Qatar Biomedical Research Institute

QBRI
معهد قطر لبحوث الطب الحيوي
Qatar Biomedical Research Institute
جامعة حمد بن خليفة
HAMAD BIN KHALIFA UNIVERSITY

Table of Contents

Overview

About QBRI

Qatar Biomedical Research Institute (QBRI) is a leading research institute under Qatar Foundation's (QF) Hamad Bin Khalifa University (HBKU), which aims to improve and transform healthcare through scientific innovation for the prevention, diagnosis, and treatment of diseases affecting the Qatari population and the region. QBRI conducts research driven by biomarker discoveries to improve individual health outcomes in pursuit of Precision Medicine (PM) or tailored medical treatments based on individual characteristics. QBRI aims to build a strong scientific community that allows Qatar to capitalize on the latest scientific advances, address immediate healthcare challenges, and develop new treatments and applications that will improve the quality of life and effectiveness of healthcare.

Overview

Vision

QBRI is a national center of excellence and a global hub for biomedical and translational research. It aims to improve and transform healthcare through innovation for the prevention, diagnosis, and treatment of diseases affecting the Qatari population and the region.

Mission

QBRI is engaged in basic and applied medical research that strongly supports the translation of new scientific discoveries into more efficient therapies and better preventative strategies, ultimately leading to the development of personalized medicine.

Strategic Objectives

Improve the diagnosis, treatment, and prevention of disease

Advance biomedical research through innovative technologies and enabling platforms

Train and retain the next generation of scientists

Promote social awareness, engagement, and participation in biomedical research

QBRI research centers are composed of interdisciplinary research teams focused on specific scientific challenges and supported by state-of-the-art research platforms to facilitate a better understanding of the enormous complexities of health sciences.

In keeping with Qatar's national health priorities, QBRI has established three scientific excellence centers to better synergize and optimize QF's investment. QBRI builds infrastructure and mandates excellence at all levels.

QBRI's Approach

The unique characteristics of the Qatari and Arab populations, combined with Qatar's commitment and investment in biomedical research, makes Qatar and specifically QBRI an ideal place to develop innovative approaches to prevent and treat diseases such as cancer, diabetes, infectious diseases, and neurological disorders. Furthermore, QBRI plays an important role in accelerating the development of innovative research and discoveries.

QBRI's approach to the nation's research priorities is based on

- Alignment with Qatar National Research Strategy (QNRS), QF strategic objectives, and thematic focus areas
- Integration with HBKU's strategic objectives
- Focusing on innovative translational research with the ultimate goal of achieving precision medicine
- Conducting local and clinically relevant research deliverables with impact across the healthcare system
- Considerations of other institutional initiatives, e.g., Qatar Precision Medicine Institute (QPMI)
- Using artificial intelligence to analyze the vast amounts of generated research data
- Pursuance of IP and commercialization opportunities
- Raising the international profile of Qatar through impactful research

QBRI and Precision Medicine

Precision Medicine (PM) is one of QF's five thematic focus areas, and it is the ultimate goal of QBRI research activities. QBRI's Research Strategy for PM focuses on utilizing multi-omics to understand the risk factors and biological mechanisms behind diseases to enable personalized biomarkers for diagnosis and precise treatments. This strategy is boosted by one of the pillars of the National AI Strategy for Qatar, published by Qatar Center for Artificial Intelligence (QCAI) at QCRI, which focuses on PM and Systems Biology. The big data generated from multi-omics and biomarkers at QBRI and Qatar Genome Program (QGP) - QPMI, lifestyle and clinical data from Qatar Biobank (QBB) - QPMI, and the medical imaging data generated through the state-of-the-art facilities at Sidra Medicine and HMC, create a fertile environment to fuel collaborative and integrative development of AI through QCAI to drive world-class PM in Qatar. Guided by QBRI's experience, Qatar is well-positioned to be a global leader in PM.

QBRI as a National Research Institute

QBRI emphasizes translational research and working on identifying unique genetic and biological markers that support precision medicine for individuals in Qatar. As a national research institute within HBKU, QBRI offers distinctive features and several competitive advantages. More importantly, QBRI plays a major leadership role in the implementation of the national health research strategies while working on the frontiers of biomedical science.

QBRI's unique features include

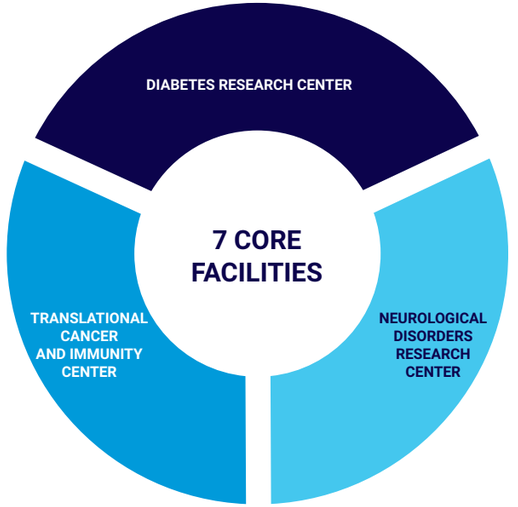
Access to unique resources and internal funding opportunities for research programs

State-of-the-art research laboratories and core technology platforms

Scientists focused on research opportunities, major challenges, and addressing national priorities

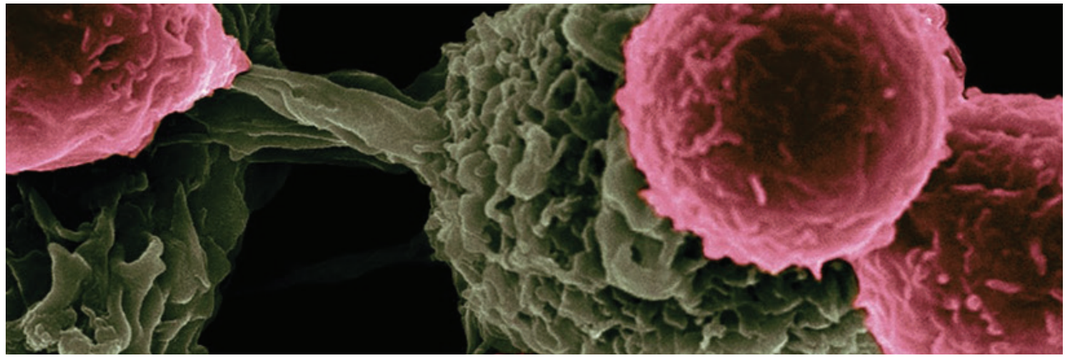
QBRI’s Structure

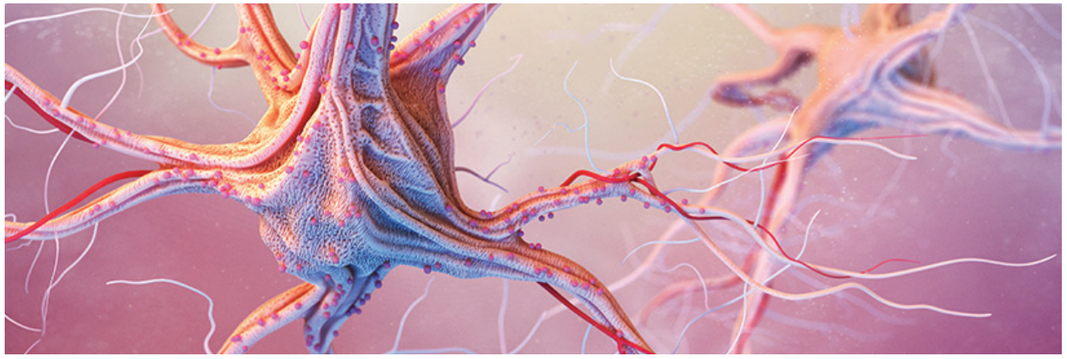
QBRI’s overall structure and funding model position the institute exceedingly well to respond to emerging health needs and challenges, as well as to initiate programs and engage in strategic partnerships aimed to advance the national biomedical and health research agenda. QBRI has a flexible structure that allows it to respond to the rapidly changing biomedical and health needs of Qatari society and the industry. This is achieved through the creation of research centers of excellence supported by state-of-the-art core facilities and enabling platforms that are on par with those existing at top institutions around the world. QBRI’s structure also enables rapid adjustment to new scientific and technological advances and allows QBRI to remain at the forefront of biomedical research in these areas. Consistent with its mission to develop and promote translational biomedical research, national and international collaboration, and knowledge sharing, QBRI has established three research centers (the Diabetes Research Center, the Translational Cancer and Immunity Center, and the Neurological Disorders Research Center). QBRI’s advanced technology platforms include: Imaging and Flow Cytometry Core, Genomics and Genome Technology Core, Proteomics Core, Bioinformatics Capabilities, Structural Biology Core, Stem Cells and Genome Engineering Core, and Clinical Research Core. Ultimately, QBRI seeks to maintain an environment that facilitates the development of homegrown innovation, thereby attracting biotechnology and pharmaceutical companies from around the world to set up operations in Qatar.



The institute houses 7 core laboratories to promote cutting-edge research:

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





QBRI’s Research Centers of Excellence

QBRI has established centers of excellence and translational research programs in four health-focused priority areas (diabetes, cancer, infectious diseases, and neurological diseases) as mandated by Qatar National Research Strategy (QNRS). These centers will support Qatar to harness the latest advances in science, medicine, and technology and attract the best minds and talents to develop new knowledge and medical advances aimed at addressing the national health priorities and improving the quality and effectiveness of healthcare in Qatar. This goal is achieved through coordination and building strategic alliances with HBKU’s colleges and partnerships with other institutions and stakeholders in Qatar and leading centers of excellence around the world. Resources are targeted towards providing new insights into the molecular basis of each of these diseases and developing diagnostic and therapeutic strategies to facilitate their early diagnosis, personalized treatment, and management.

QBRI was a pioneer in recognizing the importance of biomarkers discovery and its potential impact on national healthcare. As a result, it integrated biomarkers development into each of its research centers. It also established Interdisciplinary Research Programs (IDRPs), involving numerous researchers and multiple organizations, to guide and propel its research centers. Through its IDRPs, QBRI aims to encourage researchers to tackle scientific challenges across two or more of QBRI’s research centers while working together on biomedical research across different disciplines. This approach is expected to generate innovative problem-solving strategies that transcend individual disciplines while integrating a diverse range of skill sets and expertise. QBRI, in collaboration with several partners, has already established four IDRPs.

Translational Cancer and Immunity Center

Research Interests

Identifying diagnostic, prognostic, and predictive biomarkers and novel therapeutic targets

Investigating immunomodulatory cancer cell-intrinsic molecules with therapeutic potential

Discovering multi-omic signatures and biomarkers

Neurological Disorders Research Center

Research Interests

Using epidemiological methods to evaluate the scale of Autism Spectrum Disorders (ASD) in Qatar

Discovering the genetic causes of ASD and cognitive disabilities

Investigating the molecular mechanisms of immune abnormalities and how they correlate to ASD severity

Identifying biomarkers for the early diagnosis, prognosis, and treatment of neurological disorders

Elucidating the role of protein aggregation and synaptic plasticity in Alzheimer’s and Parkinson’s patients

Diabetes Research Center

Research Interests

Utilizing human pluripotent stem cells to investigate molecular mechanisms

Generating functional pancreatic beta cells for therapeutic use in diabetes treatment

Elucidating lifestyle interventions and treatment options that prevent Type 2 diabetes

Identifying prediabetic, diabetic, and vascular biomarkers and co-morbidities

Qatar Biomedical Research Institute (QBRI)

Core Facilities

QBRI's core facilities are major hubs for driving forward cutting-edge research and innovation in Qatar. They are positioned as modern, efficient, reliable, and tightly networked resource laboratories that guarantee strong support and scientific progress on several levels. They are embedded in a growing national and international collaborative environment, including academic, clinical, and industry partners. QBRI houses state-of-the-art core facilities that actively support scientific research by providing advanced research technologies and services to the research community in Qatar and worldwide. The core facilities include Imaging and Flow Cytometry Core, Genomics and Genome Technology Core, Proteomics Core, Bioinformatics Capabilities, Structural Biology Core, Stem Cells and Genome Engineering Core, and Clinical Research Core.

Innovation and Knowledge Economy

QBRI is a major contributor to the generation of knowledge and innovation through the active participation of its scientists and the utilization of its resources to provide new insights into the molecular basis of cancer, diabetes, neurological disorders, and infectious diseases. QBRI's scientists are actively involved in the development of new biomarkers and diagnostic/therapeutic strategies to facilitate early diagnosis, personalized treatment, and management of these debilitating diseases. Other forms of contributions include the publication of new scientific findings in prestigious journals, high-profile representation of QBRI at major international conferences, patentable discoveries, partnerships with leading research centers and industry, as well as the development of new tools and technologies, and related licensing opportunities. An example of successful QBRI innovations is QABY Biotech.

QABY is an in-house developed diagnostic technology for neurodegenerative diseases, and it is registered as a trademark with QF. QABY was used by Austrian biotechnology company AFFiRiS AG in a phase-I clinical trial to assess the impact of PD01 vaccine for Parkinson's Disease. Data from AFFiRiS phase-I clinical trial was published in prestigious journals, and QABY will be used in phase II clinical trials
to be conducted in Europe, USA, and Japan. Moreover, QBRI and the leading global pharmaceutical company H. Lundbeck A/S have established a partnership utilizing pioneering diagnostic tools and assays developed for PD by QBRI researchers. QBRI's success creates an environment that facilitates the development of homegrown innovations that will be a major attraction for biotechnology and pharmaceutical companies to set up operations in Qatar.

Research Funding

Researchers at QBRI can access research funding opportunities through internal and external grants. The QBRI Intramural Grants Program (IGP) was established to stimulate and support innovative and competitive scientific research initiatives led by QBRI researchers in basic, applied, and translational biomedical research. It provides opportunities for QBRI researchers to engage in creative high impact research to advance knowledge, education, and practice and to expand the horizons of research in the fields of neurological disorders, diabetes, cancer, and infectious diseases. Researchers with established research programs at QBRI are expected to submit research proposals to the IGP in order to help advance QBRI's mission by contributing to one or more of its research focus areas. For newly appointed scientists, QBRI has a competitive start-up research fund that provides them with the resources needed to establish successful research programs aligned with QBRI's focus areas. In addition to the IGP and start-up funds, QBRI launched several interdisciplinary research programs with preallocated budgets. Researchers across QBRI research centers are encouraged to take part in these programs and to share the allocated funds. As part of the strategic collaboration between QBRI and Harvard Stem Cell Institute (HSCI), QBRI provides funds for collaborative projects that involve investigators from both institutes.

Research Compliance Assurance

Research compliance assurance ensures that all institutional research programs comply with the rules and regulations of the national and international regulatory agencies. QBRI has two well-established research compliance committees. The first committee is the Institutional Review Board (IRB), which is a professional committee that reviews research protocols involving human subjects in various disciplines and all related processes and documentation to ensure that the participants' rights and welfare are protected. The QBRI-IRB Committee works in accordance with the guidelines and regulations of the Ministry of Public Health and supports HBKU's colleges (students and faculty) as well as other QF entities, such as Doha International Family Institute (DIFI) and Virginia Commonwealth University School of the Arts in Qatar (VCUarts Qatar). The second committee is the QBRI Institutional Biosafety Committee (IBC), which was established in 2013 to review research protocols conducted at QBRI and other QF centers, such as Sidra Medicine, Al Shaqab, QEERI, and HBKU to ensure compliance with national and international biosafety guidelines.

Partnerships

QBRI has succeeded in building collaborative and strategic partnerships with world-renowned institutions and stakeholders in Qatar, as well as with leading scientists and centers of excellence around the world. These collaborative and strategic partnerships support the development of QBRI's programs and build its scientific capacity, while engaging in groundbreaking research at the frontiers of biology, medicine, biomarkers, drug development, translational medicine, and personalized healthcare. Among the most important elements of the translational research spectrum is patient involvement. QBRI's strong partnerships with local organizations, such as HMC, Sidra medicine, QPMI, and Shafallah Center provide patients with the access needed to forge a path toward precision medicine in Qatar. The abundance of data collected at these organizations supports QBRI's scientific research and enables the institute to pursue breakthrough discoveries to better understand diseases specific to the Qatari population. QBRI's thriving research collaboration with each of these organizations is playing a pivotal role in shaping the future of precision medicine in Qatar and the region. QBRI and King Hussein Cancer Center (KHCC), in collaboration with HMC, have taken a strategic initiative to better understand the complexities of breast cancer in the Arab region. The main goal of this collaboration is to discover new susceptibility genes in Arab populations, which could help in prevention, early detection, and treatment. Additionally, this collaboration could lead to more personalized treatment options for patients by selecting the most appropriate therapies, based on their genetic backgrounds.

