

**Shared Resource Overview** Sanford Burnham Prebys Medical Discovery Institute in La Jolla has an extensive Shared Resource system with 18 core facilities. Their primary mission is to provide advanced technology, expertise, and instrumentation to investigators that may not be easily acquired by individual laboratories. The cores, staffed by technical experts, offer high quality interactive services that provide not only cost-effective sample analysis, but also assistance in experimental design, data analysis, and grant or manuscript preparation. Many of the cores offer a choice of full service, or investigator training on their advanced instrumentation for independent use. Most cores facilities can also provide expert services for outside non-profit and for-profit investigators. If you have access to Sanford Burnham Prebys intranet, detailed information on each core is available there. From outside the institute, summary and contact information for each core is accessible at: <http://www.sbpdiscovery.org/technology/sr/Pages/Home.aspx>

## Animal Resources

**Animal Facility** – A 24,000 sq ft AAALAC accredited facility that houses over 10,000 cages of mice in ventilated racks, providing full husbandry with breeding, weaning, and tail samples. The facility also provides care for a small number of rats and frogs, and has a separate BSL2 mouse facility. Many procedures can be performed by facility staff, including injections (SC, IP, IV), tumor measurements, blood collections, and surgical assistance. Mouse Reproductive Services service supports re-derivation and cryopreservation, while the creation of knockout or transgenic mice is being done under special agreement at the UCSD Moores Cancer Center transgenic core and the Salk Institute Transgenic Core.

**Animal Imaging and Analysis** – Imaging tools include LiCor Imager Pearl Impulse System for *in vivo* near infra-red fluorescence, bioluminescence and fluorescence (PE/Xenogen IVIS Spectrum), high frequency ultrasound (VisualSonics Vevo 770), and X-ray (Faxitron MX-20). Additional imaging capabilities including PET/SPECT/CT and MRI are available at the nearby Sanford Consortium for Regenerative Medicine building. A variety of widely used tumor cell lines (breast, prostate, lung, colorectal, ovarian, cervical, and melanoma) labeled with luciferase are available for xenograft tumor growth and metastasis studies. Analytical services support complete blood cell counts (CBC) and analysis of serum components revealing metabolic or organ stress, from small samples of mouse blood. **The Tumor Analysis** service assists with *in vivo* tumor studies, with injection or surgeries for cell introduction, imaging-based tumor measurements, anti-tumor compound dosing and efficacy testing, and derivation of cell cultures from patient-derived xenograft tumors.

**Additional Cardiometabolic Phenotyping analyses on** mice and rats can be performed at the Lake Nona site.

**Model Organisms** – The facility provides the infrastructure for the maintenance and analysis of *Drosophila* and *C. elegans*. The core provides advanced microscopy tools such as a Leica MZ16F fluorescence dissecting microscope, a Zeiss.M1 time-lapse microscope, and an Apotome Optical Sectioning microscope, as well as microinjection tools.

## Cell Analysis and Histopathology

**Cell Imaging** – The core houses a wide variety of microscopes, and provides investigator training and use of the instruments, as well as full-service imaging. Facility microscopes include six advanced fluorescence microscopes, three additional confocal systems (a multiphoton Zeiss LSM-710 NLO system, an Olympus FluoView 1000, and a Yokagawa Spinning Disk system). Sophisticated systems for FRET, Calcium imaging, and laser TIRF are also available. The microscopes are integrated with advanced image capture systems and analytical software, and a number are equipped with environmental chambers for extended live cell confocal analysis. TEM and SEM are available at the nearby Salk Biophotonics facility.

**Histopathology** – The facility generates slides with frozen or fixed tissue sections and processes them with various stains and antibodies, also providing expertise in pathology and tissue microarray analysis. Leica equipment (ST5010 and BOND-RX) support automated H&E and IHC staining. Leica/Aperio ScanScope AT2 and FL systems enable high resolution scanning, quantitative and morphometric analysis, digital archiving, and electronic distribution and access of standard and fluorescently stained histology slides. A Laser capture microscope system (MMI CellCut) facilitates isolation and molecular analysis of specific tissues and individual cells.

**Flow Cytometry** – The facility has five analytical flow cytometers (BD LSRFortessa and Fortessa X20, BD FACS Canto, BD Calibur, Acea NovoCyte 3000) analyzing up to 14 colors. There are two advanced BD FACS Aria

cell sorters with up to 13-color capability – both housed in biosafety enclosures, as is the Fortessa X20 analyzer. The Core also has an imaging flow cytometer (Amnis ImageStreamX MarkII) with up to 10 colors. A Muse Cell Analyzer also provides easy-to-use 2-color flow analysis. Cell sorting is performed by expert Core staff, with analytical cytometry available either as a service or for use by trained investigators.

