Philipps Universität Marburg

CORE FACILITIES:

Central Services for your successful Research

The **Core Facilities** of the Medical Faculty introduce themselves:

It is our mission to provide the scientific community at the Marburg University with high-end research equipment paired with scientific expertise and deep knowledge.

The Core Facilities are covering four central areas:

- **Microscopy**
- **Synthesis and Analysis**
- **In vivo Imaging**
- **Infrastructural Entities**

CORE FACILITIES:

Central Services for a successful Research

Extensive experience, specialized expertise and an excellent working environment are crucial prerequisites for successful biomedical research, especially in view of the steadily growing international competition. Within this framework, it is of utmost importance to have direct access to highly sophisticated methods and technologies. Core Facilities play a key role in this context as they provide the knowledge and high-end instrumentation necessary to provide state-of-the-art technical and conceptual support to the scientific community.

The importance Core Facilities nowadays play in medical research has been recognized by the Faculty of Medicine at Marburg University, which over the past years led to the implementation of a concept addressing these requirements on a long-term basis. This mission was accomplished by centralizing the financial and personal resources required to successfully operate these facilities. These continuing efforts started with the opening of the Center for Tumor Biology and Immunology (ZTI) in the spring of 2014. Since then the ZTI has become a central institution for numerous activities in the area of biomedical research hosting many of the facilities introduced in this brochure.

Prof. Dr. Rolf Müller
(Dean of Research, Faculty of Medicine)

Dr. Abdo Konur
(Manager, Research Core Facilities)

1 Microscopy

Cellular Imaging – Spinning Disc Confocal Microscopy

Spinning disc microscopy has dramatically advanced in the past decade and now represents one of the most powerful imaging technique to analyze the biological dynamics of living cells. Whereas single-beam laser confocal microscopes are limited in image acquisition speed, spinning disc microscopy allows capturing millisecond dynamic events with reasonable contrast, unraveling the intricate molecular processes occurring in living cells. The specific configuration of the microscope with FRAP and Optogenetic units further allows for rapid spatial and temporal live cell imaging.

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Multiphoton Microscopy

Multiphoton microscopy is a powerful research tool that combines the advanced optical techniques of laser scanning microscopy with long wavelength multiphoton fluorescence excitation to capture high-resolution, three-dimensional images of living cells within tissues and organs. In contrast to widefield, and to a lesser degree also to confocal fluorescence microscopy, excitation of fluorophores occurs only at the focal point resulting in blur-free images and minimized photobleaching and photo-damaging effects, allowing long-term observations of cells. The application of near-infrared excitation wavelengths permits deeper penetration into biological materials and reduces the high degree of light scattering that is observed at shorter wavelengths. Thus, multiphoton microscopy is the method of choice for experiments that require large image depths and at the same time high cell viability for a long time.

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Laser Microdissection (LMD)

Laser Microdissection allows for the contact- and contamination-free isolation of single cells or entire areas of tissue from a wide variety of samples under direct microscopic visualization. The dissected material is then available for further molecular biological methods such as real-time PCR, genomics or proteomics.

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Bioimaging

The Facility is equipped with different state-of-the-art microscopes. According to the particular scientific question, the most suitable microscope will be chosen. Besides widefield fluorescence and confocal microscopes, these include also an electron microscope, a Total Internal Reflection Fluorescence (TIRF) microscope, an Atomic-force microscope (AFM) as well as a Super-Resolution with Ground State Depletion (GSDIM) microscope. The latter one is particularly suitable for immunostaining techniques and integrates perfectly into existing workflows for fluorescence microscopy. For data and image analysis, the facility provides the image-editing programs ImageJ, Metamorph and Volocity.

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2 Synthesis and Analysis

Medicinal Chemistry

The Medicinal Chemistry unit has a strong expertise in the design, synthesis and structural optimization of small organic compounds that can be used as research tools. The further development of lead structures is also feasible. For the design and optimization of these target-specific compounds besides classical medicinal chemistry approaches, structure-based drug design as well as computational tools such as docking, de-novo design or virtual screening techniques are applied.