In September 2018, QBRI launched a strategic partnership with Harvard University to conduct joint stem cell research projects, thus paving the way for translating discoveries into clinical applications. The five-year multi-faceted partnership includes joint research projects, technical training, and future clinical trials. The primary goal is to develop the region's first cell-therapy program to combat diabetes. QBRI identifies and implements select research projects with appropriate researchers, including Qatari research fellows, to participate in training programs. QBRI established a collaboration agreement with the Cleveland Clinic Foundation (USA) to validate an autism eye-tracking tool, a test which analyzes a child's visual responses to various stimuli in order to diagnose autism. The validation of this technology in partnership with local health care providers, such as HMC, Sidra Medicine, and Shafallah Center, allow for clinical implementations that can improve healthcare for individuals and relevant populations locally and regionally.

QBRI signed commercial agreements with biotech companies, Olink and Sengenics. Through these agreements, QBRI has established cutting-edge high throughput certified platforms for protein and autoantibody biomarkers research. Establishing these platforms onsite brings the technology closer to our researchers, thus increasing the likelihood of more expedient discoveries as well as significant cost savings. As the Institute solidified its reputation as a national research institute that reliably delivers high impact, industry partners such as Lundbeck and AFFiRiS have selected QBRI-developed technologies to validate their clinical trials and to produce new diagnostic methods. These acquisitions are the first international biotech companies to procure technologies developed in the Arab World. This remarkable accomplishment positions QBRI as a powerful global partner.

Given the significant complexities associated with implementing and advancing precision medicine, productive collaborations will be fundamental to the health model's successful adoption in Qatar. Ongoing active discussions are taking place with several leading American and European biomedical institutions to develop joint initiatives aimed at leveraging the latest technologies to address local health challenges in Qatar, while pushing the frontiers in the areas of personalized healthcare.

Capacity Building

QBRI is actively contributing to the generation of a highly skilled workforce through its education, training, and professional development programs for young Qatari and resident scientists. Mentorship opportunities, educational programs, training opportunities, internships, and career guidance are provided by QBRI in basic, translational, and clinical research. QBRI is at the forefront of scientific innovation in Qatar and, through its participation in knowledge-sharing events such as symposiums and conferences, contributes significantly to the region. QBRI is committed to building local capacity. The research fellow training program was established to support recent Qatari doctorates to become independent researchers. Graduates of Cambridge and Oxford universities joined this program, received research funding, built their own research teams, and started their projects under the mentorship of QBRI senior researchers. QBRI scientists participate heavily in teaching and supervising graduate students at CHLS, HBKU. Moreover, QBRI scientists participate in teaching at other national educational institutions in Qatar such as Qatar University.

QBRI develops and offers technical training courses in collaboration with a wide range of national and international partners. For example, the institute offers instructional courses for clinicians and researchers in autism diagnosis - Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview – Revised (ADI-R). Another example is QBRI workshops that provide participants with an overview of the existing technology platforms and their importance in advancing biomedical research.

The QBRI summer research program has been quite successful, as it introduces undergraduate students to the exciting biomedical research programs and scientific opportunities available in Qatar, broadens their knowledge base, enhances their skills, and stimulates their scientific interests and career options. Such opportunities are valuable for personal development and career direction. To attract the next generation of scholars, QBRI conducts and participates in several activities, such as science competitions for school students and ‘shadow a scientist’ day for university students. These activities inspire the younger generations to choose biomedical research for a career.

Community Engagement and Outreach

QBRI organizes regular health awareness campaigns and community outreach activities that reach out to both the public and scientific communities, helping bridge the gap between them, and engaging them as partners in QBRI’s efforts to improve and enhance the nation’s health and wellbeing. Successful awareness campaigns include the Breast Cancer Awareness Month (organized in collaboration with the Qatar Cancer Society); World Alzheimer’s Day; World Autism Awareness Day; World Diabetes Day (organized in collaboration with the Qatar Diabetes Association); and World Parkinson’s Day. These campaigns help increase public understanding about the diseases and the importance of prevention, early diagnosis, and detection, while informing them about QBRI’s research activities and highlighting their importance and value. In addition to the awareness campaigns, QBRI reaches out to the public to address emerging health matters and to provide the community with credible scientific information through different communication channels and webinars.

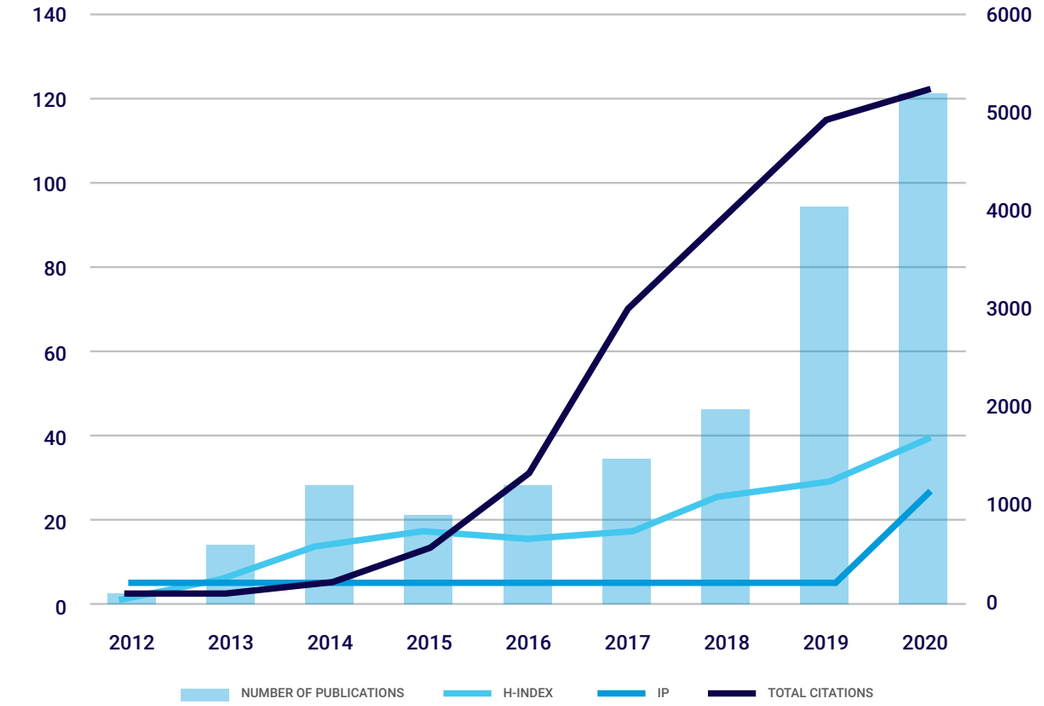
Infrastructure

Integrated Research and Development Facilities

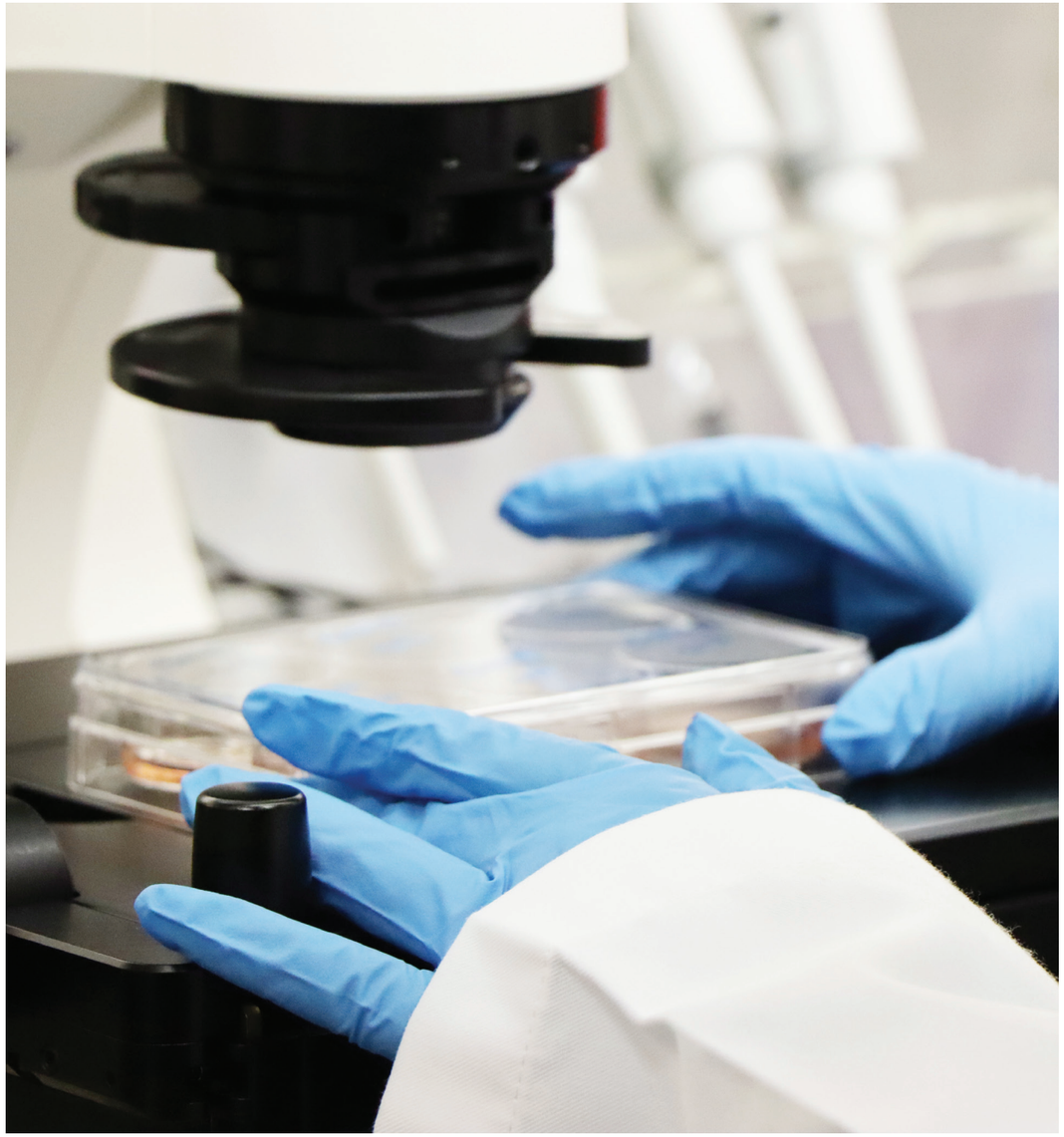
QBRI has state-of-the-art research laboratories within the purpose-built 223,000sqm HBKU Research and Development (R&D) complex located in the Education City. Inaugurated in 2017, QBRI's advanced laboratories are major hubs for driving forward cutting-edge research and innovation in Qatar and the region. Alongside QBRI, the Qatar Computing Research Institute (QCRI) and Qatar Energy and Environment Research Institute (QEERI) are also housed in the same building, thereby creating a unique and combined infrastructure that is specifically designed to address Qatar's major challenges. It further encourages interdisciplinary interaction and cross-fertilization of ideas between the primary areas of research as identified by the QNRS strategy. The institute's renowned facilities house some of the most sophisticated equipment and research apparatus in the Gulf region and worldwide, under one roof.

QBRI's Scholarly Outputs

***Data obtained from Scopus**



Research Centers



Translational Cancer and Immunity Center

Summary

The Translational Cancer and Immunity Center (TCIC) aims to achieve a better understanding of the cellular and molecular bases of cancer initiation and progression with a focus on breast cancer, which is the most common type of cancer among females globally. The TCIC's highest priority is to shed more light on cancer issues that impact Qatar and the Arab region. A new relevant and contemporary direction for the center is to conduct research in the area of infectious diseases and immunity.

Objectives

The TCIC focuses on research areas that are strongly aligned with national priorities and aims to:

- Research tumor-immune ecosystems to identify therapeutic cancer cell-intrinsic molecules
- Identify diagnostic, prognostic, and predictive biomarkers, as well as new therapeutic targets for breast cancer
- Investigate multi-omic signatures associated with infectious disease onset and progression

National and International Collaborations and Partnerships

At TCIC, both investigator and center driven collaborative initiatives have been established with stakeholders within Qatar and internationally.

Collaborations with HBKU:

- Qatar Computing Research Institute (QCRI)
- College of Health and Life Sciences (CHLS)

National Research Collaborations:

- Qatar Institute of Precision Medicine (QIPM)
- Qatar Biobank (QBB)
- Qatar Genome Programme (QGP)
- Sidra Medicine
- Hamad Medical Corporation (HMC)
- Anti-Doping Lab Qatar (ADLQ)
- Qatar University (QU)

International Research Collaborations:

- King Hussein Cancer Center (Jordan)

Interdisciplinary Research Program – Breast Cancer

Diagnostic and Predictive Biomarkers in Breast Cancer

Scientific Coordinator: Dr. Nehad Alajez
Investigators: Dr. Julie Decock, Dr. Fares Al-Ejeh, Dr. Mariam Al-Muftah, Dr. Khalid Ouararhni, Dr. Paul Thornalley, Dr. Abdelilah Arredouani, Dr. Omar El-Agnaf, Dr. Hyung Kim, and Dr. Houari Abdesselem
Collaborators: Dr. Salahddin Gehani (HMC), Dr. Salha Bujassoum (HMC), Dr. Hikmat Abdel-Razeq (KHCC, Jordan), and Dr. Omar Albagha (HBKU CHLS)

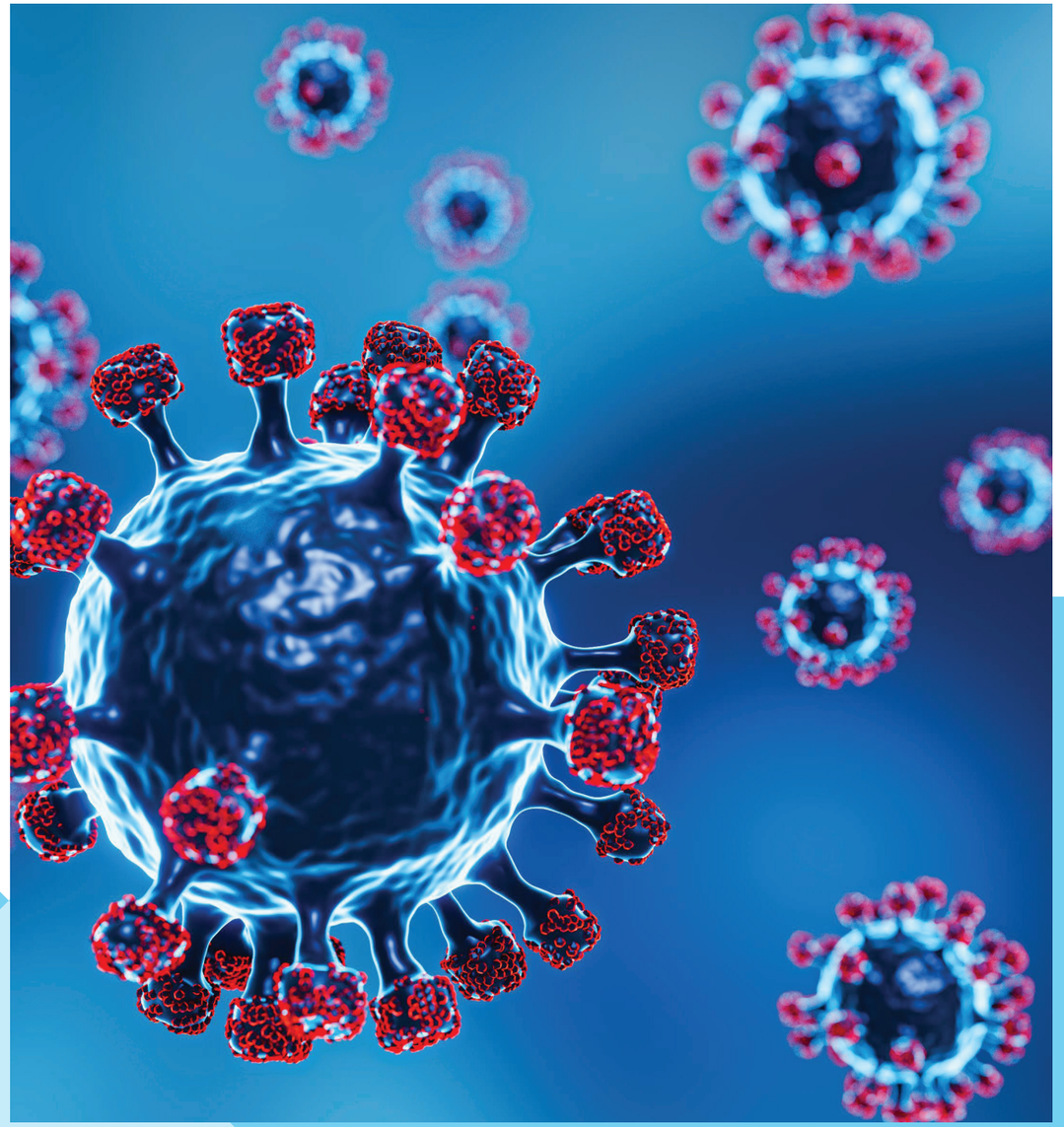
Summary
Breast cancer remains a major health issue worldwide affecting 1 out of 4 women with cancer and accounting for 15% of all cancer related deaths. In Qatar and in the Middle East and North Africa (MENA) region, breast cancer represents about 30% of female cancer cases, and data are mounting to support that there are differences in the etiology, diagnosis, and molecular features of breast cancer in Qatar and the MENA region compared to other populations. Therefore, understanding the clinical and molecular features of breast cancer in Qatar and the region is essential to improve the management and survival rates among women affected by this disease. Whole genome sequencing will be performed to identify genetic alterations in familial breast cancer patients without (likely) pathogenic BRCA1/2 mutations and to identify the genetic drivers of hereditary breast cancer beyond BRCA1/2 mutations among Arab women. In the second part, using blood from healthy individuals as well as tumor and normal breast tissue from cancer patients (treatment responders versus non-responders), genomics, transcriptomics, proteomics, metabolomics, epigenomics, immunophenotyping, and oncosome profiling will be performed and analyzed to identify potential diagnostic and predictive biomarkers, with potential implementation toward improving the clinical outcomes for breast cancer patients.

