USC’s Plan for Science and Technology Facilities

Creating the Foundation for Transformative Research

Updated September 28, 2015

Prepared by the Provost’s Office of Research in cooperation with the
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Dornsife College of Letters, Arts and Sciences
Keck School of Medicine
Ostrow School of Dentistry
Viterbi School of Engineering
School of Pharmacy

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Scientific and technological discovery promises to help people live longer and healthier lives, to improve the sustainability of the environment and the earth's resources, to provide resilience to natural disasters, and to improve the quality of life for people around the globe.

The University of Southern California is positioned to be a leader in this effort. But to do so, USC needs to create and expand its centers of excellence for fundamental scientific and technological research, providing the precision instruments that our faculty and students need to design drugs and other compounds at the molecular scale with nanoscale delivery mechanisms, to study the mechanisms that underlie the behavior of cells and organisms, to realize the goal of materials by design, and to analyze how massively complex systems interact and change over time.

USC's Plan for Science and Technology (S&T) Facilities will provide the foundation by which the university can dramatically change the trajectory of its scientific and technological research. As emphasized in USC's Strategic Vision: we must be innovative in creating the conditions for success for our faculty and students; we must be imaginative in building new types of research facilities; we must increase our commitment to translational research, creative work and practice in order to address grand challenges. The Plan for S&T Facilities creates the resources to make this happen – positioning USC to be a leader in research that addresses society's needs through fundamental research on living systems, the environment and engineered products.

The plan aims to create an integrated set of facilities that span the University Park and Health Science campuses, ensuring that faculty, students and staff have access to facilities on either campus, no matter where their labs are located. Each of the Centers of Excellence described in this document is committed to providing tools and services to support sharing of facilities across the entire university.

The Foundation for Science and Technology

USC's leadership in science and technology must be built on a foundation of outstanding facilities that enable our students and faculty to perform cutting-edge research and that attract a new and diverse faculty to the university. These facilities must provide capabilities to:

- Create data, images, models and simulations that reveal how cells, organisms and materials behave, with linkages from the scale of individual atoms and molecules through the nano- and micro-scales to real world systems.
- Decipher the mechanisms of living systems, their evolution and aging, as well as disease models, through examination of DNA, epigenetics, proteins, lipid membranes, biological markers, organ systems and fully integrated organisms.
- Precision engineer and fabricate new substances, nanostructures and devices within highly controlled environments.
- Build scientific libraries that facilitate collaborative science.
- Provide the computational backbone for scientific analyses.

We now illustrate some of the opportunities for building the next generation of such facilities at USC.

1. Revealing the Behavior of Molecules, Organisms and the Composition of Matter

Dynamic imaging and microscopy are revolutionizing all aspects of science and technology, providing the ability to create detailed pictures of how brains function, how cells behave and how they respond to stimuli, and how materials are structured down to the level of molecules and atoms. They also enable understanding at the small scale of the transport processes of momentum, mass and heat. Through "spectroscopy," we are able to generate data that explain physical, chemical, and structural properties of atoms, molecules and nanostructures. These insights are helping USC understand how materials and complex physiological systems function, so that we can engineer new materials, devices and medical therapies.

Centers of Excellence

- **Microscopy and Analysis**
- **Cell and Tissue Imaging**
- **Brain Imaging**
- **Molecular Imaging**
- **Molecular Characterization**
- **Single Cell Technology**

2. Deciphering the Codes of Life

Systems biology and "omic" technology (genomics, epigenetics, proteomics, metabolomics) will illuminate the interactions between the components of biological systems, and how these interactions give rise to the function and behavior of living systems. DNA sequencing, including the ability to sequence the whole genome, is enabling scientists to discover the pathways of evolution, how human development depends on interactions with their environment, and how drugs and other therapies can be personalized for each individual. Proteomics helps USC investigators assess markers for the presence and interactions of proteins, how diseases are expressed in individual patients and how selected proteins can be targeted to treat and diagnose disease. Chemical biology harnesses the intrinsic biosynthetic power of diverse living organisms for clean synthesis of novel therapeutic agents and diagnostic tools. These and other platform technologies will help USC scientists conduct research that reveals the underlying structures and processes of life.

Centers of Excellence

- **Therapeutic Discovery & Development**
- **Genomics & Personalized Medicine**
- **Proteomics & Biomarkers**
- **Peptide and Protein Engineering**
- **Nano BioPhysics**

3. Precision Engineering of New Substances and Devices

Research on the next generation of engineered products – digital devices, nano-fabricated compounds and cells, and innovative materials –requires highly controlled environments, often in clean rooms. This demands precision tools and equipment, highly trained staff, and facilities that fully satisfy requirements for good manufacturing practice (GMP). Through technological advances, manufacturing is being revolutionized. USC can use these new facilities to design and build new integrated circuits for faster and more compact computers, devices that efficiently convert sunlight into electricity or fuel, compounds that are precisely targeted to treat disease and materials that can be used to create precision medical devices.

Centers of Excellence

- **Nanofabrication**
- **Cell and Tissue Engineering**

4. Science Library of the Future

The science library of the future will not be limited to the written word. Instead, it will bring together research products of all sorts, including moving images, data sets, software and tools, and clinical samples in addition to books and articles. USC is creating libraries that permit our faculty and students to share research products of all forms, so that our scientific research can progress more rapidly and with greater impact. USC is also positioned to become a leader in the creation of digital representations of physical collections, including tissues and artifacts that can be studied by scholars everywhere.

Centers of Excellence

- **Digital Repository for Open Science**
- **Biobanking and Disease Discovery**

5. Computing of the Future

Research at USC has had a tremendous impact on computers, software and communication, for instance creating the domain name system that defines all world-wide-web addresses. All of these computational tools are changing how science is conducted, enabling massive data sets to be analyzed and enabling scientists to work within networks of collaborators, as well as to connect physical entities and devices. To stay at the forefront of this effort, USC needs to continually grow its high performance computing capabilities, as well as develop new technologies that answer the biggest questions facing the scientific community. In addition, the approaching end of Moore's law requires research into extending the power of computing and communications by changing the paradigms for computing, allowing us to answer new and more complex questions.

