ANNUAL REPORT

HMC – PRECISION MEDICINE
ANNUAL REPORT 2022 – 2021

مؤسسة حمد الطبية
Hamad Medical Corporation
HEALTH • EDUCATION • RESEARCH صحة • تعليم • بحوث

ANNUAL REPORT

HMC – PRECISION MEDICINE
ANNUAL REPORT 2022 – 2021

مؤسسة حمد الطبية
Hamad Medical Corporation
HEALTH • EDUCATION • RESEARCH صحة • تعليم • بحوث
حمد Hamad

Table Of Contents

Dr. Hanan Al Kuwari

Vice-Chair of the Board of Qatar Precision Medicine Institute

Acknowledgment

First and foremost, I would like to acknowledge H.H Shiekha Moza Bint Nasser for bringing the initiative to Qatar and for providing the necessary guidance required to roll out this initiative across Qatar. Secondly, I would like to acknowledge our leadership from Qatar Foundation and QPMI specially Dr. Asma Al Thani, Dr. Richard Kennedy and Dr. David Brown for all their support. A very special thanks to H.E Dr. Hanan Al Kuwari for her leadership support. I would also like to acknowledge our collaborators Qatar Biobank and Qatar Genome for their support.

In addition to this I would like to thank and acknowledge all the Precision Medicine Committee members for their contributions and efforts in the implementation of this great initiative across HMC. Specially the Assistant Chairman of Precision Medicine Committee-Dr. Salha Bujassoum for her dedication and continuous Support.

Lastly everyone who has contributed to the success of this initiative internal or external to HMC. Precision Medicine Initiative is very close to my heart because it takes the clinical and patient care to the next level of advances in medicine

Dr. Abdulla Al Ansari

Chief Medical Officer

Chairperson of HMC Precision Medicine Committee

Hamad Medical Corporation (HMC)

Contribution

HMC PRECISION MEDICINE COMMITTEE MEMBERS

- Dr Abdulla Al Ansari, CMO & Chairperson of HMC PM Committee
- Dr Salha Bujassoum, Chairperson of the Department of Medical Oncology & Assistant chair of HMC PM Committee
- Prof. Michael Frenneaux, Chief of Scientific, Academic and Faculty Affairs
- Dr. Einas Al Kuwari, Chairperson of DLMP
- Dr Ramin Badii, Clinical Scientist and Head of Molecular Genetics Laboratory
- Dr Jassim Al Suwaidi, Senior Consultant, Heart Hospital
- Dr Moza Sulaiman H Al Hail, Executive Director, Pharmacy
- Dr Reem Jawad A A Al Sulaiman, Deputy Chair of Medical Genetics
- Dr Ali R Barah, Senior Consultant, Radiology
- Dr Mahir Petkar, Senior Consultant, Anatomical Pathology
- Dr Shaban Fathy, Clinical Pharmacist, Pharmacy
- Dr Neelam Zafar, Ass Executive Director, CMO Office
- Mrs. Ayah Ziyada, Precision Medicine Coordinator

Executive Summary

Precision Medicine (PM) vision was introduced to Qatar by H.H Sheikha Moza Bint Nasser. H.H Sheikha Moza Bint Nasser initiated the genomic work of collecting and sequencing genomes though Qatar Biobank (QBB) and Qatar Genome project (QGP) in 2013. Qatar Precision Medicine institute (QPMI) was developed by H.H Sheikha Moza Bint Nasser in 2018. QPMI is now the power base of Precision Medicine within Qatar. It is working with all facilities across Qatar to lay down a strong Precision Medicine infrastructure so that it is embedded in the healthcare system like regular routine.

QPMI has developed a national level clinical council which leading the clinical implementation work under the guidance and direction of QPMI across Qatar. This national council is co-chaired by

Dr. Abdulla Al Ansari, Chief Medical Officer, Hamad Medical Corporation.

To support the QPMI initiative and to promote the Precision Medicine work in Hamad Medical Corporation (HMC) Dr. Abdulla Al Ansari developed HMC PM Committee. This committee is chaired by Dr. Abdulla Al Ansari and has representation from all key clinical areas across HMC. Most of these departments have been involved in Precision Medicine activities in the past and currently as well. Dr. Abdulla vision is to acknowledge all the past work that has been accomplished by these clinical areas as well as organize and formalize all the Precision Medicine work in HMC. The committee was established in September 2019 and since then has been creating history in Precision Medicine at HMC. The most notable accomplishments include 1st HMC Virtual Precision Medicine Conference and becoming an organizational member of US based organization Precision Medicine Coalition & UK based Genomic England.

"Applying precision medicine to clinical practice requires a deep understanding of genomic and environmental data. Therefore, developing relevant expertise in the clinical workforce will be key to the clinical implementation of Precision Medicine" .

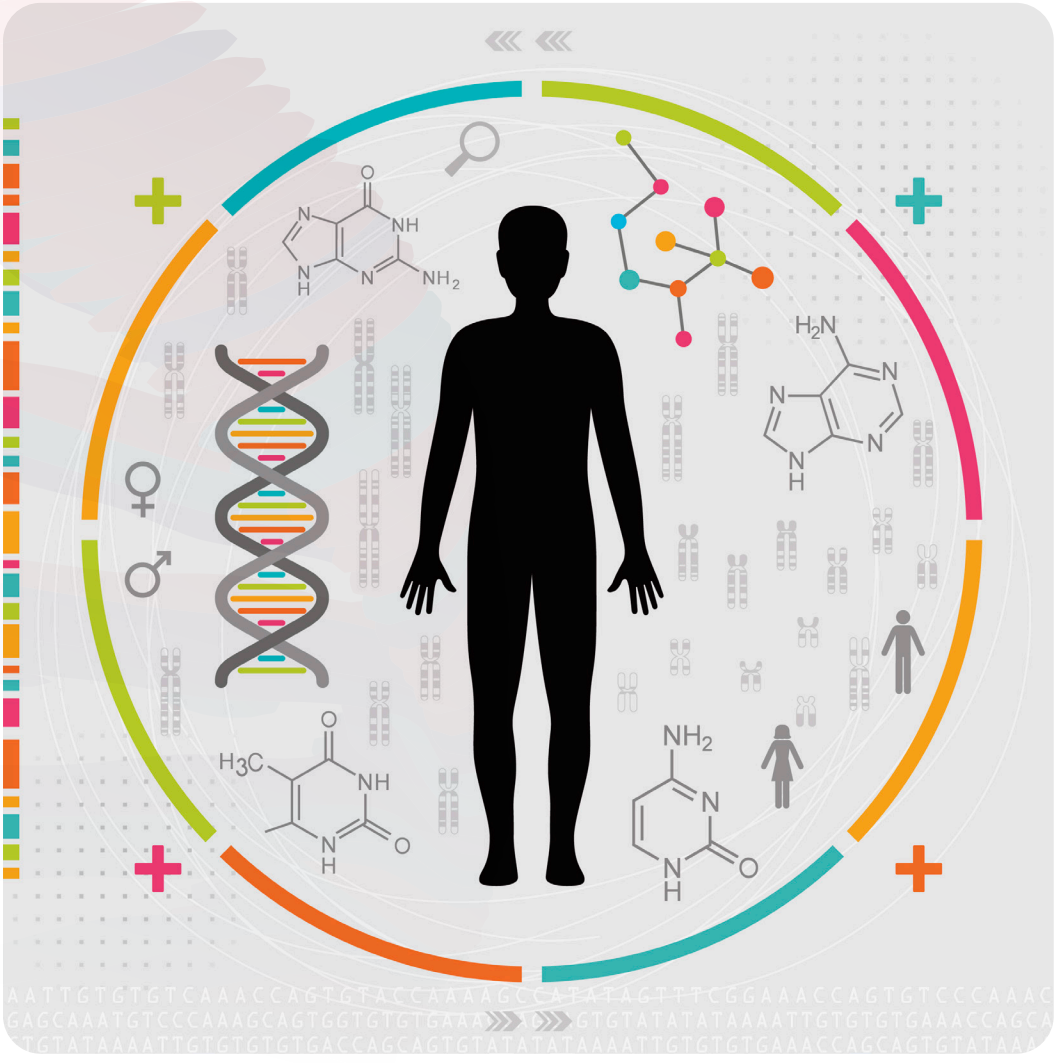
Dr. Abdulla Al Ansari, CMO"

Introduction

Precision Medicine, also called personalized or individualized medicine, is a rapidly evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms, often genetic, that cause disease or influence a patient's response to certain treatments. By combining molecular data with an individual's medical history, environment and lifestyle, health care providers can develop targeted prevention and treatment plans. Personalized health care has the capacity to detect the onset of disease at its earliest stages, pre-empt the progression of disease, and, at the same time, increase the efficiency of the health care system by targeting treatments to only those patients who will benefit.

HMC defines Precision Medicine as:

"Precision Medicine – is the tailoring of treatment or preventive measures to individuals rather than a one-size fits all approach. This can be achieved by utilizing data derived from genomics, proteomics, metabolomics, accurate phenotyping (e.g.: by advanced imaging techniques or underlying physiology), as well as familial, lifestyle and environmental data."



Background

Because our increasing understanding of human heterogeneity demands it, health care is in the midst of a transformation away from one-size-fits-all, trial-and-error medicine and toward this new, targeted approach in which, as is often said, the right patient will get the right treatment at the right time.

Precision Medicine was initiated in Qatar by H.H. Sheikha Moza bint Nasser, Chairperson of Qatar Foundation.

H.H. launched the vision for Qatar Genome Project (QGP) at the WISH summit in 2013.

Since then Qatar Genome Project (QGP) and Qatar Bio Bank (QBB) did the groundwork by collecting samples and sequencing 100,000 whole genomes to set the stage for this next level of PM implementation at a national level. This led to the creation of a new initiative by Qatar Foundation "Qatar Precision Medicine Institute (QPMI)" which was announced by Her Highness in November 2018.

QPMI is Qatar's focal point where all national stakeholders have come together to help move Qatar into being a global leader in the clinical implementation of PM. It will act as a catalyst to translate research into precision medicine in healthcare and public health - through the creation of disease cohort research datasets.

QPMI is managed by a QPMI board chaired by Her Highness Sheikha Moza bint Nasser. It was kicked off in January 2020 and Her Highness requested the development of a strategy for the PM implementation in Qatar over next 5 years.

HMC is an integral part of the QPMI - clinical implementation work group that will focus on the clinical implementation of PM through the formation of a Clinical Council (recommended by QPMI) of healthcare providers.

HMC PM Clinical Initiative will be led by Dr. Abdulla Al Ansari, CMO in HMC. In this regard, Dr. Abdulla has already established an HMC PM Committee. Dr. Abdulla will be chairing the HMC PM Committee with membership from other key HMC leaders.