Interdisciplinary Research Program – Infectious Diseases

Integrative, Translational Research Against COVID-19

Scientific Coordinator: Dr. Julie Decock
Investigators: Dr. Nehad Alajez, Dr. Khalid Ouararhni, Dr. Paul Thornalley, Dr. Prasanna Kolatkar, Dr. Abdelilah Arredouani, Dr. Heba Al-Siddiqi, Dr. Omar El-Agnaf, Dr. Hyung Kim, Dr. Yongsoo Park, Dr. Sara Abdulla, Dr. Houari Abdesselem
Collaborators: Dr. Mariam Al-Nesf (HMC), Dr. Jassim Al-Suwaidi (HMC), Dr. Ali Omrani (HMC), Dr. Nahla Afifi (QBB), Dr. Vidya Mohamed-Ali (ADLQ), Dr. Mohammed Al-Maadheedh (ADLQ), Dr. Hadi Yassine (QU), Dr. Hebah Al Khatib (QU), and Dr. Naila Rabbani (QU)

Summary
The Coronavirus (COVID-19) has been declared a pandemic by the World Health Organization. It is caused by the novel coronavirus (SARS-CoV-2), an enveloped single positive stranded RNA virus that can infect multiple cell types in humans causing serious pathological symptoms. Several studies point out that the most common co-morbidities include chronic diseases such as cardiovascular disease, diabetes, and chronic kidney disease, and pulmonary diseases. Age, 60 and above, has also been shown to predict a higher risk of death in conjunction with co-morbidities. The actual underlying causes of death from COVID-19 are not fully understood; therefore, some deaths may be directly attributed to the SARS-CoV-2 infection and respiratory failure, while others may be attributed to patients' underlying conditions. Furthermore, in patients with severe cases, SARS-CoV-2 infection can drive a profound and life-threatening inflammatory response leading to a 'cytokine storm.' The program integrates patient-based and in-vitro based studies and applies a multidisciplinary approach with dynamic interactions across experienced research teams at QBRI and with clinicians and researchers across Qatar. Blood and nasopharyngeal swab samples will be collected from COVID-19 patients in addition to blood samples from healthy individuals to study SARS-CoV-2 viral epitranscriptomics, and host immunological, genetic, transcriptomic, and protein biomarkers of COVID-19 severity and end organ complications. The program will also enable the development of in-house tools and pathogen-free in-vitro models for diagnostic and therapeutic purposes.



Innovation Activities at TCIC

TCIC aims to be the regional hub for cancer research with its state-of-the-art equipment and highly skilled staff members. The center benefits from the well-equipped and resourceful laboratories to execute inventive and innovative ideas in cancer research, resulting in several discoveries.

TCIC investigators have submitted several patent applications related to

- Targeting lactate dehydrogenase C to improve treatment response to common anti-cancer drugs
- Therapeutic potential of lactate dehydrogenase C for immunotherapy
- Identification and therapeutic potential of mRNA and lncRNA-based signatures in the resistance of Triple-Negative Breast Cancer (TNBC) to neoadjuvant chemotherapy

Training, Teaching, and Supervising Students

TCIC investigators have joint faculty positions at CHLS, HBKU, and have contributed to its graduate programs through coordinating and teaching courses, including Cancer Precision Medicine, Cancer Immunology and Immunotherapy, Cancer Cell Biology, Advanced Genetics, Advanced Molecular Biology, and Advanced Techniques in Biochemistry. TCIC investigators also participate in supervising MSc and PhD students from the CHLS, HBKU. TCIC has been actively engaged in the QBRI summer research program and work experience placements.

Research Group

Dr. Nehad Alajez

Senior Scientist

Dr. Nehad Alajez is a Senior Scientist in QBRI and an Associate Professor at the CHLS, HBKU. Dr. Alajez completed his graduate studies at San Francisco State University and the University of Pittsburgh School Of Medicine in the United States, and subsequently did his postdoctoral work at the Princess Margaret Cancer Center (University Health Network) in Toronto, Canada focusing on investigating the role of non-coding RNAs (ncRNAs) in driving cancer progression and their potential utilization for targeted therapies. Dr. Alajez is the recipient of several prestigious awards and grants, and he has published more than 80 articles in top-tier ISI-indexed journals including Blood, Cancer Research, Cell Death and Differentiation, Cell Death and Disease, EMBO Molecular Medicine, Seminars in Cancer Biology, and Science Translational Medicine. Dr. Alajez currently has more than 3000 citations and an h-index of 29 and i10-index of 60. Dr. Alajez's main research interests focus on translational oncology with emphasis on novel biomarker discoveries and targeted therapeutics and their potential applications in personalized medicine for breast cancers. Dr. Alajez is an expert on transcriptome analysis, non-coding RNAs (microRNA and lncRNA), and biomarker discovery for translational cancer research.

Current Projects

- Circulating microRNAs and lncRNAs as novel biomarkers for early breast cancer detection
- Chemotherapy in Triple-Negative Breast Cancer (TNBC) breast cancer
- Diagnostic and predictive biomarkers in breast cancer
- Integrative translational research against COVID-19
- An integrated omic approach to identifying biomarkers for type 2 diabetes associated complications

Selected Publications

- Elango, R., Alsaleh, K. A., Vishnubalaji, R., Manikandan, M., Ali, A. M., Abd El-Aziz, N., … Alajez, N. M. (2020). MicroRNA Expression Profiling on Paired Primary and Lymph Node Metastatic Breast Cancer Revealed Distinct MicroRNA Profile Associated With LNM. Frontiers in Oncology, 10, 756. https://doi.org/10.3389/fonc.2020.00756
- Elango, R., Vishnubalaji, R., Shaath, H., & Alajez, N. M. (2021). Molecular Subtyping and Functional Validation of TTK, TPX2, UBE2C, and LRP8 in Sensitivity of TNBC to Paclitaxel. Molecular Therapy - Methods & Clinical Development, 20, 601–614. https://doi.org/10.1016/j.omtm.2021.01.013
- Ito, E., Yue, S., Moriyama, E. H., Hui, A. B., Alajez, N., Shi, W., … Liu, F.-F. (2011). Uroporphyrinogen Decarboxylase: A Novel Radiosensitizing Target for Solid Human Cancers Identified from an RNAi High-Throughput Screen. Science Translational Medicine, 3(67), 67. https://doi.org/10.1126/scitranslmed.3001922
- Shaath, H., Vishnubalaji, R., Elango, R., Khattak, S., & Alajez, N. M. (2021). Single-cell Long Non-coding RNA (lncRNA) Transcriptome Implicates MALAT1 in Triple-negative Breast Cancer (TNBC) Resistance to Neoadjuvant Chemotherapy. Cell Death Discovery, 7(1), 23. https://doi.org/10.1038/s41420-020-00383-y
- Shaath, H., Vishnubalaji, R., Elkord, E., & Alajez, N. M. (2020). Single-cell Transcriptome Analysis Highlights a Role for Neutrophils and Inflammatory Macrophages in the Pathogenesis of Severe COVID-19. Cells, 9(11), 2374. https://doi.org/10.3390/cells9112374

Research Group

Dr. Fares Al-Ejeh

Senior Scientist

Dr. Fares Al-Ejeh is a Senior Scientist at QBRI, an Associate Professor (Adjunct) at the School of Medicine, University of Queensland (Brisbane, Australia), and a selected Associate Member of the Australian Academy of Health and Medical Sciences (AAHMS, Australia). He received his Bachelor of Biotech (with honors) in 2001 and PhD in 2005 from the University of Wollongong, New South Wales, Australia. His first position after receiving his PhD was industry-funded and led to two patents as a co-inventor of an agent for cancer diagnosis and therapy (theranostic). His patents were licensed out to Oncaidia Ltd. (Adelaide, South Australia), where he was the Chief Scientific Officer. The patents and product (Apomab®) were licensed to Telix Pharma in October 2019. Two cancer patients were injected with Apomab® in September 2020 as a part of a phase-I clinical trial in Australia. His group, the Personalized Medicine Group, focused on precision oncology and worked closely with the breast cancer pathology and surgery units at the Royal Brisbane Hospital. Dr. Al-Ejeh joined the Qatar Biomedical Research Institute (QBRI) in October 2019 as a Senior Scientist and is currently establishing his translational research team. In addition to his two granted/licensed patents for Apomab®, he has five additional provisional patents submitted in Australia. He also submitted an invention disclosure form for his work on COVID-19 in less than one year at QBRI based on collaborative efforts with Hamad Medical Corporation (HMC) and the Anti-Doping Laboratory Qatar (ADLQ).

Current Projects

Developing a new multi-omics biomarker to be used at first diagnosis to identify breast cancer patients who do not benefit from the current standards of care and to predict more effective treatment options for these patients.

Selected Publications

- Betts, J. A., Moradi Marjaneh, M., Al-Ejeh, F., Lim, Y. C., Shi, W., Sivakumaran, H., … French, J. D. (2017). Long Non-coding RNAs CUPID1 and CUPID2 Mediate Breast Cancer Risk at 11q13 by Modulating the Response to DNA Damage. The American Journal of Human Genetics, 101(2), 255–266. https://doi.org/10.1016/j.ajhg.2017.07.007
- Ferreira, M. A., Gamazon, E. R., Al-Ejeh, F., Aittomäki, K., Andrulis, I. L., Anton-Culver, H., … Chenevix-Trench, G. (2019). Genome-wide Association and Transcriptome Studies Identify Target Genes and Risk Loci for Breast Cancer. Nature Communications, 10(1), 1741. https://doi.org/10.1038/s41467-018-08053-5
- Saunus, J. M., Al-Ejeh, F. E., Kutasovic, J. R., Johnston, R. L., Kalita-de Croft, P., Miranda, M., … Lakhani, S. R. (2017). Multidimensional Phenotyping of Breast Cancer Cell Lines to Guide Preclinical Research. Breast Cancer Research and Treatment, 167(1), 289–301. https://doi.org/10.1007/s10549-017-4496-x
- Wiegmans, A. P., Miranda, M., Wen, S. W., Al-Ejeh, F., & Möller, A. (2016). RAD51 Inhibition in Triple Negative Breast Cancer Cells is Challenged by Compensatory Survival Signaling and Requires Rational Combination Therapy. Oncotarget, 7(37), 60087–60100. https://doi.org/10.18632/oncotarget.11065
- Wu, L., Al-Ejeh, F., Long, J., Guo, X., Michailidou, K., Beesley, J., … Zheng, W. (2018). A Transcriptome-wide Association Study of 229,000 Women Identifies New Candidate Susceptibility Genes for Breast Cancer. Nature Genetics, 50(7), 968–978. https://doi.org/10.1038/s41588-018-0132-x

Research Group

Dr. Mariam Al-Muftah

Scientist

Dr. Mariam Al-Muftah received her BS in Medical Genetics (Honors) from the University of Wales in the United Kingdom in 2005 and pursued her graduate education to complete a Master of Research (MRes) in Biological Sciences (2007) and a PhD in Medicine (cancer immunotherapy) as a joint project between the Manchester Cancer Research Institute (Cancer Research UK) and the University of Manchester in the United Kingdom. After completing her doctoral degree in 2011, she became a lecturer of Biology at Qatar University where she taught several courses on general biology and molecular biology at the Department of Biological and Environmental Sciences and was later promoted to the rank of Assistant Professor. In February 2012, she joined the Qatar Biomedical Research Institute (QBRI) as a scientist to pursue her research interests. In addition to being involved in the planning of the organizational structure and infrastructural design of QBRI, she worked on a collaborative project with Prof. Lotfi Chouchane (Weill Cornell Medicine-Qatar) focusing on the molecular mechanisms underlying the development of prostate cancer and how apoptotic pathways influence resistance and therapy efficacy. In 2015, she completed an Executive Master's degree program in Strategic Business Unit Management from HEC Paris University. Dr. Al-Muftah returned to QBRI in July 2019 as a scientist to establish a research team focused on identifying biomarkers for cancer immunotherapy efficacy with focus on immune gene signatures in triple negative breast cancer. In 2020, she submitted a patent disclosure with Dr. Fares Al Ejeh and Dr. Govinda Lenka on the identification of a unique gene signature for the prediction of benefit from immunotherapy in patients with triple negative breast cancer.

Current Projects

Dr. Al-Muftah's research team is currently focused on the validation of a unique gene signature as a predictive marker of cancer immunotherapy in triple negative breast cancer and its association with immune gene expression signatures. The overall aim of the team is to understand the role of the immune system in limiting responses to immunotherapy in triple negative breast cancer.