Centers of Excellence

- **High Performance Computing and Communications**
- **Quantum Information Science and Technology**

What USC's Centers Need

Each of USC's Centers of Excellence for science needs resources for:

- Acquisition of the most modern equipment that will keep USC at the leading edge of research.
- Staffing each center with expert researchers, able to extract the best performance from the equipment and to train newcomers in best practices.
- Endowment that supports: costs of operation (including staffing, maintenance, and equipment upgrades) as well as pilot research studies to initiate new investigations.
- Renovation or construction of new scientific buildings and facilities.
- Recruitment of transformative faculty to complement talents already at USC.

Additional information can be obtained from the Office of Research (213-740-6709) or from these USC schools:

- **Ostrow School of Dentistry**
- **Viterbi School of Engineering**
- **Davis School of Gerontology**
- **Dornsife College of Letters, Arts and Sciences**
- **Keck School of Medicine**
- **School of Pharmacy**

Information on existing core facilities can be found at http://research.usc.edu/facilities/

Centers of Excellence for Revealing the Behavior of Molecules, Organisms and the Composition of Matter

Center of Excellence for Microscopy and Analysis

Research: As scientists continue to work with structures at near-atomic and even atomic scales, tools to visualize and analyze these nano-structures have become essential to new discoveries. Recent technological advances in electron and light microscopy such as aberration correction/super resolution, high collection efficiency energy dispersive spectroscopy (EDS), and high speed electron energy loss spectroscopy (EELS) have opened up new research paths, providing insights into physical, chemical and biological phenomena in diverse domains of science.

Impact: Electron and light microscopes have fostered cross-disciplinary research at USC, leading to a convergence of man-made nanostructures (e.g., sensors and particles designed at the atomic scale) with biological molecules (e.g., lipid proteins and blood components). Continued leadership will position USC to conduct innovative research in energy (solar devices, fuel cells, storage and lighting), biomedicine (drugs, sensors, bio-surfaces and protein interactions), and materials (composites, multi-functional, and high-temperature). The Center of Excellence for Microscopy and Analysis (CEMMA), based on the University Park Campus (UPC), supports all of these research areas.

Existing Facilities: USC supports research in engineering and the physical and life sciences with a suite of modern instruments: a TEM (transmission electron microscope) with cutting-edge electron energy loss spectroscopy capable of spectroscopic imaging, a high resolution SEM (scanning electron microscope), an SEM tailored for *in situ* experiments, a combination SEM/FIB (focused ion beam) instrument for progressive sectioning and site-specific TEM sample preparation, a super-resolution light microscope, and an XPS (x-ray photoelectron spectroscopy) instrument for surface analysis, as well as technical staff support. The SEMs provide imaging of surface topography and structure, and the TEM provides angstrom resolution of internal structure of suitably thinned materials. In addition, the SEMs, XPS, and TEM provide complementary spectroscopies that enable both compositional and chemical analysis of a wide range of materials. USC purchased these instruments in the past five years.

Future Growth: CEMMA will be moved to the Michelson Center for Convergent Bioscience, within a facility designed to maximize the resolution of precision microscopes. The new facility will need to add cutting-edge instruments in three priority areas:

- **Angstrom resolution electron microscopy**. Correction of aberrations in electron microscopes has led to a factor-of-two improvement in resolution, making it feasible to obtain images with sub-angstrom resolution, leading to improvements in beam current densities, which in turn have increased collection efficiencies of EDS (energy dispersive spectroscopy) and EELS (electron energy loss spectroscopy) such that spectroscopic imaging can be accomplished at angstrom resolution. Further improvements have opened up the study of phonons at the nano-meter scale.
- **State-of-the-art Biomedical Imaging**. Titan Krios' cryo-based technology and stability permits semi-automated applications, including 2D electron crystallography, single particle analysis, cryo electron microscopy, and dual-axis cellular tomography of frozen hydrated cell organelles and cells.
- **High resolution FIB microscopy**. FIB instruments are powerful tools for milling materials at the nano scale. The resolution of FIBs has reached sub-nanometer resolution with noble gas ions. Enhanced FIB resolution translates to improved TEM sample preparation, superior SEM analysis, and more precise placement of electrical contacts using ion-beam deposition techniques.
- In coordination with the COE in Molecular Imaging, micro-CT (computed tomography) is a fourth possibility for future investment.

Center of Excellence in Cell & Tissue Imaging

Research: The Center of Excellence in Cell & Tissue Imaging on the Health Science Campus provides instrumentation and collaborative expertise for biomedical and engineering research aimed at improving human health. The Center offers state-of-the-art technologies to faculty whose interests range from the biological sciences to materials science and chemical engineering. The Center is used to investigate the normal physiological processes of cells and tissues, and how they go awry in disease. In particular, the center supports direct observation of cells and tissues – either as they function in the living organism, or within preserved specimens.

Impact: Research supported by the Center is leading to:

- better understanding of the miracle of the human brain, the normal functioning of the body's organs, and the nature of wellness;
- discovery of disease mechanisms and biomarkers;
- characterization of dangerous emerging pathogens and how they infect the body, how they cause disease, and how this may be prevented;
- novel pharmaceuticals and biomedical devices;
- application of stem cells and regenerative medicine to cure degenerative disorders.

The Center is critical to ongoing research efforts such as the "California Project to Cure Blindness" led by investigators jointly affiliated with the Keck School of Medicine and the Viterbi School of Engineering, sponsored by a $16 million grant from the California Institute for Regenerative Medicine, which is developing a stem cell therapeutic to treat macular degeneration.