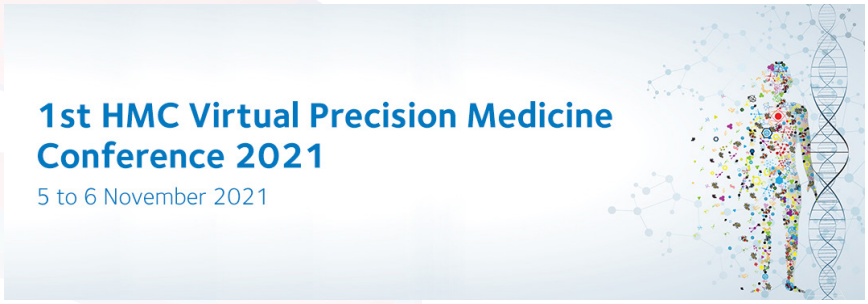
Precision Medicine (PM) is not new to Hamad Medical Corporation (HMC). We have been paving our way all along for last two decades within the organization. However, the formation of QPMI will help in recognizing and restructuring the existing PM achievements in HMC.

MILESTONES

HMC Precision Medicine (PM) Committee was founded by Dr. Abdulla Al Ansari, Chief Medical Officer in September 2019 to bring together all the subject matter experts of Precision Medicine in HMC. The committee is chaired by Dr. Abdulla Al Ansari, Chief Medical Officer (CMO). This committee meets on a regular basis every month. HMC PM team has achieved several milestones:

1. Establishment of the HMC PM Committee with representation from key clinical department that have been informally working on projects focused on Precision Medicine
2. 1st HMC Virtual Precision Medicine Conference in 2021 organized by the HCM PM Committee
3. HMC became an institutional member of the USA Based Personalized Medicine Coalition and UK based Genomics England
4. HMC Co-chairing the national clinical council for PM with representation from various HMC PM Committee members
5. Numerous past and ongoing research projects in Oncology, Pharmacology, Cardiology, Radiology and Medical Genetics that are included in this report

HMC 1st PM Conference 2021



HMC Institutional Membership

Genomics england

PMC
PERSONALIZED
MEDICINE COALITION

HMC Precision Medicine Conference 2021

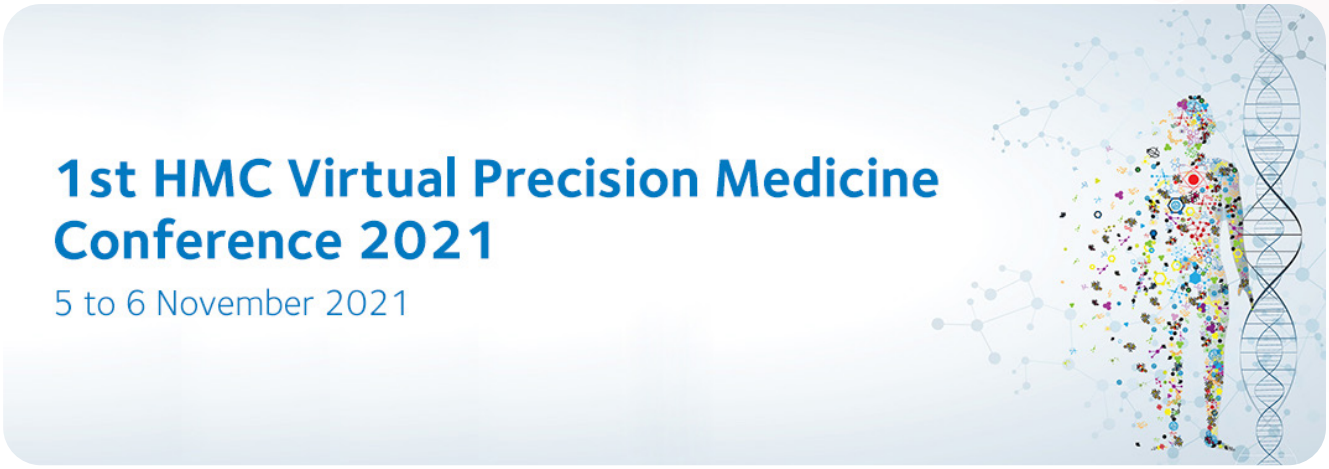
1st HMC Virtual Precision Medicine Conference 2021
A successful beginning

Hamad Medical Corporation (HMC) held its first Virtual Precision Medicine Conference that took place from 5 to 6 November 2021. A collaboration between HMC's Office of the Chief Medical Officer and the National Center for Cancer Care and Research, the educational event theme focused on "Precision Medicine in Oncology".

The conference was organized by the office of Chief Medical Officer and Dr. Salha Bujassoum Al-Bader, Senior Consultant and Chairperson of Medical Oncology at HMC, Assistant Chair of HMC - Precision Medicine and a member of the Clinical Council for Precision Medicine in Qatar; under the leadership of Dr. Abdulla Al Ansari, Chief Medical Officer at HMC and Chair of HMC - Precision Medicine and Chair of the Clinical Council for Precision Medicine in Qatar.

The event had a wide variety of local and International experts on the subject. Notably Dr. Richard Kennedy - Vice President of Research, Development & Innovation QFRDI, Dr. David Brown – Program Director for Qatar Precision Medicine Institute in Qatar foundation and Dr. Nephi Walton, Associate Medical Director, Precision Genomics, Intermountain Healthcare and Chair of the Genomic and Translational Bioinformatics Working Group, AMIA Speakers List? Agenda? How much details?

The two-day virtual conference was a milestone in the emerging and innovative field of precision medicine in Qatar, which has a goal to promote awareness of precision medicine for prevention and early intervention by identifying at-risk individuals and designing healthcare delivery around their needs.



Precision Medicine Projects in HMC Clinical Departments

Precision Medicine In Oncology Care

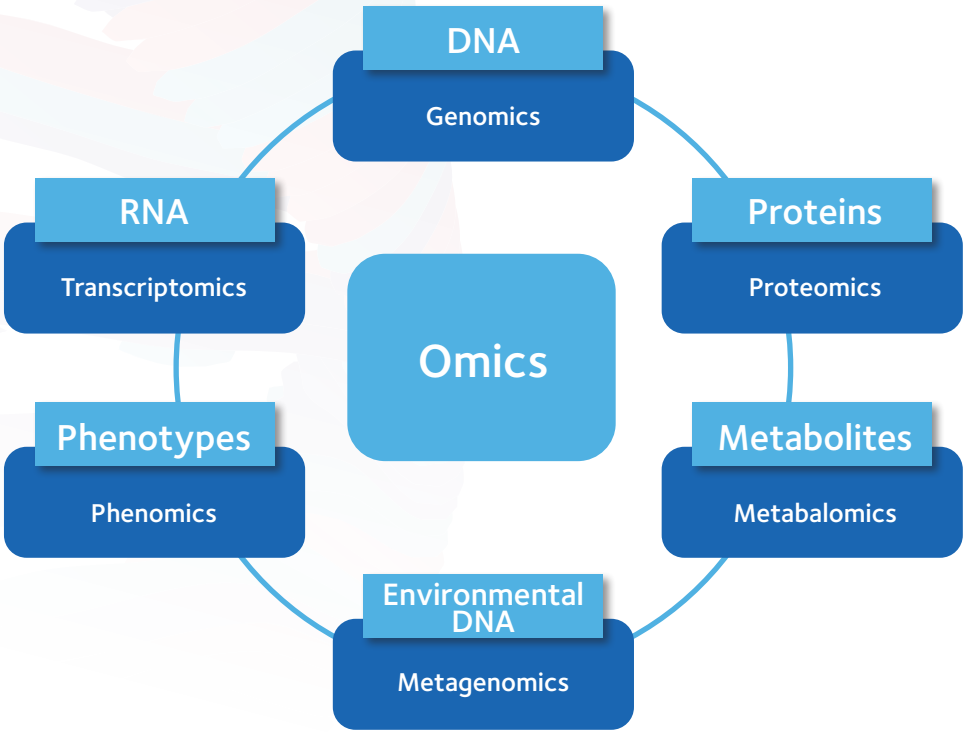
Personalized Medicine (PM) or Precision Medicine in Oncology is an emerging approach for tumor treatment and prevention that considers inter- and intra-tumor variability in genes, tumor (immune) environment, and lifestyle and morbidities of each person diagnosed with cancer. Precision Medicine tailors' therapies to classes of patients based on the differences in people's genes, environments, and lifestyles. PM aims that optimized tumor response is combined with the preservation of organ function and, thus, quality of life.

Precision Medicine requires technology development that allows us to identify key altered pathways that are susceptible to molecularly targeted or immunologic therapies. In 2017, nearly 50% of the early-stage pipeline assets and 30% of late-stage molecular entitles of pharmaceutical companies involved the use of biomarker tests. Furthermore, more than one-third of drug approvals have had DNA-based biomarkers included in their original FDA submissions.

Omics Type Data

Precision Medicine data includes but are not limited to genetic data (Genomic), radiographic features (radiomics), patient reported outcomes (person omics), and digital pathology. It is equally important to note that omics-type data can be derived from (1) the tumor, (2) the patient, (3) tissue surrounding the tumor "stroma," (4) circulating blood, and (5) other bodily fluids. Example histopathology data: assaying proteins using immunohistochemistry, supplemented by mass spectrometry.

OMICS DATA TYPES



Clinical Application Of Precision Medicine In Oncology

1. Molecular Tumor Board

The Hamad Medical Corporation (HMC) team of experts from National Center of Cancer Care and Molecular lab at HMC comes together and established the Molecular Genetic Tumor Board. Based on the American College of Medical Genetics (ACMG), American Society of Clinical Oncology (ASCO), and Association for Molecular Pathology (AMP), all recommend multidisciplinary review of somatic genetic testing to bridge the inevitable gap in knowledge between clinicians and researchers involved with genomic data, such as molecular pathologists and genetics providers, and health care providers, such as surgeons and medical oncologists and provide them with needed information to integrate into their medical practice for optimal care of their patients.

Objectives of Molecular Tumor Board:

1. Given the complexities of genomic data and its application to clinical use, molecular tumor boards with diverse expertise can provide guidance to oncologists and patients seeking to implement personalized genetically targeted therapy in practice.

2. Clarifying the potential implications of a patient's results. This includes but is not limited to prognosis, additional therapeutics, available clinical trials, and possible incidence of underlying hereditary cancer predisposition syndromes.

3. The tumor board weighed evidence for actionability of genomic alterations identified by molecular profiling and provided recommendations including US Food and Drug Administration–approved drug therapy, clinical trials of matched targeted therapy, off label use of such therapy, and additional tumor or germline genetic testing.

Clinical Tasks

1. The molecular and genetic tumor board provides oversight and acts as a referral Controller to the genomic test, monitors its implementation and provides assurance that genetic tests is being properly assessed and filled with needed information.