Selected Publications

- Castro, F. V., Al-Muftah, M., Mulryan, K., Jiang, H.-R., Drijfhout, J.-W., Ali, S., … Stern, P. L. (2011). Regulation of Autologous Immunity to the Mouse 5T4 Oncofetal Antigen: Implications for Immunotherapy. Cancer Immunology, Immunotherapy, 61(7), 1005–1018. https://doi.org/10.1007/s00262-011-1167-3
- Sastry, K. S., Al-Muftah, M. A., Li, P., Al-Kowari, M. K., Wang, E., Ismail Chouchane, A., … Chouchane, L. (2014). Targeting Proapoptotic Protein BAD Inhibits Survival and Self-renewal of Cancer Stem Cells. Cell Death & Differentiation, 21(12), 1936–1949. https://doi.org/10.1038/cdd.2014.140
- Shan, J., Al-Muftah, M. A., Al-Kowari, M. K., Abuaqel, S. W., Al-Rumaihi, K., Al-Bozom, I., … Chouchane, L. (2019). Targeting Wnt/EZH2/microRNA-708 Signaling Pathway Inhibits Neuroendocrine Differentiation in Prostate Cancer. Cell Death Discovery, 30(5), 139. https://doi.org/10.1038/s41420-019-0218-y
- Southgate, T. D., Al-Muftah, M. J., Castro, F. V., Rutkowski, A. J., McGinn, O., Marinov, G., … Stern, P. L. (2010). CXCR4 Mediated Chemotaxis Is Regulated by 5T4 Oncofetal Glycoprotein in Mouse Embryonic Cells. PLoS ONE, 5(4), e9982. https://doi.org/10.1371/journal.pone.0009982

Research Group

Dr. Julie Decock

Scientist

Dr. Julie Decock is a scientist at QBRI and an Assistant Professor at the CHLS, HBKU. She joined QBRI in November 2013 and established her research team in 2016. Dr. Decock completed her PhD in Medical Sciences in 2003 at the Catholic University of Leuven (Leuven, Belgium), focusing on the clinical utility of tumor and circulating proteases as novel biomarkers for breast cancer. Following her PhD, she undertook a postdoctoral position at the University of East Anglia (UK) where she studied the role of several protease families in breast, prostate, and pancreatic cancer. Dr. Decock is the recipient of several research grants, and her research at QBRI has resulted in two US provisional patents. Dr. Decock's research interests focus on key areas that can help accelerate research on breast cancer and infectious diseases and advance the development of new biomarkers and treatments. Part of her cancer research efforts focus on tumor-associated Cancer Testis Antigens (CTAs) as cancer biomarkers, new therapeutic targets, and immunomodulatory regulators in breast cancer, with a special emphasis on triple negative breast cancer. At the interface between cancer and infectious disease research, her group investigates disease-associated dysregulation of the host immune response and associated biomarkers

Current Projects

- Validation of LDHC as a novel target for precision medicine in breast cancer
- Mechanisms in pancreatic development and breast cancer stemness mitigated by Sox2
- How beta-cell-derived interleukin-33 shapes T cell regulation in T1D
- Integrative translational research on COVID-19
- Diagnostic and predictive biomarkers in breast cancer

Selected Publications

- Decock, J., Shaath, H., Naik, A., Toor, S. M., Elkord, E., & Thomas, R. (2020). Identification of Two HLA-A*0201 Immunogenic Epitopes of Lactate Dehydrogenase C (LDHC): Potential Novel Targets for Cancer Immunotherapy. Cancer Immunology, Immunotherapy, 69(3), 449–463. https://doi.org/10.1007/s00262-020-02480-4
- Naik, A., & Decock, J. (2020). Lactate Metabolism and Immune Modulation in Breast Cancer: A Focused Review on Triple Negative Breast Tumors. Frontiers in Oncology, 10. https://doi.org/10.3389/fonc.2020.598626
- Roelands, J., Decock, J., Zoppoli, G., Mall, R., Saad, M., Halliwill, K., … Bedognetti, D. (2020). Oncogenic States Dictate the Prognostic and Predictive Connotations of Intratumoral Immune Response. Journal for ImmunoTherapy of Cancer, 8(1), e000617. https://doi.org/10.1136/jitc-2020-000617
- Roelands, J., Mall, R., Decock, J., Thomas, R., Mohamed, M. G., Bedri, S., … Almeer, H. (2021). Ancestry-Associated Transcriptomic Profiles of Breast Cancer in Patients of African, Arab, and European Ancestry. Npj Breast Cancer, 7(1), 10. https://doi.org/10.1038/s41523-021-00215-x
- Thomas, R., Al-Khadairi, G., & Decock, J. (2021). Immune Checkpoint Inhibitors in Triple Negative Breast Cancer Treatment: Promising Future Prospects. Frontiers in Oncology, 10. https://doi.org/10.3389/fonc.2020.600573

Diabetes Research Center

Summary

Diabetes is a major healthcare challenge globally. In Qatar, diabetes affects an estimated 17% of the population - twice the global average. Qatar ranks as one of the top 10 countries in the world with the highest diabetes rates. An estimated 10% of Qatari diabetes patients have type 1 diabetes (T1D), and 90% have type 2 diabetes (T2D). A further 20% of the population have prediabetes, with 10% of these progressing into T2D every year. A key driver of the development of prediabetes and T2D is being overweight and obese, affecting over 70% of adults (with over 35% obese) and 46% of children (with 20% obese). Further concerns include the vascular complications of diabetes, such as diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, and increased risk of cardiovascular disease. These complications affect 30 – 40% of patients with diabetes. These complications are a major cause of morbidity and premature mortality among patients with diabetes, with coronary heart disease being the major cause of premature mortality. There are also co-morbidities of stroke and dementia. Accordingly, diabetes has emerged as one of the key research areas at the QNRS, which is an indication of the priority given to combating the disease.

The National Diabetes Strategy in Qatar includes a comprehensive action plan for the prevention and reversal of T2D and for improving healthcare for all diabetes patients in order to reduce risk and improve treatment options of vascular complications and co-morbidities, particularly cardiovascular diseases. In recognition of the major impact of diabetes on the health and well-being of the Qatari population, the Diabetes Research Center (DRC) at QBRI is conducting translational and innovative basic research aimed to develop biomarkers and new therapies for diabetes and its vascular complications and co-morbidities. To ensure the implementation and sustainability of these research activities, the DRC is promoting joint research programs and collaborative efforts with HBKU and with national and international partners (see below). This approach has created an exceptional research environment that fosters biomedical research on diabetes and related complications. DRC aims to quickly translate promising discoveries that's beneficial for healthcare through an integrated translational and precision medicine approach.

Research Themes

- Stem cell and beta-cell biology in the study of obesity and diabetes
- Prevention and reversal of type 2 diabetes
- Biomarkers of prediabetes, diabetes, diabetic vascular complications, and co-morbidities

Objectives

DRC has set a number of research focus areas both on T1D and T2D that are aligned with the QNRS. By integrating basic, translational, and clinical research, the primary objectives of the DRC are:

- Identifying the genetic and environmental risk factors and the mechanisms of their contribution to the pathophysiology of insulin resistance, ß-cell function, and diabetes
- Generating functional stem cell-derived pancreatic beta cells in-vitro
- Discovering and validating diagnostic biomarkers and treatments for diabetes and its vascular complications

To achieve these goals, DRC is using state-of-the-art technologies (including pluripotent stem cells) as tools for disease modeling and potential therapies. It is also employing integrated omics technologies, such as genomics, transcriptomics, proteomics, and metabolomics, as well as a wide variety of molecular and cellular biology techniques together with animal models of diabetes to identify and analyze critical genes and pathways that lead to diabetes.

Research Areas at the DRC include:

- Using human pluripotent stem cells to investigate the molecular mechanisms
- Generating functional pancreatic beta-cells for therapeutic use in diabetes
- Investigating the triggers of insulin resistance and obesity as drivers of type 2 diabetes
- Studying the biomarkers of prediabetes, diabetes, diabetic vascular complications, and co-morbidities

The ultimate goal of DRC research activities is to identify new biomarkers, develop new therapeutic targets, and treatment modalities.

National and International Collaborations and Partnerships

DRC has established several collaborations at the national, regional, and international levels, and it has a plan to expand its partnerships to other key stakeholders in the future. At the national level, scientists at DRC are collaborating closely on joint projects with clinicians and research staff at Hamad Medical Corporation. DRC is also collaborating with Sidra Medicine, Weill Cornell Medicine–Qatar, Qatar Biobank, Qatar Genome, Qatar University, and Anti-Doping Lab Qatar. The list of national collaborators is growing, and at the regional level, DRC is planning to extend its collaborations to additional institutions from the Gulf region. International collaborations and networking are also crucial for DRC at this stage of capacity building, infrastructure development, training, and technology transfer. DRC's collaborations extend to North America as it is building a strategic partnership with the Harvard Stem Cell Institute and the Joslin Diabetes Center.

Collaborations within HBKU:

- Qatar Computing Research Institute (QCRI)
- Qatar Environment and Energy Research Institute (QEERI)
- College of Health and Life Sciences (CHLS)
- College of Science and Engineering (CSE)
- College of Law (CL)
- College of Islamic Studies (CIS)

National:

- Qatar Institute of Precision Medicine (QIPM)
- Qatar Biobank (QBB)
- Qatar Genome Programme (QGP)
- Qatar Metabolic Institute (QMI)
- Sidra Medicine
- Weill Cornell Medicine-Qatar (WCM-Q)
- Hamad Medical Corporation (HMC)
- Qatar University – College of Medicine, College of Pharmacy and Biomedical Research Center
- Anti-doping Laboratory-Qatar
- World Innovative Summit in Health (WISH)

International:

- Joslin Diabetes Center, Harvard University (Boston, MA, USA)

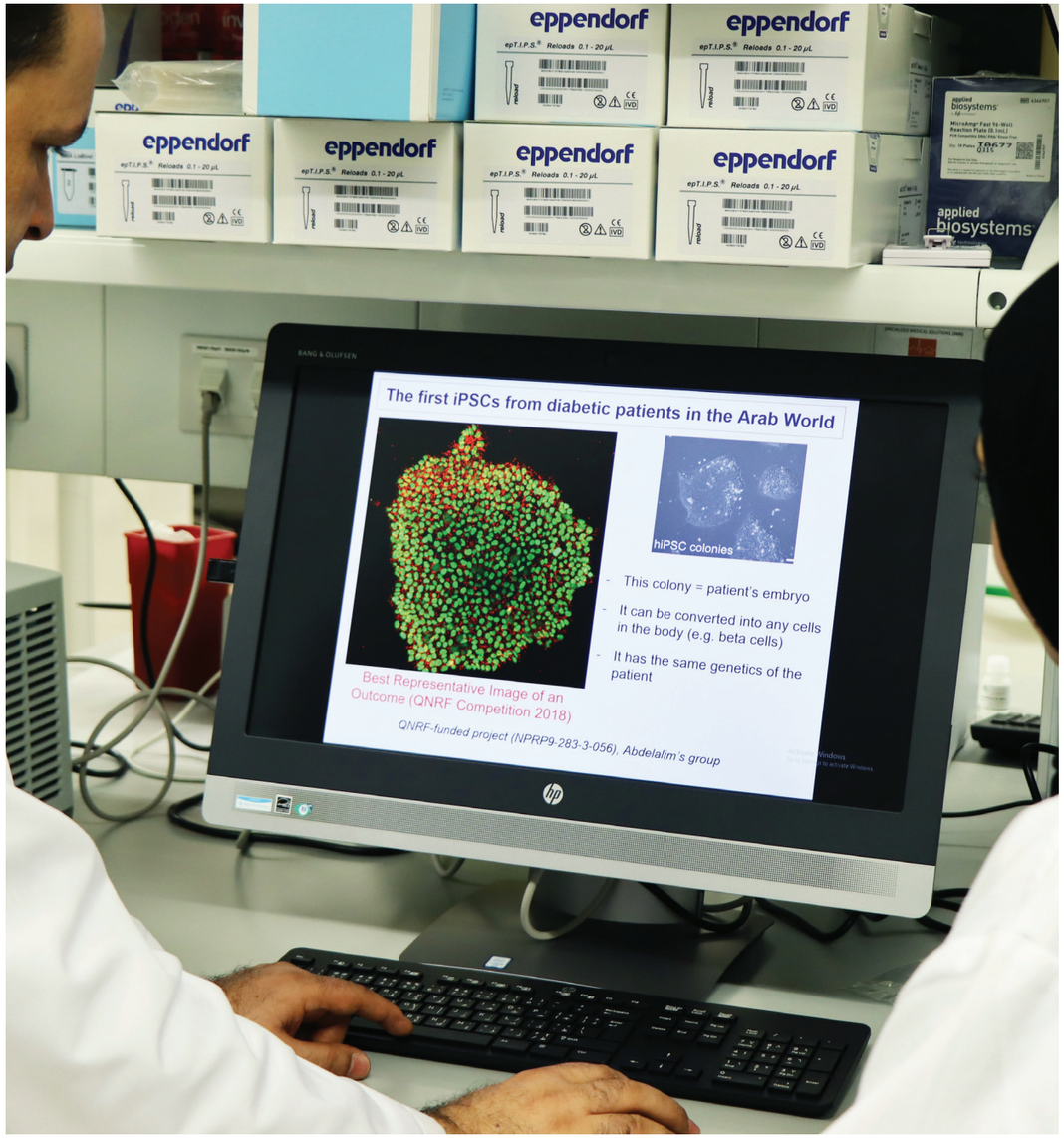
Interdisciplinary Research Program – Diabetes

An Omic Approach to Identify Biomarkers for Type 2 Diabetes-Associated Complications and Co-morbidities

Scientific Coordinator: Dr. Paul J. Thornalley
Investigators: Dr. Essam Abdelalim, Dr. Abdelilah Arredouani, Dr. Prasanna Kolatka, Dr. Julie Decock, and Dr. Nehad Alajez (Translational Cancer and Immunity Center); and Dr. Omar El-Agnaf (Neurological Disorders Research Center)
Collaborators: Dr. Omar Albagha (CHLS), Dr. Halima Bensmail (QCRI), Dr. Mohamed Emara (QU), Dr. Jassim Al Suwaidi, Dr. Ashfaq Shuaib, Dr. Aijaz Parray (HMC), and Dr. Rayaz Malik (WCM-Q)

Summary
T2D is associated with increased risk of debilitating comorbidities such as CVD, stroke, and dementia. CVD is the major cause of premature death of patients with T2D. There is an urgent need to identify biomarkers for diagnosis and progression risk to increased severit of these comorbidities. This project uses an omics approach to identify transcriptomic, proteomic, and metabolomic biomarkers of CVD, stroke, and dementia in addition to their risk of progression in patients with and without T2D. It aims to identify new biomarkers to improve diagnosis and risk prediction of disease progression for CVD, stroke, and dementia in patients with and without diabetes. The outcomes will advance our understanding of the pathogenesis of T2D co-morbidities and guide early-stage treatment for improved patient outcomes with an Artificial Intelligence (AI) and precision medicine-based approach.

Qatar Biomedical Research Institute (QBRI)



Qatar Biomedical Research Institute and Harvard Stem Cell Institute Joint Research Program

This is a multi-faceted five-year training and research program involving DRC and other QBRI investigators with the Harvard Stem Cell Institute at Harvard University (Boston, MA, USA). This strategic collaboration involves training, scholarship, and research in the field of stem cell science for the purpose of developing scientific and technical expertise at QBRI in stem cell technologies applicable to diseases relevant to Qatar and the region, particularly inducible pluripotent stem cell (iPSC)-derived pancreatic beta-cells for cell therapy of patients with T1D. The ultimate goal of this program is to conduct a clinical trial of iPSC-derived beta-cells in Doha in collaboration with HMC and Sidra Medicine.

Innovation Activities of the DRC

- Creating and developing intellectual property (IP) and commercial development
- Developing blood and urine-based tests for predicting the progression of diabetic kidney disease
- Developing dietary supplements for improved immune health and methods for treating COVID-19
- Generating induced pluripotent stem cells (iPSCs) with GLUT2 mutations
- Generating induced pluripotent stem cells (iPSCs) with FOXA2 deletion
- Establishing new human iPSC lines to study diabetes due to mutations in the glucokinase gene

Training, Teaching, and Supervising Students

DRC researchers participate in the institute's internship programs and are involved in supervising graduate students enrolled in the Biomedical and Biomedical Sciences Graduate Program at the CHLS, HBKU. They are also involved in teaching activities, offering courses on, Advanced Molecular Biology, Techniques in Biochemistry, Molecular and Cell Biology, Stem Cell Biology, Molecular Mechanisms of Cancer and Precision Medicine, Stem Cell Biology, Advances in Human Metabolism and Disease, Signal Transduction in Health and Diseases, and Omics Techniques and Molecular Biology of Neuroscience.

DRC researchers collaborate with Qatar University colleagues, supervise graduate students, and mentor students enrolled in the QNRF Undergraduate Research Experience Program.

Research Group

Dr. Paul J. Thornalley

Director, Diabetes Research Center

Dr. Paul J. Thornalley's research team at QBRI focuses on metabolic dysfunction driving the development of type 2 diabetes and diabetic vascular complications, particularly hexokinase-2 (HK2) linked glycolytic overload and increased methylglyoxal (MG), dicarbonyl stress, formation of advanced glycation end products (AGEs), and MG metabolism by the glyoxalase system.

