OVERALL FACILITIES AND OTHER RESOURCES

Yale University

Founded in 1701, the University has over 5,259 faculty members and 10,891 staff with total operating expenditures of $ 4.2 billion and includes expected revenue of approximately $5.57 billion by June 2024. The University supports 13 Graduate and Professional Schools which provide investigators with a wide range of opportunities for collaboration. Research funding for the University exceeds $787 million. The University has 6 K12 awards specifically designed to train doctoral students in patient-oriented research. The School of Medicine is also the recipient of over 29 T32 and over 25 K23/24 awards (with one T32 Award that allows medical students to work towards a Master's degree in clinical research) and over 80 program project, center, and cooperative agreement grants. As of October 2020, 65 Nobel laureates have been affiliated with Yale University. Currently, 67 Yale faculty are members of the National Academy of Sciences including 16 from the YCC.

Yale School of Medicine

The Yale School of Medicine (YSM) is located in proximity to Yale College, the Graduate School of Arts and Sciences and 10 additional professional schools. The School has 5,358 full time and part time faculty members. Over 1,704 postdoctoral research scientists are actively employed in School of Medicine laboratories. There are more than 518 MD and MD/PhD students, 695 MPH students, and 279 PA students. In addition, 416 PhD students are enrolled in the Graduate School of Arts and Sciences who are conducting thesis research in YSM laboratories. Research funding exceeds $836.2 million and the School ranked 7th nationally in total NIH funding in 2022. Organizationally, the School consists of 28 research intensive departments and sections in both clinical and basic sciences.

Yale-New Haven Hospital/Yale New Haven Health System

Yale-New Haven Hospital (YNHH*)* is a 2,681-bed university teaching hospital located next to the Medical School. In August 2012 the former Hospital of Saint Raphael located 1 mile north of the main YNHH campus joined YNHH to form a 1,541-bed general hospital under the license of YNHH. YNHH, affiliated with the Yale University Schools of Medicine and Nursing, includes a 201-bed Yale-New Haven Children's Hospital, a 76-bed Yale-New Haven Psychiatric Hospital, and Smilow Cancer Hospital (SCH). Yale-New Haven Health System is anchored by Yale-New Haven Hospital in New Haven. Bridgeport Hospital, 325-bed general hospital facility 25 miles south of New Haven, and Greenwich Hospital, with 250 beds, is 45 miles south of YNHH. All three hospitals have independent boards and operating budgets. Bridgeport Hospital serves a diverse inner-city population in the city of Bridgeport as well as several affluent suburbs in Fairfield County. In addition to serving Greenwich, Connecticut, Greenwich Hospital serves a substantial population from eastern Westchester County in New York State. Integration of the cancer programs of Bridgeport and Greenwich with YCC and SCH will be a major priority of the health system with the principal goal being increasing access to clinical trials throughout the state.

Smilow Cancer Hospital

The Smilow Cancer Hospital is the principal site of clinical care of the Yale Cancer Center. SCH is a 15-story building that incorporates radiation oncology, medical oncology, hematology, and surgical oncology. There are 168 beds in the hospital of which 115 are occupied by Smilow patients (ICU and Step Down are shared with non-SCH patients). Several multidisciplinary clinics also involve specialists such as dermatology (melanoma), pulmonary medicine (lung) and cardiology (cardiac oncology). The lower level of the hospital is the site of radiation oncology with 3 linear accelerators with multiple photon and electron energies, stereotactic body radiosurgery and gating capability, and image guided radiotherapy (IGRT/IMRT/MLC/Portal Imaging), as well

as one simulator and one gamma knife facility. The first-floor houses multidisciplinary clinics for women's cancer including infusion facilities (30 treatment chairs). The Adult and Pediatric Survivorship Programs also have clinical space on the first floor. The second floor of Smilow is diagnostic imaging including CT, MRI, and PET/CT. The third floor is the home of a dozen oncology operating theaters including the world's first three Tesla MRI embedded neurosurgical operating rooms (2). The fourth, seventh and eighth floor house multidisciplinary clinics and infusion space for solid tumors, research pharmacy, routine pharmacy, hematologic malignancy, and bone marrow transplant, respectively. Included in this space is a dedicated Phase I Unit, offices for research nurses and data managers. Smilow is also the home of the adult bone marrow transplant facility (inpatient, day hospital, infusion, and outpatient), and pediatric cancer outpatient facility. A pediatric bone marrow transplant center is contiguous to Smilow on the 8th Floor of YNHH.

In addition to the Smilow Cancer Hospital the Yale Cancer Center operates 14 regional cancer-care facilities in the following locations: Derby, Fairfield, Glastonbury, Greenwich, Guilford, Hamden, Hartford, North Haven, Orange, Torrington, Trumbull, Waterbury, Waterford and Westerly. All these sites operate under the Yale-New Haven Hospital (Smilow) license and are fully integrated faculty practice sites of the Yale Cancer Center using a provider-based model. The YCC supplies research staff to these sites to supervise enrollment of patients onto clinical research studies. A hybrid decentralization model is being implemented for patients to have access to Phase I clinical trials at the care centers, but many Phase II and III studies are open across the system. Since the practices are fully integrated, they operate under the Yale human studies committee.

