QATAR BIOMEDICAL RESEARCH INSTITUTE (QBRI)

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QATAR BIOMEDICAL RESEARCH INSTITUTE (QBRI)

Core Facilities

Located in Hamad Bin Khalifa University's (HBKU) Research and Development Complex (RDC), QBRI's state-of-the-art laboratories are major hubs in driving forward cutting-edge research and innovation in Qatar and the region. The institute's core facilities are located in the same building as QBRI's research teams. They form an integral element of HBKU's ambitious goals in driving visionary and innovative research in Qatar, and are positioned as modern, efficient, reliable, and tightly networked shared resource laboratories that guarantee idyllic support and scientific progression on several levels.

QBRI's core facilities at HBKU aim to fulfill the organization's mission through three major operational lines (Fig.1). First, its highly competitive core facilities support and drive forward the main QBRI areas of biomedical research such as diabetes, cancer, and neurological disorders. Second, they provide a backbone for progressing HBKU's leading role in training, education and knowledge transfer to students and the scientific community in Qatar and beyond. Third, the institution's core facilities are actively embedded in a growing national and international collaborative environment, including academic, clinical and industry partners. To that end, the infrastructure and services of QBRI's core facilities will include collaborations and providing services to local and international entities to increase efficiency, exchange knowledge and avoid duplication of instrumentation and services.

This setup is unique to the region, and highlights QBRI as a major hub for education, innovation, research and healthcare development in Qatar, the Middle East and beyond.

Fig. 1

DETAILS OF QBRI'S CORE FACILITIES

QBRI's core facilities at HBKU have been developed in line with the overarching QBRI strategic plan. All facilities are located in the state-of-the-art HBKU Research and Development Complex in Qatar Foundation's Education City area in Doha, Qatar. Many routine operations and services are available and delivered, and specific cores have already begun their activities in training, education and scientific innovation. A summary of available equipment and services from QBRI's core facilities are summarized in Fig. 2.

The following core facilities are currently available at QBRI:

- The Advanced Imaging and Histopathology Core
- The Flow Cytometry Core
- The Genomics Core and Genome Technology
- The Structural Biology Core
- Stem Cells and Genome Engineering Core
- Bioinformatics Capabilities
- Proteomics Core
- Clinical Research Core

CURRENT STATUS OF THE QBRI CORE FACILITIES

01 ADVANCED IMAGING AND HISTOLOGY

Major Instruments:

- Multiphoton
- Confocal
- Super Resolution
- Wide Field Fluorescence
- Microscopes

Major Services:

- Image Acquisition
- Histology
- Experimental Design
- Data Management
- Training

02 FLOW CYTOMETRY CORE

Major Instruments:

- Flow Analyzer
- Cell Sorter
- Image Stream
- CTC System

Major Services:

- Flow Analysis
- Bulk Cell Sorting
- Single Cell Sorting
- Experimental Design
- Data Analysis
- Data Management
- Training

03 GENOMICS CORE AND GENOME TECHNOLOGY

Major Instruments:

- Illumina HiSeq 4000, 2500 and Miseq
- Capillary Sequencers
- Illumina Iscan
- Nanostring System
- QuantStudio 12K Flex

Major Services:

- Experimental Design
- Whole Genome, Transcriptome, and Exome Sequencing
- Targeted Gene
- Expression Studies
- Genotyping Studies

04 STRUCTURAL BIOLOGY

Major Instruments:

- X-Ray System
- ITC
- Biacore (SPR)
- CD
- HPLC-MALS
- NanoIR
- Fermenter
- Mosquito LCP

Major Services:

- Protein Production and Crystallization
- Protein Characterization
- Structure Determination
- Protein Interaction Analysis

05 STEM CELLS AND GENOME ENGINEERING CORE

Major Instruments:

- Automated Cell Colony Picker
- Tissue Culture Capabilities
- 3D Cell Culture Expansion and Differentiation Platform
- Amaxa 4D Electroporator

Major Services:

- Generation of hiPSCs
- Karyotype and Pluripotency Characterization of hiPS and hESCs (hPSC)
- Directed Differentiation of hPSCs to Beta Cells, Neurons, and Organoids
- Genome Engineering of hPSCs by CRISPR/Cas9
- Consulting and Training

06 PROTEOMICS CORE

Major Instruments:

- BioMark HD Reader and BioMark IFC-HX Controller, Fluidigm
- SureScan Microarray Scanner G4900D, Agilent
- SIMOA HD-X Analyzer, Quanterix
- MESO Scale System S600, MesoScale Discovery (MSD)
- Biopex 3D, BioRad

Major Services:

- Olink Technology
- Sengenics Technology
- MSD Technology
- Bio-Plex 3D Technology
- Consultation and Study Design
- Data Analysis

07 CLINICAL RESEARCH CORE

Major Services:

- Storing of Biospecimens in Secure Freezers
- Dedication of Research Assistant for Short and Long-Term Projects

08 BIOINFORMATICS CAPABILITIES

Major Instruments:

- 472-core High performance cluster with 720 TB of InfiniBand-connected file storage
- 20-core servers (10)
- Major services:
- Whole exome sequencing analysis
- RNA sequencing and Differential expression analysis

Fig. 2

01 ADVANCED IMAGING AND HISTOPATHOLOGY CORE

The Advanced Imaging and Histopathology (AIH) Core is equipped with advanced and automated digital microscopy and live cell imaging instrumentation, allowing investigators to perform a variety of imaging experiments. The AIH core acts as a partner and consultant, playing a crucial role in developing the imaging experiment workflow, including experimental design, sample preparation, image data acquisition, image analysis, and presentation. QBRI's core facility alone has more than 24 microscopes, 18 imaging systems and two plate readers.

The mission of the QBRI Microscopy and Imaging Core is to offer researchers efficient, reliable and innovative imaging solutions with the highest standards of instrumentation, accuracy, quality control and professional expertise. This is achieved by providing access to state-of-the-art instrumentation and the expertise of highly skilled professionals in the fields of microscopy and imaging.

The unit is equipped with the most advanced and automated digital microscopy and live-cell imaging instrumentation. These technologies allow investigators to perform a wide variety of imaging research experiments that help them answer important biomedical questions related to their fields of study. The core also provides training and services that range from routine microscopy to cutting-edge live-animal multi-photon microscopy.

The core facility also provides cutting-edge histopathology equipment and services. Available equipment includes several up-to-date microtomes, cryostats, slide scanners and automated tissue processing, and staining systems.

The core's expertise and services cover advice and support in the planning and evaluation of histopathology experiments, tissue processing and sectioning, cryopreservation, histological staining methods and laser capture microdissection microscopy.

QBRI's Advanced Imaging and Histopathology Core currently offers the following resources and services:

Optical Microscopy and Digital Imaging Equipment

- Nikon A1+ MultiPhoton microscope
- Zeiss LSM 780 confocal microscope inclusive of incubation chamber
- Leica GSD super resolution microscope
- Zeiss Primo Star upright microscope
- Zeiss Axio Imager Z2 upright + camera fully automated fluorescence microscope
- Olympus Inverted microscope IX73 and IX83
- Zeiss Axio Imager A2 Microscope
- Several Olympus microscopes and Phase Contrast microscopes (Upright and Inverted)

Services – Optical Microscopy and Digital Imaging

- State-of-the-art microscopes for a wide variety of imaging research experiments
- Cutting-edge bright-field, dark-field and fluorescence imaging
- Standard, confocal and multi-photon microscopy applications
- Automated digital microscopy
- Advanced high-end live-cell imaging
- Image processing and analysis tools
- Training and education in microscopy and imaging
- Enhanced level of imaging research (complemented by the centralized microscopy/ imaging central care facility)
- Support with data analysis and presentation
- Data management and storage

Histopathology Equipment

- Digital whole slide scanner, Leica Aperio® AT2 Turbo
- High quality digital slide scanner, Leica Aperio CS2
- Automated upright microscope, Leica DM4000B
- Semi-motorized rotary microtome, Leica RM2245
- Cryostat, Leica Biosystems CM3050 S
- Bright Instrument 8000 Sledge (Sliding Microtome)
- Leica rotary microtome RM2125
- Leica ASP6025 Automated Tissue Processor
- Leica EG1150 modular tissue embedding center (incorporates two separate components, the Leica EGII50C cold plate and the Leica EG1150H heated embedding module)
- Leica Biosystems ST5020 Multistainer
- CryoViz robotic sectioning and imaging system
- Dako Omnis automated staining System GI100
- Dako Coverslipper

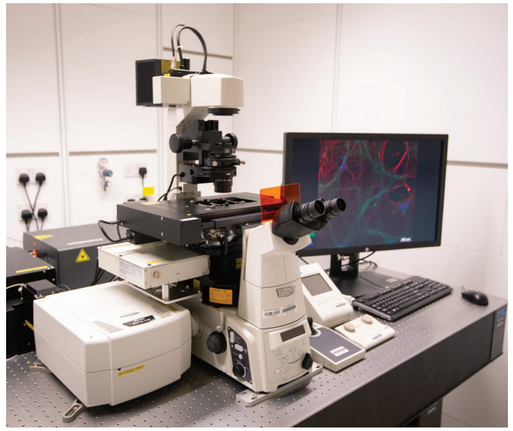
Services – Histopathology

- Tissue processing, embedding and sectioning
- Cryopreservation and cryosectioning (Leica Cryostat and Microtome systems)
- Different histological staining methods, such as H&E and special stains
- Immunohistochemical and immunofluorescence techniques
- Laser Capture Microdissection microscopy (Leica)
- Expert advice in the planning and evaluation of histopathology experiments