Current Projects

- Cellular studies on the dysregulation of methylglyoxal metabolism in obesogenic and diabetic environments
- Metabolic control of β-cell inflammation
- Regulation of glyoxalase 1 by fatty acids and implications for obesity
- Vulnerabilities of the SARS-CoV-2 virus to proteotoxicity
- Artificial intelligence for precision medicine and health technologies

Selected Publications

- Al-Motawa, M., Thornalley, P. J., Wijten, P., de la Fuente, A., Xue, M., Rabbani, N., & Abbas, H. (2020). Vulnerabilities of the SARS-CoV-2 Virus to Proteotoxicity – Opportunity for Repurposed Chemotherapy of COVID-19 Infection. Frontiers in Pharmacology , 11(1663-9812), 585408. https://doi.org/10.1101/2020.04.07.029488
- Bierhaus, A., Thornalley, P. J., Stoyanov, S., Leffler, A., Babes, A., Neacsu, C., … Nawroth, P. P. (2012). Methylglyoxal Modification of Nav1.8 Facilitates Nociceptive Neuron Firing and Causes Hyperalgesia in Diabetic Neuropathy. Nature Medicine, 18(6), 926–933. https://doi.org/10.1038/nm.2750
- Rabbani, N., & Thornalley, P. J. (2019). Hexokinase-2 Glycolytic Overload in Diabetes and Ischemia–Reperfusion Injury. Trends in Endocrinology & Metabolism, 30(7), 419–431. https://doi.org/10.1016/j.tem.2019.04.011
- Thornalley, P. J., Rabbani, N., Weston, A., Adaikalakoteswari, A., Lee, J. A., Lovblom, L. E., … Perkins, B. A. (2020). High Fractional Excretion of Glycation Adducts is Associated with Subsequent Early Decline in Renal Function in Type 1 Diabetes. Scientific Reports, 10(1), 12709. https://doi.org/10.1038/s41598-020-69350-y
- Thornalley, P. J., Weickert, M. O., Qureshi, S., Kandala, N.-B., Anwar, A., Waldron, M., … Xue, M. (2016). Improved Glycemic Control and Vascular Function in Overweight and Obese Subjects by Glyoxalase 1 Inducer Formulation. Diabetes, 65(8), 2282–2294. https://doi.org/10.2337/db16-0153

Research Group

Dr. Prasanna Kolatkar

Senior Scientist

Dr. Prasanna Kolatkar's research team at QBRI works primarily on understanding the transcriptional networks that determine cell fate using a variety of biophysical tools, including X-ray crystallography. The protein and structural biology group (PSB) works in collaboration with stem cell and bioinformatics groups within and outside QBRI to enable an integrated view of transcriptional networks. The group uses genomics to target specific transcription factors (TFs) and studies them to understand the mechanisms used by TFs to make protein-protein and protein-DNA interactions. They are currently analyzing several TFs involved in pluripotency and are working with stem cell groups that are studying pancreatic beta cell differentiation in normal and Type 2 Diabetes patients to target TFs with key roles in this process. The Kolatkar laboratory is also employing their group-specific technology to look at other disease mechanisms as well.

Current Projects

- Study and analysis of the mechanisms involved in protein-nucleic acid interactions of β cell development
- Biological conversion of fuel synthesis process water to single cell protein for aquaculture
- Mechanisms of pancreatic development and breast cancer stemness mitigated by Sox2
- Structural characterization of antibody-α-synuclein complexes for diagnostic and therapeutic applications
- The role of key transcription factors in human pancreatic beta cell development and maturation

Selected Publications

- Kolatkar, P. R., Aksoy, I., Hutchins, A. P., Ng, C. K., Tian, X. F., Chen, J., … Jauch, R. (2011). Conversion of Sox17 into a Pluripotency Reprogramming Factor by Reengineering its Association with Oct4 on DNA. STEM CELLS, 29(6), 940–951. https://doi.org/10.1002/stem.639
- Kolatkar, P. R., Jauch, R., Chen, J., Dyla, M., Divakar, U., Bogu, G. K., … Stanton, L. W. (2013). Oct4 Switches Partnering from Sox2 to Sox17 to Reinterpret the Enhancer Code and Specify Endoderm. The EMBO Journal, 32(7), 938–953. https://doi.org/10.1038/emboj.2013.31
- Kolatkar, P. R., Jauch, R., Eras, V., Chng, W.-bin A., Chen, J., Divakar, U., … Stanton, L. W. (2013). Sox Transcription Factors Require Selective Interactions with Oct4 and Specific Transactivation Functions to Mediate Reprogramming. STEM CELLS, 31(12), 2632–2646. https://doi.org/10.1002/stem.1522
- Kolatkar, P. R., Mall, R., Kunji, K., Rawi, R., Islam, Z., Chuang, G.-Y., … Bensmail, H. (2019). BCrystal: An Interpretable Sequence-based Protein Crystallization Predictor. Bioinformatics, 36(5), 1429–1438. https://doi.org/10.1093/bioinformatics/btz762
- Kolatkar, P. R., Prokoph, N., Girbig, M., Wang, X., Huang, Y.-H., Srivastava, Y., … Jauch, R. (2016). Structure and Decoy-mediated Inhibition of the SOX18/Prox1-DNA Interaction. Nucleic Acids Research, 44(8), 3922–3935. https://doi.org/10.1093/nar/gkw130

Research Group

Dr. Essam Abdelalim

Scientist

Dr. Essam Abdelalim leads the stem cell research group for diabetes modelling and the treatment of T1D and T2D at DRC. The focus of the stem cell research program is to use patient-specific induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) to investigate the molecular mechanisms underlying T2D, insulin resistance, and pancreatic β-cell differentiation. T2D has a strong genetic component and often occurs as a result of insufficient insulin secretion by pancreatic β-cells and/or the inappropriate response to insulin by target tissues (insulin resistance). Patient-specific iPSCs are being used as tools to: (1) investigate the mechanisms and pathways implicated in the pathogenesis of specific forms of T2D and insulin resistance, and (2) screen novel drugs and therapies for the treatment of T2D. A similar approach will also be used for T1D.

Current Projects

- The role of key transcription factors in pancreatic beta cell development and maturation using human iPSCs
- Metabolic control of β-cell inflammation
- Signaling pathways underlying the generation of pluripotent stem cell-derived pancreatic progenitors
- The mechanisms involved in protein-nucleic acid interactions of beta cell development
- Insulin resistance in a Qatari cohort using patient specific induced pluripotent stem cells

Selected Publications

- Abdelalim, E. M., Ali, G., Elsayed, A. K., Al-Khawaga, S., Hussain, K., & Aqel, Y. W. (2020). Generation of Two Human iPSC Lines from Patients with Maturity-onset Diabetes of the Young Type 2 (MODY2) and Permanent Neonatal Diabetes due to Mutations in the GCK Gene. Stem Cell Research, 48, 101991. https://doi.org/10.1016/j.scr.2020.101991
- Abdelalim, E. M., Memon, B., Elsayed, A. K., & Aigha, I. I. (2018). Differentiation of Human Pluripotent Stem Cells into Two Distinct NKX6.1 Populations of Pancreatic Progenitors. Stem Cell Research & Therapy, 9(1), 83. https://doi.org/10.1186/s13287-018-0834-0
- Abdelalim, E. M., Younis, I., Elareer, N. R., Nasser, S., & Karam, M. (2020). Scalable Generation of Mesenchymal Stem Cells and Adipocytes from Human Pluripotent Stem Cells. Cells, 9(3), 710. https://doi.org/10.3390/cells9030710
- Elsayed, A. K., Abdelalim, E. M., Al-Khawaga, S., Hussain, K., & Aghadi, M. (2020). Derivation of a Human Induced Pluripotent Stem Cell Line (QBRIi007-A) from a Patient Carrying a Homozygous Intronic Mutation (c.613-7T>G) in the SLC2A2 gene. Stem Cell Research, 44, 101736. https://doi.org/10.1016/j.scr.2020.101736
- Memon, B., Abdelalim, E. M., Al-Khawaga, S., & Karam, M. (2018). Enhanced Differentiation of Human Pluripotent Stem Cells into Pancreatic Progenitors Co-expressing PDX1 and NKX6.1. Stem Cell Research & Therapy, 9(1), w15. https://doi.org/10.1186/s13287-018-1002-2

Research Group

Dr. Abdelilah Arredouani

Scientist

Dr. Abdelilah Arredouani is involved in the identification of specific secondary metabolites that precede the onset of diabetes. The comprehensive analysis of low-molecular weight metabolites carried out by a metabolomics approach is becoming a powerful tool for disease diagnosis and biomarker identification. Identification and characterization of such metabolites using a metabolomics approach is paramount to identifying at-risk individuals, especially that this can be achieved during early asymptomatic stages when treatment is likely to be most effective. Dr. Arredouani is implementing this technology at DRC in combination with multivariate data analysis tools to identify diabetes predictive biomarkers, as well as other risks associated with the development of diabetes and obesity.

Current Projects

- The impact of a low energy diet intervention on non-alcoholic fatty liver disease in type 2 diabetes
- Metabolic and molecular profiling of lean and obese subjects with T2DM in Qatar

Selected Publications

- Al-Akl, N., Thompson, R. I., & Arredouani, A. (2020). High Plasma Salivary α-Amylase, but not High AMY1 Copy Number, Associated with Low Obesity Rate in Qatari Adults: Cross-sectional Study. Scientific Reports, 10(1), 17918. https://doi.org/10.1038/s41598-020-74864-6
- Arredouani, A., Errafii, K., Abbas, M., Mall, R., Lattab, A., Ullah, E., & Bensmail, H. (2020). Simple Risk Score to Screen for Prediabetes: A Cross-sectional Study from the Qatar Biobank Cohort. Journal of Diabetes Investigation, in press. https://doi.org/doi: 10.1111/jdi.13445.
- Arredouani, A., Stocchero, M., Culeddu, N., Moustafa, J. E.-S., Tichet, J., Balkau, B., … Falchi, M. (2016). Metabolomic Profile of Low–Copy Number Carriers at the Salivary α-Amylase Gene Suggests a Metabolic Shift Toward Lipid-Based Energy Production. Diabetes, 65(11), 3362–3368. https://doi.org/10.2337/db16-0315
- Arredouani, A., Yengo, L., Dechaume, A., Canouil, M., Castelain, M., Roger, E., … Froguel, P. (2017). Relationship between Salivary/Pancreatic Amylase and Body Mass Index: A Systems Biology Approach. BMC Medicine, 15(1), 37. https://doi.org/10.1186/s12916-017-0784-x
- Yengo, L., Arredouani, A., Marre, M., Roussel, R., Vaxillaire, M., Falchi, M., … Froguel, P. (2016). Impact of Statistical Models on the Prediction of Type 2 Diabetes Using Non-targeted Metabolomics Profiling. Molecular Metabolism, 5(10), 918–925. https://doi.org/10.1016/j.molmet.2016.08.011

Research Group

Dr. Heba Al-Siddiqi

Research Fellow

Dr. Heba Al-Siddiqi focuses on the generation of insulin-secreting pancreatic beta cells from Human Pluripotent Stem Cells (hPSCs), using both Human Induced Pluripotent Stem Cells (hiPSCs) and Human Embryonic Stem Cells (hESCs).

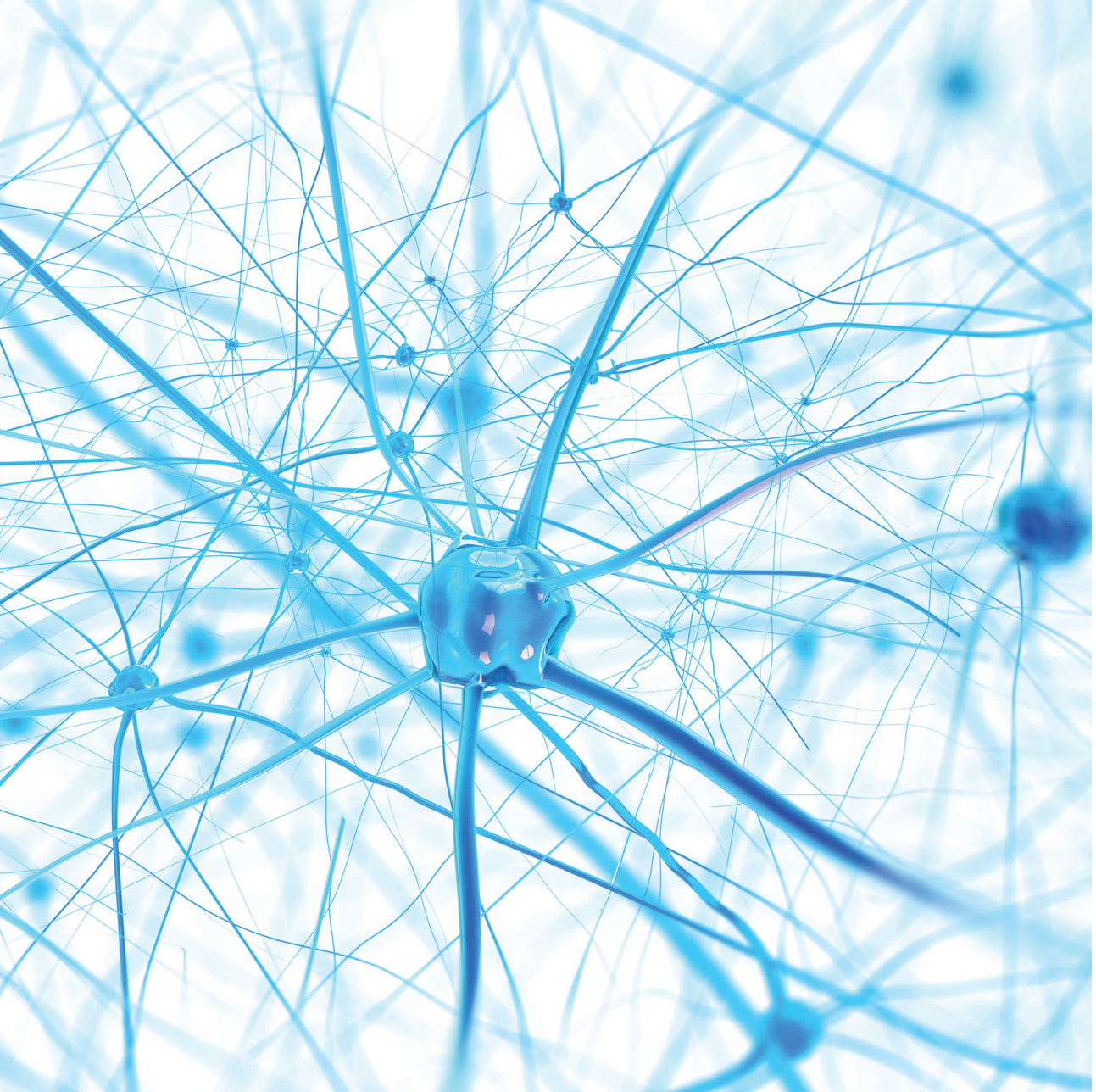
Her research group is establishing 2D and 3D in-vitro pancreatic beta cell differentiation protocols. They aim to analyze the efficiency and maturation of hPSC-derived pancreatic beta cells by studying the expression and role of transcription factors involved in the development and maturation of pancreatic beta cells and the functionality of the generated beta cells. Dr. Heba received the Early Career Researcher Grant (ECRA) from QNRF, and her research group is involved in the collaborative projects with Harvard Stem Cell Institute.

Current Projects

- The role of key transcription factors in pancreatic beta cell development/maturation using hPSCs
- Gene expression profiling and role during directed differentiation of hPSCs to pancreatic β-cells

Selected Publications

- Ahfeldt, T., Schinzel, R. T., Al-Siddiqi, H., Hendrickson, D., Kaplan, A., Lum, D. H., … Cowan, C. A. (2012). Programming Human Pluripotent Stem Cells into White and Brown Adipocytes. Nature Cell Biology, 14(2), 209–219. https://doi.org/10.1038/ncb2411
- Lopez, C. A., Al-Siddiqi, H. H., Purnama, U., Iftekhar, S., Bruyneel, A. A., Kerr, M., … Carr, C. A. (2021). Physiological and Pharmacological Stimulation for In-vitro Maturation of Substrate Metabolism in Human Induced Pluripotent Stem Cell-derived Cardiomyocytes. Scientific Reports, 11(1), 7802. https://doi.org/10.1038/s41598-021-87186-y
- Malandraki-Miller, S., Lopez, C. A., Al-Siddiqi, H., & Carr, C. A. (2018). Changing Metabolism in Differentiating Cardiac Progenitor Cells—Can Stem Cells Become Metabolically Flexible Cardiomyocytes? Frontiers in Cardiovascular Medicine, 5, 119. https://doi.org/10.3389/fcvm.2018.00119



Neurological Disorders Research Center

Summary

Research at NDRC focuses on the neurological disorders of high prevalence in Qatar and the Arab region in order to elucidate their underlying molecular mechanisms to facilitate diagnosis and therapeutic interventions. These disorders are diverse and range from neurodevelopmental diseases, such as Autism Spectrum Disorder (ASD), Intellectual Disability (ID), and epilepsy, to neurodegenerative diseases, such as Alzheimer's Disease (AD) and Parkinson's Disease (PD). NDRC has the potential to significantly impact the visibility of neurological disorders in Qatar and the region, not only by bringing new treatment options and hope to patients, but by also significantly accelerating the pace of therapeutic development using new technologies, such as genome sequencing, experimental disease modeling, biomarker discovery, gene therapy, and stem cell biology. This integrated approach combines basic and translational research and paves the way for the development of personalized medicine, which aligns well with the QNRS in improving the quality of healthcare in Qatar.

