



***Research Facilities
at the University of Kansas***

*Lawrence Campus
Kansas City Campus*

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Research Facilities

The sections below describe campus-level research facilities available to support COBRE investigators at The University of Kansas in Lawrence and The University of Kansas Medical Center in Kansas City.

A. KU-Lawrence

The Molecular Structure Group (MSG) (www.msg.ku.edu/~msg/)

The Molecular Structures Group (MSG) is comprised of six service laboratories: (1) the Nuclear Magnetic Resonance Laboratory (NMR), (2) the Mass Spectrometry Laboratory (MSL), (3) the Biochemical Research Service Laboratory (BRSL), (4) the Molecular Graphics and Modeling Laboratory (MGM), (5) the X-ray Crystallography Laboratory, and (6) the Protein Structure Laboratory (PSL). Each laboratory has a Ph.D. level director, plus technical staff who in some cases work in more than one lab. Together, they manage the shared instruments and computers used for determining molecular structure on behalf of investigators across the Lawrence campus. They work collaboratively with faculty and students, acquire data for users, train users to operate instruments, help with planning experiments and interpreting data, and frequently are co-authors on publications and investigators on grant proposals. They have also worked in collaboration with investigators at the KU Medical Center and at Kansas State University. Instrument operation and maintenance are underwritten by user fees. A steering committee, consisting of four faculty members and the four directors, oversee the technical aspects of the operation. Administratively the MSG is a unit of the University of Kansas Center for Research, Inc.

The Nuclear Magnetic Resonance Laboratory (NMR) (Director David VanderVelde, Ph.D., www.msg.ku.edu/~msg/nmr2) The NMR laboratory is responsible for maintaining the high field NMR spectrometers, training users, providing spectra on a service basis, and assisting users with design, execution, and interpretation of NMR experiments. Its capabilities extend from small molecules to isotopically enriched proteins, solids, and flow samples. The laboratory manages six modern and frequently updated instruments; the two most relevant to studies of proteins are a four-channel Bruker Avance 800 with triple resonance cryoprobe and warm probe, and a four-channel Varian Inova 600 with triple resonance cold probe and warm probe, and a z-gradient broadband probe. The lab also has a 500 and three 400 MHz instruments used primarily for small molecule work. The addition of the cryoprobes and the 800MHz instrument gives us one of the best-equipped, most modern NMR facilities in the region.

The Mass Spectrometry Laboratory (MSL) (Director Todd Williams, Ph.D., www.msg.ku.edu/~msg/mass) is a core facility to provide mass spectral analysis for researchers at the University. The MSL is staffed with 4 FTEs, a Ph.D. trained director, two research assistants and a research instrument operator. The lab occupies about 2100 square feet in rooms B025, 1008, and 3007 Malott Hall. The lab operates six mass spectrometers with dedicated computer based data systems. The instruments are: a VG ZAB-HS high resolution sector instrument, a VG AUTOSPEC -Q sector based tandem hybrid of EBEqQ configuration, a Micromass Quattro Ultima LC/MS/MS instrument of QQQ configuration and a Micromass Q-TOF2 tandem hybrid of Quadrupole/ Time-of-Flight configuration. Ionization methods supported are EI, CI, FAB APCI and Electrospray. The MSL supports MS, MS/MS and exact mass types of experiments. HPLC equipment includes a Waters Acquity UPLC with autoinjector and dual wave length UV/Vis detector for high pressure HPLC (>4000 psi), a Waters 2690 with autoinjector and uv/vis detector for conventional separations at 250 ul/min, a Waters capLC XE and a Micro-Tech Ultra Plus II capillary HPLC for low (10 ul to 200 nl/min) flow rate separations. An additional auto-injector (CTC analytics miniPal) is used for automated introduction of infusion samples on the Ultima and Q-Tof2. Two open access instrument are operated in Malott Hall for

users to “walk up and inject” on a Waters Quattro Micro GC for GC/MS or on a Waters LCT premier for ESI tof data. The MSL also collaborates with the Biochemical Research Service Laboratory (BRSL) in the Analytical Proteomics Laboratory (APL) located on West Campus in the Structural Biology Center. The APL utilizes two high-resolution MALDI-TOF instruments, a Voyager DESTR and an ABI 4700 MALDI-TOF/TOF for protein/peptide characterization. For high performance HPLC/MS/MS the APL also has a ThermoElectron LTQ-FT hybrid instrument with linear ion trap and high resolution ICR cell for FT MS.

The Biochemical Research Services Lab (BRSL) (www.brsl.ku.edu) provides state-of-the-art biochemical and bioanalytical services to advance the research interests of investigators at the University of Kansas and at other institutions in the State. Highly trained and experienced laboratory personnel maintain and operate the sophisticated research instrumentation. They also assist investigators in the design of experiments and interpretation of data. In addition, researchers can come to the laboratory to use equipment and/or to learn techniques useful to their research. The following services are currently available: Amino Acid Analysis; Peptide Synthesis; Analytical (and Preparative HPLC; Fermentation and Cell Culture; Molecular Imaging; and Mass Spectrometry of Biomolecules. Assistance with expression and purification of recombinant proteins is provided by our sister laboratory, the KU Protein Purification Group (www.medchem.ku.edu/cobre). The Bio-Rad FX Molecular Imager is a walk-up instrument that is used to analyze a wide variety of electrophoretic applications, such as: Southern, northern and western blotting, 2-D gels, and band shift assays The FX also system provides a state-of-the-art phosphorimaging capability for autoradiography. We also operate two complete HPLC systems, a Dionex Summit and a Beckman Gold, that allow us to solve almost any kind of analytical and preparative HPLC problem. Our Voyager DE-STR Biospectrometry Workstation is a state-of-the-art MALDI TOF mass spectrometer equipped with PSD, CID, reflectron, and delayed extraction. Mass accuracy of this instrument is better than 10 ppm and typical sensitivity is in low femtomole range. Recent additions to the BRSL instrumentation are a MALDI TOF/TOF 4700 Proteomics Analyzer and a Beckman 2D HPLC system.