**Stem Cells** – The Institutional Stem Cell Core has been discontinued, with the functions of the former Core now split into two separate operations. **iPSCs:** The generation and characterization of induced Pluripotent Stem Cells (iPSCs) is now being performed on a collaborative basis for both internal and external investigators with the Snyder lab. For information regarding iPSC projects, contact Dr. Evan Snyder. **Shared Laboratory:** A well-equipped shared laboratory dedicated to the culture and analysis of stem cells is available to Sanford Burnham Prebys investigators. This shared stem cell lab is managed by Chun-Teng Huang, who also manages the adjacent Viral Vectors Core.

## Structural Biology

**X-ray Crystallography** – The facility is equipped with a Rigaku FR-E SuperBright X-ray generator and two independent detectors. High throughput crystallization studies are supported by a Phoenix microdrop liquid handling system and Formulatrix incubators with automated image analysis for detecting crystal growth.

**NMR** – The facility has two 600 MHz Bruker instruments equipped with cryoprobes, with one of these also equipped with a sample changer. There are also two Bruker 500MHz instruments - one equipped with a sample changer and a probe for solution analysis, the other a wide bore probe for solid-state analysis. A highly automated JEOL 400 MHz NMR with a sample changer supports small molecule analysis.

**Protein Analysis** – The core focuses on analytical services for proteins by Isothermal Titration Calorimetry, (Two MicroCal ITC200 instruments), MicroScale Thermophoresis (Monolith NT.115), Differential Scanning Calorimetry (DSC), fluorescence spectroscopy, and analytical ultracentrifugation (AUC).

## Genomics Technologies

**Next Gen Sequencing** The facility provides high throughput 3<sup>rd</sup> generation DNA sequencing using a NextSeq 500 and NeoPrep automation (Illumina), as well as Ion Proton and Ion Torrent PGM (Life Technologies) instruments coupled with 2 Ion OneTouch and 1 Ion Chef. These instruments provide rapid throughput and up to 120 Gb of sequence per run, supporting analysis of mutational hotspots as well as ChIP, transcriptome, and exome sequencing. RNA quality analysis is performed utilizing Bioanalyzer, NanoDrop, and Qubit instruments.

**Other Genomics Services** RNA profiling services with a NanoString nCounter are also offered through the Core. Full-service quantitative real-time PCR analysis (Stratagene MX3000, Roche LC480 and LC96), including SYBR green primer design and validation, is provided. STR-based cell line authentication and mycoplasma testing services are also provided. Access is provided to shared instruments including: Phosphorimager/fluorescent scanner (Fuji FLA-5100 with 4 lasers), Cooled CCD imaging systems (Bio-Rad ChemiDoc, Alpha Innotech FluorChem), Near IR imagers (LI-COR), Microplate luminometer, Real-time PCR Instruments (Stratagene, AB, Roche), and Nanodrop spectrophotometers.

**Functional Genomics** – The facility provides transfection testing, assay development, siRNA libraries, and high throughput screening service for RNAi-based analysis. The core has a comprehensive human genome-wide (18,301 genes) modified Dharmacon ONTARGET-Plus siRNA library, in both pooled format and 4 individual siRNAs per target. Additional libraries include focused siRNAs targeting human Kinases, Proteases, Ubiquitination-associated genes, and Cancer signaling. Also available are libraries of genome-wide miRNA mimics and antagonists, each targeting 988 miRNAs, allowing the functional analysis of relevant miRNAs. The core has a cDNA expression library of 2,400 ORFs, and screening technologies utilizing viral-mediated shRNA vectors available through the Viral Vector core and cDNA expression constructs are being developed.

**Viral Vectors** – Starting with vector plasmid DNA, the core provides custom packaging, concentration, and titration of lentiviral particles. Several ready-to-use lentiviral supernatants are available to fluorescently mark cells. The facility also provides vector backbones and assistance in creating effective constructs.

## Proteomics and Metabolomics

**Proteomics facility** – This facility provides protein identification from IP enriched material, or complex samples. Additionally, analysis of post-translational modifications, peptide mapping and comparative proteomics using mass tagging or label-free analysis can be performed. Following initial digestion and sample preparation utilizing a robotic Bravo AssayMap system, samples are separated by 1D or 2D UHPCL (EASY nLC 1200, and 2D NanoAcquity) and then analyzed by mass spectrometry. Core mass spectrometry instruments include two state-of-the-art Thermo Orbitrap Fusion Lumos Tribrid systems, an Orbitrap Velos Elite, Thermo Q-Exactive Plus, and a Thermo Quantiva. There is also a Bruker Autoflex MALDI-TOF-TOF. These instruments enable analysis targeted or complex (whole proteome) samples as well as phosphoproteomics and global characterization of other post-translational modifications. Data analysis is via a pipeline comprised by a number of open-source tools for protein identification, statistical and functional analyses of large proteomic datasets.