Objectives

- Applying epidemiological methods to evaluate the burden of ASD on Qatari families and residents
- Identifying novel genetic causes for neurodevelopmental diseases (ASD and ID)
- Deriving neurons from patient-specific stem cells to understand the molecular basis of ASD
- Revealing novel biomarkers for the early diagnosis, prognosis, and treatment of neurological disorders
- Elucidating the mechanisms of protein aggregation and deposition in AD and PD
- Investigating the mechanisms associated with synaptic plasticity and pathology
- Investigating the molecular mechanisms of immune abnormalities in ASD

National and International Collaborations and Partnerships

NDRC has a well-defined plan for collaboration, which is underway and continues to expand to include more national and international partnerships.

Collaborations within HBKU:

- Qatar Computing Research Institute (QCRI)
- Qatar Environment and Energy Research Institute (QEERI)
- College of Health and Life Sciences (CHLS)
- College of Science and Engineering (CSE)

National Research Collaborations:

- Shafallah Center
- Qatar Institute of Precision Medicine (QIPM)
- Qatar Biobank (QBB)
- Qatar Genome Programme (QGP)
- Sidra Medicine
- Weill Cornell Medicine-Qatar (WCM-Q)
- Hamad Medical Corporation (HMC)
- Child Development Center Rumailah (CDC)
- Qatar University (QU)

International Research Collaborations:

- Department of Neurology at Cleveland Clinic (USA),
- Rush University Medical College (USA)
- Sultan Qaboos University (Oman)
- AFFiRiS (Austria), Lundbeck (Denmark)
- Herantis (Finland)

Interdisciplinary Research Program – Autism

Identifying Potential Molecular Biomarkers for Autism Spectrum Disorder (ASD)

Scientific Coordinators: Dr. Lawrence Stanton and Dr. Sara Abdulla
Investigators: Dr. Omar El-Agnaf, Dr. Hyung Goo Kim, Dr. Fouad Al-Shaban, Dr. Yongsoo Park, Dr. Abeer Al-Shammari, and Dr. Abdelilah Arredouani (Diabetes Research Center); Dr. Julie Decock, and Dr. Nehad Alajez (Translational Cancer and Immunity Center)
Collaborators: Dr. Adolis Ali and Dr. Rihab Alozeib (Hamad Medical Corporation, Child Development Center Rumailah); Dr. Mohamed Tolefat (Shafallah Center); and Dr. Halima Bensmail (Qatar Computing Research Institute)

Summary
Autism Spectrum Disorder (ASD) is a complex, heterogeneous, and neurodevelopmental disorder characterized by core symptoms that include social interaction deficits and language difficulties. Our goal is to apply a blend of omic approaches to blood collected from a large and well-phenotyped cohort of ASD individuals to identify biomarkers that will help address our research objectives. Blood samples drawn will be used to prepare the matrices (DNA, plasma, serum, and PBMCs) required for the different objectives of the study. Next generation sequencing technologies, including whole genome sequencing, will be used to identify the gene variants associated with ASD and controls. RNA sequencing will be used to identify total RNA, as well as specific non-coding RNAs, as biomarkers to better understand the ASD heterogeneity. Proteomics, using the Olink platform and Sengenics Immunome Protein Array, will be used to screen blood samples to identify novel biomarkers (proteins and autoantibodies). Metabolomics profiling will also be used to screen blood samples to identify novel metabolomics signatures of ASD. From this study, we will identify and validate molecular biomarkers for early diagnosis of ASD. These markers will facilitate the development of clinical targets for early intervention to prevent, delay, or reduce the severity of the disorder.

Qatar Biomedical Research Institute (QBRI)

Innovation Activities at NDRC

The innovative research efforts led by the NDRC investigators have resulted in a number of inventions that are impacting patient care. Examples include

- Patent applications for antibodies directed against alpha-synucein linked to Parkinson's disease
- Agreements with biopharmaceuticals (AFFiRiS, Idorsia, Herantis, and Lundbeck) to use in-house technologies
- Registration of QABY Biotech as a trademark with QF
- Licensing agreements with Abcam and Euroimmun to distribute in-house developed reagents
- The first AI Arabic digital phenotyping for social communication (a diagnostic tool for Autism)

Training, Teaching, and Supervising Students

NDRC staff members participate in training students through its internship programs and in supervising MA and PhD students from CHLS, HBKU. NDRC faculty members are also regular lecturers at HBKU and QU in undergraduate and graduate courses including: Advance Biochemistry, Molecular and Cellular Biology of Neurodegenerative Diseases, Advanced Techniques in Biochemistry, Molecular Biology, and Stem Cell Biology.

Research Group

Dr. Omar El-Agnaf

Executive Director

Dr. Omar El-Agnaf's major research goals include developing novel diagnostic tools for neurodegenerative diseases characterized with abnormal protein aggregation and developing new therapeutic strategies for their treatment. Such diseases include Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB), Alzheimer's Disease (AD), and Multiple System Atrophy (MSA). Importantly, his studies seek to develop novel biomarker diagnostic approaches and new therapeutic tools that can prevent the neurotoxic processes, particularly the alpha-synucleinopathies that contribute to the pathogenesis of these common neurodegenerative diseases.

Current Projects

- Developing new diagnostic and therapeutic tools for Parkinson's disease and related disorders
- Identifying potential molecular biomarkers for ASD
- Revealing biomarkers for Type 2 Diabetes-associated complications such as dementia
- Integrative and translational COVID-19 research

Selected Publications

- El-Agnaf, O. M., Nioche, A., Dovero, S., Arotcarena, M.-L., Camus, S., Porras, G., … Bezard, E. (2020). Identification of Distinct Pathological Signatures Induced by Patient-derived α-synuclein Structures in Non-human Primates. Science Advances, 6(20), eaaz9165. https://doi.org/10.1101/825216
- Fayyad, M., El-Agnaf, O. M., Majbour, N. K., Vaikath, N. N., Ghanem, S. S., Sudhakaran, I. P., … Erskine, D. M. (2020). Investigating the Presence of Doubly Phosphorylated α-synuclein at Tyrosine 125 and Serine 129 in Idiopathic Lewy Body Diseases. Brain Pathology, 30(4), 831–843. https://doi.org/10.1111/bpa.12845
- Gupta, V., El-Agnaf, O. M., Hmila, I., Vaikath, N. N., Sudhakaran, I. P., Ghanem, S. S., … Salim, S. (2020). Fibrillar form of α-synuclein-specific scFv Antibody Inhibits α-synuclein Seeds Induced Aggregation and Toxicity. Scientific Reports, 10(1), 8137. https://doi.org/10.1038/s41598-020-65035-8
- Majbour, N. K., El-Agnaf, O. M., Hustad, E., Thomas, M. A., Vaikath, N. N., Elkum, N., … Aasly, J. O. (2020). CSF Total and Oligomeric α-Synuclein along with TNF-α as Risk Biomarkers for Parkinson's Disease: A Study in LRRK2 Mutation Carriers. Translational Neurodegeneration, 9(1), 15. https://doi.org/10.1186/s40035-020-00192-4
- Mesleh, A. G., Abdulla, S. A., & El-Agnaf, O. (2021). Paving the Way toward Personalized Medicine: Current Advances and Challenges in Multi-OMICS Approach in Autism Spectrum Disorder for Biomarkers Discovery and Patient Stratification. Journal of Personalized Medicine, 11(1), 41. https://doi.org/10.3390/jpm11010041
- Volc, D., El-Agnaf, O., Vaikath, N., Majbour, N., Lührs, P., Kutzelnigg, A., … Medori, R. (2020). Safety and Immunogenicity of the α-synuclein Active Immunotherapeutic PD01A in Patients with Parkinson's Disease: A Randomised, Single-blinded, Phase 1 Trial. The Lancet Neurology, 19(7), 591–600. https://doi.org/https://doi.org/10.1016/S1474-4422(20)30136-8

Research Group

Dr. Nasser H. Zawia

Research Director

Dr. Nasser H. Zawia's research deals with two aspects: the latent effects of environmental factors on the developing brain and the discovery of a novel class of mechanism-based drugs for the treatment of Alzheimer's Disease (AD). He is a leader in the epigenetics of AD, and his work has been featured by national and international media outlets such as ABC News, CBS, and CNN. His research group focuses on lead (Pb) as a model environmental hazard to which early life exposure reprograms gene expression impacting the neurodegenerative process in the aging brain. His group has provided the first basic science evidence of the role of epigenetic pathways and factors in mediating latent effects on disease due to developmental exposure. He has generated the first evidence for the developmental origins of Alzheimer's Disease. In addition to exploring environmental risk factors for neurodegenerative diseases, his lab has repurposed a novel class of mechanism-based drugs for the treatment of neurodegenerative diseases, including tolfenamic acid, which has been designated as an orphan drug by both the FDA and EMA for both progressive supranuclear palsy and frontal dementia and is pending final approval for clinical trials. He has published over 100 papers (Google Scholar: 135+ pubs, Citations approx. 5000, h-index 37, i10-index 72; ResearchGate: RG Score 40 (Publication reads about 14,000) and book chapters and has edited a book on molecular toxicology and a journal issue for Current Alzheimer's Research. His research has been supported by the National Institutes of Health (NIH), the National Science Foundation (NSF), and the Environmental Protection Agency (EPA). He has chaired NIH grant study sessions and served as a reviewer on numerous international journals and funding agencies, as well as on the editorial board of Journal of Neurotoxicology, Current Alzheimer's Research, and Journal of Alzheimer's Disease (JAD).

Current Projects

- Developing drugs for the treatment of neurodegenerative diseases
- Identifying biomarkers associated with neurodegenerative diseases
- The role of epigenetics in Alzheimer's Disease

Selected Publications

- Chang, J. K., Zawia, N. H., Subaiea, G. M., Lahouel, A., Masoud, A., Mushtaq, F., Deeb, R., Eid, A., Dash, M., Bihaqi, S. W., & Leso, A. (2018). Tolfenamic Acid: A Modifier of the Tau Protein and its Role in Cognition and Tauopathy. Current Alzheimer Research, 15(7), 655–663. https://doi.org/10.2174/1567205015666180119104036
- Eid, A., Bihaqi, S. W., Renehan, W. E., & Zawia, N. H. (2016). Developmental Lead Exposure and Lifespan Alterations in Epigenetic Regulators and their Correspondence to Biomarkers of Alzheimer's Disease. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 2(1), 123–131. https://doi.org/10.1016/j.dadm.2016.02.002
- Eid, A., Bihaqi, S. W., Zawia, N. H., Gaspar, J. M., Hart, R. P., & Hemme, C. (2018). Histone Acetylation Maps in Aged Mice Developmentally Exposed to Lead: Epigenetic Drift and Alzheimer-related Genes. Epigenomics, 10(5), 573–583. https://doi.org/10.2217/epi-2017-0143
- Hill, J., & Zawia, N. H. (2021). Fenamates as Potential Therapeutics for Neurodegenerative Disorders. Cells, 10(3), 702. https://doi.org/10.3390/cells10030702
- Subaiea, G. M., Ahmed, A. H., Adwan, L. I., & Zawia, N. H. (2014). Reduction of Amyloid-β Deposition and Attenuation of Memory Deficits by Tolfenamic Acid. Journal of Alzheimer's Disease, 43(2), 425–433. https://doi.org/10.3233/jad-132726
- Zawia, N. H. (2017). Unique aspects of the Epigenetic Code in the Brain. Epigenomics, 9(9), 1157–1159. https://doi.org/10.2217/epi-2017-0069
- Zawia, N. H., Bihaqi, S. W., Masoud, A., Chang, J. K., Lahouel, A., & Leso, A. (2019). Loss in Efficacy Measures of Tolfenamic Acid in a Tau Knock-out Model: Relevance to Alzheimer's Disease. Experimental Biology and Medicine, 244(13), 1062–1069. https://doi.org/10.1177/1535370219871249

Research Group

Dr. Lawrence Stanton

Director, Neurological Disorders Research Center

Dr. Lawrence Stanton's lab is generating Induced Pluripotent Stem Cells(iPSC) from patients with neurodevelopmental disorders. These patient-specific iPSCs are converted into neurons and organoids, thus providing an opportunity to understand the molecular pathology of diseases such as autism and establishing a foundation for the development of diagnostics and therapeutics. Dr. Stanton's lab also works closely with the Stem Cell Core lab at QBRI and in partnership with the Harvard Stem Cell Institute to develop cell-based therapies for treatment of diabetes. Dr. Stanton has extensive collaborations with academic neuroscientists from the USA, UK, and Singapore. In Qatar, he is a Co-PI on a funded research project (HBKU Thematic Grant Call 2020) with Dr. Bori Mifsud from the CHLS, HBKU.).

Current Projects

- Identifying the genes associated with ASD in the Qatari population
- Creating stem cell lines from autistic Qataris and their non-affected family members to study autism
- Analyzing the generation and functional characterization of autistic neurons and brain organoids

Selected Publications

- Stanton, L. W., Göke, J., Cukuroglu, E., Dranias, M. R., Van Dongen, A. M. J., & Lin, L. (2016). Molecular Features Underlying Neurodegeneration Identified through In-Vitro Modeling of Genetically Diverse Parkinson's Disease Patients. Cell Reports, 15(11), 2411–2426. https://doi.org/10.1016/j.celrep.2016.05.022
- Stanton, L. W., Jenjaroenpun, P., Bhinge, A., Angarica, V. E., Del Sol, A., Nookaew, I., … Wang, J. (2017). Single-cell Gene Expression Analysis Reveals Regulators of Distinct Cell Subpopulations among Developing Human Neurons. Genome Research, 27(11), 1783–1794. https://doi.org/10.1101/gr.223313.117
- Stanton, L. W., Namboori, S. C., Zhang, X., Van Dongen, A. M. J., & Bhinge, A. (2017). Genetic Correction of SOD1 Mutant iPSCs Reveals ERK and JNK Activated AP1 as a Driver of Neurodegeneration in Amyotrophic Lateral Sclerosis. Stem Cell Reports, 8(4), 856–869. https://doi.org/10.1016/j.stemcr.2017.02.019
- Stanton, L. W., Narayanan, G., Ma, S., Tam, W. L., Chai, J., & Sheila, M. (2019). Phenotypic and Molecular Features Underlying Neurodegeneration of Motor Neurons Derived from Spinal and Bulbar Muscular Atrophy Patients. Neurobiology of Disease, 124, 1–13. https://doi.org/10.1016/j.nbd.2018.10.019
- Stanton, L. W., Ng, S.-Y., Brand, H., Wang, H., Plummer, L., Best, L., … Crowley, W. F. (2020). A Balanced Translocation in Kallmann Syndrome Implicates a Long Noncoding RNA, RMST, as a GnRH Neuronal Regulator. The Journal of Clinical Endocrinology & Metabolism, 105(3), e231–e244. https://doi.org/10.1210/clinem/dgz011

Research Group

Dr. Fouad Al Shaban

Senior Scientist

Dr. Fouad Al Shaban focuses on applying epidemiological methods to evaluate the burden of ASD on Qatari families and other families residing in Qatar through studying the prevalence of ASD and the contributing risk factors associated with the disorder. The group is also working to establish the first ASD registry in Qatar and working to develop innovative early diagnostic and screening tools using eye tracking technology in collaboration with the Cleveland Clinic. In addition, the group is working on establishing the first Arabic digital phenotyping for social communication behaviors as a diagnostic tool for Autism, using machine learning and artificial intelligence in collaboration with Argus Cognitive Inc., USA. The group is committed to establishing a regional center for autism research that will contribute to improving early diagnosis, intervention, and treatment of autism spectrum disorders. Dr. Al Shaban has a strategic collaboration with the Autism Center and the Department of Neurology at the Cleveland Clinic, supporting his ongoing autism prevalence study and a new study on using an eye-tracking system for the early diagnosis of autism, which is a cutting-edge technology that enables diagnosing autism as early as six months of age. He also collaborates with Argus Cognitive Inc. in association with Rush University in Chicago to develop a digital diagnostic technique for ASD using machine learning and artificial intelligence.