The Molecular Graphics and Modeling Lab (MGM) (Director Dr. Gerald H. Lushington, www.msg.ku.edu/~msg/mgm). Molecular modeling entails computational simulations of molecular structure and phenomena, whereas interactive graphics and visualization tools allow users to assemble and analyze complex simulations. The MGM Laboratory's goal is to provide access to high-performance computational tools for these purposes, with a focus on support and assistance to university research workers through consultation and training in their independent application of computational chemistry approaches to their specific problems. An important secondary mission is to track developments in computational chemistry software and hardware and to keep the University's capabilities up to date. The MGM's primary interactive tools are the Tripos Associates' SYBYL software suite, the Insight-II and Cerius2 environments from Accelrys, Inc., and the Molecular Operating Environment (MOE) from Chemical Computing Group, each of which provide the capacity for constructing and manipulating small- and macromolecular systems; computing energies and geometries, analyzing covalent and non-covalent interactions, searching conformational space, ascertaining intermolecular interactions (including pharmacophore characterization), aligning and comparing structures, computing a wide range of molecular properties, and interfacing with data presented in a wide variety of standard or specialized formats. Additional drug design tools include various docking utilities (FlexX, FlexE, Flex-Pharm, CScore, AutoDock), QSAR/CoMFA, VolSurf, and UNITY. Chemical informatics suites include JChem and CACTVS. Biomolecular analysis tools include the BioPolymer suites (both Tripos and Accelrys versions), MPSA, Modeller and DeepViewer. The MGM Lab also possesses a huge virtual chemical library collection (more than 15 million 3D structures) including the ChemNavigator collection, the PubChem small molecules database, plus smaller Maybridge, NCI, ChemDiv, ChemBridge, IBS and LeadQuest libraries. MGM lab

hardware includes 7 SGI R10K workstations, 3 Linux workstations, a 16 processor Linux cluster, a 10 processor workstation / cluster hybrid, and a 4 processor database server. Total disk storage capacity is on the order of 1 TB.

X-Ray Crystallography Lab (Director Victor Day, Ph.D., xrayweb.msg.ku.edu) This lab uses diffraction methods to determine high-precision three-dimensional crystal structures of small molecules and to identify polycrystalline materials. Single crystals are studied with molybdenum radiation using the in-house Bruker SMART APEX diffractometer that is equipped with a charge-coupled device (CCD) area detector and an Oxford Cryostream low temperature device. Most single-crystal studies are conducted at a temperature of 100K but studies can be performed at any temperature between room temperature and 80K. Data for very small or poorly-diffracting single crystals or samples which require highly accurate anomalous dispersion data are presently collected off-campus using copper radiation on a Bruker CCD area detector equipped with a rotating anode. The single crystal studies range from the use of x-ray crystallography as a routine analytical tool for identifying reaction products to detailed studies of bonding subtleties in complex inorganic molecules and hydrogen-bonded organic species. Although the lab always prefers to work with single-domain specimens, it routinely determines structures for twinned samples with multiple domains when single-domain crystals cannot be obtained. Final structural results can usually be obtained within 24 hours of the start of data collection.

The Protein Structure Laboratory (PSL) (Dr. Weijun Huang, Director; www.psl.ku.edu) assists investigators with crystallization of target proteins, collection of complete X-ray diffraction data sets (locally and/or at a Synchrotron site), phase determination, model building and refinement, preparation of presentation graphics, and writing manuscripts and grant applications. Major equipment includes an 18 kW high brilliance rotating anode generator (Rigaku RU-H3RHB), Blue Max-Flux (Osmic) confocal optical system, two-theta stage and inverse Phi axis, R-AXIS IV++ imaging plate systems, X-stream cryogenic system, data collection PC, graphics workstations, and software. Individual investigators are responsible for purification and concentration of their protein to make it ready for crystallization. After purification, the PSL performs or assists with any or all of the functions mentioned above. In addition, experienced users are provided with access to the X-ray beam and other facilities of the PSL. The lab operates on a fee-for-service basis.

The Applied Proteomics Laboratory (APL) occupies approximately 2100 square feet in the Structural Biology Center, and it includes a prep room and two instrument suites. The prep room contains chromatographs, plate spotter/digester and a clean hood. One instrument suite contains two MALDI instruments; the other has the LTQ-FT mass spectrometer and chromatograph. The facility is equipped with five computers networked and equipped with laser and color printer, and a dedicated server for proteomics organizing packages, Genomic Solutions and Protein Databases. Search engines include Mascot, Profound and Sequest. Utilities for manipulating MS data for peptides and proteins are ABI's BioAnalyst and Finnigan's Bioworks 3.2. The mass spectrometers are ThermoFinnigan LTQ-FT linear ion trap/FTICR tandem mass spectrometer, ABI 4700 MALDI-TOF/TOF, and Perseptive VOYAGER DE-STR MALDI-TOF. Other instruments in the facility include Ultimate micro LC system with Probot fraction collector, Beckman Protein 2DF HPLC system, Symbiot Robotic Sample Plate loading workstation, PropPrep Protein Digestion and Mass Spec Preparation Station, Flow hood, Bio-Rad FX Molecular Imager, HPLC and FPLC equipment, Bio-Rad Protean IEF Cell, and Bio-Rad preparative electrophoresis unit and Rotofor.