VA Connecticut Healthcare System (West Haven and Newington Campus)

VA Connecticut is a 250-bed general hospital that provides general oncology and hematology services as part of its ongoing mission. The VA Connecticut Comprehensive Cancer Center diagnoses and treats approximately 550 new cases of cancer per year (excluding non-melanoma skin cancer). There are 4 Yale Cancer Center faculty members in hematology and medical oncology at VA Connecticut. Most VA Connecticut patients receive radiation therapy at the SCH. The cooperative group clinical trials are available through the VA Cooperative Trials Program, which is nationally recognized for its successful conduct of multi-center clinical trials. This program employs personnel in biostatistics, epidemiology, and data management, and provides resources for methodological and biostatistical collaboration for intervention trials and access to large databases for analysis which complement existing YCC resources. Some VA Connecticut patients are also referred for clinical trials at the YCC main campus when appropriate trials are not available locally.

Yale Cancer Center (YCC)

The Yale Cancer Center has been an NCI-designated comprehensive cancer center (NIH 3P30 CA16359) for over 49 years. It is one of 54 such Centers in the nation and the only one in Southern New England. The Center combines a tradition of cancer research, innovative cancer treatment, and quality care for its patients. It harnesses the resources of the Yale School of Medicine and Yale-New Haven Hospital to advance cancer research, prevention, and patient care, as well as community outreach and education. The total research and office space occupied by all Cancer Center members consists of more than 650,000 net square feet.

YCC Administration: YCC Administration Offices are in 3 principal locations. The YCC Director's Office is on the second floor of the Winchester Building in the Yale School of Medicine. The location is also near the offices of the YCC Deputy and Associate Directors to enhance interactions with key leadership. Conference facilities for Leadership meetings are located as part of the YCC Director's suite. The director has a second office suite embedded in the Smilow

Cancer Hospital for his role as the Physician-in-Chief of the Smilow Cancer Hospital. In this location the director is joined by the Chief Medical Officer of Smilow, the Senior Vice President for Smilow and the Director of Clinical Programs/Chief Nursing Officer. Finally core administrative functions (finance, grants and contracts, human resources) are housed on the periphery of the Cedar Street Campus at 100 Church Street South, a 5-minute walk from the Director's office.

YCC Facilities: The more than 300 YCC members occupy space throughout the Cedar Street, Science Hill (Central) and West Campuses of Yale University. As a matrix cancer center, YCC members have primary appointments in basic and clinical departments of the YSM, YSPH, YSN or FAS and principally the home department administers their space. The great majority of these laboratories are newly constructed or recently renovated and represent state-of-the-art research facilities and totals nearly 462,886 ft^2 of research space. In addition, the Cancer Biology Institute (CBI) at Yale West Campus provides an additional 30,000 ft^2 for 12 new faculty recruits. The 7 Shared Resource facilities and Clinical Trials Office supported by the YCC are located in the Cedar Street Campus and the West Campus and occupy approximately 23,000 ft^2.
The YCC is administrative home for the 32,000 ft^2 of laboratory and office space used by the >40 faculty in Hematology and Medical Oncology as well as the YCC administration. This space is in 2 locations adjacent to the YCC Director's office and in the George Street and Congress Avenue location.

1)The Yale Center for Genome Analysis (YCGA)
The YCGA at Yale's West Campus provides rapid and cost-effective, state-of-the art genomic technologies to the largest possible number of cancer investigators. YCGA occupies 9,000 ft^2 of custom-designed laboratory space and is well equipped with several microarray (Affymetrix, Illumina, Sequenom and NimbleGen) and high throughput sequencing (two Illumina NovaSeq6000, one Illumina HiSeqs, one illumina MiSeq, one each of PacBio RS, MiSeq and Ion Torrent) platforms. The YCGA provides >30 genomic services including: i) gene expression and whole transcriptome analysis, ii) SNP genotyping and copy number variation, iii) Whole-exome (WES), whole-genome (WGS), targeted sequencing, mRNA-Seq, ChIP-Seq, methyl-Seq, microRNA-Seq and de novo genome sequencing analysis, v) analysis of formalin-fixed paraffin-embedded tissue, vi) methylation analysis, vii) miRNA analysis and discovery, viii) chromatin immunoprecipitation to study protein-DNA interactions, ix), single cell RNAseq, and x) spatial transcriptiomics (Visium, Illumina, MERFISH spatial multiomics), and xi) single cell genomics and single cell multiomics (DNA+protein). Together, the microarray and sequencing technologies of YCGA offer comprehensive support to study genetic events in cancer development which has the potential to aid in identification of genetic and biochemical causes of the disease, develop better diagnostic methods, and to improve therapeutic outcomes and patient care. In addition, the bioinformatics team has extensive experience in conducting high level analyses by developing new algorithms and data analyses tools. They work very closely with the HPC team to manage data storage and develop analysis pipelines.