Existing Facilities: The Center is sponsored by the National Institutes of Health core grant to the USC Norris Comprehensive Cancer Center. Major instrumentation includes: (1) laser scanning confocal microscopy (2) multiphoton laser scanning confocal microscopy (Zeiss LSM510), (3) spinning disk confocal microscopy (PerkinElmer Ultraviewer spinning disk confocal), (4) transmission electron microscopy (JEOL JEM 2100 LaB6), (5) scanning electron microscopy (JEOL JSM/6390LV), (6) fluorescence microscopy, (7) quantitation of immunocytochemical procedures (Leica and Olympus Microscopes), and (8) single molecule super-resolution fluorescence microscope system (Nikon N-Storm). Other equipment includes a vacuum evaporator, sputter coater, critical point dryer, two print processors, two dissecting microscopes, a tissue cryostat, and a tissue chopper. Additional resources for intravital imaging of living, intact organs (kidney, liver, pancreas, lung, skin, eye, brain, etc.) in mice and rats are available in the specialized Multi-photon Microscopy Core facility located in the Zilkha Neurogenetic Institute (Leica SP5). Aiding in the utility of dynamic cell-focused imaging approaches, both the Keck School and the School of Pharmacy offer state-of-the-art histology laboratories.

Future Growth: The Center must remain up-to-date with state-of-the-art instrumentation to support research on the cutting edge, including a super-resolution confocal microscope and (in coordination with the Single Cell COE) an upgraded laser capture microdissection microscope. In addition, there is a need for more sensitive multi-laser confocal microscopes to establish support for investigators across satellite facilities**.**

Center of Excellence in Brain Imaging

Research: Despite remarkable progress in the neurosciences, the workings of the human brain remain a considerable mystery. The knowledge that we lack is important for understanding what makes us human (the goal of cognitive neuroscience) and for the management of brain diseases (the goal of neurology, psychiatry, and allied medical specialties). Impairments of language or movement, emotions, memory, and decision-making lead to loss of independence and delay recovery from brain damage, resulting in cost and suffering, a problem that only gets worse as our population ages. The Center of Excellence in Brain Imaging marshals the strengths of USC's neuroscience community in an attack on the challenges posed by fundamental cognitive neuroscience and brain disease.

Impact: Biomedical imaging technologies are essential to elucidate the structure and operations of the normal human brain, and how it is disrupted by disease. Neuroimaging technologies make it possible to:

- identify brain circuitries that are associated with specific cognitive and motor functions;
- identify brain characteristics that provide clinicians with the power to distinguish among brain diseases with overlapping symptoms;
- identify biomarkers of conditions such as Alzheimer's disease and Parkinson's disease, so that preventive and therapeutic measures can be instituted;
- test in experimental systems the impact of new drugs for the treatment of diseases such as multiple sclerosis, and select the brain circuits most suitable as targets of treatment in schizophrenia, depression, autism and epilepsy;
- document brain changes related to recovery and response to drug and behavioral treatments.

The National Institutes of Health (NIH) has emphasized the incorporation of brain imaging into research endeavors, and is directing increasing resources into large-scale national imaging consortia. Strengthening neuroimaging would help establish USC's leadership in these areas. In addition, a revolutionary grid system developed at USC's Information Sciences Institute called Globus MEDICUS has enabled physician and scientists to exchange high-resolution medical images online. This is now being adapted for use in sharing of neuroimaging data, and will serve as a resource to the Center.

Existing Facilities: Key instrumentation already exists on the Health Sciences Campus within Keck Medicine and the Mark and Mary Stevens Neuroimaging and Informatics Institute (GE 3-Tesla brain scanner and other high-resolution research tools located within the Keck Hospital clinics and the 3-Tesla Siemens TIM Prisma MRI (magnetic resonance imaging), 128 RF (radio frequency) Channels and 7-Tesla Siemens TIM Terra actively shielded MRI, 32 RF Channels pending installation) and at the University Park Campus (with a Siemens 3-Tesla brain scanner and an adjoining EEG (electroencephalogram) laboratory at the Dana & David Dornsife Cognitive Neuroscience Imaging Center).

Future Growth: Additional instrumentation is needed to keep USC at the cutting edge:

- MR-PET (simultaneous magnetic resonance-positive emission tomography) Siemens mMR scanner;
- high density MEG (magnetoencephalography);

Other supporting instrumentation can be found in the COE in Molecular Imaging.

Center of Excellence in Molecular Imaging

Research: With the development of new techniques to acquire information it has become possible to "see" the internal structures of the human body at work without invasive surgery. The Center of Excellence in Molecular Imaging supports state-of-the-art instrumentation, technical services, and collaborative expertise in molecular imaging technologies for use by USC biomedical scientists, engineers, psychologists, and physicians. This Center synergizes with and provides essential resources to, the Center of Excellence in Brain Imaging.

Impact: Molecular imaging uses biological probes to image the living subject via means of sound (ultrasound), magnetism (MRI or magnetic resonance imaging), radioactivity (PET or positron emission tomography), or light (optical techniques of bioluminescence and fluorescence) as well as other emerging techniques. Research projects include:

- quantitative measurements of brain physiology and biochemistry in diseases and disorders such as Alzheimer's Disease and vascular dementia, Parkinson's Disease, stroke and epilepsy;
- novel imaging probes for diagnosis and early assessment of response to therapy in cancer;
- imaging probes to enhance delivering of therapeutic substances leveraging, advances in biotechnology, nanotechnology, and engineering;
- imaging to facilitate drug discovery and development by exploring the pharmacology, metabolism, and efficacy of parent drugs using labeled analogues.