**Cancer Metabolism** – The scientific focus of the core is to investigate the role of metabolism in cancer on both the cellular and organismal level, combining *in vitro* and *in vivo* analysis. To that effect, the facility provides measurement of metabolites in cells, tissue samples, plasma and media. A GC-MS is available for broad metabolic flux analysis using stable isotope labeling. A YSI 2950 Analyzer allows for focused analysis of specific metabolites, and a SeahorseXFp for real-time measurement of mitochondrial respiration and glycolysis. Lastly, a Shimadzu HPLC is available for the measurement of metabolites not generally accessible by GC/MS.

## Informatics

**Informatics and Data Management** – The Bioinformatics core with PhD-level staff provides assistance in data analysis and management for large projects, and in implementing or developing specific bioinformatics tools and pipelines. This includes analysis of large datasets generated in the Shared Resources (e.g., DNA sequence, Microarray or Proteomic data) or in investigator laboratories, as well as data comparison with other available databases. A biostatistician provides expert statistical support. High throughput (next-gen) DNA sequence is supported utilizing a variety of software packages. The facility assists with Systems Biology and Pathway Analysis, utilizing tools such as Ingenuity Pathways, NextBio, and GeneGo MetaCore. A growing area of focus is systems biology integrating analysis across multiple data types (data generated in-house or mined), such as genomics, proteomics, and metabolomics.

## Chemical Biology and Drug Discovery

*These cores are part of the Conrad Prebys Center for Chemical Genomics (CPCCG)*

**High Throughput Assay Development** – The facility provides assistance in HTS-compatible assay development (384 or 1536 wells), including assay optimization, and miniaturization. The core staff is experienced in a wide variety of assay types for biochemical or cell-based assays, enabling selection and development of assays most suitable to each particular project, with an emphasis on optimal assay sensitivity in identification of hits. The core also provides support for Structure-Activity Relationship (SAR) studies aimed at characterization and optimization of hits obtained in primary screening. Assistance in preparing screening-related grants is also provided.

**Chemical Libraries & Screening** – The facility provides access to small molecule libraries (the 320K Sanford Burnham Prebys and the 350K NIH collections, as well as smaller collections of drug-like, bioactive, and other focused libraries), along with the robotics, compounds, instrumentation, and expertise to perform the screens, typically in 1536 or 384 well format. The core is equipped with 3 integrated robotic HTS systems, their centerpiece is a High Res Biosolutions POD system with a Staubli arm equipped for integrated biochemical or cell-based screening. Core robotics can screen up to 350,000 wells per day. Major equipment in the core includes plate readers such as the PE ViewLux, Hamamatsu FDSS 7000, PE Envision, and BMG Pherastar, liquid handling workstations include two Labcyte Echo acoustic pipettors (including one that is integrated into a stand-alone LabCytte Access robotic workstation) and a V11 Bravo as well as the two Beckman Coulter FX core systems. Two BSL-2 labs support tissue culture and cell-based screening in the core. Instrumentation for High Content Screening is described below. The system is controlled by the same Cellario software as in the Lake Nona Core, facilitating smooth transfer of assays developed in La Jolla for large-scale screening in Lake Nona.

**High Content Screening** – The facility supports assay development, screening, and data analysis for high content screens, where the readout is typically images from high-throughput microscopy. The Core's flagship instrument is a PerkinElmer Opera Phenix with confocal imaging and an integrated robotic plate loader. The facility also has a PerkinElmer Evotec Opera, an open frame Vala IC-200 equipped for live cell screening, and a Cytellect Celigo Cytometer.

**Cell-based Disease Modeling and Screening** – This facility supports development of cell based disease models for screening and testing small molecules and drugs, and specializes in culture, scaling, and directed differentiation of human embryonic and induced pluripotent stem cells. Resources and expertise are provided to facilitate development of stem cell-based assays and patient-specific disease models in screenable formats, supporting HTS/HCS analysis.

**Cheminformatics** – The Cheminformatics facility provides informatics support for analyzing screening data, SAR follow-up of hits, and *in silico* screening through docking and other informatics approaches. The core also supports compound registration, inventory, HTS data collection and analysis, using the Cheminnovation CBIS software. This constantly updated database from reputable commercial compound vendors currently contains over 12 millions compounds which properties can be filtered with user-built settings

**Medicinal Chemistry** – The core provides researchers with medicinal chemistry expertise for follow-up of screening hits and library design. The core is equipped for synthetic chemistry functions from milligram to multi-gram scale, with a wide array of equipment to synthesize and modify organic molecules for both initial lead generation and subsequent structure-activity relationship (SAR) studies. Parallel synthesis of small molecule libraries and the synthesis of natural product analogues are also supported. Equipment includes automated Syrris AFRICA microfluidic synthesizers, advanced liquid chromatography and mass spectrometry systems, and access to 400MHz and 500 MHz NMR spectrometers for further characterization of small molecules.