2) The Yale Center for Molecular Discovery (YCMD)
Yale Center for Molecular Discovery (YCMD) is a core facility providing high throughput and high content assay development, screening and hit validation services to the scientific community. The YCMD supports and makes available for screening a diverse collection of drug-like small molecules (over 250,000 compounds) and genomic libraries (human arrayed genome-wide sgRNA/CRISPR and siRNA collections). YCMD also maintains a sophisticated infrastructure, including cutting-edge screening instrumentation and analysis databases, to support high throughput and high content assay design, testing, liquid handling, and reformatting needs. YCMD

develops biochemical, cell-based, and model organism-based assays with both plate reader and quantitative microscopy-based readouts.

The mission of the Center is to blend innovative research capabilities and practical experience to create statistically robust and rigorous approaches, developing nimble means to accelerate basic scientific concepts into innovative applications. Highly trained and experienced staff has unique and deep expertise in assay optimization, screening, and validation, offering services that span a range of investigator-driven goals. Established in 2003, YCMD continues to be successfully utilized by YCC members to understand basic biological processes, facilitate discovery and validation of new therapeutic targets, and help discover novel small molecule probes that may serve as tool molecules or starting points for new therapeutics.

3) Yale Pathology Tissue Services (YPTS)

Yale Pathology Tissue Services (YPTS) is committed to providing the maximum amount and quality of human tissue for research at Yale Cancer Center and Yale University without impacting diagnostic quality, accuracy, and safety in anatomic pathology. YPTS, established in 2007, based in the Department of Pathology, serves as a shared resource for YCC. The resource includes 3 divisions that work together to provide a full range of tissue services. The Tissue Distribution and Analysis (TDA) has about 40 active standard operating procedures (SOPs) for tissue acquisition, over half of which provide tissue to members of YCC including a series of federated tissue banks including banks for the Lung and HNSCC SPORE biobanks. Two of these SOPs are for the new Yale Biobank (a new University-wide, centrally supported tissue bank anticipated to replace the federated tissue banking system in the future). The TDA division also provides slide scanning and quantitative analysis services for Yale investigators. The Developmental Histology division provides comprehensive human and animal histology services, including chromogenic immunohistochemistry, bespoke fixation and processing, frozen sections, TMA construction and distribution and access to the Yale Pathology archives for historical diagnostic tissue. DH/TMA has nearly 600 master blocks, some with as many as 20 replicates, and distributes 10,000-50,000 TMA slides per year. Clinical Trials Tissue Services provides rapid access to tissue for patient enrollment in trials requiring tissue samples both within Yale and for outside institutions. The resource has been directed by Dr. David Rimm since 2007 with a 5-member leadership team that helps manage about 15 FTEs. The services are ordered online, supported by a dedicated IT person from the Department of Pathology's IT unit. The software was built at Yale and is maintained and updated by our IT person (Sudha Kumar) including "eHisto", the tissue and services ordering and accounting system and "Aquamine", a PHI-free database for tissue microarrays and whole slide cohorts available from YPTS.

4) The Biostatistics Shared Resource (Biostatistics)

This Shared Resource provides support for the four broad major programmatic areas of YCC: clinical science; basic science; translational science and population science. It provides a highly interactive team of cancer biostatisticians and bioinformaticians who work collaboratively with basic, clinical**,** translational and population science researchers to advance the frontiers of cancer medicine and public health. The Biostatistics Shared Resource includes faculty and staff in the Yale School of Public Health (YSPH) who collaborate actively on a wide range of cancer research projects and develop new methodologies and software related to these projects. The services provided by the Biostatistics Shared Resource include: biostatistical and bioinformatics support to grant applications, protocol development and experiment design, data analysis and management support to studies, and training. Additionally, this shared resource makes major contributions to protocol review as well as data and safety monitoring. As such, it is vital to cancer research design, execution, analysis, and reporting.

5) Flow Cytometry Shared Resource

The Flow Cytometry Shared Resource supports clinical, basic and population sciences research at YCC. The services provided include comprehensive cytofluorometric analyses and sorting to the YCC investigators and the broader YSM community. This facility provides access to a large collection of cell sorters and analytic flow cytometers, as well as staff to operate the cell sorters, maintain the analytic instruments, and provide advice on fluorophore panel design. Staff assistance is also available on a fee-for-service basis for sample preparation, data acquisition or data analysis. For cell sorting, the facility has a Sony SH800, and 6 BD Aria sorters staffed with FTE operators and distributed across the Medical School Campus in 4 buildings including the TAC, Amistad and 300 George St buildings. An Aria cell sorter is located within the BSL3 facility to enable the sorting of samples that are potentially infectious with Risk Group 3 pathogens. One of the Arias can accept clinical samples on same day notice, which facilitates the sorting of fresh clinical specimens that have arrived unexpectedly. In addition, two Bigfoot cell sorters have been recently installed that offer the option to sort using either spectral unmixing or traditional light separation and compensation. Despite being high-speed, the Bigfoot sorters are exceptionally gentle on cells and have the added advantage of sorting simultaneously into any combination of 1.5 ml, 5ml, 15ml or 50 tubes. This core facility supports multiple models of analytic cytometers that are maintained and overseen by facility staff: 2 CytoFlex LXs (5 laser, 20 detectors for fluorescence), 4 BD LSRII analyzers (4-5 lasers, 20 detectors), 2 BD Fortessas (4 lasers, 16 detectors) and 2 BD Symphony cytometers (6 lasers including a 780 nm laser, 30 detectors). Custom filters are made available for infrequently demanded specialty detections such as side populations, or GFP/YFP discrimination. Both CytoFlex and Fortessa cytometers have robust plate loaders that permits sample acquisition directly from 96-well plates. This facility also maintains an Amnis Imagestream Mark II for image flow cytometry and a Luminex 200 analyzer. Software analysis programs available for use at workstations include Diva for BD instruments and IDEAS for the analysis of Amnis data. Finally, we manage a site license for FlowJo (PC and Mac) that charges users a low monthly rate per computer.