Existing Facilities: The Center is comprised of three comprehensive sites on the Health Sciences Campus (HSC). HSC's Small Animal Imaging Laboratory instrumentation at the USC Molecular Imaging Center (MIC) includes: microCT**,** nanoCT, photoacoustics, microPET, high-Resolution ultrasound, and optical imaging. The HSC's Cyclotron and Radiochemistry Laboratories at MIC offers support for radiopharmaceutical development and production for molecular imaging studies. The center houses a state of the art GE PET trace 860 Cyclotron and ancillary equipment. HSC's Clinical PET Imaging Center houses a state-of-the-art Siemens PET-CT Biograph True Point scanner for whole body and brain tomography. The CT scanner is a 64 slice, offering diagnostic quality spiral CT imaging for image co-registration and attenuation correction and/or diagnostic evaluation.

Future Growth: Instrumentation needs include:

- new animal imaging instrumentation, also supporting the COE in Brain Imaging: high field preclinical MRI scanner (7-11T); preclinical PET/MR scanner; mobile high resolution ultrasound, optical/CT scanner; cryogen free preclinical MRI; preclinical nanoSPECT/CT, autoradiography imager, translational human PET/CT ;
- surgical support suite for animal prep for imaging procedures and large animal imaging;
- support suite for GLP (good laboratory practice) imaging;
- high precision hot cell manipulators;
- radiochemistry support synthesis modules for preparation of research radiotracers containing isotopes such as F-18, C-11, I-124, Cu-64 and Zr-89.

In addition, upgrades are needed in ancillary laboratory equipment (HPLC, MS, GC, etc.), high precision hot cell manipulator upgrades, IT hardware and software, high end imaging software and pneumatic tube transport system upgrade.

Center of Excellence for Molecular Characterization

Research: The Magnetic Resonance Spectroscopy Center provides nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR) instruments for interdisciplinary research spanning chemistry, chemical engineering, biology, pharmacology, medicine, and physics. Modern NMR and EPR instruments are needed to conduct research in most areas of basic and applied chemistry and biochemistry. Essential for fundamental research on the structure and interactions of molecules in solution, our existing NMR and EPR instrumentation complements our nearby X-ray diffractometers and our optical and mass spectrometry instruments.

Impact: NMR provides a dynamic view of proteins, useful for examining natively unfolded proteins and enzyme active sites. NMR can detect weak transient structural interactions, and it is useful for studying functionally important protein–protein and protein–ligand interactions, combining protein binding and dynamics with structural data. The center has been critical to recent discoveries in areas ranging from energy storage to translational drug discovery. Our goal now is to augment existing capabilities at USC with state-of-the-art equipment and facilities to create a center that would be the best in the nation, enabling advances in two key research areas: medicinal chemistry/chemical biology, and energy/nanoscience. The envisioned center will also support our effort to develop custom designed molecular and cellular vesicles for drug delivery.

Existing Facilities: Thanks to National Science Foundation and National Institutes of Health grants as well as university support, we have strengthened our NMR instrumentation with the addition of a 600 MHz, two 500 MHz and three 400 MHz NMR spectrometers, each equipped for a number of specialized structural measurements. Our EPR instrumentation is anchored on a NIH-funded pulsed EPR/electron-nuclear double resonance (ENDOR) spectrometer. This Bruker E580 FT/CW pulsed EPR platform is operated at X-band, and is capable of multiple-resonance measurements, such as pulse-ELDOR (Electron-Electron Double Resonance) for measuring nanometer distances between electron spin centers and pulse-ENDOR for measuring sub-nanometer distances via hyperfine interactions between electron and nuclear spins. A He liquefier and recovery system is being installed to protect our cryogenic instrument infrastructure from Liquid He supply disruption due to market fluctuations or a natural disaster.

Future Growth: Our vision incorporates the following additions to the center:

- modernized technical support and infrastructure for the instruments with broadened access to diverse users, strengthened staff support and enhanced student user training, including onsite cryogen regeneration (LN) and site renovation/maintenance;
- state-of-the-art EPR instrumentation that provides high frequency capabilities (S-, Q-, W-band and beyond) and also EPR imaging (L-band). Strengthened auxiliary capabilities in mass and optical spectroscopies;
- ultra high-field (750-900 MHz) NMR spectrometer that supports future advances in chemical biology, pharmacology and molecular medicine.

Center of Excellence in Single Cell Technology

Research: Individual cells can differ by size, protein levels, and expressed mRNA transcripts, even within homogeneous cell populations. Single-cell genomics and proteomics is the next frontier in molecular biology, offering unprecedented access to study how genetic variability and gene expression impacts on individual cells and cell types. Novel technologies and methods allow us to isolate and analyze the limited genetic material present within a single cell, enabling us to gain a whole-genome view of genetic variability and gene expression at single-cell level. This field of research is opening up developmental and disease biology. For example, this approach can identify distinct sub-populations of cells within a tumor and reveal how they contribute to cancer development. Single-cell sorts, laser-capture micro-dissection or microfluidic-mediated cell isolation are other new approaches to single-cell analysis. It is also possible to use intra-cellular flow cytometry to analyze cell internal proteins of interest using suitable antibodies. Other new techniques are on the horizon.

Impact: The impact on biomedicine of new single cell technologies is revolutionary. Previous gene expression studies related to disease have been based on tissue samples or blood specimens containing large numbers of heterogeneous cells, and thus reflect an average of cell properties. For example, the mechanisms that regulate the survival of circulating tumor cells can be pursued, allowing the biophysical factors implicated in the endurance of individual circulating tumor cells while in the blood stream and in their progression to metastatic disease to be defined. Fluid phase biopsies from epithelial cancers such as lung cancer can assess and model the physical attributes of these tumor cells over the course of the disease across various body compartments. In addition, this center will utilize highly sophisticated, quantitative physical science techniques to analyze patient samples in terms of cell size, mechanical properties and ultrastructural complexity. This unprecedented approach should deliver a rich database for further longitudinal statistical and mathematical analysis and yield much needed insight into the behavior, survival and destination of circulating tumor cells, which propagate metastatic cancers.