Examples of the state-of-the-art microscopes

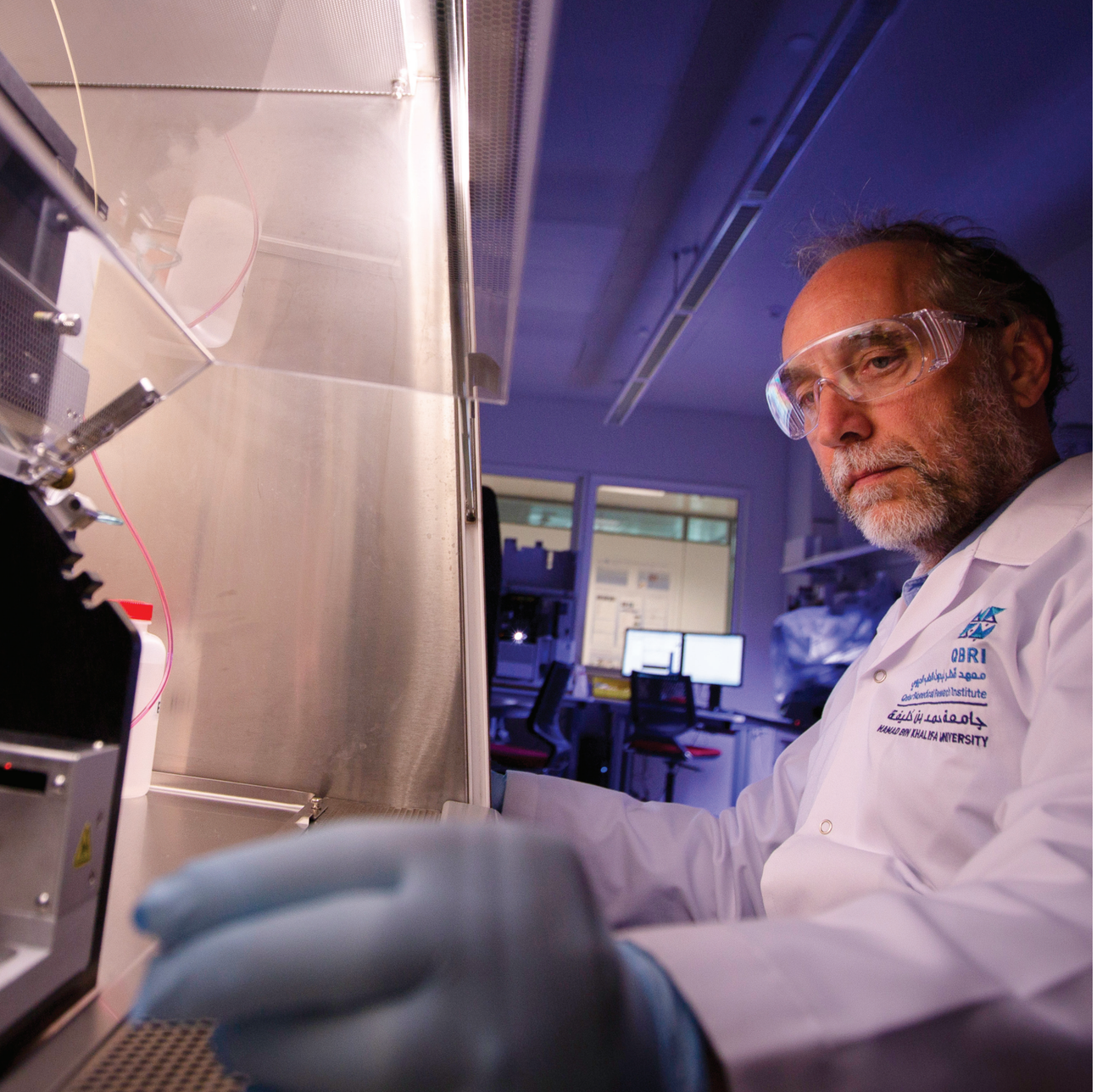
Confocal, multiphoton and high-resolution microscopy

- Nikon A1R multiphoton microscope
- Zeiss LSM-780 confocal microscope with incubation chamber