6) Yale Cancer Center (YCC) Translational Immuno-oncology Laboratory

Overview: This YCC platform aims to produce and support high quality immune-monitoring, translational and biomarker studies in immuno-oncology through standardized analyses of tissue biomarkers and cross-integration with other resources including flow cytometry, CyTOF Helios, STS CLIA lab, the Center for Genome Analysis (YCGA) and the new Mass Cytometry Imaging platform.

Structure/organization: The platform is directed by Kurt A. Schalper, MD/PhD and supported by a scientific oversight committee composed of Drs. David Rimm (Pathology/biomarkers), Mario Sznol (Oncology/immuno-oncology) and David Hafler (Immunobiology/neurology). The administrative lead is Dr. Edward Kaftan, PhD from the Yale Cancer Center. The immunology co-lead is Dr. Khadir Raddasi. Our team has prominent experience performing immuno-oncology translational studies in samples from cancer patients and we have developed rigorous validation and experimental protocols.

Supported studies: Available resources include standardized biospecimen collection/storage and archive protocols for specialized immuno-oncology studies, conventional pathology/tissue services, digital pathology imaging station for bright field slide analyses, laser capture microdissection, validated quantitative immunofluorescence panels for protein & nucleic acid measurement in tumor tissues using multiplexed staining and automated target quantification by 3 independent multispectral imaging platforms (AQUA, Vectra3 and Mantra). Additional studies include analysis of solid tumor tissues and peripheral blood/PBMCs using a 38-marker immune marker CyTOF panel. Capacities for measurement of cytokines in liquid samples using the

Luminex technology and cell sorting of immune cell subpopulations for functional studies are also available. In collaboration with the YCGA and external partners we support high throughput genomic studies including whole exome DNA sequencing, RNA-sequencing, and T-cell receptor clonality. We also support specific immuno-oncology related bioinformatic analysis pipelines (e.g., WES-based HLA-typing, mutational load and neoantigen analyses).
Innovative methods/services: Our group has recently acquired the new Mass Cytometry Imaging platform (Fluidigm Corporation) with capacity of in situ measuring up to 40-60 protein targets simultaneously, with quantitative output and preservation of the morphological context. Studies in this equipment are amenable for both fresh and FFPE tissue samples.

7) Yale Center for Precision Cancer Modeling
The goal of the Center for Precision Cancer Modeling (CPCM) is to enable scientifically informative preclinical studies for cancer drug development. CPCM offers a wide variety of *in vivo* cancer models as well as unique models developed at Yale, including models that enable the evaluation of anti-cancer immune responses. CPCM is fully equipped to perform left ventricle injection metastasis models and has developed 3D patient tumor explant models that may be very useful for studying tumor microenvironment and therapeutic responses. These cancer models can be utilized for the investigation of drug candidates as single agent therapy, comparative efficacy studies, or combination studies with standard of care therapies. The CPCM can organize and carry-out a full suite of preclinical evaluation of the drug candidates of interest including Toxicology (Tox), Pharmacokinetics (PK), and Pharmacodynamics (PD). The experiments can be highly customized to suit the candidate drug. The CPCM can collaborate in developing animal protocols and generating high quality data for academic publications or commercial development. In addition, CPCM oversees training, access, and performance of integrated bioluminescent, fluorescence and X-ray imaging of small animals using a dedicated IVIS Spectrum and IVIS LuminaX5.