2. To develop, review and update related policies and guidelines materials.

3. The molecular and genetic tumor board shall oversee the molecular / genetic testing and reporting results.

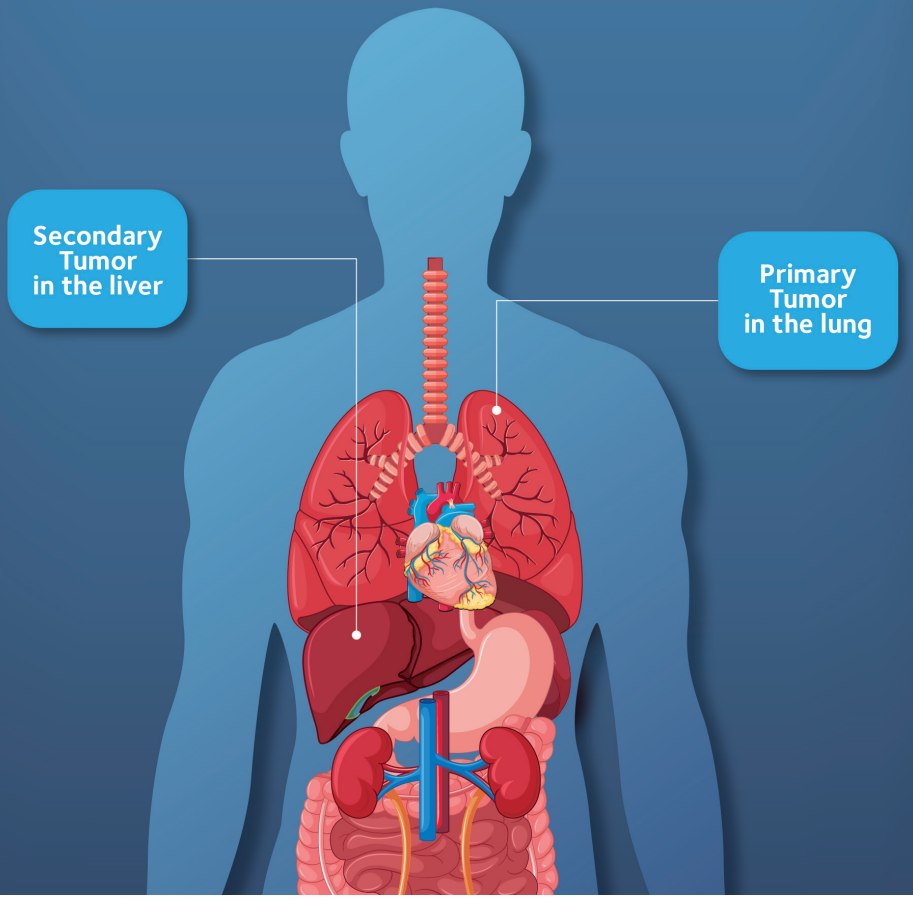
2. Diagnostic Genomic Test:

The Diagnostic Genomic Division (DGD) within the Hamad Medical Corporation, Department of Laboratory Medicine and Pathology (DLMP) has been providing molecular genetics testing for cancer patients since 2016 and was successfully able to introduce long list of comprehensive Genomic test. As the molecular pathology does not only provide tumour diagnosis and prognosis but also guide for therapeutic decisions. The targeted therapies have become available for several cancer types based on the genetic profile and the detected biomarkers. The laboratory is well equipped with different advanced and high standard technologies for detection of defects in patient's chromosome number and structure and a deep genomic analysis (to the level of DNA mutations). Different cytogenetics and molecular genetics techniques are up and running in the DGD that can be listed as following: The cytogenetics techniques (for analysis and detecting defects in chromosomal number and / or structure): • Fluorescent In Situ Hybridization (FISH) • Karyotyping The Molecular Genetics techniques [for analysis and detecting defects in DNA changes or mutations (such as point mutations, deletion, insertion, inversion, duplication), fusion driver detection by analysis of RNA sequence and Copy number variation (CNV)]: • Real Time – PCR • PCR • Fragment analysis • Sanger Sequencing • Next Generation Sequencing (NGS) • DNA Microarray Samples from different sources are analyzed in the DGD including: Blood, CVS, amniotic fluid, soft tissue, Bone marrow, FFPE

In the DGD, many different specialties are running in parallel to provide clinical diagnostic services for inherited diseases, Haemato-oncology, cytogenetics, solid tumors, and premarital screening program. Every specialty has long list of tests, further improvement of services is crucial to reduces the number of samples that are sent abroad for molecular testing, not only for cancer services, but for other conditions and will have great impact in implementing precision medicine.

OVERVIEW OF GENOMIC TEST

Specimen type	Preservation technique	Analysis
Core Biopsy Surgical Excisions	FRESH, FFPE FROZEN	Somatic And Germline From (DNA, RNA)
blood liquid biopsy body fluid (urine, saliva,..etc.)	Target components (circulating tumor cell) free DNA, Exosomes	Somatic and germline (DNA, RNA)



3. Prevention - Hereditary Cancer genetic program

Although most cases of cancers are thought to be sporadic and multifactorial in etiology, about 5% – 10% of cancers are hereditary and are due to germline mutations in cancer predisposition genes. These hereditary cancers are often (but not always) observed in families with positive family history of the relevant cancer types, and frequently involve features such as young age at diagnosis in addition to specific histopathological features.

The Qatari population has a unique genetic profile and patterns in disease presentation and incidence, including familial clusters in cancer, therefore, cancer genetics high risk screening program was established in 2013 at the NCCCR. This service serves high risk individuals affected with cancer or unaffected but carries high risk of developing cancer because of hereditary solid and hematological malignancies and their families by offering them personalized treatment strategies and preventative measures.

4. Prognosis

Prognosis depends critically on both cancer biology such as measures of somatic gene aberration, histological biomarkers, and host fitness such as performance status and the presence of comorbidity.

Staging also remains chiefly anatomic site of cancer location, although biomarkers, which are indirect measures of genetic aberration, have been incorporated into the staging. It was recognized that certain karyotypic abnormalities were also associated with relatively good or poor prognosis in acute myeloid leukemia (AML)

Molecular diagnostic devices using predictive genetic information provide valuable information regarding genetically defined subgroups of patients who would benefit from a specific therapy.

For example, several recurrence scores area available in the market which uses a 21-gene signature to determine whether women with early-stage, hormone receptor positive, HER2 negative breast cancer are likely to benefit from chemotherapy and inform physicians whether patients would be treated successfully with hormone therapy alone or may require more aggressive chemotherapy treatment.

Major international guidelines are now recommending this testing to be offered to this subgroup of breast cancer patients and now considered as standard of care for this type of breast cancer.

Biomarkers are reliable and accurate measurement that indicates the normal biological processes, pathogenic process, and pharmacological response to therapeutic interventions.

For example Breast cancer can be classified into several sub-types based on the observed presence of certain breast cancer-associated biomarkers, such as oestrogen receptor (ER), progesterone receptor (PR), Ki-67 and human epidermal receptor 2 (HER2), in the tumours with prognostic and predictive potential for adjuvant chemotherapy.

5. Treatment:

- **Multidisciplinary team**

The National Cancer Strategy 2011-2016 was a significant step on our country's journey to delivering excellence in all aspects of cancer services.

HMC has developed 15 cancer site specific MDTs, made up of physicians, surgeons, radiologists, pathologists, nurses and oncologists with specialist knowledge and skills in a specific cancer type. The MDTs focus on the clinical, radiological and pathological features of each individual patient and make recommendations about treatment to ensure care is tailored to individual needs based on type of cancer, stage of the disease, performance status of patient, associated comorbidities, histopathology, biomarker and genetic profile.

- **Target therapy**

The recognition that some, if not all, cancers are oncogene-addicted led to the quest for genomic targeted treatments such as gefitinib targeting amutated epidermal growth factor receptor (EGFR) in lung adenocarcinoma, Imatinib, targeting the fusion protein BCR-ABL ,in chronic myeloid leukemia

In addition, imatinib was shown to be an effective KIT inhibitor and to be useful for the treatment of KIT-mutated gastrointestinal stromal tumor.

This important recognition that targeted therapies can have multiple modes of "actionability" has led to a complex and promising ecosystem of targeted treatments and the guidance of their selection by molecular profiling panels.

- **Personalizing cancer immunotherapy**

Immunotherapy has now firmly established itself as a novel pillar of cancer care, from the metastatic stage to the adjuvant and neoadjuvant settings in different cancer types.

Cancer immunotherapy became part of standard of care in Qatar and world wide . It works by boosting specific immune capabilities, reactivating effector T lymphocytes which were previously blocked by cancer. This underlines the fundamental distinction between cytotoxic chemotherapy, attacking generic cell-cycle mechanisms, and targeted drugs, interfering with specific aberrant biologic pathways in cancer cells

- **Re-treatment**

Treatment selection at the time of progression or relapse will likely require extensive genomic analysis in most cases can be done in HMC lab and some of it send abroad.

Some oncogene-addicted cancers will have stereotyped genomic escape mechanisms, leading to progression (for example, ABL kinase domain mutations in CML and gain of EGFR p.T790M mutation in EGFR-mutated lung adenocarcinoma, When such mechanisms are identified, next-generation treatments can be developed, such as ponatinib for CML with ABL p.T315I mutation and Osimertinib and rociletinib for non-small-cell lung cancer with EGFR p.T790M mutation.

- **Monitoring disease activity:**

Most oncogene-driven cancers recur or progress under the pressure of targeted therapy disease status can be monitored through measurement of the quantity or character of the target protein. E.g. BCR-ABL in CML.

For the solid malignancies, radiologic monitoring using standard response criteria (for example Response Evaluation Criteria in Solid Tumors RECIST]) remains the most common approach. Most recently, measurement of the genomes of circulating tumor DNA as a means of monitoring response has been established in certain diseases .

Examples of HMC Contributions in Cancer Precision Medicine Research:

1. Cancer Metabolism: Target and Predictor of Therapeutic Choices Award Active/ NPRP12S-0205-190042

   Qatar National Research Fund and Hamad Medical Corporation (HMC), scientists from WCM-Q, Weill Cornell Medicine (WCM) and clinicians from HMC have collaborated to explore the pathology of breast cancer to gain a more precise understanding of the tumor by focusing on its metabolomics in addition to genomic analysis studying tumor tissue metabolomics can help us better understand how the tumor grows and what kind of nutrients it relies on to fuel its growth and how this can be used to optimize treatment.