Existing Facilities: USC is already a leading institution for conducting single cell proteomics in translational clinical trials in oncology, with state-of-the-art rare cell identification (Epic Sciences), single cell genomics (Epic/CSHL with Jim Hicks) and single cell proteomics (Fluidigm) platforms. Leadership can be provided in the Bridge Institute and the Norris Cancer Center. In a unique partnership, USC is the only current Early Access Partner for Fluidigm in academia.

Future Growth: The COE will require high end infrastructure, expert staff and faculty leadership in rare cell identification, single cell genomics and single proteomics. Specific needs are to acquire:

- suite of genomic and cell culture platforms from Fluidigm and Illumina;
- single-cell sorters, laser-capture micro-dissection or microfluidic-mediated cell isolation in partnership with the flow cytometry core for upstream single cell capture;
- time-of-flight cytometry that combines mass spectrometry and flow cytometry and allows simultaneous detection of dozens of antigens in single cells;
- ability to “fingerprint” single cells in terms of the complement of genes expressed in it over time and, through advanced imaging technology, its evolution can be monitored in vivo as well as in vitro.

These capabilities should be completed by a partnership with clinical and biorepository infrastructure to leverage the diversity of patient populations along the translational continuum (bench to bedside and back) and translation of single cell research to clinical decision making through distinct setup of Research Use and CLIA (clinical laboratory) setup for laboratory developed tests.

Centers of Excellence for Deciphering the Codes of Life

Center of Excellence in Therapeutic Discovery and Development

Research: As early-stage drug development increasingly transitions from industry to academia, USC is focusing on the development of unique technologies to create novel biological and chemical therapeutics. Drug effectiveness will be optimized based on discoveries of molecular mechanisms and biological pathways of diseases and sophisticated targeting and encapsulation strategies. Such efforts are a key part of USC's biomedical research portfolio and a critical driver of translational research.

Impact: Development of more effective therapies for society's most pressing and unmet health challenges including obesity, infection, cancer, neurodegenerative and inflammatory diseases, by providing more effective, targeted approaches to therapeutic discovery and development.

Existing Facilities: The School of Pharmacy's Translational Research Laboratory features a range of medium- and high-throughput instruments covering molecular biology, cell and immunobiology, protein and nanoparticle and analytical applications. Additional shared facilities in the School of Pharmacy include computer modeling capabilities, mass spectrometers, Nuclear Magnetic Resonance equipment, as well as a Histology Laboratory, which provides services on tissue processing, sectioning and staining. These facilities enable researchers to perform experiments essential for drug discovery and development. Researchers can analyze biological outputs from experimental systems, enabling the rapid design and analysis of drug candidates to treat the gamut of human diseases. The provision of high-throughput DNA, protein, and metabolite analysis instruments enables the rapid investigation of the effect of candidate drugs on animal and human subjects while high-end computer modeling provides for the rapid design and development of drug candidates at the molecular level. Together with instrumentation for molecular and cellular analysis within Keck, USC investigators design, synthesize, and test candidate drugs and delivery vehicles on a variety of biological systems, from *in vitro* testing of drug effects on cell cultures, to *in vivo* analysis in animal models, through to clinical samples from human subjects.

Future Growth: To excel in drug discovery and development, USC will need to invest in these key facilities:

- state-of-the-art software systems to upgrade the computational chemistry facilities to enhance molecular modeling and cheminformatics, improving the design and development of candidate drugs, and leading to more specific and less toxic therapeutic agents;
- expansion of our preparative capabilities for high-throughput generation and analysis of diverse chemical libraries and molecular arrays for the identification and optimization of new drug candidates, representing an important strategic move to expand our efforts in drug discovery;
- new capabilities for the production and purification of larger quantities of candidate drugs while retaining quality. Establishment of a GLP facility will be one of our primary goals. A GMP (good manufacturing practice) facility will be considered for the long-term plan for the translation of drug discovery into clinical trials. Pipelines and process will be established for feeding candidate drugs into GLP partner facilities and for transition of these agents into Clinical Trials Units (CTUs), administered by the SC-CTSI.

Center of Excellence in Genomics & Personalized Medicine

PLAN IS UNDER DEVELOPMENT

Center of Excellence in Proteomics & Biomarkers

Research: DNA sequence information in the "genome" (or genes) is copied into RNA transcripts, which are then translated into proteins within the cell. Proteins are the building blocks of living organisms, as well as molecular machines that operate cellular functions. The Center of Excellence in Proteomics and Biomarkers provides high-sensitivity and high-resolution mass spectrometry for protein analysis. A major goal is to expand multidisciplinary research and education that utilize mass spectrometry and other proteomics technologies to tackle complex biological and medical problems.

Impact: Analogous to the genome, the "proteome" is the entire complement of proteins, including the modifications made to a particular set of proteins, produced by an organism or system. This will vary with time and distinct requirements, or stresses, that a cell or organism undergoes. A biomarker is a substance used as an indicator or "proxy" of a biological state. This can be a protein or another type of molecule. In medicine, a biomarker correlates with the risk or progression of a disease, or with the susceptibility of the disease to a given treatment. Protein biomarkers are often used in clinical trials, where they are derived from bodily fluids that are easily accessible for analysis.

Existing Facilities: The Center is located on the Health Science Campus, managed and supported by the Keck School of Medicine. Major instrumentation includes:

- Q Exactive™ Hybrid Quadrupole-Orbitrap Mass Spectrometer coupled with EASY-nLC 1000 Liquid Chromatography, one of the most advanced LC-MS/MS system for proteomics profiling and biomarker discovery and quantitation;
- Eksigent NanoLC-2D, a fully automated 2-dimensional chromatography system ideal for whole proteome profiling, low abundance protein identification, and post translational modification;
- ThermoElectron Finnigan LTQ, a linear ion trap mass spectrometer equipped with an electrospray ionization source;
- Thermo Scientific LTQ Orbitrap XL ETD, an instrument for proteomics analyses: It combines three different and complementary fragmentation techniques with the proven benefits of Orbitrap™ technology.