8) The W.M. Keck Biotechnology Resource Laboratory
The W.M. Keck Biotechnology Resources Laboratory provides proteomic capabilities mainly based on mass spectrometry, including extensive phosphoproteomic capabilities and supporting chemistry resources. The Keck Lab is organized into three genomic resources (Sanger DNA sequencing, Microarray and next- generation sequencing and Oligonucleotide synthesis), two proteomic resources (Mass Spectrometry and Biophysics), and three multidisciplinary resources (Bioinformatics, Biostatistics, and High-Performance Computing). These resources have served hundreds of investigators who depend upon the expertise of their staff and their highly sophisticated and expensive instrumentation to support their genomic and proteomic research. The facility's major equipment includes: Affymetrix GeneChip system, Illumina iScan, one Tecan Robotics, Pacific Biosciences Sequel II third generation sequencing system, four 10x Genomics' Chromium single cell genomics system, One MissionBio Tapestri Single Cell DNA analysis system, one PhenomeX IsoSpark single cell proteomic and transcriptomic system, one PerkinElmer Chemagic 360 nucleic acid isolation system, Agilent Fragments analyzer, tapestation and bioanalyzer, three Applied Biosystems 3730xl DNA Analyzers, Tecan Freedom Evo 150 Liquid Handling System, two Beckman NX Lab Automation Workstations, Agilent 2200 Tape Station, two x BioLytic Dr. Oligo-192 High-Throughput DNA/RNA Synthesizer, 10 x ABI 394 DNA/RNA Synthesizer, K&A H-16 Synthesizer, Perkin-Elmer LabChip GX microfluidic electrophoresis system, BioLytic Dr. Oligo Processor purification system, SGI-DNA BioXP 3200 Gene Synthesizer, DAWN HELEOS II multiangle laser light scattering detector, Agilent 1200 HPLC system, which comprise the Size Exclusion Chromatography coupled with Multiangle Light Scattering (SEC/MALLS) system, VP-ITC; Isothermal MicroCalorimeter (ITC), Chirascan, Circular Dichroism (CD) spectrophotometer, Biacore T200; Surface Plasmon Resonance (SPR) Sensor, two HPLC systems with DAD, FL, refractometer and light scattering (static and dynamic) detection,

Eclipse 3 Asymmetric flow Field-Flow Fractionation coupled with Multiangle Light Scattering (AFFF/MALLS), nanoparticle tracking analysis (NTA) system and standalone Dynamic Light Scattering system (DLS) three proteomics mass spectrometers (Orbitrap Fusion Tribrid, Q-Exactive HFX, and Q-Exactive Plus) coupled to individual nanoUPLC systems, and a 4000 QTRAP LC MS/MS mass spectrometer for quantitative small molecule analyses. The Keck Laboratory is making an important contribution to biological and biomedical research that extends far beyond Yale University.

9) Yale Center for Cellular and Molecular Imaging

The Yale Center for Cellular and Molecular Imaging provides training services for students and fellows, sample preparation, and access to light and electron microscopy equipment.

Light Microscopy. Confocal and two-photon instrumentation includes Zeiss LSM 510, LSM 510 Meta, and Zeiss LSM 710 Duo NLO/Multiphoton Microscope. The meta feature records a complete spectrum at each pixel of an image allowing sophisticated spectral un-mixing to be performed.

Electron microscopy (EM) services include both biological and cryo electron microscopy. We have 4 transmission electron microscopes (TEM) for room-temperature and cryo samples. A scanning electron microscope (SEM) and Focused-ion-beam SEM for whole cell volume imaging, and various EM sample preparation equipment. As a full-service lab, our experienced staff members prepare and image biological samples for investigators. We also offer training for users who want to operate the electron microscopes independently.

10) Yale Macromolecular X-ray Core Facility

The Yale macromolecular X-ray Core Facility provides equipment, training, assistance, and technological innovations for determining three-dimensional structures of proteins and other macromolecules. The facility is dedicated to X-ray diffraction and crystallographic studies and uses state of the art technology to understand the structural basis for biological function. The Center for Structural Biology houses a core X-ray diffraction, graphics, and computation facility with three phosphorimaging plate detector systems, a small angle X-ray scattering station using a multiwire area detector, and three rotating anode X-ray generators.

11) Magnetic Resonance Research Center (MRRC)

The Yale MRRC is dedicated to the development of novel approaches to imaging and imaging related research studies. The center contains all the computing resources needed for software development and analysis. Imaging supporting infrastructure includes all the facilities needed for construction of magnets, coils, data acquisition modules, and associated interface boxes. A more detailed description of each of the major components of the center is given below. Note that all these systems are dedicated 100% to research activity.

The Computing lab at MRRC are used to program pulse sequences, reconstruct images, analyze data, and develop and test new analysis algorithms. The shared workstations in the computing lab are utilized for data analysis including preprocessing, clustering, predictive modeling, and imaging tasks such as image registration, motion correction, functional MRI analysis and connectivity analysis including high-level network analyses. We have several data science investigators on this proposal who are experts at programming (Matlab, python, Java script, C++). BioimageSuite will be used for all the image analysis and predictive modeling, including, motion correction, data editing, general linear model statistics and multiple approaches for corrections for multiple comparisons as well as k-fold validation. All the data is housed in the data center located at the MRRC. The data center houses several servers, which are built with fault tolerant design and can currently store over 14 terabytes of imaging data. Computers and software are upgraded and patched on a regular basis and the computing environment is highly secure, and

HIPAA compliant. Access to the computers is password restricted and available only to the members of MRRC.