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Protein Biochemistry and Spectroscopy

The Core Facility is equipped with devices for the (anaerobic) purification of proteins and has spectroscopic methods available allowing for the quantitative biophysical analysis of proteins as well as of their binding partners, including DNA, RNA, and low molecular weight compounds. Protein-protein and protein-ligand interactions can be evaluated by microscale thermophoresis (MST) and fluorescence anisotropy (polarization). Use of an electron paramagnetic resonance (EPR) system is possible. If required, UV-Vis, fluorescence, and circular dichroism (CD) spectrometers may be connected to a stopped-flow system in order to measure rapid kinetics.

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Metabolomics/Mass Spectrometry

The Core Facility offers an up-to-date infrastructure to analyze small molecules associated with intermediary metabolism or lipid signaling as well as synthetic drugs in biological samples. Analyses are performed by gas- or liquid-chromatography coupled to single- or tandem mass spectrometry. Trained staff provides support with project design, acquisition of biological specimens as well as sample preparation for analytic procedures. Measurements are executed by the staff under state-of-the-art quality control. The service of the Core Facility includes qualitative and quantitative analyses of low molecular weight biomolecules, e.g. metabolites of energy and lipid turnover, as well as pharmacokinetic analyses of synthetic compounds.

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Cell- and Tumor Metabolism

The Facility has the technical and human resources for project planning, implementation and evaluation of individual experiments, small-scale projects and research in the field of cellular metabolism of mammalian cells, with an emphasis on energy metabolism.

The determination of the metabolic phenotype of cells is carried out by real-time measurement of O_2 consumption (OCR= O_2-Consumption Rate) and the lactate release (ECAR = Extracellular Acidification Rate) using a Metabolic Flux Analyser (Seahorse XFe96). For the analysis of metabolic processes under normoxia / hypoxia, O_2-incubators and a noninvasive online measuring system type SensorDish Reader are available.

Other services of the Unit include non-invasive cell analysis (proliferation/migration/invasion) in real time (impedance-based) using a Real-Time Cell Analyzer (RTCA).

The quality management for the implementation and documentation of the experiments are carried out in accordance with the principles of GxP.

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Genomics

The Genomics Core Facility holds the infrastructure for various genome-wide analysis techniques and provides access for research groups to several instrument- and cost-intensive technologies of modern biomedicine. With next generation sequencers (Illumina HiSeq, Illumina MiSeq), a high content imaging system (BD Pathway), liquid handling robotics (Hamilton STARlet and STARplus), and genome-wide human siRNA and shRNA libraries the facility offers state-of-the-art resources to the research community.

Trained staff provides support with project design and sample preparation and performs as a service genome-wide sample analyses (RNAseq, ChIPseq, targeted resequencing) under stringent quality control.

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Flow Cytometry

The Flow Cytometry Core Facility is equipped with instruments for phenotypic cell analysis (Becton Dickinson, LSR II) and cell sorting (BD FACSAria II; Beckman Coulter MoFlo Astrios and Dako MoFlo XDP). Two of the sorters are running within a fully sealed sort chamber (BSL II cabinet) according to Biosafety Level II for sterile sorting of gene-modified and/or pathogenic cells. The flow cytometers are equipped with up to five lasers and twenty detectors (eighteen colors) allowing for the characterization and simultaneous sorting of up to six low frequency cell populations from heterogeneous cell mixtures. The staff members support the scientists at each step of the experiment from planning to analysis and interpretation of data.

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3 In vivo Imaging

Small animal Ultrasound and Multimodal Imaging

The Vevo2100 Ultrasound System represents a high-resolution, non-invasive unit for pre-clinical research. The system not only enables precise localization, but also volumetric analysis of tumors in tissues and organs with high precision. Furthermore, contrast agent-assisted sonography offers additional options for non-invasive analyses in the context of therapeutic interventions, e.g. concerning functional vascularization of tumors. Ultrasound data can be readily correlated with other imaging data (e.g. small animal MRT or PET). The system also enables precise monitoring of interventions such as needle biopsy procedures or targeted injection of cells into specific organs or embryos.

A Bruker in Vivo Extreme multimodal imaging station enables fluorescence and bioluminescence as well as X-ray modalities and radioisotope detection. Based on the combination of four different imaging modalities in a single system, many potential applications are possible related to in vivo tumor models and other in vivo applications as well as ex vivo studies of tissues and organs. The system is especially suited for therapeutic intervention studies, since parameters such as tumor localization and tumor size can be combined with simultaneously timed functional studies in the same animal.