The Instrumentation Design Laboratory (IDL) (Director Dr. Kenneth Ratzlaff, www.idl.ku.edu) is an analytical resource laboratory which provides collaborative support to research scientists in order to enhance their research through custom instrumentation and laboratory automation, often based on small computers and workstations. Instrumentation solutions to laboratory

problems may be developed as "turnkey" systems in which the IDL develops all hardware and software or as a coordinated project where the IDL both consults with a member of a research group and provides hardware and software modules as needed. Services are available to research groups in the natural sciences including chemistry, physics, medicinal chemistry, pharmaceutical chemistry, pharmacology and toxicology, botany, physiology, entomology, systematics and ecology, the Natural History Museum and the Higuchi Biosciences Center. The IDL designs and fabricates electronic and computer-based instrumentation as well as programmable mechanical devices that interact with the computer. It is fully equipped with test equipment and fabrication equipment, as well as significant stocks of integrated circuits, passive components, connectors, *etc.* CAD systems are used for printed circuit board layout and documentation preparation. Lab personnel are also responsible for a wire-bonding machine. The IDL typically develops software in C or C++, but also uses Visual Basic, LabView, Delphi or Assembly Language for a variety of microprocessors and micro controllers. The lab has extensive experience with high-density Field Programmable Gate Arrays (FPGAs) and gigahertz logic. Applications involving precision data acquisition (up to a gigahertz) and control, real-time graphics, communications and concurrent processes are common. Dedicated microcontrollers can be used for data acquisition or miniaturized circuits.

The KU Microscopy & Analytical Imaging Laboratory (Director/Assistant Scientist Dr. David Moore) The Microscopy & Analytical Imaging Laboratory at the University of Kansas is a core facility maintained under the auspices of the Kansas University Center for Research, Inc. The laboratory recently underwent extensive renovations, expanding its space and its range of analytical imaging devices: The lab houses a Zeiss Meta 510, multi-line laser scanning confocal microscope with, advanced spectroscopic analysis functions, spectral mapping and advanced FRET/FLIP/FRAP capabilities. It also has a fast acquisition, multi-line laser-based Yokogawa spinning disk confocal microscope custom designed for rapid kinetics optical imaging of live cell systems. This microscope is also fully equipped for ratio-metric fluorescence measurements (UV and Visible) and is capable of total internal reflection-based fluorescence assays. Detection capabilities are sensitive to the single molecule level (EMBTCCD's). Systems are available for environmental control and temperature/gas mixture maintenance/modulation. Drug perfusion/application is also available for pharmacological manipulations. This microscope is on an inverted frame and possesses the same multi-well plate manipulation system found on many commercial high content imaging systems. Drug dispensation, image capture, and data analysis are all automated through a customized data acquisition/instrument control software interface. An additional pair of optical microscopes, one inverted, one upright, are available for standard, non-laser based epi-fluorescence imaging. All optical microscopes in the lab are equipped with phase contrast and DIC optics, automated objective/filter set switching, computer driven Z -axis motor drives, and auto-focusing under software control. Point-spread based iterative deconvolution is available for both epi-fluorescence and confocal imaging systems. Within the lab, a wide range of optics, high speed shutters, and spectral analysis tools are also available, permitting flexible configurations of devices for specialized applications including, but not limited to, total internal reflection imaging, measurement of multi-spectral polarization anisotropy, dynamic measurements of fluorescent single dipole orientation, fluorescence correlation spectroscopy, and high speed FRET detection. Limited high content imaging capabilities, including automated plate handling and exchange will be assembled and functioning by autumn of 2006. Data Acquisition and on-the-fly analysis for all systems except the Zeiss Meta 510 may be alternately driven via Image Pro, sildebook, or Labview-based software packages, depending on the requested assay conditions. Commercial Software capabilities include automated, customizable, segmentation-based, on-the-fly analysis of 2-D data sets (static images as well as timelapse data sets), 3-D multi-color time-lapse image capture, montage imaging for tissue sections, stereology, and 4-D particle tracking. Offline image analysis is also available for all

imaging modalities. Recently a 2-D Gel fluorescence/phosphorescence/bioluminescence scanner & a 2-D gel analysis Software for DIGE/proteomics applications were acquired (GE HealthCare Typhoon Imager/Phoretix Progenesis 240). Funds also are now available to purchase a new 200kV HRTEM system including Cryo-Imaging capabilities, STEM, EDAX, & HAADF. The base model of the TEM that will be purchased will be the Tecnai G2 F20 X-TWIN. This TEM will be capable of tomographic reconstructions within biological samples, and will be very well equipped for doing through-focus analysis for single protein/protein complex structural mapping. Anticipated purchase of this instrument will be in the early spring of 2007.

The High Throughput Screening Laboratory (HTS) (Director to be named, www.hts.ku.edu) provides researchers with high throughput technologies and libraries to assist in identifying biological probes and to provide leads for drug discovery. The laboratory is equipped with an Integrated Automation System (ORCA Robot and the SAGIAN™ Core System, Beckman), robotics for liquid handling (Biomek FX Liquid Handling Workstation, Beckman; MultiDrop Bulk Reagent Dispensers, LabSystems), and integrated signal detection instruments (Victor2 V Multilabel Platereader, Perkin-Elmer Life Sciences; SpectraMax Plus 384 Absorbance Platereader, Molecular Devices; SpectraMax Gemini XS Fluorescence Platereader, Molecular Devices). The HTS supports several compound libraries (ChemBridge Library-45,000 Compounds; ChemDiv Library-56,000 Compounds; Prestwick Library-880 Compounds), and software for chemical and biological information management.

The DNA Sequencing Laboratory (Director Dr. Mike Grose, www.nhm.ku.edu/dnalab/) provides full service automated DNA sequencing and genotyping using an Applied Biosystems 3130xl genetic analyzer. This 16 capillary machine processes up to two 96 well sequencing plates within a 24 hour period. We can accommodate post sequencing/fragment clean-up and, or injection only rates at a competitive price. Within the past year, we have added microsatellite detection and AFLP typing to compliment the work flow of the genetic analyzer.