12) Yale Center for Research Computing

The Yale Center for Research Computing (YCRC) supports and provides access to four high performance computing (HPC) clusters located in an HPC data center at Yale's West Campus facility. Yale operates a high-performance network infrastructure in support of research computing and HPC throughout the campus. To facilitate high-speed data transfers, the YCRC holds a site license for the Globus file transfer and sharing software. The YCRC supports several Globus endpoints for the HPC clusters. Other Yale departments and laboratories can create endpoints supported by departmental or IT staff. Other Yale departments and laboratories can create endpoints supported by departmental or IT staff. All endpoints are connected to Yale's Science Network and Science DMZ, enabling high-speed data transfers among Yale, national supercomputing facilities, and other universities with whom Yale researchers collaborate world-wide. Starting July 1, 2022, each research group is allocated 25,000 hours of usage on institutionally funded nodes per year (July 1 - June 30) at no charge. Usage in excess of 25,000 incurs modest charges at rates well below the actual cost to provide the service. No charges are incurred for usage on researcher-funded nodes including those funded by grants. For research data in active use, the Storage@Yale file storage system provides mirrored storage that is optimized to provide research labs, departments, schools, and individual researchers the ability to store and use large quantities of data on the HPC clusters or any Windows, Mac or Linux computer connected to the Yale network. For archive storage, Yale operates an archive cloud storage service which can be accessible to the HPC clusters. Throughout its campus, Yale operates a high-performance network infrastructure in support of research computing and HPC. The 100-Gbps Science Network connects the HPC datacenter and the main campus. It also provides a direct connection to the Internet2 through a non-firewalled Science DMZ, currently running at 10 Gbps, but scalable up to 100 Gbps should that be required in the future. Virtual LAN technology is used to segregate access and applications on the network, and 10-Gbps connections are provided via the VLANs to several individual laboratory and departmental storage and server facilities.

To facilitate high-speed data transfers, the YCRC holds a site license for the Globus file transfer and sharing software. The YCRC supports several Globus endpoints for the HPC clusters. Other Yale departments and laboratories can create endpoints supported by departmental or IT staff. All endpoints are connected to Yale's Science Network and Science DMZ, enabling high-speed data transfers among Yale, national supercomputing facilities, and other universities with whom Yale researchers collaborate world-wide.

Yale has a separate main campus network based on a 10-Gbps backbone, with most buildings connected via 1-Gbps local networks. The main campus network is currently used for all university purposes other than high-speed data transfer through the Science Network VLANs. It also provides commodity Internet connectivity via multiple 1-Gbps connections from several commercial vendors. In addition to the direct connection from the Science DMZ, Yale provides one firewalled 10-Gbps connection to Internet2 from the main campus network. Over the next several years, Yale is upgrading its main campus network, incorporating both a faster backbone and software defined networking technology.

13) Yale Genome Editing Center

This facility creates genetically engineered mice (knockouts, knockins, point mutations, conditional (floxed) alleles) via CRISPR/Cas genome editing, gene targeting via homologous recombination in ES cells, and traditional transgenic mouse technology. YGEC also cryopreserves sperm or embryos of inherently valuable genetically altered mouse strains.

Assisted reproduction technologies include strain reanimation or rescue via in vitro fertilization and/or embryo transfer.

14) Yale Animal Resources Center

The Yale Animal Resources Center (YARC) is a comprehensive, University-wide AAALAC-accredited program with rodent housing, animal biosafety level (ABSL)-2, ABSL-3, aquatics, large animal, non-human primate, quarantine, surgery, imaging, and gnotobiotic housing facilities. In addition to husbandry and veterinary care, YARC's umbrella also includes: 1) a Rodent Services unit which provides colony management and technical services for rodent-based research; 2) a Yale Genome Editing Center which produces genetically engineered mice, cryopreserves sperm or embryos, and reanimation from cryopreserved embryos or sperm and/or the rescue of unique mouse lines; 3) a Zebrafish Research Center which provides expert resources to create transgenic zebrafish and provide assistance in phenotyping them. In addition to YARC, the Department of Comparative Medicine (CMed), an academic department within the School of Medicine, supports the animal program through diagnostic, phenotyping services and histology services.

15) Yale Center for Clinical Investigation (YCCI) Research Services

Clinical Research Services is an essential shared resource that provides centralized, integrated, and coordinated support for cancer clinical trials conducted through Yale Cancer Center. Clinical Research Services is comprised of the Clinical Trials Office (CTO) and Office of Protocol Review and Monitoring (OPRM) as well as resources for contracts and budgeting and protocol development. A Protocol Review Committee (PRC) and a Data and Safety Monitoring Committee (DSMC) oversee all clinical trial activities for the Yale Cancer Center, along with the Institutional Review Board (IRB) and Human Investigation Committee (HIC) at Yale School of Medicine.

The purpose of the Clinical Trials Office (CTO) is to provide support to clinical investigators in initiating and conducting clinical trials, as well as collecting and preparing clinical trial data for the reporting of results from clinical trials. Clinical trials and data monitoring plans are required to be registered with the CTO. The CTO is responsible for: the initiation and maintenance of regulatory files, identification and extraction of source documentation for entry into centralized clinical databases and/or corresponding case report forms, assistance with the processing of protocol specimen collection and shipping, collaboration with the research team to maintain and coordinate the efficient and accurate collection of data and regulatory documentation, regular communication with the research team regarding study-related data collection and reporting issues, assistance in the preparation and submission of regulatory applications, including any ongoing amendments, annual renewals, data safety reports as determined by the Yale Cancer Center Data and Safety Monitoring Committee (DSMC) and submission of all other related protocol documents, maintenance of individual research subject records by obtaining medical records, lab reports, treatment schedules, and other vital protocol-related information and assistance in HIC submissions, protocol revisions, and renewal processes as required.