2. Title: Precision immunology implications for aggressive types of breast cancer: genomic determinants of immune response to neoadjuvant chemotherapy

   Award Tech. Completed / in NPRP9-459-3-090

3. Title: A Novel Microchip Based Spatial Gene Expression Analysis Assay for Breast and Prostate Cancer

   Award Active / in NPRP10-0120-170211

4. Influence of Pharmacogenetics on the Clinical Outcome of Patients with Early Breast Cancer Treated with Neoadjuvant Chemotherapy in Qatar

   In collaboration between QGP and HMC - approved

5. Identification of genetic risk factors in inherited cancers in Qatar- Towards precision treatment and prevention.

   Approved by HMC -MRC

6. Cost Effectiveness Analysis of the Use of Ribociclib Versus Palbociclib for Hormone? Receptor Positive and HER2? Negative Stage. IV Breast Cancer in Qatar

   in collaboration between Qatar university and HMC approved by HMC-MRC

7. Clinical application of precision medicine utilizing unselected adult biobank participants for BRCA1/2 screening as early cancer detection and prevention in state of Qatar"

   submitted Approved from QBB, Hamad-MRC

8. Qatar Biomedical Research Institute (QBRI) part of Qatar Foundation member Hamad Bin Khalifa University and the King Hussain Cancer Center (KHCC) in Jordan, together with Hamad Medical Corporation (HMC), have launched a strategic initiative aimed at developing a better understanding of breast cancer complexity in the Arab region through research title Genetic determinants of high-risk non-BRCA1/2 familial breast cancer in Qatar."

   Aim to help to identify genetic risk other than BRCA associated gene that increase risk of developing breast cancer; and to enable prevention, early detection, and treatment, Leading to more personalized treatment for patients, by allowing the most appropriate therapy to be selected based on their genetic background.

Precision Medicine In Clinical Research

National Reliance agreement

Historically, gaining approval to undertake multi-site clinical studies in Qatar has been very time consuming. IRB approval has been required for each site. The IRBs for the different institutions often require amendments which must then be accepted by the other IRBs.

We have been working to establish a National Reliance agreement that would ensure that the application would be submitted to a clinical IRB of record (usually the clinical site of the CI) and, following approval, the other institutions would accept this IRB approval and they would simply need to provide site approval (to confirm local capability). We have established a tripartite agreement between three clinical IRBs of record (HMC, WCMQ, Sidra) which is now functioning. QBB is about to join as a clinical IRB. We have been in protracted negotiations with PHCC, but at this stage they do not wish to join such an arrangement. We will now invite non clinical sites (principally universities) to become members of this agreement.

Regulatory System for Clinical Trials involving IMPs and IMDs.

Currently, Qatar does not have in place a regulatory framework for the approval and conduct of clinical trials involving investigational medicinal products (IMPs) or investigational medical devices (IMDs). There is an ad hoc arrangement for approval of a small number of low- risk clinical trials. The absence of such a structure is impeding the development of a strong clinical trials program in Qatar and also represents a risk.

We have been liaising with local partners (including MoPH, who ultimately would ultimately manage this process) and with external stakeholders regarding establishing such a process. We have identified an external expert who is willing to advise us on a consultancy basis, and we hope he will be appointed very soon.

Clinical Research Facility

We have secured approval to establish an out- patient clinical research facility in building 316 of Medical City. the funding is being provided by AHS. The facility will be staffed by skilled personnel and will be well equipped. This facility will be available for all disciplines to utilize it's resources.

It will assess and complement the facilities planned for the Precision Medicine department on the 4th floor of the "TRI' which would have 'beds' and would facilitate high risk studies including phase 1 studies.

Clinician Scientist Posts

A joint clinical academic department is being established between HMC and QU which will appoint clinician scientists who will have joint appointments between the two institutions. Their work allocation will be 50% clinical and 50% academic. The intention is that they will be appointed as 'double acts' in a particular specialty, typically one very senior and the other more junior, so that the former can mentor the latter. By working as a 'double act' protection of academic time may also be facilitated. Administrative support and technician/RA PhD student support will also be provided. These posts will be appointed progressively over the next three years or so. It has been agreed that Precision Medicine will be a priority.

Training of the next generation of clinician scientists

A business case has been submitted by HBKU to establish a clinical PhD program in Precision Medicine for aspiring clinician scientists. Further work is required to develop an integrated career development program for such individuals. The clinician scientists appointed to the joint clinical scientist posts (above) will play a key role in mentoring these individuals. In the longer term, the concept can be extended to include academic training in other disciplines.

Training of Existing Specialists in Precision Medicine

Prior to COVID HBKU was providing training course for clinicians in Precision Medicine. These will be re-established. HBKU are also developing master's level courses in Precision Medicine which would be suitable for research active clinicians. Queen Mary's University of London is also interested in developing such program for Qatar clinicians.

Precision Medicine In Medical Genetics

Medical Genetics Services at HMC: Opportunities in the era of Precision Medicine for genetic and rare diseases

Background:

It is estimated that 1 in 10 suffering from 1 of 10,000 known rare genetic diseases, and this risk increase in consanguineous populations. For the majority of patients, diagnosing the rare genetic disease is a challenge, particularly for those lacking treatments. However, with developing the precision medicine for rare genetic diseases and tailoring treatment directly to the specific phenotypic characteristics of an individual patient is very promising. This will mainly be achieved by unraveling the root molecular cause of the genetic diseases in the era of advanced genomic technologies. Innovative genetic and genomic technologies have the great potential to unprecedently revolutionize medicine and public health. The pace of change in this area is rapid and a clear strategy is needed to ensure that opportunities are grasped. Genomic Medicine is the backbone of Precision Medicine (PM). This Strategy sets out the HMC's plan to create a sustainable, globally competitive environment for genetics and genomics to advance health and healthcare provision for the people of Qatar.

There a significant shifting of the landscape for rare genetic diseases by the availability of genomic sequencing which enable the diagnosis of rare genetic diseases, leading to a surge in discoveries of novel diseases and genes. Furthermore, applications of precision treatment approached, building the necessary infrastructure as well as identifying targeted therapies will ultimately benefit our patients and their families here in Qatar and the region.

Qatar has magnificent efforts and extended funds in founding highly informative genomic resources. Qatar Biobank for Medical Research and Qatar Genome Programs are examples of such efforts. There are certain challenges as well as opportunities in the utilization of these resources for feeding the nationally funded research. This includes determining which actionable plans that require implementation to maximize the benefits and output of these genomic resources. The employment of genomic and large data programs in translational research and national clinical trials is the ultimate goal we aim to accomplish. Taking into consideration the trials readiness and outcome measures that will address the best genetic disorders examples to bring precision medicine to practice in Qatar.

The development of clinical, genomic, and proteomic sets of databases for Qatar patients should aid the Qatar National Plans in the field of genetics of rare monogenic diseases (Ismail et al., 2020).

PM can be applied to diagnose and treat a variety of diseases, most notably in more precisely diagnosing cancer. (Adopted from Report of the WISH Precision medicine Forum 2016) (Ginsburg GS, 2016) (Figure 1).

PM has the potential to enter all parts of the health service – from diagnostics and delivery to prevention and patient safety. PM inventions will provide targeted treatments and ease health burdens. However, it is a long process before the analysis can provide clinical or preventative guidance. The path from gene sequencing to patient benefit is illustrated in (Figure 2). Now, the field is only starting to scale-up evaluation and management of genomic data. We first need to develop standards for data and algorithms that can interpret its clinical relevance

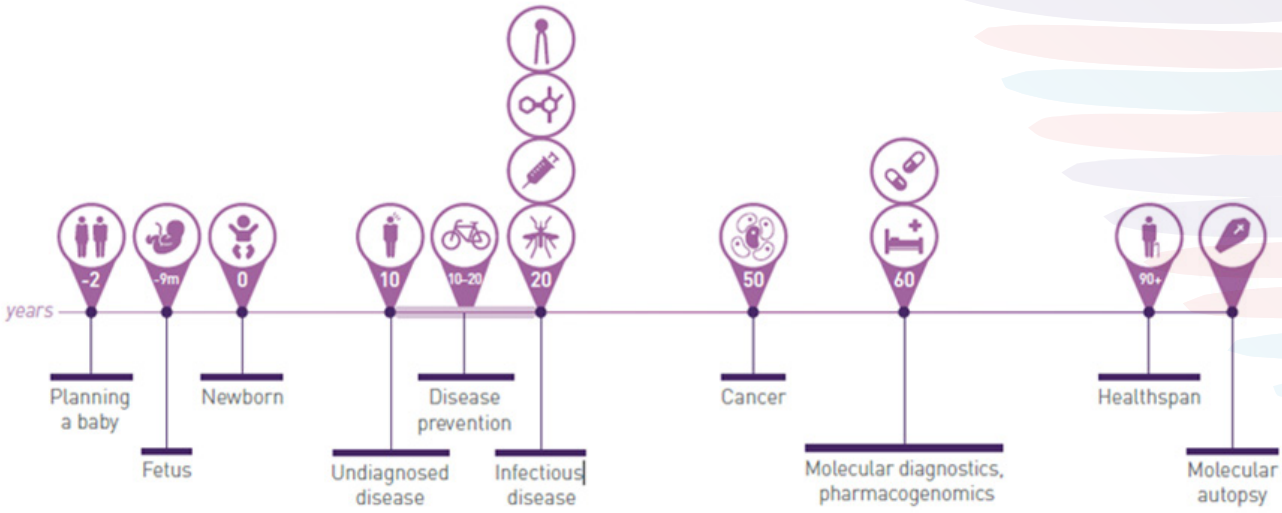


Figure 1: Application of precision medicine across the lifetime
Precision medicine: Qatar personalized genomics and healthcare initiative (Qatar Genome Project-QGP, Qatar Biobank-QBB, Sidra Medicine, Hamad Medical Corporation-HMC, WISH, and other stakeholders).(A. L.-Dewik & Qoronfleh, 2019)

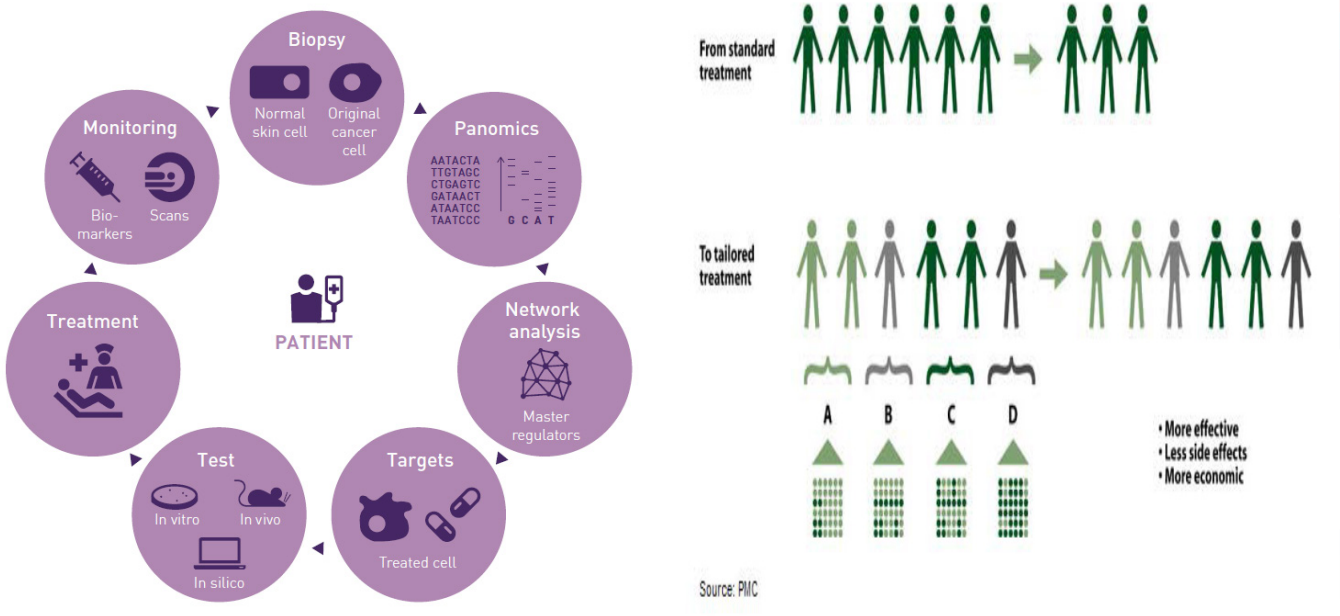


Figure2: The PM cycle from gene sequencing to treatment. The path from gene sequencing to patient benefit (Adopted from Report of the WISH Precision Medicine Forum 2016) (Ginsburg GS 2016)