The Tissue Culture Laboratory (TCL) (Jennifer Bean, Technical Coordinator, www.hbc.ku.edu/tcl.shtml) This facility occupies ~2,000 sq. ft. of space in Malott Hall. The cell and tissue culture component is a ~1,000 sq. ft. positive pressure lab totally designed for preparation and maintenance of cell and organotypic cultures. The ante-room is designed for media preparation and is equipped with a large Primus PSS 500 computer-controlled steam sterilizer, a Millipore Milli-Q synthesis A10 water purification system, a Revco -80 °C freezer, and standard refrigerators and freezers. The inner tissue culture room is equipped with 2 NuAire and 2 Baker biological safety cabinets, 8 NuAire CO₂ incubators, 1 double-chamber NuAire Trigas incubator, an Integra Tecnomouse bioreactor, a BTX 2001 Electroporator/electrofusion unit for cell transfection or fusion, Cryomed liquid N₂ tanks for cell preservation, an Olympus CK2 inverted microscope, a Thermo-Electron Centra CL3R refrigerated centrifuge, a Wescor 5520 vapor pressure osmometer, and other small equipment items required for cell culture. An adjacent instrument provides several items relevant for studies with cell and tissue culture systems, including a Packard Lumicount Chemiluminescence plate reader, a Bio-Tek FL600 microplate fluorescence reader, a Molecular Devices SPECTRAMax 190 microplate absorbance reader, a Becton Dickinson FACScan flow cytometer with two workstations, a Nikon Eclipse TE200 inverted microscope with Nikon TE-PS100 fluorescence, a Dage-MTI 3CCD video-camera, and Flashpoint digital conversion/frame grabber software. The Facility is under the direction of an experienced tissue culture expert, who handles maintenance of the equipment and efficient utilization of the facility. University lab staff members have access to all of the instrumentation, based on a sign-up system to reserve items for use as needed.

The Transgenic Mouse Facility (Director Jeff Staudinger, Ph.D., people.ku.edu/~stauding/transgenic/htm) provides transgenic and gene-targeted mice for

researchers in KU and other regional institutions. The mission of this facility is to facilitate gene-targeting and transgenesis. The facility is currently supported by University of Kansas Research Development Fund (RDF). The facility prepares transgenic and knockout mice from DNA supplied by investigators, and assists with genotyping. The facility has two labs: one embryonic stem cell culture & manipulation lab, and one animal care lab. The facility is equipped with state-of-art instrumentation for making transgenic and knockout mice including an inverted Nikon TE-2000 microscope equipped with Nomarski DIC optics and two Eppendorf Microman NK micromanipulators. The workstation is equipped with a Sony color video camera that delivers very high-resolution pictures of the microinjection process to a video monitor. This equipment enables the microinjection technician to visualize the microinjection process. The microinjection microscope is equipped with a temperature-adjustable warming/cooling stage and this workstation is solely dedicated for microinjection use. The microinjection and holding pipets are Eppendorf CellTram Air and CellTram Oil micromanipulators that are used for either pronuclear or blastocyst injection. A sutter P-97 needle-puller and a Narshige MF-900 micro-forge are utilized for making holding and injection pipettes. A BTX square wave electroporator is used for efficient transfection of ES cells. The embryonic stem cell lab is equipped with a laminar flow hood and two Lab-Line CO₂ Incubators.

The facility provides customer-oriented services to suit various needs in making transgenic and knockout mice. Investigators who are interested in expanding the role of transgenic technology in their research effort are encouraged to contact the facility. A requisition form for production of transgenic and knockout mice and other related services needs to be completed and submitted and is available on the web-site. For each construct accepted for microinjection, two microinjection time slots will be assigned in order to produce a minimum of two founders. Two progress reports will be sent to the investigators following the microinjection session: first at the birth of the pups and the second after weaning. Tail samples from weaned pups will be provided for DNA analysis. The investigators will be expected to prepare and analyze tail DNA to identify founders within one week of receiving tail samples. Positive animals will be assigned to the investigator's research animal per diem charge at that time.

The AAALAC-accredited Animal Care Unit (Director James Bresnahan, D.V.M., www.ku.edu/~acu/acu.html) is under the direction of veterinarian Dr. James Bresnahan, board certified in laboratory animal medicine, and includes a staff of more than thirteen animal science technicians and administrators. Campus-wide a total of 34,000 square feet are devoted to animal care. Facilities include procedure rooms, surgery suite, radiology, necropsy, carcass disposal, and animal housing. The use of laboratory animals carries with it unique professional and moral obligations. The university is committed to ensuring that all animal use under its auspices is responsible, judicious, and humane. Practices for ensuring appropriate use and benevolent care for laboratory animals are in accordance with the Animal Welfare Act (and its subsequent amendments) and the Health Research Extension Act of 1985. Standards for housing and care, established by the Animal Care Unit, meet or exceed these federal laws and guidelines. The excellence of the program has been recognized by the American Association of Accreditation of Laboratory Animal Care (AAALAC) in granting full accreditation following thorough, regular evaluations.