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Molecular Imaging: SPECT-PET-CT

The Core Facility for Molecular Imaging, operated by the Department of Nuclear Medicine, provides expertise for scientists in different research areas, including oncology, neurology, immunology and cardiology. One focus of the unit is the development and analysis of radiopharmaceuticals using small animal tumor models. The Core Facility uses advanced imaging technologies, such as SPECT, PET and CT, in different multimodal setups and in combination with MRI to study functional and morphologic parameters. In order to meet these high requirements state-of-the-art imaging devices are currently procured and will go into operation at the end of 2016.

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7T-small animal MRI

The Core Facility offers non invasive magnetic resonance imaging for all scientists, independent from their research background. Due to the high contrast resolution, 7T MRI permits visualization of structural and functional changes in organ systems in experimental animals with a weight of up to 1.2 kg. It also offers the ideal opportunity for imaging of tissue samples and non-organic probes. Furthermore, this Core Facility is equipped for magnetic resonance spectroscopy (^{1}H), (^{31}P) and (^{13}C), diffusion imaging (DWI, DTI), molecular and cardiac imaging and vessel imaging (TOF, ceMRA).

Besides the 7T-high field magnetic resonance imaging system diverse measuring coils, animal beds and ample means of anesthesia and animal monitoring (breathing, ECG, temperature) are available.

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Magnetic Resonance Brain Imaging

The Core-Unit Brain Imaging is a core resource that offers technical expertise and administrative assistance to permit scientists of the Philipps University Marburg and their collaborators to initiate and conduct human brain imaging research. This is accomplished by offering access to state of the art imaging technology, infrastructure, and personnel assistance. We use various magnetic resonance imaging methods, including functional magnetic resonance imaging (fMRI), structural magnetic resonance imaging (sMRI), diffusion tensor imaging (DTI) and magnetic resonance spectroscopy (MRS). Our highly experienced team is composed of physicists, computer scientists, radiographers and system administrators. The laboratory is equipped with a 3T scanner (Siemens Tim Trio), a MR-compatible EEG system and various MR compatible eye-tracker systems.

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4 Infrastructural Entities

Irradiation Facility

The facility provides the capability to expose small animals and mammalian cells in culture to a highly homogenous X-ray beam. The self-contained X-ray system operates with energies up to 320 keV and is connected to a password protected operator interface with programmed exposure parameters. Additional X-ray beam conditioning filter offers the opportunity to irradiate with soft or hard beam quality. The adjustable collimator allows users to shape the beam to the contour of orthotopic and ectopic growing tumors.

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BSL4 Facility

The BSL4 Core facility at the Institut für Virologie in Marburg is the only Institution of this kind at german universities. The major task of the BSL4 laboratory is to enable research on highly pathogenic viruses with the goal to improve our understanding of virulence factors and develop antiviral therapy and prophylaxis. Since the first Marburg virus outbreak in 1967, the Institut für Virologie focuses on highly pathogenic, zoonotic viruses.

Using reverse genetics, we investigate mechanisms of virus pathogenicity in infected cell cultures and small animal models. The BSL4 facility provides service for researchers of the section "Emerging Infections" of the German Center for Infection Research (DZIF) to investigate the efficacy of candidate vaccines and antivirals.

Furthermore, the team of BSL-4 scientists offers support to scientists interested in investigating the stability of highly pathogenic viruses, efficacy of disinfectants, antiviral drugs and detection of infection-triggered immunity.

As part of the emergency response chain of the Federal State of Hessen, we provide diagnostics of highly pathogenic viruses (24/7).

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Biomaterial Bank – Comprehensive BioMaterial Bank Marburg (CBBMR)

Structured biomaterial collections contribute to future translational biomedical research by facilitating acquisition, documentation and dissemination of quality-controlled bio-specimens. Linking samples to corresponding clinical data represents an added value for etiological research and novel therapeutic approaches. CBBMR offers two modules of bio-repositories: By building up a faculty-wide bio-repository, CBBMR affords scientists at the Marburg medical faculty a rapid access to bio-samples collected with a non-hypothesis driven approach to collaborate in interdisciplinary projects. Bio-specimens collected within clinical and epidemiological studies could be pre-analytically processed, aliquoted and stored under quality-controlled and cost-effective conditions in CBBMR with guaranteed limited access only for study team members.

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