Current Projects

- Developing innovative tools for early screening and diagnosis of ASD in Qatar
- Studying the impact of COVID-19 on ASD in Qatar
- Researching adults with ASD in Qatar

Selected Publications

- Alshaban, F. A. (2020). Qatar and Autism. Encyclopedia of Autism Spectrum Disorders, 1–7. https://doi.org/10.1007/978-1-4614-6435-8_102230-2
- Alshaban, F., Aldosari, M., Al-Shammari, H., El-Hag, S., Ghazal, I., Tolefat, M., … Fombonne, E. (2019). Prevalence and Correlates of Autism Spectrum Disorder in Qatar: A National Study. Journal of Child Psychology and Psychiatry, 60(12), 1254–1268. https://doi.org/10.1111/jcpp.13066
- Alshaban, F., Aldosari, M., El Sayed, Z., Tolefat, M., El Hag, S., Al Shammari, H., … Fombonne, E. (2017). Autism Spectrum Disorder in Qatar: Profiles and Correlates of a Large Clinical Sample. Autism & Developmental Language Impairments, 2, 17. https://doi.org/10.1177/2396941517699215
- Alshaban, F., Fombonne, E., Aldhalaan, H., Ouda, M., El Hag, S., Alshammari, H., … Aldosari, M. (2019). Validation of the Arabic Version of the Social Communication Questionnaire. Autism, 23(7), 1655–1662. https://doi.org/10.1177/1362361318816065
- Kilshaw, S., Al Raisi, T., & Alshaban, F. (2015). Arranging Marriage; Negotiating Risk: Genetics and Society in Qatar. Anthropology & Medicine, 22(2), 98–113. https://doi.org/10.1080/13648470.2014.976542

Research Group

Dr. Hyung Goo Kim

Senior Scientist

Dr. Hyung Goo Kim is specialized in positional cloning approaches. Dr. Kim's team focuses on patients with balanced and unbalanced chromosomal anomalies to zero in on the genomic locations of disease genes by mapping the molecular breakpoints. This approach has resulted in identifying two new autism genes, NRXN1 and PHF21A. Apart from whole exome/genome sequencing, the research team also employs homozygosity mapping in consanguineous families to identify autism genes. This project is based on the view that a de-novo balanced translocation disrupting a single gene, a CNV encompassing deleted/duplicated gene(s), or the presence of a de-novo variant within the open reading frame of a candidate gene found by WES/WGS, does not by itself represent compelling evidence to directly pinpoint a causative autism gene. The team combines the WES approach with the positional cloning of chromosomal rearrangements. This two-tiered approach is an extremely powerful and cost-effective means to disease gene identification. The discovery of autism genes will help elucidate the underlying mechanism and molecular etiology of this disorder to advance molecular diagnosis, genetic counseling, and therapeutic interventions. Dr. Kim is engaged in extensive on-going collaborative efforts with Harvard Medical School, Max-Planck-Institute for Molecular Genetics, University of Michigan, Baylor College of Medicine, Hamad Medical Corporation, Augusta University, and Chungnam National University to identify the genetic etiologies of neurodevelopmental disorders and their underlying molecular mechanisms.

Current Projects

- Identifying autism genes and their underlying mechanisms in Qatar
- Discovering disease genes in autosomal dominant syndromic and non-syndromic ASD/intellectual disability
- Studying loss-of-function of PTPRD in syndromic intellectual disability and autism in 9p23 microdeletion syndrome
- Developing a new locus for intellectual disability and Kallmann syndrome at 12p11

Selected Publications

- Kim, H.-G., Kim, H.-T., Leach, N. T., Lan, F., Ullmann, R., Silahtaroglu, A., … Gusella, J. F. (2012). Translocations Disrupting PHF21A in the Potocki-Shaffer-Syndrome Region Are Associated with Intellectual Disability and Craniofacial Anomalies. The American Journal of Human Genetics, 91(1), 56–72. https://doi.org/10.1016/j.ajhg.2012.05.005
- Kim, H.-G., Kishikawa, S., Higgins, A. W., Seong, I.-S., Donovan, D. J., Shen, Y., … Gusella, J. F. (2008). Disruption of Neurexin 1 Associated with Autism Spectrum Disorder. The American Journal of Human Genetics, 82(1), 199–207. https://doi.org/10.1016/j.ajhg.2007.09.011
- Kim, H.-G., Rosenfeld, J. A., Scott, D. A., Bénédicte, G., Labonne, J. D., Brown, J., … Kim, C.-H. (2019). Disruption of PHF21A Causes Syndromic Intellectual Disability with Craniofacial Anomalies, Epilepsy, Hypotonia, and Neurobehavioral Problems Including Autism. Molecular Autism, 10(1), 35. https://doi.org/10.1186/s13229-019-0286-0
- Labonne, J. D., Driessen, T. M., Harris, M. E., Kong, I.-K., Brakta, S., Theisen, J., … Kim, H.-G. (2020). Comparative Genomic Mapping Implicates LRRK2 for Intellectual Disability and Autism at 12q12, and HDHD1, as Well as PNPLA4, for X-Linked Intellectual Disability at Xp22.31. Journal of Clinical Medicine, 9(1), 274. https://doi.org/10.3390/jcm9010274
- Talkowski, M. E., Rosenfeld, J. A., Blumenthal, I., Pillalamarri, V., Chiang, C., Kim, H.-G., … Gusella, J. F. (2012). Sequencing Chromosomal Abnormalities Reveals Neurodevelopmental Loci that Confer Risk across Diagnostic Boundaries. Cell, 149(3), 525–537. https://doi.org/10.1016/j.cell.2012.03.028

Research Group

Dr. Yongsoo Park

Scientist

Dr. Yongsoo Park's research team at QBRI focuses on the development of exosome biomarkers for ASD, Alzheimer's Disease, and Parkinson's disease. Exosome biomarkers can facilitate the development of clinical targets for early intervention to prevent, delay, or reduce the severity of ASD, AD, and PD. Dr. Park's research team is also working on a functional assay to validate patient-specific hiPSC-derived neurons using calcium imaging, whole-cell patch clamping technique, and Micro-Electrode Array (MEA) in order to model neurodevelopmental and neurodegenerative diseases. Dr. Park has established international collaborations with neuroscientists from Max-Planck-Institute for Biophysical Chemistry, Yale University, and Seoul National University for synaptic plasticity and vesicle fusion. He has extensive national collaborations with Dr. Jean-Charles Grivel at Sidra Medicine for exosome biomarkers and Dr. Khaled Machaca at Weill Cornell Medicine-Qatar for calcium signaling in neurological disease models.

- Exosome biomarkers for ASD, AD, and PD
- Electrophysiological studies on neuronal differentiation of human induced pluripotent stem cells (hiPSC)
- Molecular mechanisms of neuronal degeneration in Parkinson's disease and Alzheimer's Disease

Selected Publications

- Park, Y. (2017). MicroRNA Exocytosis by Vesicle Fusion in Neuroendocrine Cells. Frontiers in Endocrinology, 8, 355. https://doi.org/10.3389/fendo.2017.00355
- Park, Y., Hernandez, J. M., van den Bogaart, G., Ahmed, S., Holt, M., Riedel, D., & Jahn, R. (2012). Controlling Synaptotagmin Activity by Electrostatic Screening. Nature Structural & Molecular Biology, 19(10), 991–997. https://doi.org/10.1038/nsmb.2375
- Park, Y., Preobraschenski, J., Ganzella, M., Jahn, R., & Birinci, Y. (2020). Isolation of Large Dense-core Vesicles from Bovine Adrenal Medulla for Functional Studies. Scientific Reports, 10(1), 7540. https://doi.org/10.1038/s41598-020-64486-3
- Park, Y., Seo, J. B., Fraind, A., Pérez-Lara, A., Yavuz, H., Han, K., … Jahn, R. (2015). Synaptotagmin-1 Binds to PIP2-containing Membrane but not to SNAREs at Physiological Ionic Strength. Nature Structural & Molecular Biology, 22(10), 815–823. https://doi.org/10.1038/nsmb.3097
- Park, Y., Yildiz, R., Eren, E., Karakülah, G., Ünver, T., GENÇ, Ş., & Gümürdü, A. (2017). MicroRNA Exocytosis by Large Dense-core Vesicle Fusion. Scientific Reports, 7(1), 45661. https://doi.org/10.1038/srep45661

Research Group

Dr. Sara Abdulla

Research Fellow

Dr. Sara Abdulla's research lab conducts experiments to elucidate the impact of total and non-coding RNA on the fundamental and developmental networks of the brain during pregnancy and early childhood and its association to ASD. Furthermore, Dr. Abdulla aims to identify biomarkers in children that will improve our understanding of ASD severity as well as contribute to the advancement of current clinical diagnostic methods of identifying ASD, navigating it away from a more subjective approach to a more objective one. Dr. Abdulla is utilizing a multidisciplinary approach to identify maternal, prenatal, and fetal components that influence and alter a normal neurodevelopmental trajectory, ultimately contributing to the emergence of ASD. This further opens up new pathways of discovery for very early, predictive, and diagnostic biomarkers of ASD. Dr. Abdulla's research lab utilizes platforms that incorporate proteomics, genomics, transcriptomics, calcium imagining, electrophysiology, behavioral neuroscience, and the derivation of cellular models including cerebral organoids and neuronal cell cultures to address her research questions. Dr. Abdulla has established extensive ongoing collaborative initiatives with Hamad Medical Corporation's Child Development Center at Rumailah Hospital, the Primary Health Care Clinics, Qatar Foundation schools, and the Ministry of Education to facilitate the recruitment of a well-phenotyped ASD cohort for QBRI's IDRP project entitled 'Identifying Potential Molecular Biomarker for ASD', as well as with Qatar Biobank to identify prenatal influences that may contribute to the outcome of ASD.

- Analyzing transcriptomics to identify biomarkers for early diagnosis of ASD and its severity
- Studying transcriptomics and proteomics within exosomes as biomarkers for ASD
- Generating patient derived cerebral organoids and neuronal cultures of ASD
- Establishing a birth cohort to identify biological prenatal components that influence the outcome of ASD
- Understanding the role of transcription factors in neuronal cell differentiation and organoid developmen

Selected Publications

- Ardah, M. T., Ghanem, S. S., Abdulla, S. A., Lv, G., Emara, M. M., Paleologou, K. E., … El-Agnaf, O. M. (2020). Inhibition of Alpha-synuclein Seeded Fibril Formation and Toxicity by Herbal Medicinal Extracts. BMC Complementary Medicine and Therapies, 20(73), 1–21. https://doi.org/10.1186/s12906-020-2849-1
- Gupta, V., Abdulla, S., Hmila, I., Vaikath, N. N., Sudhakaran, I. P., Ghanem, S. S., … El-Agnaf, O. M. (2020). Fibrillar Form of α-synuclein-specific scFv Antibody Inhibits α-synuclein Seeds Induced Aggregation and Toxicity. Scientific Reports, 10(1), 1–14. https://doi.org/10.1038/s41598-020-65035-8
- Mesleh, A. G., Abdulla, S. A., & El-Agnaf, O. (2021). Paving the Way toward Personalized Medicine: Current Advances and Challenges in Multi-OMICS Approach in Autism Spectrum Disorder for Biomarkers Discovery and Patient Stratification. Journal of Personalized Medicine, 11(1), 41. https://doi.org/10.3390/jpm11010041
- Salloum-Asfar, S., Satheesh, N. J., & Abdulla, S. A. (2019). Circulating miRNAs, Small but Promising Biomarkers for Autism Spectrum Disorder. Frontiers in Molecular Neuroscience, 12(253), 1–10. https://doi.org/10.3389/fnmol.2019.00253
- Swaidan, N. T., Abdulla, S., Palangi, F., Errafii, K., Soliman, N. H., Aboughalia, A. T., … Emara, M. M. (2020). Identification of Potential Transcription Factors That Enhance Human iPSC Generation. Scientific Reports, 10(1). https://doi.org/10.1038/s41598-020-78932-9

Research Group

Dr. Abeer Al-Shammari

Research Fellow

Dr. Abeer Al-Shammari is interested in the crosstalk between the nervous system and the peripheral immune system in autism. Dr. Al-Shammari's lab uses a multidisciplinary approach to study autism, in which human participants with autism and their matching controls are recruited, and data are collected and integrated from the fields of psychology, medical history, immunology, genomics, and neurosciences. Some of the research techniques used in the lab for analyzing human blood samples include flow cytometry, immunohistochemistry, proteomics, and transcriptomics. This is in addition to functional studies in which patient-specific induced pluripotent stem cells (iPSC) are generated and converted into brain-specific cells to further understand the disease mechanisms in cell culture models. The ultimate goal of Dr. Al-Shammari's lab is to understand the underlying cause of immune dysfunction in autism and to confirm their functional relevance to the disorder as a future target for autism therapy. Dr. Al Shammari has established strong collaborations with national organizations such as the Child Development Center at Rumailah Hospital (HMC) for an ongoing research project involving children with autism. Moreover, she is collaborating with the Primary Health Care Corporation for the recruitment of matching controls. Dr. Al-Shammari has been awarded the Early Career Researcher Grant (ECRA) from QNRF to achieve her research objectives.

Current Projects

- Studying cell-specific immune phenotypes in autism and its association with clinical severity
- Investigating the underlying molecular mechanisms and network interactions for immune abnormalities
- Relevance of the peripheral immune alterations in autism to the phenotype and function of brain-related cells in cell culture models

Selected Publications

- Al-Shammari, A. R., Bhardwaj, S. K., Musaelyan, K., Srivastava, L. K., & Szele, F. G. (2018). Schizophrenia-Related Dysbindin-1 Gene is Required for Innate Immune Response and Homeostasis in the Developing Subventricular Zone. *Npj Schizophrenia*, 4(1). https://doi.org/10.1038/s41537-018-0057-5
- Bardella, C., Al-Shammari, A. R., Soares, L., Tomlinson, I., O'Neill, E., & Szele, F. G. (2018). The Role of Inflammation in Subventricular Zone Cancer. *Progress in Neurobiology*, 170, 37–52. https://doi.org/10.1016/j.pneurobio.2018.04.007

Core Facilities

Qatar Biomedical Research Institute Core Facilities

QBRI's core facilities provide a wide spectrum of innovative cutting-edge services and equipment. They are maintained by highly skilled and trained scientists and staff. QBRI's core facilities are located in the HBKU Research and Development Complex (RDC) and are closely integrated with QBRI's research teams in the same building. QBRI's core facilities aim to fulfill the organization's mission through three major operational lines (Fig.1).

These core facilities support QBRI's main biomedical research areas, such as diabetes, cancer, immunity, and neurological disorders. QBRI's core facilities are the backbone for fulfilling HBKU's leading role in training, education, and knowledge transfer for students and the scientific community in Qatar and beyond. QBRI's core facilities are actively embedded in a growing national and international collaborative environment, including academic, clinical, and industry partners.

To this aim, the infrastructure and services of QBRI's core facilities include collaborations with 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's role as a major hub for education, innovation, research, and healthcare development in Qatar, the Middle East, and beyond.

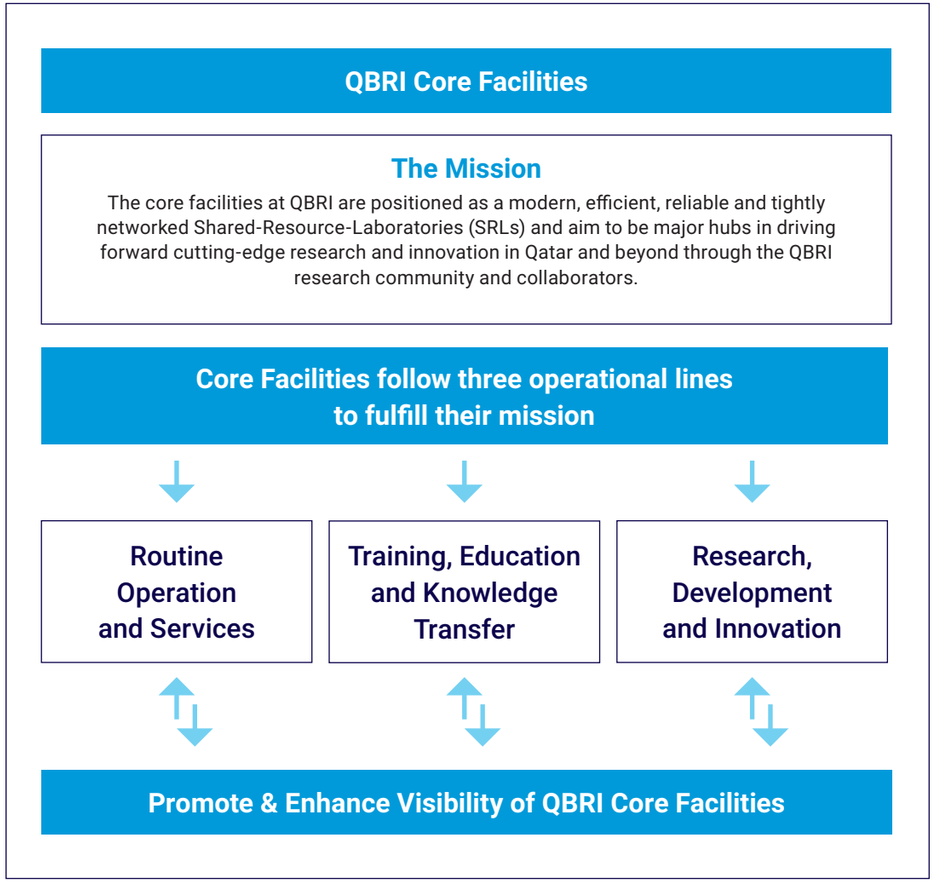


Fig. 1

A summary of equipment and services available at QBRI's core facilities.