The Office of Protocol Review and Monitoring (OPRM) is an administrative arm of Yale Cancer Center dedicated to the management and coordination of the Center's Protocol Review and Monitoring System (PRMS) and Data and Safety Monitoring (DSM) functions to support, facilitate, and assure the highest quality clinical research at Yale. Two major components provide for clinical research review and oversight: the Protocol Review Committee (PRC), and the Data and Safety Monitoring Committee (DSMC). YCCI has partnered with the Yale Human Subjects Protection Program (HRPP) to create a quality assurance and safety monitoring system to support investigators and improve the quality of clinical research at Yale. The Office of Quality Assurance

and Monitoring supports the oversight committees' administrative support, study monitoring, and Quality Assurance specialists.

16) Clinical Research Support Laboratory (CRSL)

The Yale CRSL's purpose is to collect, stabilize and process samples from patients participating in clinical trials as directed in the study protocols in collaboration with physicians, research and chemotherapy nurses, project and data managers and pharmaceutical company representatives. The CRSL also participates in the feasibility team discussions and site initiation visits for each study. The fourteen-member staff of the CRSL is comprised of a lab manager/director, one research associate and twelve lab technicians, all of whom have either a Bachelor's degree, LPN degree, or Master's degree. The 415 ft^2 laboratory space is located within the Smilow hospital with nearby storage space of 105 ft^2. Additional wet lab space of 270 ft^2 and storage space of 300 ft^2 are located in two adjacent buildings. Major equipment includes a) 11 tabletop centrifuges with most being capable of up to 3,000 g-force, and with ambient and/or refrigerated operation and swinging or fixed angle rotors; b) two micro-centrifuges capable of up to 18,000 g-force; c) a biohazard level-2 safety cabinet; d) a refrigerator; 3) three -20°C freezers; f) three -80° C freezers; and g) liquid nitrogen freezers. The CRSL staff regularly monitors the patient locations when collections are expected, so the samples are retrieved for processing as soon as possible after they are collected and are processed according to the protocol requirements. This may include fixation, centrifugation, refrigeration and freezing of samples, and some special procedures, such as making blood smears for differential counts, and the isolation of mononuclear cells from whole blood by Ficoll separation. After processing, the samples can be immediately stored or shipped directly to the analyzing laboratory or repository. In 2014, the CRSL processed almost 11,000 samples and sent out over 2,000 shipments. These samples included blood and urine, biopsy tissue or fine needle aspirate from biopsies, cheek cells from buccal swabs and hair follicles. Sample collections were performed for many high-profile clinical trials conducted at Yale, including many early therapeutics trials that collected serial blood and tumor samples and required patient consenting and extensive sample processing and shipping.

17) Rapid Case Ascertainment

The Rapid Case Ascertainment program (RCASR) was originally developed in 1986-1987 in response to a Connecticut Hospital Association (CHA) request to establish a single entity that would be responsible for all population-based cancer epidemiology studies that directly involve Connecticut hospitals. It was incorporated as a YCC Shared Resource on January 1, 1995, and approved by the NCI for July 1, 1998. RCASR assists cancer researchers in implementing and executing their studies by providing high-quality and cost-effective study management, cancer case identification, patient enrollment and interview, medical record abstraction, and specimen collection services so that investigators can accomplish their scientific goals. The Rapid Case Ascertainment Shared Resource (RCASR) also facilitates cancer research and population-based studies of cancer for YCC investigators, as well as outside ones, who wish to conduct research in the state of Connecticut (YCC catchment area). RCASR addresses the many administrative tasks common to all proposed hospital-based research in the state and provides a uniformly high-quality, well-coordinated interface with those individuals, institutions, and agencies crucial to the success of cancer research. RCASR also supports rapid cancer case identification for research and clinical purposes, and functions as an agent of the Connecticut Tumor Registry, as designated by the Commissioner of Public Health. The Specific Aims of the RCASR Shared Resource are to: (1) Provide consultation and assistance to investigators in protocol writing in appropriate areas (protection of human subjects, HIPAA regulations, confidentiality, study feasibility, etc.); (2) Obtain approvals to conduct the research and submit annual reports and re-approvals to IRB's; (3) Perform overall project management; (4) Identify patients with incident cancers; (5) Serve as an honest broker in studies that require the investigators to not know the

identity or the individuals whose data or specimens are being used for research (de-identified research); (6) Perform data collection and pathology specimen collection; (7) Manage blood and other specimen collections (i.e., stool, cerebral spinal fluid, biopsy cores) at YCC Care Centers; (8) Facilitate research across the state of CT (YCC catchment area), as well as targeting areas of higher cancer risk (e.g., cities of Hartford, New Haven. and Bridgeport).