Fluorescent, bright field and phase contrast microscopy

- Zeiss Axio Imager Z2
- Zeiss Primovert inverted microscope
- Olympus Inverted microscope IX73



02 FLOW CYTOMETRY CORE

The Flow Cytometry Core Facility at QBRI is a key facility within HBKU's research landscape and is equipped with state-of-the art flow cytometry hardware, software and intellectual capabilities. The core very actively interacts with all research teams and the other core facilities to address reliable, accurate and innovative solutions in line with HBKU's focus on cancer research, metabolic disorders and neurological diseases. In that sense, the Flow Cytometry Core serves as a veritable Shared Resource Lab (SRL), providing its instrumentation, infrastructure and knowledge to optimize the scientific output for any flow-related project within HBKU.

The mission of the QBRI Flow Cytometry Core is to offer researchers efficient, reliable and innovative flow cytometry and cell sorting solutions with the highest standards of instrumentation, quality control, biosafety and productivity. This is achieved by providing access to state-of-the-art instrumentation and professional flow cytometry and cell sorting services and is supported by a highly motivated staff with extensive skills and profound expertise in the field of flow cytometry.

Recently established scientific collaborations include specific research teams at QBRI, such as the cancer and the stem cell research teams, as well as the advanced imaging and genomics cores. The collaborations aim to develop, evaluate, establish and optimize advanced flow cytometry and single-cell sorting applications. As a vivid player and innovative flow cytometry hub in Qatar and beyond, the QBRI Flow Cytometry Core is also in collaborative exchange with partners from industry (e.g. BD, sedeer) and external research institution (e.g. QCM-Q, HBKU, HMC). As such, the flow cytometry core assists with experimental design, sample preparation, data acquisitions and analysis.

In addition, the QBRI Flow Cytometry Core also provides support and guidelines with regards to flow cytometry education, operation of instruments, software workflows and biosafety to fulfill the mission of a fruitful, collaborative and highly innovative environment for research and development. To that aim, the QBRI Flow Cytometry Core started to establish its education and knowledge transfer channels by organizing and hosting a very successful flow cytometry symposium in May 2017 and has offered several training and laboratory courses for QBRI and HBKU staff and students since then.

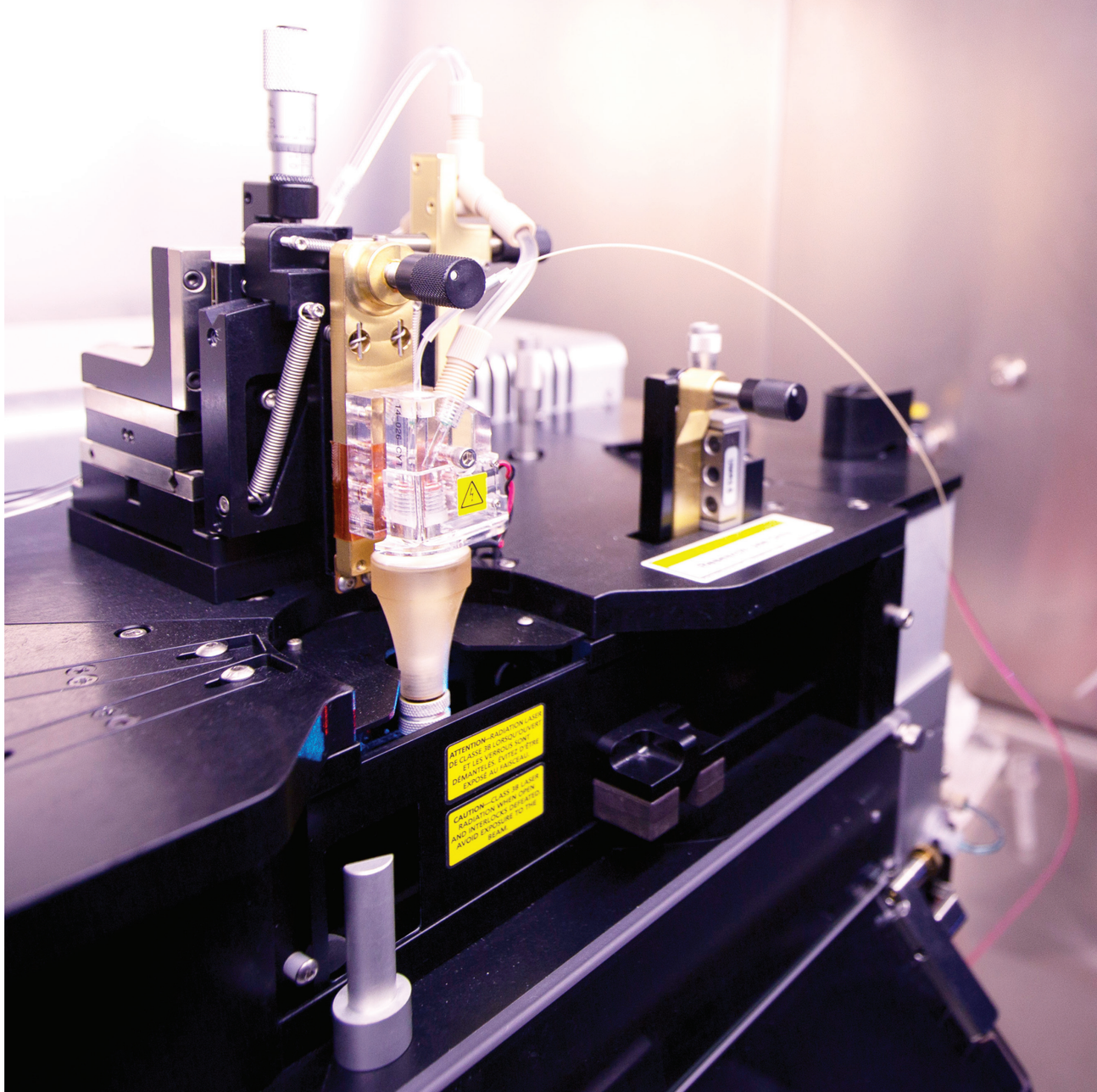
The following resources and services are currently offered by QBRI's Flow Cytometry Core:

Equipment

- BD Accuri C6 flow cytometer (2 lasers, 6 detectors)
- BC Gallios flow cytometer (3 lasers, 12 detectors)
- BD LSR Fortessa X-20 SORP flow cytometer (5 lasers, 20 detectors)
- Amnis Image Stream MKII imaging flow cytometer (2 lasers, 6 detectors)
- CellSee CTC Single Cell Analysis System
- 2 x BD FACSAria SORP cell sorter (5 lasers, 18 detectors)
- BD FACSJazz cell sorter (3 lasers, 8 detectors, in BSL-2 cabinet)
- Flow cytometry software analysis (BD FACSDiva, FlowJo, BD Sortware, ModFit LT, etc.)

Services

- Advice on sample preparation (reagent selection, protocol design & optimization)
- Advice and support on multicolor panel design (negative controls, compensation setup, and multicolor panels)
- Multicolor sample acquisition and analysis
- Single cell analysis and sorting applications
- Aseptic cell sorting and biosafety advice
- Surface phenotyping and intracellular staining
- Apoptosis, cell cycle analysis, and proliferation
- Flow cytometry training and education of researchers and students
- Support with data analysis and presentation
- Data management and storage



03 GENOMICS CORE AND GENOME TECHNOLOGY

The Genomics Core and Genome Technology Facility at QBRI actively supports scientific research by providing advanced research technologies and services to the research community at HBKU and QBRI, and their collaborators from academia and industries to address the complex biomedical problems of QBRI's research interests in the field of cancer biology, metabolic disorders and neurological diseases. The genomics core laboratory is equipped with various state-of-the-art, high-throughput technological platforms to sequence the nucleic acids by next-generation sequencing (NGS) as well by capillary sequencing methods; as well as capillary sequencing methods and different array platforms. Our applications include sequencing of different nucleic acid templates, high throughput genotyping, epigenome analysis, gene expression analysis, single-cell technologies, NanoString technologies and digital PCR methods.

Genomics core laboratory operation is aligned to support the vision and mission of QBRI-based fundamentals; assisting the researchers with design of an experiment, providing intellectual support and novel method development for genomics experiments; interface with other core technological platforms to facilitate integrated biology research; and collaborative research.

Facilities and Capabilities

The facilities and instruments that are available at QBRI's Genomics Core Facility are classified broadly under the following categories

Next Generation Sequencing

- Illumina HiSeq 4000 and 2500 platforms (high throughput sequencing for whole exome sequencing , and RNA sequencing "total RNAseq, mRNAseq, miRNAseq, 3'-Tag-Seq,...")
- Illumina MiSeq (for smaller genome, amplicon sequencing and targeted sequencing)

Large Scale Genotyping Analysis

- Illumina iScan array scanner (Illumina Bead Array technology for high-throughput SNP genotype analysis)
- ABI 3730xl 96 capillaries, ABI 3500xl 24 capillaries and ABI 3100xl 16 capillaries Genetic Analyzers (Sanger sequencing)
- NanoString Technology (Copy number variation analysis of up to 800 target regions)