01 IMAGING AND FLOW CYTOMETRY CORE

ADVANCED IMAGING AND HISTOPATHOLOGY

Major Instruments:
- Multiphoton
- Confocal
- Super Resolution
- Wide Field Fluorescence
- Microscopes

Major Services:
- Image Acquisition
- Histology
- Experimental Design
- Data Management
- Training

FLOW CYTOMETRY

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

02 GENOMICS AND GENOME TECHNOLOGY CORE

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
- Genotyping Studies

03 PROTEOMICS CORE

Major Instruments:
- BioMark HD Reader and BioMark IFC-HX Controller, Fluidigm
- SureScan Microarray Scanner G4900D, Agilent
- HD-X Analyzer, Quanterix

Major Services:
- Olink Technology
- Sengenics Technology
- Simoa Technology
- Consultation and Study Design
- Data Analysis
- Data Management
- Training

04 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

05 STRUCTURAL BIOLOGY CORE

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

06 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

07 CLINICAL RESEARCH CORE

Major Services:
- Storing of Biospecimens in Secure Freezers
- Dedication of Research Assistant for Short and Long Term Projects
- Data Storage for Future Research

01 IMAGING AND FLOW CYTOMETRY CORE

Imaging

The mission of the QBRI Imaging Core is to provide researchers with efficient, reliable, and innovative imaging solutions at the highest standards of instrumentation, accuracy, quality control, and professional expertise. This is achieved by providing access to state-of-the-art equipment and the expertise of highly skilled professionals in microscopy and imaging. The core is equipped with the most advanced and automated digital microscopy and live-cell imaging instrumentation. These technologies allow investigators to conduct a wide range of imaging research experiments that help answer important biomedical questions related to their fields of study. The core also provides training and easy access to researchers, as well as services that range from routine microscopy to cutting-edge live-animal multi-photon microscopy. The core's expertise and services provide support in the planning and evaluation of histopathology experiments, tissue processing and sectioning, cryopreservation, histological staining methods, and laser caption microdissection microscopy.

The following resources and services are offered:

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

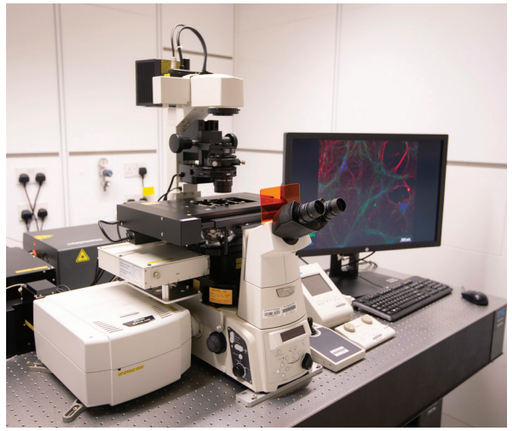
- State-of-the-art microscopes for a wide variety of imaging research experiments
- Cutting-edge bright-field, dark-field and fluorescence imaging
- Standard, confocal and multi-photon microscopy applications
- Automated digital microscopy
- Advanced high-end live-cell imaging
- Image processing and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

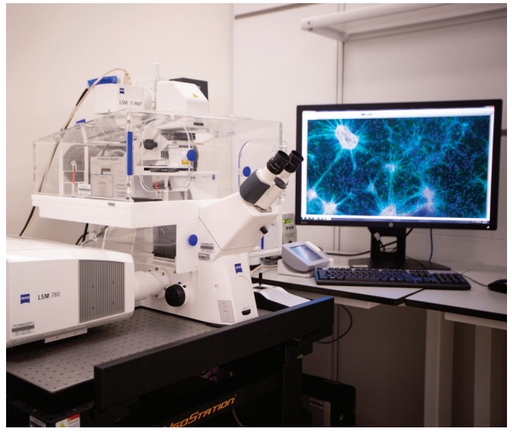
Histopathology Equipment

- 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
- Leica Biosystems ST5020 Multistainer
- CryoViz robotic sectioning and imaging system
- Dako Omnis automated staining System GI100
- Dako Coverslipper

Services – Histopathology

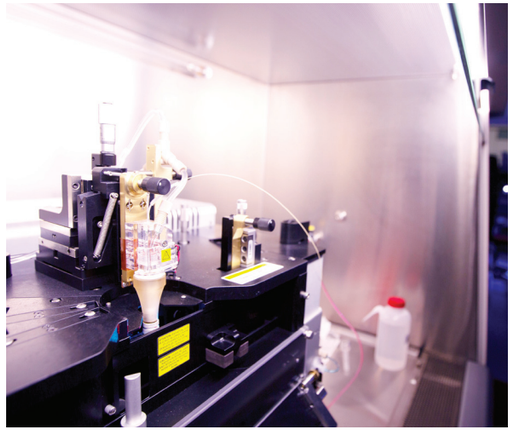
- Tissue processing, embedding and sectioning
- Cryopreservation and cryosectioning (Leica Cryostat and Microtome systems)
- Different histological staining methods, such as H&E and special stains
- Immunohistochemical and immunofluorescence techniques
- Laser Capture Microdissection microscopy (Leica)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





Flow Cytometry

The mission of the QBRI Flow Cytometry Core is to offer researchers efficient, reliable, and innovative flow cytometry and cell sorting solutions at the highest standards of instrumentation, quality control, biosafety, and productivity. This is achieved by providing access to state-of-the-art instruments and professional flow cytometry and cell sorting services supported by highly motivated staff with extensive skills and expertise in flow cytometry. In addition, the Flow Cytometry Core provides support and guidance regarding flow cytometry education, operation of instruments, software workflows, and biosafety to fulfil its mission to create a productive, collaborative, and highly innovative environment for research and development.



The following resources and services are currently offered:

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

02 GENOMICS AND GENOME TECHNOLOGY CORE

The Genomics Core at QBRI actively supports research by providing advanced research technologies and services to the research community at HBKU and QBRI, and their collaborators from academia and the industry. The Genomics Core facility houses various state-of-the-art technological platforms to sequence nucleic acids by Next-Generation Sequencing (NGS) as well as capillary sequencing methods and different array platforms. 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.

The following resources and services are offered:

Next Generation Sequencing

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

Genetic Analyzers

- ABI 3500xL Dx (24-capillary electrophoresis)
- ABI 3730XL (96-capillary electrophoresis)

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

Single Cell Genomics

- 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)

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

03 PROTEOMICS CORE

The Proteomics Core provides services and supports investigators at QBRI, HBKU colleges, and other institutions in Qatar and abroad with the aim of addressing and solving protein-based challenges related to their research projects. This core operates a cutting-edge technological platform, offering users access to high throughput, affinity-based proteomics assays such as Olink, Sengenics, and Simoa. In addition to analytical capabilities, the core also offers additional services, including technological consultation, study design, custom panel selection, experimental design optimization, and biostatistical analysis.

Equipment

- Fluidigm Biomark HD: Used for proximity extension assays (known as Olink technology)
- SureScan detection system: Used for Sengenics proteomics technology
- HD-X analyzer, Quanterix (measurements of proteins at the femtomolar scale)

The following resources and services are offered:

OLINK technology: Protein Biomarker Discovery

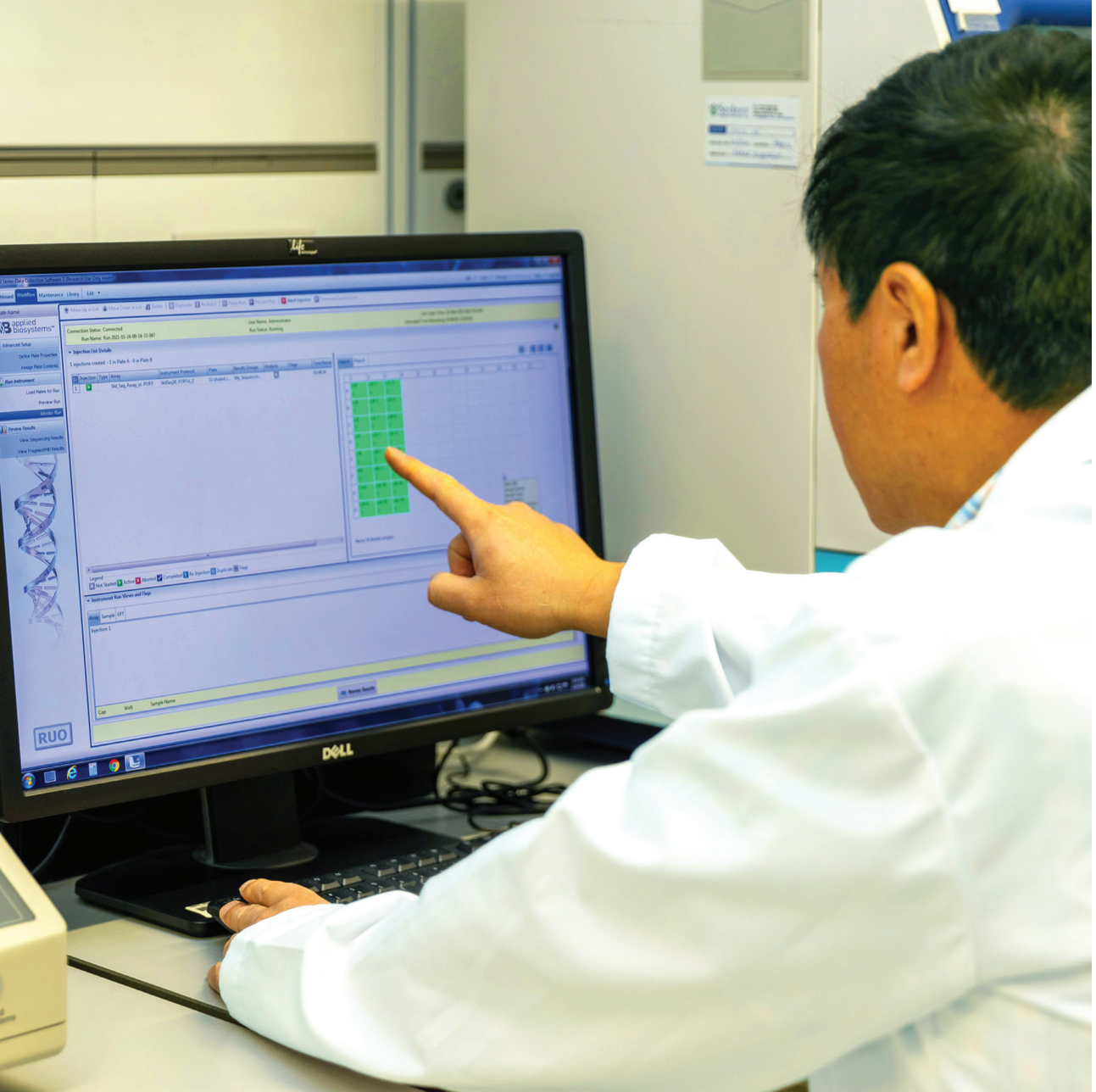
Olink technology provides high-multiplex immunoassays using a Proximity Extension Assay (PEA) technology capable of measuring 92 biomarker proteins across 88 samples simultaneously using only 1 µl of plasma, serum, saliva, or CSF. Olink services offer 13 different panels, targeting a total of 1200 established and/or exploratory human biomarkers panels: cardio-metabolomic, cardiovascular, metabolism, inflammation, immune response, neurology and neuro-exploratory, oncology, organ damage, and cell regulation/development. Each panel is focused on a disease or key biological process.

Sengenics technology: Auto-antibody Biomarker Discovery

Sengenics technology is based on detecting and identifying of novel auto-antibodies in plasma or serum using KREX protein array technology. Protein arrays made with the KREX technology are characterized by correct folded proteins that ensure high specificity, reproductivity, and sensitivity. Sengenics services offer three different panels and also the possibility of making custom panels. The main panel that is used in the core laboratory is the Immunome Discovery Array, which contains up to 1600 human proteins including kinases, signaling molecules, cytokines, interleukins, chemokines, and cancer antigens. Autoantibody binding is detected and quantified using a Cy3-labelled anti-human IgG and Cy5-labelled anti-human IgM polyclonal antibodies. Signals are recorded using a microarray scanner at 10µm resolution. The output from the microarray scanner (a raw .tiff image file) is extracted using GenePix Pro 7 software and analyzed using the Sengenics data processing pipeline.

SIMOA Technology

The HD-X Analyzer from Quanterix is a fully automated digital immunoassay instrument capable of analyzing samples using the proprietary single-molecule array (Simoa) technology and delivering ultra-sensitive measurements of the targeted proteins over a wide dynamic range and with low CV's. Simoa detects thousands of single protein molecules simultaneously on a variety of different matrices (Serum, plasma, SCF, urine, and cell extract) at femtomolar (fg/ml) concentrations, offering a 1000-fold improvement in sensitivity.



04 BIOINFORMATICS CAPABILITIES

The Bioinformatics Capabilities provides support for data analysis and interpretation, as well as software and pipelines for analyzing next-generation data sets from DNA and RNA based experiments. 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. The QBRI HPC enables the rapid computational analysis of large data sets across a wide range of informatics tasks. In line with the computational needs of QBRI, 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 protein analysis.

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 storages
- 10 Individual 20-core servers with 128GB of memory to carry out pipeline development and testing
- 400TB of Network Storage

The following resources and services are offered:

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

05 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 equipment. The needs of protein studies are quite diverse, including studies of single proteins, protein complexes, and interactions among 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 CPAD detector. The unit also has a cryostream with an air compressor. This equipment facilitates the 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 collaborative initiatives with various stakeholders are ongoing, including with QBRI's diabetes and neurological disorders teams.

The following resources and services are offered:

Equipment

- Shaker/Incubator (Innova 44R)
- Fermenter (BioFlow 115)
- Ultracentrifuge (Beckman)
- 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

- Mosquito LCP for crystallization screening (TTP Labtech)
- D8 VENTURE X-ray Diffractometer for 3-D structure determination (Bruker)
- Circular Dichroism (CD Spectrometer)
- Isothermal Titration Calorimetry (ITC) from GE Healthcare Lifesciences

06 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 expertise, iPSCs derivation, directed differentiations, and genome engineering services to researchers. The facility is 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 and diabetes research teams, as well as with the Harvard Stem Cell Institute for generating and engineering iPSCs and their directed differentiation into cortical neurons, brain organoids, and pancreatic beta cells.

The following resources and services are offered:

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
- Gene knockout/in via CRISPR/Cas9, TALENs, Recombinases, and transposases
- 3D adoption and directed differentiation of ESCs and iPSCs in a small-scale bioreactor setting
- Directed differentiation of ESCs and iPSCs into cortical neurons, organoids, and pancreatic beta cells
- Training and thesis supervision for students using ESCs and iPSCs in research projects

07 CLINICAL RESEARCH CORE

In line with QBRI's vision to improve and transform healthcare through innovation in the 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 clinical and translational research activities at QBRI.

The following resources and services are offered:

Equipment

- BL2 biosafety cabinets
- Freezers (-80, -150 and -20°C) with backup freezers
- Fridges (4°C)
- Brooks BioStoreTM IIIv -80°C automated storage system
- Refrigerated centrifuges
- Labeling system (BRADY)
- Barcode reading system

Services and Resources

- Standard operating procedures for collecting different biospecimens: blood, saliva, and urine, etc.
- Processing biospecimens
- Labeling biospecimens
- Storing biospecimens in secure freezers
- Training research assistants
- Research assistants for short and long-term projects
- Consumables for biospecimens processing and storage
- Streamlining data and/or biospecimens transfer
- Data storage for future research

Qatar Biomedical Research Institute

qbri.hbku.edu.qa
qbriinfo@hbku.edu.qa
+974 4454 8143

P.O. Box: 34110
Doha – Qatar

QBRI
Qatar Biomedical Research Institute
Qatar Biomedical Research Institute