18) Interventional and Diagnostic Radiology

The state-of-the-art 22,000 sq. ft. research Positron Emission Tomography (PET) Center was opened at Yale University in July 2004. The PET Center has a GE PETtrace cyclotron, with targetry for producing C-11, F-18, N-13, and O-15 radioisotopes. Chemistry modules are available for the production of a wide variety of radiotracers. The Center has 7 scanners, 3 for clinical imaging (HRRT, mCT-X PET/CT, and Vision PET/CT) and 4 for small animal imaging (3 Focus-220, Inveon PET/CT). The next-generation brain PET system, the NeuroEXPORER will be installed in spring of 2023. Two laboratories for blood and metabolite analyses are available. The Center also has an image analysis laboratory for investigators, with several workstations running image analysis software applications. To date, over 14,000 administrations of PET radiopharmaceuticals as part of quantitative *in vivo* PET studies have been performed with over 150 different radiopharmaceuticals, 62 of which have been used in human studies.

PET Center consists of four laboratories including PET radiochemistry laboratory; PET radioligand quality control (QC) laboratory; organic chemistry laboratory; blood and metabolite analysis laboratory.

Magnetic Resonance Imaging Facilities

Magnetic Resonance Center houses a total of eight Siemens MR systems including three Siemens 3.0T Verio scanners, one Siemens 1.5T Aera, one Siemens 1.5T Avanto, one Siemens 1.5T Espree, and one Siemens 3.0T Verio-IMRIS intra-operative magnet. The four Siemens 3.0T Verio scanners (used for the studies in this grant) are equipped with excellent gradient capabilities with 40mT/m maximum amplitude, and a slew rate of 200T/m/sec with a 100% duty cycle. The Siemens 3.0T Verio MR systems also have 32-channel head coils with fast parallel imaging capabilities. Research MR facilities houses MRI and MRS research groups from the Departments of Radiology & Biomedical Imaging and facilities dedicated to research. The center has three Siemens 3.0T Prisma scanners equipped with excellent gradient capabilities with 80mT/m maximum amplitude, and a slew rate of 200mT/ (m sec). These systems are dedicated to research studies for anatomic, functional, diffusion and metabolic MR.

Computed tomography:

Computed Tomography Imaging Facilities consists of a total of 12 CT scanners (combination of General Electric and Siemens) spread across both the main campus and ambulatory sites. This includes eight 64-slice CT machines, 3 Dual Energy CT scanners (number of acquired slices = 384; 2 x 192 slices) and one 128-slice CT system. There is an additional 16-slice CT system used primarily for Interventional Radiology guided procedures, with few, if any, diagnostic studies performed on this machine.

Cyclotron: A GE PETtrace cyclotron for radioisotope production is in the lower level of the PET Center. The cyclotron uses 16.5 MeV protons and 8.4 MeV deuterons to produce radioisotopes. A total of six targets are mounted in the cyclotron: two C-11 targets, two F-18 targets for production of [^{18}F] fluoride and [^{18}F] fluorine, one O-15 target, and one N-13 target.

PET Scanners: The Yale PET Center has two whole body PET/CT scanners: Siemens Vision with 3-4 mm spatial resolution and ~200 ps timing resolution, as well as simultaneous dual-energy

CT capability, .and Siemens mCT-X, with 109 PET slices with resolution of ~ 5x5x5 mm resolution, 128-slice CT). In addition, there is one brain-dedicated scanner (Siemens High Resolution Research Tomograph (HRRT), 104 rings, 207 slices with resolution of better than 3 x 3 x 3 mm). In June of 2023, the brain dedicated NeuroEXPLORER PET/CT was installed. This system has an axial field-of-view of 49.5 cm, 236 psec timing resolution, spatial resolution of < 2mm, and embedded stereovision camera system for continuous motion correction. For animal imaging, there are three small animal PET scanners (Siemens Focus 220, 48 rings, 95 slices with a resolution of ~ 1.4 x 1.4 x 1.4 mm at center field of view), and one small animal PET/CT (Siemens Inveon, 159 slices, with 0.8 mm slice separation, axial coverage of 127 mm, transaxial field-of-view of 100 mm, resolution < 1.5 mm, peak sensitivity > 9%). Adjacent to each human scanner room are patient prep rooms. All PET systems acquire list-mode data reconstructed on each scanner's reconstruction system. In addition, list-mode data files are transferred over the local Gigabit network (behind a hardware firewall) to a dedicated Linux cluster with 40 nodes and 352 processors (3.0-3.2 MHz). Images are reconstructed with the MOLAR algorithm (Motion-compensation OSEM List-mode Algorithm for Resolution-recovery Reconstruction). For brain studies, subject motion information is collected with a Vicra (NDI, Canada), which records head motion at a rate of up to 20 Hz. These are stored in a time-synced file and used by MOLAR to correct head motion. Continuous bed motion is available on the mCT and the Vision. Respiratory and cardiac gating are available on the Vision, mCT and Inveon.

19) Yale Library

The University maintains 21 libraries that make up the third largest library system in the world. The Cushing/Whitney Medical Library serves the biomedical and health care information needs of the Yale-New Haven Medical Center and the University and provides service to area physicians and medical libraries. The collections cover clinical medicine and its specialties, the pre-clinical sciences, public health, nursing, and related fields. A new level of partnership with ITS is providing a new vision for information services. In addition, Yale library's resources also include extensive licensed e-resources and extraordinary special collections that represent early printed books and a growing body of digital materials.