Targeted Gene Expression Analysis

- NanoString Technologies (targeted gene expression for up to 800 targets "mRNA expression, long non coding lncRNA expression, Leukemia fusion gene analysis and miRNA expression)
- QuantStudio 12K Plus for qPCR and Digital PCR and Gene Expression Panels studies
- ABI 7900 Real-Time PCR System

Single Cell Genomics

- Fluidigm C1 Single-Cell Auto Prep (single-cell mRNA sequencing, single-cell target gene expression, Single-cell miRNA expression and single-cell whole exome sequencing)
- Bio-Rad ddSEQ System and NGS platform (single cell RNA sequencing)

DNA methylation analysis

- Illumina HiSeq 4000 platform (Methylated DNA immunoprecipitation sequencing "MeDIP-Seq", whole-genome bisulfite sequencing and amplicon methyl-seq or target enrichment)
- Illumina iScan array scanner (methylation profiling microarray of over 850,000 methylation sites)

Core Laboratory Services

- Advice on experimental design and sample preparation
- Quality control of nucleic acid materials by LabChip and Bioanalyzer
- Different types of sequencing library preparation and data generation by high-throughput sequencing methods
- Quantitative PCR for differential gene expression analysis
- Helping researchers with the generation of preliminary data for grant applications
- Data management and storage

04 STRUCTURAL BIOLOGY CORE

The Structural Biology Core is currently the only advanced, comprehensive protein laboratory in Qatar, and is unique to the region. This advanced core provides full biochemical and biophysical characterization, including protein-protein and protein-nucleic acid interactions. In addition, X-ray crystallography and other structural tools are available to afford atomic level descriptions of systems.

The core supports protein biophysics and structural biology. The nature and complexity of protein research requires highly sophisticated technologies and advanced instrumentation. The needs of protein studies are very diverse, comprising studies of single proteins, protein complexes and interactions of groups of proteins, which may relate to structure, function or biology. This core is committed to facilitate these needs within QBRI and Qatar. The Protein Biophysics unit houses a Mosquito LCP crystallization robot, which can carry out both membrane and non-membrane protein crystallizations. X-ray crystallography is supported by the latest generation microfocus source with high intensity, as well as a robust and sensitive CMOS detector.

The unit also has a cryostream with an air compressor. Instrumentation facilitates rapid screening of macromolecular crystals, as well as data collection for structure determination. In addition, several nitrogen dewars are housed for the storage and transport of crystals to synchrotron facilities. Support staff maintains all crystallographic software.

QBRI's Structural Biology Core is well established and highly functional. Research collaborations with various stakeholders are ongoing, including with QBRI's diabetes and neurological disorders teams.

QBRI's Structural Biology Core currently offers the following resources and services:

Protein Biophysics Equipment

- Nikon A1+ MultiPhoton microscope
- Shaker/Incubator (Innova 44R)
- Fermenter (BioFlow 115)
- Ultracentrifuge (Sorvall)
- FPLC (AktaXpress)
- TyphoonScanner (FLA 9500)
- Sonicator (Qsonica)
- CD (Applied Photophysics)
- ITC (Microcal AutoITC-200)
- Crystallization Robots (Mosquito LCP)
- X-ray Diffractometer (Bruker D8 Venture with Cobra Cooling system)
- NanoIR (Anasys/Bruker)

Bimolecular and Macromolecular Analysis

(e.g., X-ray Crystallography, Thermodynamics, etc.)

- Mosquito LCP for crystallization screening (TTP Labtech)
- D8 VENTURE X-ray Diffractometer for 3-D structure determination (Bruker)
- Circular Dichroism (CD Spectrometer) for detailed structure analysis of biomolecules, e.g., secondary structure and protein refolding (Applied Photophysics)
- Isothermal Titration Calorimetry (ITC) from GE Healthcare Lifesciences for the characterization of biomolecular and macromolecular interactions, and thermodynamic analysis

05 STEM CELLS AND GENOME ENGINEERING CORE

Human pluripotent stem cells (hPSCs) that include induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) provide an excellent platform for studying human development, disease progression modeling, drug screens and cell-based therapies.

The main objective of the Stem Cells and Genome Engineering Core is to facilitate the development of basic and translational stem cell research by providing scientific advice, iPSCs derivation, directed differentiations and genome engineering services to researchers. The facility s fully equipped with standard and state-of-the-art cell culture, cell biology and molecular biology equipment.

The Stem Cells and Genome Engineering Core is currently working with QBRI's Neurological disorders, Diabetes teams and with Harvard Stem Cell Institute for generation and engineering of iPSCs and their directed differentiation into cortical neurons, brain organoids as well as pancreatic beta cells.