Medical Genetics Services in HMC: Existing and Current services employing precision medicine

The department of medical genetics is the main referral department for genetic and biochemical genetic disorders in the State of Qatar established since 2009, that provide patient and family centered clinical care to both children and adults patients. Services that are being offered by the department and through collaborations with other specialties entails diagnosis, treatment and prevention of genetic disorders in the following subspecialities:

- Adult and Pediatrics Clinical and Metabolic Genetics
- Adult and Pediatric Cancer Genetics
- Prenatal Genetics
- Managing positive cases from National Screening Programs (New-born screening and Premarital).
- Reproductive Genetics

Clinical activities and Collaborative Achievements

Date of establishment	Current activity	Impact on patient care
2020	Genomic Newborn Screening pilot study in Collaboration with Heidelberg	This is the first pilot study of its kind in the region to study the feasibility and specificity of the Genomic NBS in addition to the standard NBS in detecting genetic disorders. The aim is to identify genetic disorders that can't be detected through the regular NBS such as SMA to improve early detection which will lead to early intervention and better quality of life of babies living in Qatar.
2019	Gene Therapy for Spinal Muscular Atrophy	Hamad Medical Corporation (HMC) has become the second healthcare organization outside the United States and Canada to treat children with congenital spinal muscular atrophy using a new gene therapy. Spinal muscular atrophy (SMA) is a genetic disorder and a leading cause of death in children under two years of age. The disease is characterised by weakness and atrophy in the muscles used for movement, breathing, and swallowing. Zolgensma (onasemnogene abeparvovec-xioi), the first gene therapy approved to treat children less than two years of age with spinal muscular atrophy (SMA), the most severe form of SMA and a leading genetic cause of infant mortality. The vector delivers a fully functional copy of human SMN gene into the target motor neuron cells. A one-time intravenous administration of Zolgensma results in expression of the SMN protein in a child's motor neurons, which improves muscle movement and function, and survival of a child with SMA.

		This treatment is considered a breakthrough in the world of precision medicine that gives a window of hope to treat such a lethal disease Since its launching, HMC has provided gene therapy for a total of 9 patients and the clinical outcomes will be published soon (in press)
2018	National Center of Rare Diseases	The Center of rare disease was launched back on 2018 at HMC in collaboration with Heidelberg University Hospital (HUH), The first of its kind in the Middle East, is the main point of contact for many patients with rare diseases. Through expert multidisciplinary teamwork between HMC and HUH, the Center aims to support the diagnosis and management of patients with rare and complex diseases. In addition to providing clinical care, the National Center for Rare Diseases in Qatar also supports state-of-the-art research targeted toward precision medicine and provides education to local clinicians in the management of rare diseases. This centre is chaired by Dr Saad Al Kaabi and assisted by Dr Reem Al Sulaiman Clinical genetics play a core entity at the centre of rare disease since most of the rare diseases are of genetic etiologic. One of the biggest achievements of the rare disease center is the launching of the gene therapy for patients with SMA and the ongoing pilot research study on Genomic Newborn screening, the first of its kind in the Middle East targeted toward preventative precision medicine.
2013	Prenatal Genetics Program	The Prenatal Genetics clinic is a unique service which was established in collaboration between medical genetic department and Fetal Maternal Unit (FMU). The aim of establishing this clinic was to provide proper prenatal genetics service to high risk pregnancies, offer early diagnosis of at the prenatal stage through different methods of genetic testing for early intervention and improved informed decisions and and coordinate postnatal care. Genetic testing is done prenatally in a targeted manner based on several assessments including ultrasound findings and family history.
2013	Cancer Genetics Program	This program was established through the medical oncology department and specifically under the caner precision medicine program lead by Dr Salha Bujassoum. This program is defined as an example of an integrated multidisciplinary and well-established service targeted toward achieving excellence in cancer care through offering prevention and personalized medicine for patients with cancer and patients at risk for

		cancer; these goals align closely with Qatar's 2022 vision of achieving excellence in cancer care (Qatar's National Cancer Framework, 2017–2020) (Al-Bader et al., 2018). It is the first regional program designed to manage affected and unaffected, high-risk patients, and their families and offer genetic risk assessment, genetic counselling, and thus offering targeted therapies as well as risk-reducing strategies to reduce mortality and morbidity of cancer in Qatar. Family relatives of the patient with hereditary cancer syndrome can benefit through receiving targeted genetic testing in addition to allowing reproductive options. The cancer genetics program is an example of a well-established, multidisciplinary service targeted toward achieving excellence in cancer care through offering prevention, and personalized medicine. With the advances in the field of genomics and precision medicine, programs like the cancer genetics is becoming a core part of the care of patients and their families in Qatar.
2003	Metabolic Genetics-National Newborn Screening Program (NBS)	The genetic department provides clinical management for positive cases discovered via the NBS. The role of clinical metabolic and genetics department is to identity suspected cases and confirms diagnoses for early intervention and treatment. The future direction is to build a new entity of newborn screening which the genomic newborn screening to identify diseases that can't be detected through the standard newborn screening, this project is on-going through a collaborative effort with the center of rare disease.
2009	Premarital Genetics-National Premarital Screening Program	The department of medical genetics provides comprehensive targeted genetic counseling for couples at risk for having children with genetic disorders. Couples are particularly educated about their risk of having certain genetic disorders and counseled on reproductive risks and available reproductive options. The screening is offered by designated primary healthcare centers and selected private hospitals for hemoglobinopathies (thalassemias, sickle cell disease); classical homocystinuria; cystic fibrosis; and optionally spinal muscular atrophy (SMA) The above-mentioned conditions were selected for screening because of high carrier frequencies in the population of Qatar. Screening for hemoglobinopathies is performed by complete blood count (CBC) and hemoglobin electrophoresis, followed by molecular genetic testing as indicated. Screening for classical homocystinuria and cystic fibrosis is primarily offered for known founder mutations.

		Carrier testing for SMA is performed by targeted deletion/ duplication testing to detect the common exon 7 deletion in the SMN1 gene. A challenge in screening for SMA in Qatar was highlighted after the identification of newborns with SMA born to couples in which one parent was an SMA "silent carrier" with two copies of the SMN1 gene (OMIM 600354) on one chromosome 5 and a second chromosome 5 with zero copies (also known as "2 + 0" genotype). The purpose of premarital genetic counseling is to screen for the most common genetic disorders in Qatar in order to make couples more informed about their risk and reduce the burden of such diseases on the society through offering targeted reproductive options.
2015	Reproductive Genetics Preimplantation Genetic Diagnosis (PGD)	Through the collaboration with the assisted reproductive unit, the role of clinical genetics department play an important role in selecting families who can benefit from PGD in order to prevent genetic disorders in the upcoming generation. This is done by selecting high risk families with known genetic diseases and by offering them targeted genetic assisted reproductive technology such as PGD to reduce the burden of the diseases in the un-born generations in high risk families.
2020	Adult Cardiogenetic streamlined care	Through the collaboration with Dr Jassim Alsuwadi from Cardiology department, the referral and care of adult patients identified with hereditary cardiac disorders are streamlined through proper collaboration for such as high risk patients. Those high risk patients and their families require targeted surveillance programs and care.

Research activities:

We successfully built our research culture in Medical Genetics through carrying out collaborative clinical, translational and basic sciences research projects with local institutes as well as international prestigious centers/universities. Our mission is to further the understanding of the genetic components of inherited diseases pertinent to the population of Qatar and the region, such as Classical Homocystinuria and others Autosomal Recessive conditions.

Our research in the division is crafted to support three major themes:

- Disease gene discovery
- The development of new treatment strategies
- Targeted Prevention

Our current research activities include a multidisciplinary approach to identify the underlying genetic factors of metabolic and genetic disorders as well as the effects of founder mutations in the Qatari population for certain high priority diseases such as Classical Homocystinuria and White Matter and clinical trials in order to translate research discoveries and findings into practical applications.

We secured numerous funding from Qatar National Research Fund (QNRF), HMC and Qatar Innovation Promotion Award (QIPA) (Total funding successfully obtained: $6,106.095 between 2011 - 2020) (For more details about s publications please refer to appendix 1)

Our center is recognized at the international level to carry out so far three clinical trials (MOR4, MO5 and SMA) which are registered in ClinicalTrials.gov (a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world under the U.S. National Institutes of Health) and we are currently receiving several feasibility packages to participate in future clinical trials in homozygous familial hypercholesterolemia (HoFH) and Pompe disease.

Furthermore, our center attracts the international scientific community i.e prestigious centers and universities such as McGill University and Genome Quebec Innovation Center, Canada; Boston Children's Hospital, Boston, USA; The Rockefeller University & New York Genome Center, USA; University Hospital Freiburg-Germany; University of Zurich- Switzerland as well as local universities such as Weill Cornell Medical College, Qatar University and Shafallah Medical Genetic Center to collaborate in translational and basic research activates.

We have published several peer-reviewed original articles in high impact and prestigious international journals (like Science, Science translational medicine, Neuron and American journal of human genetics) and participated in numerous conference presentations (including invited and peer-reviewed oral presentations and panel discussions) on the topic of Medical Genetic. The outcomes of the above research work have been published in following international journals.

Furthermore, the launch of Qatar Genome Project and its mission towards personalized medicine will also dramatically increase the load of genetic referrals and consultations for evaluation and genetic counseling.