Future Growth: Expansion of the Center should occur by:

- upgrading the current Eksigent NanoLC-2D, LTQ Orbitrap XL ETD, and LTQ;
- acquiring automated sample preparation and handling instruments;
- creating a bioinformatics infrastructure;
- adding the ability to assess protein post translational modification as well as lipidomics, glycomics, and small molecule assessment through the Orbitrap Fusion Mass Spectrometer.

Center of Excellence for Peptide & Protein Engineering (CPPE)

Research: USC's center for Peptide and Protein Engineering provides new, highly specific, engineered peptide and protein ligands in the areas of basic biology, imaging, diagnostics, and therapy. Key goals include provision of new polypeptides to: 1) assist structural biology and therapeutic studies of GPCRs (G protein coupled receptors) and 2) imaging and trafficking of proteins and nucleic acids in neurons.

Impact: High quality, engineered, molecular scale tools can support visualizing, understanding, and controlling biological systems. This center will use new technology developed to generate peptide and protein tools—providing a means to initiate cross-cutting collaborations and explore new areas of research at the interface of medicine, engineering, and science. The impact of this center is to improve fundamental knowledge of living systems by providing, 1) new tools and approaches for analysis of disease and health, 2) leads for therapeutic development, and 3) intellectual property, by generating patented methods and compositions of matter.

Existing Facilities: Existing facilities are housed within the Viterbi School of Engineering and leverage the technology and infrastructure in the Roberts laboratory. The facility provides fast protein liquid chromatography (FPLC), high performance liquid chromatography, peptide synthesizer, scintillation counter, and gel electrophoresis capabilities.

Future Growth: Short term goals include acquisition of:

- integrated high-performance liquid chromatography system and electrospray mass spectrometer (HPLCMS);
- second FPLC, and a magnetic bead-handling device.

In the longer term, the center is pursuing the development of innovative microfluidic technologies that should allow the increase of protein design by ten-fold or more.

Center of Excellence in NanoBiophysics

Research: The Center of Excellence in NanoBiophysics supports faculty and students across the university in the study of molecular nano-assembly, structures and functions. Housed in the Dornsife College, the center is used by research programs in structural biology, nanotechnology, nanomedicine, molecular biology, biochemistry, and materials sciences. While the scope of research supported by the center is wide and diverse, the majority of the activity focuses on fundamental problems of nanobiology, structural biology, and molecular medicine. For example, the core has supported studies that examine biomolecule and drug interactions, by determining X-ray atomic structures, characterizing the thermodynamics and kinetics, and understanding the nanoscale molecular assembly and disassembly.

Impact: The Center aims to contribute to the discovery of new drugs that can be used to treat cancer and other disease, as well as to understand the basic principles governing cellular signaling pathways. The center provides powerful technology for basic and medical sciences, and offers ample collaborative opportunities between scientists and clinicians. Its work is highlighted in publications in *Nature*, *Cell*, the *Proceedings of the National Academy of Sciences* and others, which has helped increase USC's academic prestige and visibility.

Existing Facilities: The center features two core facilities. The NanoBiophysics Core has a range of instruments including: a Biacore T100, a DLS System (Wyatt Technologies), a Multitask Spectrofluorometer, two Atomic Force Microscopes, and a CD Spectrometer. The X-Ray Crystallographic Core has an X-ray generator (007), two X-ray diffraction detectors, a multi-task screening robot, and high-power computer system for simulation and modeling. The center core facility is located on the University Park Campus, and is led by a headed by a renowned USC Professor who is well-recognized in the fields of biophysical, biochemical, and structural molecular biology. Recently funded acquisitions include a Microplate Reader Synergy H4, a Microcalorimeter to measure thermodynamic parameters of reactions and an X-Ray Crystallization robot.

Future Growth: The current equipment only provides a part of what is needed for the structural and biophysics characterization of molecules. USC has the potential to significantly expand the impact of its research through additional instruments, including:

- micro-liquid handler for precise multi-channel robotic handling of biological samples;
- Zetasizer to measure particle and molecular size;
- analytical ultracentrifuge to study molecular properties of proteins, nucleic acids and protein complex interactions;
- advanced multi-angle light scattering system coupled with an HPLC chromatography system;
- graphic computer work station for imaging and simulation;
- high-end atomic force microscopy system (coordinated with microscopy COE).

Additional staffing is also needed to assist faculty, students and postdocs in the exacting use of the most sophisticated instruments available.

Centers of Excellence for Precision Engineering of New Substances and Devices

Center of Excellence in Nanofabrication

Research: Advanced material and device fabrication are essential to performing cutting-edge research in the physical sciences, life sciences, and biomedicine. Nanofabrication and nanosynthesis tools, which enable design and manufacture at the atomic scale, are also required to engineer high-performance devices, materials and medicines. Nanofabrication tools benefit research across engineering (electrical, chemical, materials, biomedical, mechanical), science (physics, chemistry, biology) and medicine, particularly in emerging areas that are inherently multidisciplinary.

Impact: Nanofabrication will position USC to create the next generation of electronics and photonics. As current integrated circuit technology reaches its performance limits, innovative approaches are needed to develop both classical and quantum computers that surpass the speeds of today's computers. Miniature biomedical devices for prostheses and novel therapies stand to revolutionize medicine. Early detection and monitoring of disease, tissue repair, and devices for clinical diagnostics will increasingly rely on nanofabrication technology. Nanofabrication can also be used to develop probing biological systems for the study of cells, viruses, and organisms as well as transform bioenergy production, materials biosynthesis, and drug delivery. Last, we can use nanofabrication to make solar energy economical, improve water quality and synthesize better medicines.

Existing Facility: USC's nanofabrication research is centered in the 5,000 square foot W. M. Keck Foundation Photonics Research Laboratory, located in Vivian Hall, providing class 100 clean-room operation with a class 10 photolithography area. The facility is equipped with research tools for two-sided contact lithography, e-beam lithography, electron cyclotron reactive dry etching of semiconductors and insulation, e-beam metal deposition, e-beam and PECVD dielectric deposition, rapid thermal processing, oxidation diffusion and metrology.