All proposals for projects requiring vertebrate animals must be reviewed by the Institutional Animal Care and Use Committee (IACUC). Serving on this committee are at least five faculty representatives who are knowledgeable of appropriate use of animals in research; a representative from the Museum of Natural History, where living vertebrates are used in exhibits and in public education programs; two graduate student representatives; a representative from the Office of Research and Public Service; an Animal Care Unit representative; the Director of the Animal Care Unit; and two representatives from the Douglas County community. The

committee considers the propriety of each proposal, the adequacy of anesthetic and analgesic agents and acceptability of euthanasia methods. If the procedure is deemed inhumane or the project frivolous, it is prohibited. Whenever IACUC members express concern regarding animal welfare relative to a particular procedure, the procedure is monitored by an IACUC delegation, in which the Animal Care Unit Director is included. The IACUC is empowered to terminate any project found not to adhere to the original proposal or which is in violation of federal regulations. The IACUC is vigilant in identifying new technology which may refine, reduce or replace animal use for research.

The Genomics Facility (Director Xinkun Wang, Ph.D.) provides equipment and expertise for gene array and other functional genomics experiments. The facility director is experienced in genomics, DNA microarray construction, hybridization protocols and extensive data analysis. The staff provides service at various levels to meet the individual investigator's needs. The facility is equipped with the latest equipments for high-density Affymetrix microarrays and variety of software for data analysis.

Major equipments available at the Facility include: an Affymetrix GeneChip microarray system (including the GeneChip Hybridization Oven 640, the Fluidics Station 450, and the latest GeneChip Scanner 3000 with autoloader, operated with the latest GeneChip Operating Software), an Agilent Bioanalyzer 2100, an Applied Biosystems 7500 Fast Real-time PCR System, and a Beckman Biomek NX Laboratory Automation Workstation as well as an Arcturus PixCell Ile Laser Capture Microdissection system. For data analysis, the Facility is equipped with the latest versions of GeneSpring, Spotfire DecisionSite, GeneTraffic (server version), PathwayAssist and other open-source software packages.

The Bioinformatics Core Facility (Director Dr. Gerry Lushington, www.bcf.ku.edu/index.htm) at the University of Kansas provides access to high-performance computational tools to study the biology, genetics and proteomics of many organisms from simple (viruses, bacterial) to the most complex (humans). Through the analysis of diverse biological information, synthetic models can be constructed to better approximate many complex processes responsible for life-science systems and greatly increase our knowledge of comparative genetics. The facility is equipped with A 64-bit LINUX cluster with 16 CPUs, 16 GB memory, and ~500 GB hard drive, a Dell PowerEdge 4600 LINUX server, a Dell Precision workstation, a HP 4600DN laserjet color printer, and a videoconference workstation. Several software systems are used including Tracker System, developed at KU to monitor protein searches using Blast-N and PubMed databases; BLAST server; EMBOSS package; DS Gene and MacVector; GeneSpring; MOE; Alignment of cDNA in codon-codon mode; and AMBER. The facility supports and assists researchers from K-INBRE institutions through consultation, training in their independent application of bioinformatics approaches to their specific problems, and development of software and data structures relevant to large scale data-intensive projects.

The NIH Center for Combinatorial Methodologies and Library Development at KU (CMLD) (Principal Investigator Jeffrey Aubé, Ph.D., jaube@ku.edu). The CMLD's primary mission is to (1) validate newly developed synthetic methodology for applications towards diversity oriented synthesis of expanded compound libraries, (2) apply newly-developed chemical methodologies and strategies to the generation of chemical diversity libraries for HTS biological screening and (3) to design and synthesize follow-up libraries from hit or lead structures in close collaboration with chemists and biologists. The CMLD's chemical synthesis core is four laboratories (1,300 sq. ft.) located in the KU Life Sciences Laboratory, directly adjacent to the High Throughput Screening (HTS) Laboratory and the COBRE Center for Cancer Experimental Therapeutics. Two of the laboratories are fully equipped for modern chemical synthesis; the others house the 400 MHz NMR and a prospective MS spectrometer. Automation is critical for meeting the analytical needs of the CMLD. The CMLD has its own Bruker Avance 400 MHz NMR equipped

for auto-sampling from 96 well plates with the Bruker BEST system, and a 1H/13C dual flow probe with an active volume of 120 microliters. This instrument has high sensitivity for proton experiments. In addition a Bruker Avance 500 with a $^{13}\text{C}/^1\text{H}$ dual cryoprobe and a 24 position NMR-CASE sample changer is available. This instrument has extremely high sensitivity for ^{13}C and can acquire a good carbon spectrum on 1 mg of sample in about 10 minutes. The following combinatorial chemistry equipment is available: one Quest 205 and three Quest 210 synthesizers from Argonaut for parallel solution and solid phase work, Two Radley Discovery Technology Carousel® Reaction Stations for conducting 10 simultaneous reactions, and five custom-made parallel synthesis units that allow the simultaneous synthesis of up to 100 compounds each in (mg) to gram quantities. A custom-made parallel solid phase synthesis unit (up to 12 parallel reactions) that utilizes glass reaction flasks with fritted ends which allow for convenient resin washing is also used. An additional fully automated system is the HP 7686 Solution-Phase Synthesizer capable of bar code reading, solvent and reagent addition, mixing, heating, cooling, aqueous work-up, phase separation, and chromatography on silica gel. Two Personal Chemistry/Biotage microwave chemical reactors (Optimizer and Creator) are available for microwave-assisted synthesis and offer significant synthetic advantages in library generation. For chromatography needs, the CMLD houses 4 Biotage Horizon purification systems and 10 individual Biotage FLASH (12i, 25i, and 40i) Purification Systems. The center also houses the IRORI AccuTag MicroKan system (radiofrequency tag) and the IRORI MicroKan (encoded by bar codes) system for solid phase synthesis of compounds. An IRORI Synthesis Manager equipped with IRORI's proprietary software is used to manage library information. Final sorting of the compounds is carried out into the AccuCleave-96 and the products are collected in 96-well plates after resin cleavage. The identity of each compound in the 96 wells is known through geographic partitioning. We have all the necessary parts of this system: a bench-top RF scanning station, bench top bar code reader, dry resin filling station, and two AccuCleave-96s. The system also includes the LED Sorting Accessory that increases the speed of sorting MicroKans manually and ensures accuracy. For solvent evaporation, the CMLD has a DD4 Centrifugal Evaporator from GeneVac. The built-in VC1500 dual chamber refrigerated condenser is a powerful cryopump and solvent recovery system and is capable of evaporating 4 microtiter plates at once.