In the era of genomic and Precision Medicine (PM), the breakthrough and the substantial advances in Genomic Diagnostic technologies (Next Generation Sequencing) like Whole Exome and Whole Genome sequencing, this will create a critical need for more medical geneticists and genetic counselors, scientists for next generation phenotypic delineation, clinical analysis and massive Genomic data analysis. Accordingly, hospitals, academic medical centers, and research institutes will need to attract and support medical Geneticists if they want to participate in these exciting developments or be left on the sidelines.

Current Clinical Trials activities

Titles	Impact on patient care
Protocol title: "An Open-Label Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of Multiple Doses of ISIS 396443 Delivered Intrathecally to Subjects with Genetically Diagnosed and Presymptomatic Spinal Muscular Atrophy" Sponsored by: Biogen Idec Research Limited	Gene therapy of antisense olonucleotide that alters the splicing of SMN2 pre-mRNA to promote expression of full-length SMN protein has been introduced to Spinal muscular atrophy (SMA) a fatal genetic condition SMA is an autosomal recessive neurodegenerative disease associated with progressive and often severe muscle weakness and atrophy and is a leading cause of death in infants. Early treatment allows for gains in motor function closer to normal development than that expected in SMA individuals. The clinical trail showed that early identification of infants with SMA through NBS and support the value of treatment initiation in presymptomatic infants. This treatment changes the natural history of SMA disease and patients achieved major motor milestone timelines consistent with normal development. as healthy individuals

Future Clinical Trials activities

Titles	Impact on patient care
Phase 1/2 study for subjects with A Double-blind, Randomized, Placebo-controlled, Phase 1/2 Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Effects on Clinical Outcomes of OT-58 Administered Subcutaneously in Patients with Cystathionine Beta-Synthase Deficient Homocystinuria.	Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics of OT-58 enzyme therapy in Patients with Cystathionine Beta-Synthase Deficient Homocystinuria

Past Clinical Trials activities

Protocol title: "A Multicenter, Multinational, Extension Study to Evaluate the Long-Term Efficacy and Safety of BMN 110 in Patients with Mucopolysaccharidosis IVA (Morquio A Syndrome)"
Protocol title: "A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multinational Clinical Study to Evaluate the Efficacy and Safety of 2.0 mg/kg/week and 2.0 mg/kg/every other week BMN 110 in Patients with Mucopolysaccharidosis IVA (Morquio A Syndrome)"
Qatar Foundation 250,000 Euro ($308,115 USD) grant for the project "Clinical trial for investigations and treatment of inherited glutamine synthetase deficiency".

Current Research Activities

Research activities	Impact on patient care
Pilot Study: Genomic Newborn Screening in Collaboration with Heidelberg MRC -01-19-293	This is the first pilot study of its kind in the region to study the feasibility and specificity of the Genomic NBS in addition to the standard NBS in detecting genetic disorders. The aim is to identify genetic disorders that can't be detected through the regular NBS such as SMA to improve early detection which will lead to early intervention and better quality of life of babies living in Qatar.
Gene Therapy for Spinal Muscular Atrophy: The Qatari Experience	The first study in the region to present the outcomes of gene therapy in patients with Spinal Muscular Atrophy
Identifying a founder BRCA1 variant in the Qatari population with unique genotype-phenotype correlations	To describe founder mutations in the BRCA1 gene in Qatar which will impact early diagnosis, treatment and prevention for high risk patients and their families
Exploring the prevalence of Lynch syndrome and its genotype-phenotype correlation in the State of Qatar	To explore the prevalence of Lynch syndrome in Qatar and target high frequent genes to identify patients early on and provide targeted therapies and prevention.
Identification of genetic risk factors in inherited cancers in Qatar- Towards precision treatment and prevention	To identify the prevalence of hereditary cancers in Qatar and set a platform to establish in house testing for all hereditary cancers.
Clinical, biochemical and Molecular characterization of Dihydrolipoamide dehydrogenase (DLD) deficiency in the Qatari patients	Describe the clinical characteristics and molecular findings of the DLD deficiency patients in the state of Qatar in comparison to international counterparts' findings.

Woodhouse-Sakati Syndrome: Clinical, biochemical and Molecular characterization in the Qatari population MRC-01-20-779, (2020-2021)	Early identification of WHSS among Qatari patients guide early and appropriate treatment and prevent adverse outcomes.
Prenatal Genetic clinical experience in the state of Qatar MRC-01-18-274(2020-2021)	Early detection of diseases at prenatal stage guide early and suitable therapy and prevent fatal outcomes.

Past Research Activities

1	Reem Al-Sulaiman, Amna Othman, Karen El-Akouri1, Shehab Fareed, Hajer AlMulla, Aseel Sukik, Mariam Al-Mureikhi, Noora Shahbeck, Rehab Ali, Fatma Al-Mesaifri, Sara Musa, Mariam Al-Mulla, Khalid Ibrahim, Khalid Mohamed, Maryam Ali Al-Nesef, Mohammad Ehlayel, Tawfeg Ben-Omran. A Founder RAB27A Variant Causes Griscelli Syndrome Type 2 with Phenotypic Heterogeneity in Qatari Families. 2020, AJMG-A.
2	Ali, R., Al-Dewik, N., Mohammed, S., Elfituri, M., Agouba, S., Musa, S., Mahmoud, L., Almulla, M., El-Akouri, K., Mohd, H., Bux, R., Almulla, H., Othman, A., Al-Mesaifri, F., Shahbeck, N., Al-Muriekhi, M., Khalifa, A., Al-Sulaiman, R. and Ben-Omran, T., 2021. Expanding on the phenotypic spectrum of Woodhouse-Sakati syndrome due to founder pathogenic variant in DCAF17 : Report of 58 additional patients from Qatar and literature review. American Journal of Medical Genetics Part A, 188(1), pp.116-129.
3	Al-Dewik N, Al-Mureikhi M, Shahbeck N, Ali R, Al-Mesaifri F, Mahmoud L, Othman A, AlMulla M, Sulaiman RA, Musa S, Abdoh G, El-Akouri K, Solomon BD, Ben-Omran T. Clinical genetics and genomic medicine in Qatar. Mol Genet Genomic Med. 2018 Sep;6(5):702-712. doi: 10.1002/mgg3.474.
4	Al-Bader SB, Alsulaiman R, Bugrein H, Ben Omran T, Abbaszadeh F, Bakheet N, Apsa Kusasi S, Abdou N, Solomon BD, Ghazouani H. Cancer genetics program: Follow-up on clinical genetics and genomic medicine in Qatar. Mol Genet Genomic Med. 2018; 6(6):865-872. doi: 10.1002/mgg3.534.
5	Bujassoum S., Bugrein H., & Al-Sulaiman R. (2017). Genotype and phenotype correlation of breast cancer in BRCA mutation carriers and noncarriers. Journal of Cancer Science and Therapy, 9(2), 358–364.
6	Bujassoum S., Bugrein H., Al-Sulaiman R., & Ghazouani H. (2016). Qatar's experience with hereditary breast and ovarian cancer and high risk clinic: A retrospective study 2013–2016. International Journal of Research, 5(10), 184–196.

7	Bujassoum, S. , Alsulaiman, R. , Elmalik, H. , Junejo, K. , Mahfouz, A. , & Farghaly, H. (2018). Identifying Lynch syndrome in two families with classical hereditary breast and ovarian cancer syndrome phenotype: A case report. Journal of Cancer Science and Therapy, 10(9), 235–239. 10.4172/1948-5956.1000550
8	Chong JX, Talbot JC, Teets EM, Previs S, Martin BL, Shively KM, Marvin CT, Aylsworth AS, Saadeh-Haddad R, Schatz UA, Inzana F, Ben-Omran T, Almusafri F, Al-Mulla M, Buckingham KJ, Harel T, Mor-Shaked H, Radhakrishnan P, Girisha KM, Nayak SS, Shukla A, Dieterich K, Faure J, Rendu J, Capri Y, Latypova X, Nickerson DA, Warshaw DM, Janssen PML; University of Washington Center for Mendelian Genomics, Amacher SL, Bamshad MJ. Mutations in MYLPF Cause a Novel Segmental Amyoplasia that Manifests as Distal Arthrogryposis. Am J Hum Genet. 2020. doi: 2020.06.014.
9	Arisha Rasheed, Evren Gumus, Maha Zaki , Katherine Johnson, Humera Manzoor , Geneva LaForce, Danica Ross, Jennifer McEvoy-Venneri , Valentina Stanley, Sangmoon Lee, Abbir Virani , Tawfeg Ben-Omran , Joseph G Gleeson , Sadaf Naz , Ashleigh Schaffer . Bi-allelic TTC5 variants cause delayed developmental milestones and intellectual disability. J Med Genet 2020. doi: 10.1136.
10	Ben-Omran T, Al Ghanim K, Yavarna T, El Akoum M, Samara M, Chandra P, Al-Dewik N. Effects of consanguinity in a cohort of subjects with certain genetic disorders in Qatar. Mol Genet Genomic Med. 2020. PMID:31793205.
11	De Vivo DC, Bertini E, Swoboda KJ, Hwu WL, Crawford TO, Finkel RS, Kirschner J, Kuntz NL, Parsons JA, Ryan MM, Butterfield RJ, Topaloglu H, Ben-Omran T, Sansone VA, Jong YJ, Shu F, Staropoli JF, Kerr D, Sandrock AW, Stebbins C, Petrillo M, Braley G, Johnson K, Foster R, Gheuens S, Bhan I, Reyna SP, Fradette S, Farwell W; NURTURE Study Group. Nusinersen initiated in infants during the presymptomatic stage of spinal muscular atrophy: Interim efficacy and safety results from the Phase 2 NURTURE study. Neuromuscul Disord. 2019. PMID:3 1704158
12	Genetic, clinical and biochemical characterization of a large cohort of patients with hyaline fibromatosis syndrome. Cozma C, Hovakimyan M, Iuraşcu MI, Makhseed N, Selim LA, Alhashem AM, Ben-Omran T, Mahmoud IG, Al Menabawy NM, Al-Mureikhi M, Martin M, Demuth L, Yüksel Z, Beetz C, Bauer P, Rolfs A. Orphanet J Rare Dis. 2019. PMID: 31455396
13	Gupta S, Gallego-Villar L, Wang L, Lee HO, Nasrallah G, Al-Dewik N, Häberle J, Thöny B, Blom HJ, Ben-Omran T, Kruger WD. Analysis of the Qatari R336C cystathionine ş-synthase protein in mice. J Inherit Metab Dis. 2019. PMID: 31240737
14	Ben-Omran T, Masana L, Kolovou G, Ariceta G, Nóvoa FJ, Lund AM, Bogsrud MP, Araujo M, Hussein O, Ibarretxe D, Sanchez-Hernández RM, Santos RD. Real-World Outcomes with Lomitapide Use in Paediatric Patients with Homozygous Familial Hypercholesterolaemia. Adv Ther. 2019. PMID: 31102204
15	Al-Dewik N, Ali A, Mahmoud Y, Shahbeck N, Ali R, Mahmoud L, Al-Mureikhi M, Al-Mesaifri F, Musa S, El-Akouri K, Almulla M, Al Saadi R, Nasrallah GK, Samara M, Abdoh G, Rifai HA, Häberle J, Thöny B, Kruger W, Blom HJ, Ben-Omran T. Natural history, with clinical, biochemical, and molecular characterization of classical homocystinuria in the Qatari population. J Inherit Metab Dis. 2019. PMID: 30968424.