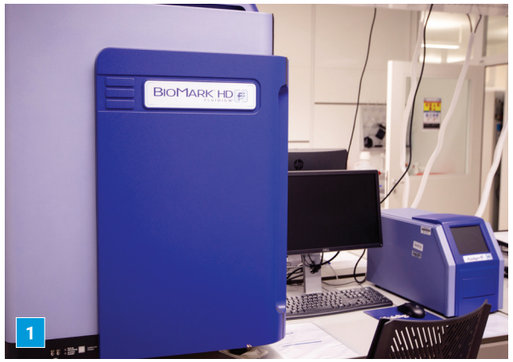
QBRI's Stem Cells and Genome Engineering Core currently offers the following resources and services:

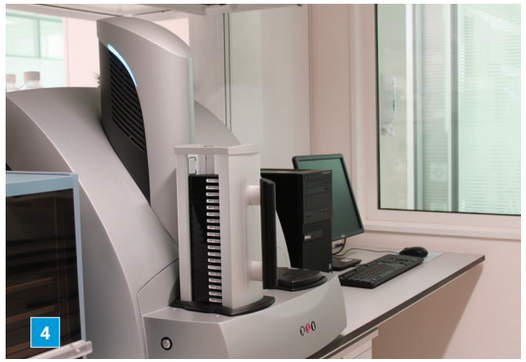
Equipment

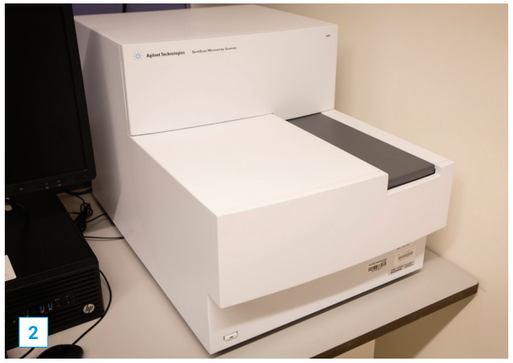
- Fully equipped cell culture facilities
- Quarantine tissue culture room
- Automated cell colony picker
- 3D cell culture expansion and differentiation platforms
- Amaxa 4D and Neon Electroporators

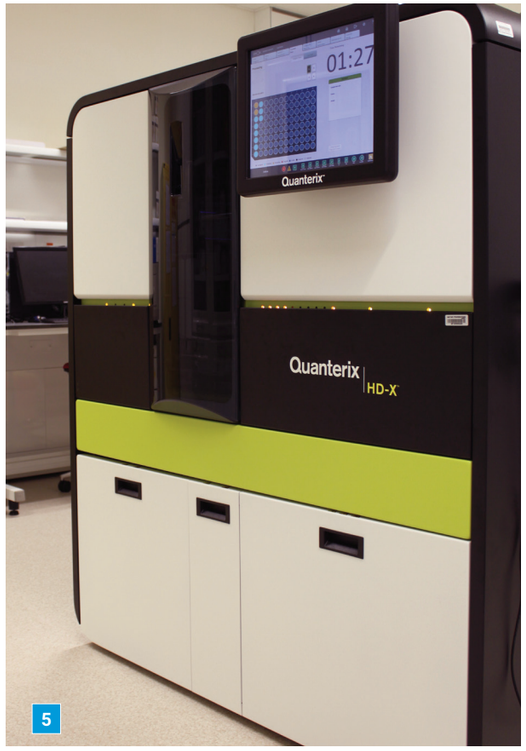
Services

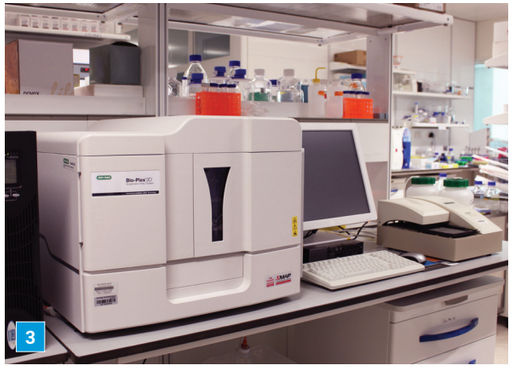
- Consultation and project design.
- Generation of human induced pluripotent stem cells (iPSCs).
- Karyotypic and pluripotency characterization of human iPSC and embryonic stem cells (ESCs).
- Genome engineering services to create isogenic human pluripotent stem cell (ESCs and iPSCs) lines as well as gene knockout/in via CRISPR/Cas9, TALENs, Recombinases and transposases.
- 3D adoption and directed differentiation of human pluripotent stem cells (ESCs and iPSCs) in a small-scale bioreactor setting.
- Directed differentiation of human pluripotent stem cells (ESCs and iPSCs) into cortical neurons, brain organoids and pancreatic beta cells.
- Training and supervision of thesis students utilizing ESCs and iPSCs in research projects.