The University of Kansas Libraries (Dean of Libraries Stella Bentley, www2.lib.ku.edu/anschutzlib/) are housed in six buildings on the Lawrence campus. The science print collection, along with business and government documents, and maps are located in **Anschutz Library on the Lawrence campus**. Monographs are purchased through an approval plan for North American, University press, and major European publications. Books are received automatically that adhere to a plan based on subject and publisher profiles. Designated bibliographers in chemistry, pharmaceutical sciences, and molecular biosciences purchase additional monographs pertinent to current research and teaching programs within the departments. Reference assistance to library patrons is offered through several options: in person or by phone to staff at the reference desks, e-mail, or a chat service.

Access to the current journal literature is moving toward electronic availability that augments and at times replaces the print titles. Based on feedback from the faculty and students, desktop access is highly desirable to serials, particularly in the sciences. The KU Libraries have expanded extensively within the past 2-3 years the number of full-text journals available electronically. The following publisher packages with extensive science offerings are accessible on campus and remotely:

1. ACS Web editions and complete archives (34 titles)
2. Annual Reviews (33)
3. Blackwell Synergy (694)
4. Dekker Online (81)

5. Journals of the American Medical Association (10)
6. Kluwer Online Journals (842)
7. Wiley InterScience (442)

The Libraries subscribe to some of the titles and years accessible online through the following publishers:

1. ScienceDirect Elsevier Journals (338 titles)
2. Nature Journals Online (22 titles including all of the Reviews and most of the Nature subject titles)
3. Royal Society of Chemistry (13)

Selected titles are available through other publishers and aggregators.

A separate “e-journal title search” is provided on the Libraries’ web page to allow quick identification of those journal titles and volumes available electronically. Through this mechanism, the Libraries also provide records to those publishers and societies offering open access to backfiles of their journal content (e.g. Highwire Press; PubMed Central).

As to the bibliographic databases offered at KU, the Libraries subscribe to *Biological Abstracts* (1969+), *International Pharmaceutical Abstracts*, *Web of Science* (1983+), and *SciFinder Scholar* with the structure searching module. Presently, the subscription to *SciFinder Scholar* allows for five simultaneous users. Convenient links are provided to the public on the Libraries’ web site to the free resource, *PubMed*. To expedite access from the bibliographic databases to the subscribed electronic journal titles, the Libraries are beginning to implement a linking mechanism from the database citations directly to the electronic version of the journal title.

For materials not available at KU in print or electronic formats, the Libraries’ interlibrary loan and document delivery service borrows and scans materials held at institutions from across the world. Requests are submitted by KU patrons through an online system. Copies of articles from print journals held in the KU Libraries can also be requested through the same service. Most copies of articles are provided to the patrons as .pdf files on a web page which is accessible via the Libraries’ website. The interlibrary loan/document delivery department understands the need for quick turnaround time and has developed high standards of performance.

A variety of supportive reference materials are available in the print and electronic collections. Examples of print reference sources include *Encyclopedia of Reagents for Organic Synthesis*, *Houben Weyl Methods of Organic Chemistry*, *Beilstein Handbook of Organic Chemistry* which is complete through the fourth supplementary series, and *Comprehensive Organic Chemistry*. *CHEMnetBASE* is an electronic resource to Chapman & Hall chemistry reference sources including the *CRC Handbook of Chemistry and Physics*. *Clinical Pharmacology* is an electronic drug handbook tool.

Videoconferencing facilities are available through the Higuchi Biosciences Center (HBC). The HBC videoconference equipment has the ability to link as many as three external sites through IP (data lines), and can transmit dual images (e.g., camera and PowerPoint images). Five audience microphones allow for audio transmission from up to 30 different audience members. Facilities in the Simons Auditorium allow for satellite downlink and 2-way compressed video.

B. University of Kansas Medical Center

The Archie R. Dykes Library (library.kumc.edu/) at the University of Kansas Medical Center currently contains about 63,000 monograph volumes and 170,000 bound journal volumes. The library subscribes to approximately 1,000 current print journals and 9,000 electronic journals. The Dykes Library supports biomedical and health sciences programs in medicine, nursing and allied health. More specifically, the Library supports Medicine with resources for clinical

sciences and the following basic sciences: Biochemistry, Anatomy, Physiology, Pharmacology, Microbiology, and Pathology.

Generalized scientific resources include online access to Science Citation Index, Medline, the Cumulative Index to Nursing and Allied Health Literature, PsycInfo, and the International Pharmaceutical Abstracts.

The journal collection includes online access to packages of titles available from the American Chemical Society, Blackwell-Synergy, Kluwer, Wiley Interscience, Lippincott-Williams-and-Wilkins, Proquest Nursing Journals, BioOne, Science Direct, Marcel Dekker, and the Nature Publishing Group.

The Dykes Library has active interlibrary loan relationships with the Kansas Regents' Universities, Linda Hall Library, and with regional medical schools. Courier service between Dykes and the KU main campus provides daily deliveries.

