, FITC, TRITC, mPlum, and DIC-II for 10x and 20x objectives.

Olympus fluorescent dissection stereoscope with filter sets for use with CFP, YFP, and mCherry.

Zeiss Axio fluorescence dissection stereoscope with filter sets for use with CFP, GFP, and mCherry.

Home built compound microscope in an upright configuration with a 10x air objective and 20x water immersion/dipping objective. This microscope has filters for CFP, GFP, RFP, and far-red imaging.

Facility software:

Huygens by Scientific Volume Imaging

Huygens is a full-featured 3D image analysis and visualization software, especially well known for its deconvolution package.

Imaris and Stitcher by Bitplane

Imaris is a core scientific software module that delivers all the necessary functionality for stitching large (500GB+) 3D tiled data sets, visualization, analysis, segmentation and interpretation of 3D and 4D microscopy datasets.

HySP by HySP

HySP is a python-based program to process and analyze multi-spectral images in phasor space. It provides a graphical way to segment out individual fluorescent components from complex fluorescent images. This software package also includes a fluorescence lifetime module for analysis of FLIM data.

SIM-FCS by Globals Software

SIM-FCS allows users to acquire, process, and analyze fluorescence lifetime images as well as perform and analyze fluorescence correlation spectroscopy (FCS) and all its derivatives: ICS, RICS, STICS, etc.

Matlab by Mathworks

Matlab is a high level language used for rapid prototyping and modeling. Its platform allows for fast visualization of ideas and easy collaboration across disciplines.

DNASStar by Lasergene

DNASStar software package is used for applications ranging from genomics, structural biology, molecular biology and cloning suites.

Snappgene by Snappgene

Snappgene is a molecular biology software used to document electronically DNA constructs made in the lab. Its platform allows for simple sharing with colleagues and collaborator around the world.

FACILITIES AND OTHER RESOURCES

USC Translational Imaging Center & Light Microscopy Imaging Center

Unless otherwise stated, all facilities and resources are located on the 4th floor of Michelson Hall, 1002 Childs Way.

Drs. Fraser, Cutrale, Trinh, and Truong have research space and offices in the state-of-the-art Michelson Hall/Michelson Center for Convergent Bioscience which opened November 2017. Michelson Hall was designed to be a convergent community resource, with dedicated meeting space on the first floor that can accommodate the large and routine programmatic meetings associated with this effort.

The Translational Imaging Center (TIC) and the Light Microscopy Imaging Center bring together advanced light and fluorescence microscopy systems, providing facilities and instruments for scientists engaged in translational research. The TIC is focused on developing new technologies for automating and providing advanced imaging technologies not yet commercially available.

Laboratory:

The laboratory/research space includes: Main laboratory (1151 SF); Developmental Microscope room (439 SF); Commercial Microscope rooms (2 rooms: 382 SF total); Microscope Rooms (2 rooms: 210 SF total); Imaging corridor (287 SF); Embryology room (250 SF)

Shared in the same wing of 4th floor: Chemical room (212 SF); Cell Culture room, (211 SF); Equipment room (182 SF), Gel Doc room (148 SF); Equipment corridors (407 SF and 265 SF); Cold room (133 SF), CO2 manifold (34 SF)

Microscope rooms (600 SF); Fish room (360 SF); zebrafish facility that contains 15-rack system from Aquaneering. Located at Ray R Irani Hall, 1050 Childs Way, adjacent to Michelson Hall.

Shared autoclave and glass washing facilities (262 SF) are available and shared among 6-8 wet-laboratory operations that reside on the 4th floor.

Animal:

Approved animal facilities for mice, fish and quail are provided in the vivarium section of Ray R Irani Hall (1050 Childs Way, adjacent to Michelson Hall), supervised by a full time veterinarian. Procedure space is provided near the animal holding space.

Computer Resources:

Computer equipment includes: Linux, Windows and Mac workstations, with conventional image processing and figure composition software. In addition, two major workstations are provided with Bitplane's Imaris software package for 3D and 4D image analysis and rendering.

The TIC Imaging Core utilizes two main data servers as a link between the imaging instruments and the analysis workstations. The servers function as a both cloud data-storage and -transfer from the Core's various acquisition and analysis workstations to the final users, within or outside the university.

The first server is built on the FreeNAS operating system which is based on FreeBSD and OpenZFS in order to secure and serve our users' files. The server is kept and managed onsite with a current maximum storage of 150TB and an Ethernet connection of 1Gbe. Both storage capacity and speeds are further upgradable depending on necessity. Files are accessible through SSH, FTPS, SFTP, and SMB protocols, allowing for ease of access while preventing any unauthorized usage. Backups are regularly performed and stored on a separately managed server in order to prevent any loss of data due to any technical malfunctions.

Our second server is managed by the University of Southern California's Dornsife Technology Services and housed at the university's data center. This server has a current maximum capacity of approximately 140TB with an Ethernet connection of 10Gbe. The system is designed to allow for further upgrades to both storage

capacity and speed when necessary. Files are accessible through SMB protocols on the USC networks or by connecting through VPN.

Office:

Advanced Light Microscopy Core office (100 SF); Imaging Analysis office (156 SF); Technical staff, Postdoc, Students offices (660 SF); PI offices (2 offices: 273 SF total); Administrative Staff offices (2 rooms; 242 SF total)

Shared Office support (104 SF); Shared Conference room (267 SF)

Shared: Michelson Hall has several shared/community spaces that tenant research groups have access to including: Conference (10 rooms; 1600 SF; 969 SF; 184 SF; 134 SF; 303 SF; 363 SF; 431 SF; 401 SF; 196 SF and 154 SF); Circulation/Workspace and kitchen (6 rooms; 3742 SF; 224 SF; 4532 SF; 262 SF; 3456 SF and 230 SF). Each of these spaces is equipped with secure wifi network connections and large touch-screen monitors for data sharing and collaboration.

Other:

The USC has Core Facilities including: Center for Electron Microscopy and Microanalysis; Chemistry NMR Facility; High Performance Computing Center; Biostatistics Core; Proteomics Core Facility; Flow Cytometry Core; Cell and Tissue Imaging Core; HTP Sequencing Core; Mass Spectroscopy; Resources Department; Glasswashing Facilities; Machine Shop Facilities; Supply Center; and X-Ray Crystallography Facility.