Future Growth: The Center of Excellence in Nanofabrication is planned to be located within a new 10,000 square-foot facility in the soon to be constructed Michelson Center for Convergent Bioscience. Design, fabrication, synthesis and characterization tools will be provided in class 1,000 and class 100 clean-rooms. The tool set will need to be significantly expanded to enhance our ability to pattern at the submicron scale as well as integrate a range of materials and functionalities onto traditional silicon substrates. Capabilities will include:

- nanodevice fabrication, including advanced patterning, lithography, and etching;
- synthesis of nanoparticles, such as quantum dots, plasmonic particles, nanowires;
- microfluidics, including their integration into hybrid devices;
- assembly and packaging, to integrate nanoscale devices into larger systems.

The Center will also provide "plug-and-play" access to nanotechnology for research groups across the university. With appropriate support staff, nanofabrication and nanosynthesis tools will be available to faculty across the university, particularly those who are "non-experts" in these domains. Such a capability will dramatically expand USC's research in the convergence of science and engineering.

Center of Excellence in Cell & Tissue Engineering

Research: Stem cells are truly remarkable. They have the potential to become any cell type and thus may be a uniquely powerful tool to treat a wide range of degenerative diseases, including diabetes, neurodegenerative diseases, spinal cord injury, heart disease, and periodontal disorders. The Center of Excellence in Cell & Tissue Engineering provides the facilities, technical support, and collaborative expertise for the use of stem cells in basic science investigations and in clinical applications.

Impact: USC has built an exceptional group of stem cell researchers centered on the Broad Center, a magnificent new facility that opened on the Health Sciences Campus in 2010. The Center is based within the Keck School of Medicine, but is a cross-school collaboration that also involves the Ostrow School of Dentistry, the School of Pharmacy, and the Viterbi School of Engineering. Remarkable breakthroughs in stem cell technology have already emerged from the Center, one selected by *Science* magazine as among the 10 top world breakthroughs of 2010. Several promising stem cell therapeutics are currently in preclinical development, including:

- A new stem cell therapeutic to treat macular degeneration
- A method to genetically alter blood stem cells for the treatment of HIV/AIDS
- Use of autologous periodontal ligament (PDL) stem cells in the form of cell sheets to regenerate periodontal tissue for patients with periodontitis

Therapeutics arising from the stem cell program, currently in or entering clinical trials include:

- A small molecule pharmaceutical PRI-724, that selectively attacks stem cells that are a source of aberrant growth. Clinical trials at USC began in October 2010 for patients with colorectal cancer.
- Use of Allopregnanolone (AP), to prevent and treat Alzheimer's disease. AP promotes the ability of brain to regenerate itself by increasing the number and survival of newly generated neurons.

Additional efforts involve development of regenerative tissue models that provide insights into normal and pathological development, while also allowing screening for discovery and analysis of therapeutics.

Existing Facilities: The Broad Center's Stem Cell Core Facility provides comprehensive support service for human embryonic stem cell (hESC) researchers at USC. The laboratory maintains and supplies stock of quality-controlled hESC lines, including many not on the National Institutes of Health (NIH) registry. The provision of space, equipment and expertise enables investigators new to hESC research to undertake pilot projects and generate preliminary data, including projects utilizing non NIH-approved cell lines. The staff members who operate this facility develop and evaluate new methodology for hESC propagation and provide formal training in practical aspects of hESC experimentation. The hESC laboratory can also derive new hESC lines and supports induced pluripotent stem (iPS) cell technology.

Future Growth: The next steps for resource development in the area of stem cells and regenerative medicine at USC is the creation of a Good Manufacturing Practice (GMP) laboratory. GMP guidelines set out quality standards for manufacturing medicinal products. The FDA requires the use of a GMP facility for taking stem cell-based therapies into clinical trials. The GMP facility is a clean-room laboratory that ensures the therapeutic products will be safe and contamination-free for patients. Dedicated instrumentation and equipment must be purchased to outfit the lab and staff must be hired to manage the facility and provide technical assistance.

Centers of Excellence for the Science Libraries of the Future

Center of Excellence for the Digital Repository for Open Science (DROS)

Research: The USC Digital Repository (USCDR) offers state-of-the-art resources for the digitization, cataloging, and preservation of scientific and scholarly collections, as well as the means to manage and host such collections online. USC's long-term vision is for DROS to be an internationally recognized digital library for the sciences, accessed through a cloud-based archival system. Currently, the USCDR manages 40 petabytes of online data tape and eight petabytes of online disk storage, with preservation systems located in multiple locations in the United States. The USCDR builds on USC's strengths in technology and librarianship to capture and preserve collections of significant research, educational, and cultural value. The Digital Repository for Open Science (DROS) will be a scientific library within the USCDR, dedicated to preserving and making available a range of scientific materials, including large data sets, video simulations, clinical samples, books, and articles. The USCDR's commitment to long-term preservation will ensure that the digital materials stored in DROS will be accessible to researchers for years to come, making DROS a valuable scientific resource for researchers around the world.

Impact: Digitizing, hosting, and preserving scientific materials are time-intensive, highly specialized activities that can unnecessarily detract from time that scientists would otherwise devote to research. Moreover, professional services for large-scale collections can require costly equipment and facilities. DROS would provide a cost-effective, time-efficient way for USC researchers to share scientific data sets and other research materials, enabling them to fulfill the data management plans required by the NSF, NIH, and other grants regardless of the size of the collection. DROS services would make the research findings of USC scientists accessible to departments and researchers within USC, as well as to researchers and organizations around the world.