The Biotechnology Support Facility (BSF) (Manager Bo Wisdom, M.A., BSF@kumc.edu) is a full service core laboratory that includes protein-peptide sequencing, peptide synthesis, amino acid analysis, oligonucleotide synthesis, and DNA sequencing. DNA sequencing is performed using an ABI Prism 377XL sequencer. Standard sequencing primers are provided by the facility at no additional cost. Oligonucleotide synthesis is performed on an ABI 394-08 DNA/RNA Synthesizer. Synthesis is accomplished on controlled pore glass supports in a 3' to 5' direction. Scale of synthesis on the 394-08 is 40-50 nanomole, 200 nanomole, or 1 micromole. Peptide synthesis is performed on a Rainin Symphony Quartet Peptide Synthesizer. This instrument is capable of simultaneously synthesizing four peptides using Fmoc chemistry. Routine levels of synthesis are 25-50 micromoles. Multiple Antigenic Peptides (MAPs) can also be synthesized with the Quartet by using a 4- or 8-branched immunologically inert lysine core resin. Amino acid analysis is performed on a Hitachi L-8800 Amino Acid Analyzer. Protein or peptide sequencing is performed on the facility's ABI Procise 491 Protein Sequencer using standard Edman degradation chemistry. This chemistry derivatizes and removes one amino acid at a time from the amino-terminal end of the protein or peptide that is being sequenced.

The Laboratory Animal Resources (Director David Pinson, D.V.M., Ph.D., ACVP, ACLAM, www.kumc.edu/lar/index.html) at the University of Kansas Medical Center is charged with the housing and care of research animals at the Medical Center campus. It is independent of the Lawrence campus facilities. Animals are maintained at two locations. The principal site is the Research Support Facility (RSF), which includes conventional rodent rooms, clean corridor rooms, biohazard suites, and isolation cubicles. Other rooms are designed for larger laboratory animals. The second animal facility occupies the fifth floor of the Mental Retardation Research Center (MRRC). The MRRC is a self-contained biomedical research operation that includes an animal facility with support space as well as conventional rooms for housing rodent species, chickens, and monkeys. A third animal facility is nearing completion (Oct 2006). This facility includes approximately 15,000 sq ft of housing and support space. The new facility will include a cagewash, procedure rooms, the transgenic core facility, a rodent behavioral core, and an ABSL3 laboratory. Animal care and use facilities are detailed in the table below. The Director of Laboratory Animal Resources is responsible for management of the department including meeting all regulatory requirements and maintaining AAALAC accreditation. Departmental staff includes two veterinarians, a departmental accountant (CGFM), and an assistant director for facilities. Dr. Nathan Culley (DVM) is the associate director. Dr. Pinson currently serves as interface to the Experimental Therapeutics Program. He has work experience in drug studies, contract laboratories and Good Laboratory Practices regulations. He is also a board certified veterinary pathologist. The day-to-day operation now includes 35 full time employees.

Animal Housing Sites

Location (Building/site name)	Distance from main facility	Approx. sq.ft./m animal care & use (net)	Approx. sq.ft./m support space (net, not including hallways)	Species housed	Person in charge of site
Research Support Facility	Main housing area	75,896 gross ft ² Administration: 4918 ft ² Net Animal: 14049 ft ² Mechanical: 5972 ft ² Support: 20,399 ft ²		Rats Mice Macaques Sq. monkeys Chickens Pigs Hamsters Rabbits Frogs Cats Dogs Gerbils Guinea pigs	Director, LAR
Hall Biomedical Research Building	<0.1 mile	~ 15,000 gross ft ² Administration: available Net Animal: Not available Mechanical: Not available Support: Not available Includes Rodent Behavior Core and ABSL3 Laboratory	Not	Mice Rats	Director LAR
2035 WHW	<0.1 mile	110 gross ft ² No administration support space	or	Mice	Director, LAR
5020E WHE 2027 WHE	<0.1 mile	Zebrafish tanks		Zebrafish	Director, LAR
Hoglund Brain Imaging Center G033	<0.1 mile	322 ft ² No administration support	or	Mice Rats	Director, LAR
Smith Mental Retardation Research Center	Located 0.25 mile from the main facility	6170 gross ft ² Administration: 105 ft ² Net Animal: 2713 ft ² Mechanical: 306 ft ² Support: 1376 ft ²		Macaques Sq. Monkeys Rats Mice Hamsters Chickens	Director, LAR

The Hoglund Brain Imaging Center (HBIC) (Director William (Bill) Brooks, Ph.D., www.kumc.edu/hoglund/) is an 11,500 sq. ft. free-standing building located near the University of Kansas Hospital and adjacent to the Animal Research Facility. Human MR imaging studies are carried out on a 3 Tesla Siemens Allegra system, which provides a full array of state-of-the-

art imaging and spectroscopy capabilities including anatomic imaging, functional MRI, angiography, diffusion weighted imaging and tractography, magnetization transfer imaging, and both proton and phosphorus with proton decoupling magnetic resonance spectroscopy for metabolic studies. Human cortical MEG studies are carried out using a 151-channel biomagnetometer system manufactured by CTF Systems Inc. Visual, auditory, and somatosensory stimulation equipment is available, as is data analysis software for single and multiple spatio-temporal modeling of both MEG and EEG data. Clinical studies are supported by changing rooms, consultation rooms, and clinical space for nursing support, and for participant preparation such as placing venous lines for injections and preparation for MEG studies. Animal MR imaging and spectroscopy studies are carried out on a 9.4 Tesla Varian system equipped with an actively shielded magnet to minimize the stray magnetic field. The 31cm horizontal bore and three sets of gradients allow studies of small animals including mice, rats, and small primates. For animal studies, there are animal preparation areas where anesthesia can be invoked, minor surgery can be carried out, and where animals can be held for short durations before and after examinations.