16	Almannai M, Felemban R, Saleh MA, Faqeih EA, Alasmari A, AlHashem A, Mohamed S, Sunbul R, Al-Murshedi F, AlThihli K, Eyaid W, Ali R, Ben-Omran T, Blau N, El-Hattab AW, Alfadhel M. 6-Pyruvoyltetrahydropterin Synthase Deficiency: Review and Report of 28 Arab Subjects. Pediatr Neurol. 2019. PMID: 30926181
17	Al-Dewik N, Mohd H, Al-Mureikhi M, Ali R, Al-Mesaifri F, Mahmoud L, Shahbeck N, El-Akouri K, Almulla M, Al Sulaiman R, Musa S, Al-Marri AA, Richard G, Juusola J, Solomon BD, Alkuraya FS, Ben-Omran T.Clinical exome sequencing in 509 Middle Eastern families with suspected Mendelian diseases: The Qatari experience. Am J Med Genet A. 2019. PMID: 30919572
18	Friedman J, Smith DE, Issa MY, Stanley V, Wang R, Mendes MI, Wright MS, Wigby K, Hildreth A, Crawford JR, Koehler AE, Chowdhury S, Nahas S, Zhai L, Xu Z, Lo WS, James KN, Musaev D, Accogli A, Guerrero K, Tran LT, Omar TEI, Ben-Omran T, Dimmock D, Kingsmore SF, Salomons GS, Zaki MS, Bernard G, Gleeson JG. Biallelic mutations in valyl-tRNA synthetase gene VARS are associated with a progressive neurodevelopmental epileptic encephalopathy. Nat Commun. 2019;10(1):707. doi: 10.1038/s41467-018-07067-3.
19	Keller R, Chrastina P, Pavlíková M, Gouveia S, Ribes A, Kölker S, Blom HJ, Baumgartner MR, Bártl J, Dionisi-Vici C, Gleich F, Morris AA, Kožich V, Huemer M; and individual contributors of the European Network and Registry for Homocystinurias and Methylation Defects (E-HOD), Bariş I, Ben-Omran T, Blasco-Alonso J, Bueno Delgado MA, Carducci C, Cassanello M, Cerone R, Couce ML, Crushell E, Delgado Pecellin C, Dulin E, Espada M, Ferino G, Fingerhut R, Garcia Jimenez I, Gonzalez Gallego I, González-Irazabal Y, Gramer G, Juan Fita MJ, Karg E, Klein J, Konstantopoulou V, la Marca G, Leão Teles E, Leuzzi V, Lilliu F, Lopez RM, Lund AM, Mayne P, Meavilla S, Moat SJ, Okun JG, Pasquini E, Pedron-Giner CC, Racz GZ, Ruiz Gomez MA, Vilarinho L, Yahyaoui R, Zerjav Tansek M, Zetterström RH, Zeyda M. Newborn screening for homocystinurias: Recent recommendations versus current practice. J Inherit Metab Dis. 2019;42(1):128-139. doi: 10.1002/jimd.12034.
20	Besnard T, Sloboda N, Goldenberg A, Küry S, Cogné B, Breheret F, Trochu E, Conrad S, Vincent M, Deb W, Balguerie X, Barbarot S, Baujat G, Ben-Omran T, Bursztejn AC, Carmignac V, Datta AN, Delignières A, Faivre L, Gardie B, Guéant JL, Kuentz P, Lenglet M, Nassogne MC, Ramaekers V, Schnur RE, Si Y, Torti E, Thevenon J, Vabres P, Van Maldergem L, Wand D, Wiedemann A, Cariou B, Redon R, Lamazière A, Bézieau S, Feillet F, Isidor B. Biallelic pathogenic variants in the lanosterol synthase gene LSS involved in the cholesterol biosynthesis cause alopecia with intellectual disability, a rare recessive neuroectodermal syndrome. Genet Med. 2019 Feb 6. doi: 10.1038/s41436-019-0445-x
21	Aartsma-Rus A, Hegde M, Ben-Omran T, Buccella F, Ferlini A, Gallano P, Howell RR, Leturcq F, Martin AS, Potulska-Chromik A, Saute JA, Schmidt WM, Sejersen T, Tuffery-Giraud S, Uyguner ZO, Witcomb LA, Yau S, Nelson SF. Evidence-Based Consensus and Systematic Review on Reducing the Time to Diagnosis of Duchenne Muscular Dystrophy. J Pediatr. 2019; 204:305-313.e14. doi: 10.1016/j.jpeds.2018.10.043.
22	Al-Dewik N, Ben-Omran T, Zayed H, Trujillano D, Kishore S, Rolfs A, Yassin MA. Clinical Exome Sequencing unravels new disease-causing mutations in the myeloproliferative neoplasms: A pilot study in patients from the state of Qatar. Gene. 2019, 20;689:34-42. doi: 10.1016/j.gene.2018.12.009.

23	Stephen J, Maddirevula S, Nampoothiri S, Burke JD, Herzog M, Shukla A, Steindl K, Eskin A, Patil SJ, Joset P, Lee H, Garrett LJ, Yokoyama T, Balanda N, Bodine SP, Tolman NJ, Zerfas PM, Zheng A, Ramantani G, Girisha KM, Rivas C, Suresh PV, Elkahloun A, Alsaif HS, Wakil SM, Mahmoud L, Ali R, Prochazkova M; Undiagnosed Diseases Network members, Kulkarni AB, Ben-Omran T, Colak D, Morris HD, Rauch A, Martinez-Agosto JA, Nelson SF, Alkuraya FS, Gahl WA, Malicdan MCV. Bi-allelic TMEM94 Truncating Variants Are Associated with Neurodevelopmental Delay, Congenital Heart Defects, and Distinct Facial Dysmorphism. Am J Hum Genet. 2018 Dec 6;103(6):948-967. doi: 10.1016/j.ajhg.2018.11.001.
24	Ismail HM, Krishnamoorthy N, Al-Dewik N, Zayed H, Mohamed NA, Giacomo VD, Gupta S, Häberle J, Thöny B, Blom HJ, Kruger WD, Ben-Omran T, Nasrallah GK. In silico and in vivo models for Qatari-specific classical homocystinuria as basis for development of novel therapies. Hum Mutat. 2019 Feb;40(2):230-240. doi: 10.1002/humu.23682. Epub 2018 Nov 23.
25	Maffucci P, Chavez J, Jurkiw TJ, O'Brien PJ, Abbott JK, Reynolds PR, Worth A, Notarangelo LD, Felgentreff K, Cortes P, Boisson B, Radigan L, Cobat A, Dinakar C, Ehlayel M, Ben-Omran T, Gelfand EW, Casanova JL, Cunningham-Rundles C. Biallelic mutations in DNA ligase 1 underlie a spectrum of immune deficiencies. J Clin Invest. 2018 Dec 3;128(12):5489-5504. doi: 10.1172/JCI99629.
26	Balobaid A, Ben-Omran T, Ramzan K, Altassan R, Almureikhi M, Musa S, Al-Hashmi N, Al-Owain M, Al-Zaidan H, Al-Hassnan Z, Imtiaz F, Al-Sayed M. Delineating the phenotypic spectrum of hyperphosphatasia with mental retardation syndrome 4 in 14 patients of Middle-Eastern origin. Am J Med Genet A. 2018 Dec;176(12):2850-2857. doi: 10.1002/ajmg.a.40627.
27	Maddirevula S, Alzahrani F, Al-Owain M, Al Muhaizea MA, Kayyali HR, AlHashem A, Rahbeeni Z, Al-Otaibi M, Alzaidan HI, Balobaid A, El Khashab HY, Bubshait DK, Faden M, Yamani SA, Dabbagh O, Al-Mureikhi M, Jasser AA, Alsaif HS, Alluhaydan I, Seidahmed MZ, Alabbasi BH, Almogarri I, Kurdi W, Akleh H, Qari A, Al Tala SM, Alhomaidi S, Kentab AY, Salih MA, Chedrawi A, Alameer S, Tabarki B, Shamseldin HE, Patel N, Ibrahim N, Abdulwahab F, Samira M, Goljan E, Abouelhoda M, Meyer BF, Hashem M, Shaheen R, AlShahwan S, Alfadhel M, Ben-Omran T, Al-Qattan MM, Monies D, Alkuraya FS. Autozygome and high throughput confirmation of disease genes candidacy. Genet Med. 2018 Sep 21. doi: 10.1038/s41436-018-0138-x.
28	Patel N, Alkuraya H, Alzahrani SS, Nowailaty SR, Seidahmed MZ, Alhemidan A, Ben-Omran T, Ghazi NG, Al-Aqeel A, Al-Owain M, Alzaidan HI, Faqeih E, Kurdi W, Rahbeeni Z, Ibrahim N, Abdulwahab F, Hashem M, Shaheen R, Abouelhoda M, Monies D, Khan AO, Aldahmesh MA, Alkuraya FS. Mutations in known disease genes account for the majority of autosomal recessive retinal dystrophies. Clin Genet. 2018 Dec;94(6):554-563. doi: 10.1111/cge.13426.
29	Hamilton EMC, van der Lei HDW, Vermeulen G, Gerver JAM, Lourenço CM, Naidu S, Mierzewska H, Gemke RJBJ, de Vet HCW, Uitdehaag BMJ, Lissenberg-Witte BI; VWM Research Group, van der Knaap MS. Natural History of Vanishing White Matter. Ann Neurol. 2018 Aug;84(2):274-288. doi: 10.1002/ana.25287.