Existing Facilities: DROS will help researchers create, manage, and preserve important scientific materials by uniting the expertise and resources of the USCDR's three founding partners: the USC Libraries, the USC Shoah Foundation Institute (SFI), and USC's Information Technology Services (ITS). The USC Libraries bring expertise in imaging services, physical preservation, metadata, and online access to digital collections. USC's SFI offers the technological infrastructure for mass-conversion media preservation and cataloging systems, as well as facilitates library and classroom delivery of collection-based content for primary, secondary, and higher education environments. USC's ITS will contribute to the infrastructure for digital preservation through the processing power of one of the nation's most powerful academic supercomputers.

Future Growth: Through DROS, the networking and storage needs for the USCDR will grow dramatically. To achieve the university's vision and ensure that the materials stored in DROS are preserved for future generations, the USCDR will require funding to:

- upgrade the technology of its digital preservation systems at regular intervals;
- dedicate staff to help meet the specialized cataloging and access needs of scientific researchers;
- upgrade servers to maintain high-speed access to the collection for large-scale processing;
- dedicate high-capacity equipment to guarantee continual access to the material preserved in DROS.

Center of Excellence for Biobanking and Disease Discovery

PLAN IS UNDER DEVELOPMENT

Centers of Excellence for Computing of the Future

Center of Excellence for High-Performance Computing and Communications (HPCC)

Research: USC's Center for High-Performance Computing and Communications (HPCC) provides a foundation and model for research in computational sciences and engineering by bridging USC's unique strengths in scientific computing, computer science, medical research, and communications. HPCC supports approximately 125 research groups, representing more than 1,200 researchers in a variety of disciplines, including computational biology, bio-nano interface and biophotonics, cosmology, geophysics, linguistics, medicine, materials science, nanosciences and engineering, and pharmacology.

Impact: The compute power of HPCC enables USC researchers to tackle grand-challenge class problems in a broad range of disciplines. With its advanced computing and communications resources, HPCC allows researchers to develop the models, simulations, and visualizations that will lead to ground-breaking advances in medicine, new materials for clean energy technologies, earth sciences, defense, and oceanography. HPCC resources have helped researchers at the Southern California Earthquake Center (SCEC) conduct seismic hazard research and researchers at USC's Collaboratory for Advanced Computing and Simulations develop stress corrosion cracking simulations that deepen our understanding of chemically influenced corrosion. Detailed examples of scientific discoveries enabled by HPCC are provided below.

Existing Facilities: Housed in USC's state-of-the-art data center, HPCC has two Linux clusters. The primary cluster is a 56-GB low-latency bandwidth cluster. This cluster was ranked as the 9^{th}-fastest academic computer in the U.S. and the 127^{th} fastest computer in the world.

HPCC includes the USC Center for Data Visualization and Collaboration, whose resources allow researchers to study high-resolution simulations and computer-generated models. The tile wall enables researchers to project these images onto a 14-foot-wide by 8-foot-high, all-glass screen for multi-perspective analysis.

Future Growth: Future Growth: HPCC requires continual upgrading of its hardware and software to return to the ranks of the world's top 100 supercomputers and to offer USC's faculty and graduate students the necessary infrastructure for scientific discovery. Investment is needed in the following areas:

- hardware and software upgrades, including graphics processing units, or GPUs, which accelerate computationally intensive processing;
- upgraded technology for interactive and immersive 3-D visualization, which would include 14 stereo projectors for the tile wall, along with infrared technology for wireless synchronization, computing and visualization nodes, and software;
- additional staff to support researchers and HPCC's infrastructure.

Center of Excellence in Quantum Information Science and Technology

Research: Quantum information science and technology is concerned with the study of the new possibilities quantum mechanics offers for the acquisition, transmission, and processing of information. Quantum computers are predicted to solve classically intractable tasks such as breaking cryptographic codes, efficiently searching large databases, and efficiently simulating quantum dynamics. Quantum cryptography offers unconditional security. And quantum information theory has revolutionized our understanding of the capacity of communication channels. Theoretical and experimental quantum information processing and quantum control research at USC spans electrical engineering, physics, and chemistry. Researchers are creating new quantum computing algorithms, quantum error correction, the interplay between quantum information theory and condensed matter physics, device development for quantum information processing, and experimental quantum computing.

Impact: Quantum computing research at USC has catapulted to a world leadership position with the establishment of the Center for Quantum Information Science & Technology (CQIST), and especially the USC-Lockheed Martin Quantum Computing Center. CQIST has already been awarded $7 million from the iARPA (Information Advanced Research Projects Administration) and a $6.5 million multi university grant from the Department of Defense. We have attracted stellar young faculty and organized a major conference on quantum computing, attracting more than 180 researchers from around the world. Two *Nature* papers were recently co-authored by CQIST members. We expect this research to lead to significant advances in the practical realization of quantum computing using solid state devices, which are expected to ultimately lead to large scale quantum information processing, capable of outperforming the most powerful classical computers.

Existing Facilities: CQIST has acquired a D-Wave One 128-qubit "Rainier" processor, the world's first specialized quantum optimizer, at the Information Sciences Institute. A focus area of the Center is theoretical and experimental quantum adiabatic optimization, including both algorithm development and fundamental physics research. Adiabatic quantum optimization has the potential to dramatically speed up the solution of problems in, for example, machine learning, image recognition, software debugging, database searching, and drug design.

Future Growth: To keep USC as an undisputed leader in quantum information processing, investment is needed in these new technologies:

- D-Wave Inc. is developing the 512 qubit Vesuvius chip, which we expect to be the first ever quantum chip to beat classical computers in optimization problems. An upgrade to Vesuvius will enable USC to be the undisputed leader in quantum optimization, the first large-scale application of quantum information processing.
- In addition, CQIST anticipates development of a new custom D-Wave system, designed to do more detailed investigations into the physics underlying the processor and how processor performance and scaling depend on the quantum resources present. The acquisition of such a custom (yet unbuilt) D-Wave system would bridge the gap between our current strength in adiabatic quantum optimization and the need to gain a complete bottom-up understanding of the underlying physics.