06 PROTEOMICS CORE

The Proteomics Core provides services and supports the investigators within QBRI, HBKU's colleges, and other institutions in Qatar and abroad, with the aim of addressing and solving the protein-based challenges related to their research fields. This core operates a cutting-edge technological platform, offering users access to high-throughput, affinity-based proteomics assays such as Olink, Sengenics, MesoScale Discovery (MSD), Luminex Bio-Plex 3D and Simoa.

Besides pure analytical capabilities, the core will also offer additional services, including technological consultation, study design, custom panel selection, experimental design optimization, as well as biostatistical analysis.

Services

Services and Resources provided by QBRI's Proteomics Core:

- Consultation
- Study design
- High-throughput, targeted proteomics analysis using the following technologies: Olink, Sengenics, MSD, Bio-Plex 3D and Simoa
- Data analysis

Equipment

The Proteomics Core facility is equipped with:

1. **Fluidigm Biomark HD:** Used for proximity extension assays (known as Olink technology)
2. **SureScan detection system:** Used for Sengenics proteomics technology
3. **Bio-Plex 3D system**
4. **MSD MESO Scale system:** Both technologies will be used for multiplexing assays ranging up to 70-plex.
5. **Simoa HD-X analyzer:** The only available digital immunoassay instrument capable of analyzing samples using the proprietary Single Molecule Array (Simoa) technology. It delivers ultra-sensitive measurements of proteins of interest over a wide dynamic range at the femtomolar scale, offering a roughly 1000-fold improvement in sensitivity.

07 CLINICAL RESEARCH CORE

In line with QBRI's vision to improve and transform healthcare through innovation in prevention, diagnosis, and treatment of diseases, the investigators at QBRI are involved in clinical and translational research projects in collaboration with local, regional and international clinicians and hospitals. The main mission of the Clinical Research Core (CRC) is to provide standard operating procedures and resources to collect different bio-specimens to support QBRI's researchers in order to advance and promote the clinical and translational research enterprise at QBRI.

Services and Resources

- Standard Operating Procedures and templates for collecting different biospecimens, including blood, saliva and urine
- Processing of biospecimens
- Labeling of biospecimens
- Storing of biospecimens in secure freezers
- Training for Research Assistants
- Research assistant for short and long-term dedication to projects
- Consumables for biospecimens processing and storage
- Streamlining of Data and/or biospecimens transfer between QBRI investigators and between QBRI investigators and external collaborators

Equipment

The CRC is equipped with the necessary equipment required for the proper and safe handling of different types of biospecimens.

- BL2 biosafety cabinets
- Freezers (-80, -150 and -20°C)
- 4°C Fridges
- Brooks BioStoreTM IIIv -80°C automated storage system (holds 120,000 1ml cryotubes or 63000 2ml cryotubes)
- Refrigerated centrifuges
- Labeling system (BRADY)
- Barcode reading system

08 BIOINFORMATICS CAPABILITIES

The Bioinformatics Capabilities provides support for data analysis and interpretation, as well as utilizing software and pipelines to analyze next-generation datasets from DNA and RNA based experiments. For example, interpreting OMIC datasets to identify the candidate genes and elucidate relevant biological pathways.

The Bioinformatics Capabilities contributes to a wide range of research projects and collaborates closely with the Genomics and Proteomics Cores to provide high quality informatics support to all users.

Services

- Whole Exome Sequencing analysis
- RNA Sequencing and Differential Expression analysis
- Single-Cell Sequencing analysis
- Custom pipeline development
- Bioinformatics training

Equipment

- HPC: 472-core High-Performance Cluster, made up of:
  - 10 36-core compute nodes with 256GB of memory
  - Two 56-core compute nodes with 1TB of memory
  - 720 TB of InfiniBand-connected file storage
- 10 Individual 20-core servers with 128GB of memory to carry out pipeline development, testing, and small-scale projects.
- 400TB of Network Storage

The QBRI HPC enables the rapid computational analysis of large datasets across a wide range of informatics tasks. In line with the computational needs of QBRI, the HPC is primarily used for the analysis of whole-exome sequencing for variant analysis; RNA sequencing for differential expression analysis; ChIP-Seq analysis; MeDIP analysis; and Single-Cell Sequencing de-multiplexing and analysis.