The Electron Microscopy Research Laboratory (EMRL) (Barbara Fegley, Lab Manager, www.kumc.edu/emrl/) is well equipped for routine EM applications and technical personnel are available to assist investigators. The EMRL is equipped with transmission electron microscopes (a JEOL 100CX II with Gatan Bioscan Digital Camera, and a JEOL 100S), a scanning electron microscope (Hitachi 2700 with Quartz PCI digital capture system) and microtomes (LKB Nova Ultramicrotome, Leica UCT Ultramicrotome, Leica-S Ultramicrotome, LKB Historange microtome), as well as critical point drier, carbon evaporator and sputter coater.

The Confocal Imaging Center (Director Michael J. Werle, Ph.D., www.kumc.edu/cic/index.htm) provides state-of-the-art laser confocal microscopy services. The Center is equipped with an LSM 510 Laser Scanning Microscope which offers four simultaneous confocal channels for reflection and fluorescence, plus an extra channel for transmitted-light examination. The LSM 510 resolves no less than 2048 x 2048 pixels, with four independent 12-bit analog-to-digital converters providing up to 4096 brightness levels. This is ideal for morphology and physiology, for experiments such as calcium ratio imaging, release of caged compounds or FRAP. The Center also has a Leica Laser Microdissection Microscope – ASLMD. Laser microdissection offers researchers a tool for precise non-contact and contamination-free preparation of cell groups or single cells cut out of histological tissue sections. The laboratory is staffed by a full time manager.

The KUMC Transgenic and Gene-Targeting Institutional Facility (TGIF) (Director Melissa Larson, Ph.D., www.kumc.edu/TGIF/) provides a centralized service for production of transgenic and gene-targeted mice for researchers in KU and other regional institutions. Our mission is FIGT: Facilitate Innovations in Gene-targeting and Transgenesis. The facility is currently supported by the School of Medicine.

The facility has two labs: one embryonic stem cell culture laboratory and one animal care laboratory. The facility is equipped with state-of-the-art instruments for making transgenic and knockout mice. A Nikon TE2000 inverted microscope with Nomarski optics and temperature-adjustable warming/cooling stage is used for microinjection. This microscope is equipped with Narishige manipulators, a pair of Narishige micrometers and an Eppendorf CellTram micrometer to accomplish pronuclear and blastocyst injection. A de Fonbrune microforge, a Kopf vertical pipette puller and a Sutter P-97 horizontal puller are utilized for making holding and injection pipettes. A Bio-Cool controlled-rate freezer is available for cryopreserving embryos and gametes. The ES cell laboratory has equipment available to support the culture and manipulation of embryonic stem cells, including a BioRad GenePulser II electroporator for the transfection of DNA into ES cells.

The TGIF will be moving to new laboratory space in the Fall of 2006 in the newly constructed Biomedical Research Center on the University of Kansas Medical Center campus. Coincident with this move, the facility will be purchasing another Nikon TE2000 inverted microscope equipped with DIC, HMC and fluorescence, as well as Eppendorf Cell Tram air and vario micrometers, an Eppendorf Femtojet and a Piezo drill. Other new equipment purchases include four Sanyo MCO-18M tri-gas incubators; new stereo and tissue culture microscopes with video and high resolution camera capabilities; a new controlled-rate freezer; an auto-fill liquid nitrogen storage tank and a vapor shipper. The facility will then be equipped to offer a full range of embryo services, including generation of transgenics, chimeras and targeted embryonic stem cells; cryopreservation of sperm, embryos and oocytes; and assisted reproductive techniques such as rederivation, in vitro fertilization, and intracytoplasmic sperm injection. The new laboratory space will centralize our operations, with accommodations for embryo manipulations and cryogenics, distinct cell culture space, animal holding rooms and offices.

Biospecimen Shared Resource (BSR) (Director Ossama Tawfik, M.D., Ph.D., otawfik@kumc.edu) is a core facility supported by the Kansas Masonic Cancer Research Institute (KMCRI). It specializes in the collection, preservation, and distribution of human tissues and blood samples obtained from patients undergoing surgical procedures for the breast and prostate. In addition, ovary, endometrium, and uterine tissues have been collected. The BSR has also obtained approval to collect intestine, lung, and liver samples. The overall objective is to serve as a resource for investigators who require a comprehensive, well-documented storehouse of human tissue and blood samples to conduct cancer research. The goals of the BSR are to promote translational research activities among basic and clinical scientists. Priority is given to cancer investigators who are KMCRI members.

The Center for Biostatistics and Advanced Informatics (CBAI) (Director Mathew S. Mayo, Ph.D. biostatistics.kumc.edu/) mission is to provide and infrastructure of biostatistical and advanced informatics expertise to support and enhance the research, service and educational needs of the University of Kansas Medical Center. The CBAI has up-to-date hardware and software facilities. The Center provides expertise in data entry, management, study design, database design, sample size and power calculations, statistical analysis and graphics, as well as grant and manuscript preparation in support of basic, clinical and population-based research.

Flow Cytometry Facility (Director Joyce Slusser, Ph.D.) at the Kansas University Medical Center is dedicated to providing analysis of both patient and research specimens for the purpose of immunophenotypic type of analyses and DNA ploidy and cell cycle analyses. The facility is equipped with a Coulter XL flow cytometer powered by a Pentium III 500MHz system for both data acquisition and analysis. In addition, the facility has three workstations for post analysis requirements. The facility is staffed with three technicians. Two of the technicians are medical technologists specifically trained in analysis of patient samples as related to leukemias, lymphomas, bone marrow transplant progenitor cell enumeration, and CD4+ enumeration. The third technician is responsible for all research related aspects of analysis and all patient and research related DNA analysis. The instrument is capable of four color analysis and can analyze specimens as small as bacteria and chromosomes and as large as macrophage or larger fibroblast type cells. The facility can accommodate total sample preparation through and including data analysis or can receive investigator prepared specimens for data analysis only. The instrument is located within the Clinical Laboratories Department at the Bell Memorial Hospital.