30	Schaffer AE, Breuss MW, Caglayan AO, Al-Sanaa N, Al-Abdulwahed HY, Kaymakçalan H, Yılmaz C, Zaki MS, Rosti RO, Copeland B, Baek ST, Musaev D, Scott EC, Ben-Omran T, Kariminejad A, Kayserili H, Mojahedi F, Kara M, Cai N, Silhavy JL, Elsharif S, Fenercioglu E, Barshop BA, Kara B, Wang R, Stanley V, James KN, Nachnani R, Kalur A, Megahed H, Incecik F, Danda S, Alanay Y, Faqeih E, Melikishvili G, Mansour L, Miller I, Sukhudyan B, Chelly J, Dobyns WB, Bilguvar K, Jamra RA, Gunel M, Gleeson JG. Biallelic loss of human CTNNA2, encoding αN-catenin, leads to ARP2/3 complex overactivity and disordered cortical neuronal migration. Nat Genet. 2018 Aug;50(8):1093-1101. doi: 10.1038/s41588-018-0166-0.
31	Keller R, Chrastina P, Pavlíková M, Gouveia S, Ribes A, Kölker S, Blom HJ, Baumgartner MR, Bártl J, Dionisi Vici C, Gleich F, Morris AA, Kožich V, Huemer M; and individual contributors of the European Network and Registry for Homocystinurias and Methylation Defects (E-HOD), Barić I, Ben-Omran T, Blasco-Alonso J, Bueno Delgado MA, Carducci C, Cassanello M, Cerone R, Couce ML, Crushell E, Delgado Pecellin C, Dulin E, Espada M, Ferino G, Fingerhut R, Garcia Jimenez I, Gonzalez Gallego I, González-Irazabal Y, Gramer G, Juan Fita MJ, Karg E, Klein J, Konstantopoulou V, la Marca G, Leão Teles E, Leuzzi V, Lilliu F, Lopez RM, Lund AM, Mayne P, Meavilla S, Moat SJ, Okun JG, Pasquini E, Pedron-Giner C, Racz GZ, Ruiz Gomez MA, Vilarinho L, Yahyaoui R, Zerjav Tansek M, Zetterström RH, Zeyda M. Newborn screening for homocystinurias: recent recommendations versus current practice. J Inherit Metab Dis. 2018 Jun 15. doi: 10.1007/s10545-018-0213-0.
32	Musa S, Eyaid W, Kamer K, Ali R, Al-Mureikhi M, Shahbeck N, Al Mesaifri F, Makhseed N, Mohamed Z, AlShehhi WA, Mootha VK, Juusola J, Ben-Omran T. A Middle Eastern Founder Mutation Expands the Genotypic and Phenotypic Spectrum of Mitochondrial MICU1 Deficiency: A Report of 13 Patients. JIMD Rep. 2019;43:79-83. doi: 10.1007/8904_2018_107.
33	Al Mutairi F, Alfadhel M, Nashabat M, El-Hattab AW, Ben-Omran T, Hertecant J, Eyaid W, Ali R, Alasmari A, Kara M, Al-Twaijri W, Filimban R, Alshenqiti A, Al-Owain M, Faqeih E, Alkuraya FS. Phenotypic and Molecular Spectrum of Aicardi-Goutières Syndrome: A Study of 24 Patients. Pediatr Neurol. 2018;78:35-40.
34	Anazi S, Maddirevula S, Salpietro V, Asi YT, Alsahli S, Alhashem A, Shamseldin HE, AlZahrani F, Patel N, Ibrahim N, Abdulwahab FM, Hashem M1, Alhashmi N, Al Murshedi F, Al Kindy A, Alshaer A, Rumayyan A, Al Tala S, Kurdi W, Alsaman A, Alasmari A, Banu S, Sultan T, Saleh MM, Alkuraya H, Salih MA, Aldhalaan H, Ben-Omran T, Al Musafri F, Ali R, Suleiman J, Tabarki B, El-Hattab AW, Bupp C, Alfadhel M, Al Tassan N, Monies D,, Arold ST, Abouelhoda M, Lashley T, Houlden H, Faqeih E, Alkuraya FS. Expanding the genetic heterogeneity of intellectual disability. Hum Genet. 2017
35	Marin-Valencia I, Gerondopoulos A, Zaki MS, Ben-Omran T, Almureikhi M, Demir E, Guemez-Gamboa A, Gregor A, Issa MY, Appelhof B, Roosing S, Musaev D, Rosti B, Wirth S, Stanley V, Baas F, Barr FA, Gleeson JG. Homozygous Mutations in TBC1D23 Lead to a Non-degenerative Form of Pontocerebellar Hypoplasia. Am J Hum Genet. 2017.
36	Elsaid M, Chalhoub N, Ben-Omran T, Kamel H, Al Mureikhi M, Ibrahim K, Ross ME, Abdel Aleem A. Homozygous Nonsense Mutation in SCHIP1/IQCJ-SCHIP1 Causes a Neurodevelopmental Brain Malformation Syndrome. Clin Genet. 2017.

37	Shamseldin HE, Kurdi W, Almusafri F, Alnemer M, Alkaff A, Babay Z, Alhashem A, Tulbah M, Alsahan N, Khan R, Sallout B, Al Mardawi E, Seidahmed MZ, Meriki N, Alsaber Y, Qari A, Khalifa O, Eyaid W, Rahbeeni Z, Kurdi A, Hashem M, Alshidi T, Al-Obeid E, Abdulwahab F, Ibrahim N, Ewida N, El-Akouri K, Al Mulla M, Ben-Omran T, Pergande M, Cirak S, Al Tala S, Shaheen R, Faqeih E, Alkuraya FS. Molecular autopsy in maternal-fetal medicine. Genet Med. 2017.
38	Gallego-Villar L, Hannibal L, Häberle J, Thöny B, Ben-Omran T, Nasrallah GK, Dewik AN, Kruger WD, Blom HJ. Cysteamine revisited: repair of arginine to cysteine mutations. J Inherit Metab Dis. 2017.
39	Maddirevula S, AlZahrani F, Anazi S, Almureikhi M, Ben-Omran T, AbdelSalam GMH, Hashem M, Ibrahim N, Abdulwahab FM, Meriki N, Bashiri FA, Thong MK, Muthukumarasamy P, Azwani Mazlan R, Shaheen R, Alkuraya FS. GWAS signals revisited using human knockouts. Genet Med. 2017.
40	Almusafri F, Elamin HE, Khalaf TE, Ali A, Ben-Omran T, El-Hattab AW. Clinical and molecular characterization of 6 children with glutamate-cysteine ligase deficiency causing hemolytic anemia. Blood Cells Mol Dis. 2017
41	Lakhani S, Doan R, Almureikhi M, Partlow JN, Al Saffar M, Elsaid MF, Alaaraj N, James Barkovich A, Walsh CA, Ben-Omran T. Identification of a novel CNTNAP1 mutation causing arthrogryposis multiplex congenita with cerebral and cerebellar atrophy. Eur J Med Genet. 2017.
42	Gramer G, Abdoh G, Ben-Omran T, Shahbeck N, Ali R, Mahmoud L, FangHoffmann J, Hoffmann GF, Al Rifai H, Okun JG. Newborn screening for remethylation disorders and vitamin B12 deficiency-evaluation of new strategies in cohorts from Qatar and Germany. World J Pediatr. 2017.
43	Kambouris M, Thevenon J, Soldatos A, Cox A, Stephen J, Ben-Omran T, AlSarraj Y, Boulos H, Bone W, Mullikin JC . NISC Comparative Sequencing Program, Masurel-Paulet A, St-Onge J, Dufford Y, Chantegret C, ThauvinRobinet C, Al-Alami J, Faivre L, Riviere JB, Gahl WA, Bassuk AG, Malicdan MC, El-Shanti H.Biallelic SCN10A mutations in neuromuscular disease and epileptic encephalopathy.; Ann Clin Transl Neurol. 2016.
44	Tărlungeanu DC, Deliu E, Dotter CP, Kara M, Janiesch PC, Scalise M, Galluccio M, Tesulov M, Morelli E, Sonmez FM, Bilguvar K, Ohgaki R, Kanai Y, Johansen A, Esharif S, Ben-Omran T, Topcu M, Schlessinger A, Indiveri C, Duncan KE, Caglayan AO, Gunel M, Gleeson JG, Impaired Amino Acid Transport at the Blood Brain Barrier Is a Cause of Autism Spectrum Disorder. Novarino G. Cell. 2016.
45	Elsaid MF, Chalhoub N, Ben-Omran T, Kumar P, Kamel H, Ibrahim K, Mohamoud Y, Al-Dous E, Al-Azwani I, Malek JA, Suhre K, Ross ME, Aleem AA. Mutation in noncoding RNA RNU12 causes early onset cerebellar ataxia. Ann Neurol. 2017.

46	Morris AA, Kožich V, Santra S, Andria G, Ben-Omran TI, Chakrapani AB, Crushell E, Henderson MJ, Hochuli M, Huemer M, Janssen MC, Maillot F, Mayne PD, McNulty J, Morrison TM, Ogier H, O'Sullivan S, Pavlíková M, de Almeida IT, Terry A, Yap S, Blom HJ, Chapman KA Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency.. J Inherit Metab Dis. 2017
47	Reis LM, Tyler RC, Weh E, Hendee KE, Kariminejad A, Abdul-Rahman O, Ben-Omran T, Manning MA, Yesilyurt A, McCarty CA, Kitchner TE, Costakos D, Semina EV .Analysis of CYP1B1 in pediatric and adult glaucoma and other ocular phenotypes.. Mol Vis. 2016.
48	Jerber J, Zaki MS, Al-Aama JY, Rosti RO, Ben-Omran T, Dikoglu E, Silhavy JL, Caglar C, Musaev D, Albrecht B, Campbell KP, Willer T, Almuriekhi M, Çağlayan AO, Vajsar J, Bilgüvar K, Ogur G, Abou Jamra R, Günel M, Gleeson JGBiallelic Mutations in TMTC3, Encoding a Transmembrane and TPRContaining Protein, Lead to Cobblestone Lissencephaly.. Am J Hum Genet. 2016.
49	Al-Dewik NI, Morsi HM, Samara MM, Ghasoub RS, Gnanam CC, Bhaskaran SK, Nashwan AJ, Al-Jurf RM, Ismail MA, AlSharshani MM, AlSayab AA, Ben-Omran TI, Khatib RB, Yassin MA. Is Adherence to Imatinib Mesylate Treatment Among Patients with Chronic Myeloid Leukemia Associated with Better Clinical Outcomes in Qatar? Clin Med Insights Oncol. 2016
50	Johansen A, Rosti RO, Musaev D, Sticca E, Harripaul R, Zaki M, Çağlayan AO, Azam M, Sultan T, Froukh T, Reis A, Popp B, Ahmed I, John P, Ayub M, Ben-Omran T, Vincent JB, Gleeson JG, Abou Jamra R. Mutations in MBOAT7, Encoding Lysophosphatidylinositol Acyltransferase I, Lead to Intellectual Disability Accompanied by Epilepsy and Autistic Features. Am J Hum Genet. 2016, (16)30293-2.
51	Elsaadany L, El-Said M, Ali R, Kamel H, Ben-Omran T. W44X mutation in the WWOX gene causes intractale seizures and developmental delay: a case report. BMC Med Genet. 2016, 17(1):53.
52	Anazi S, Maddirevula S, Faqeih E, Alsedairy H, Alzahrani F, Shamseldin HE, Patel N, Hashem M, Ibrahim N, Abdulwahab F, Ewida N, Alsaif HS, Al Sharif H, Alamoudi W, Kentab A, Bashiri FA, Alnaser M, AlWadei AH, Alfadhel M, Eyaid W, Hashem A, Al Asmari A, Saleh MM, AlSaman A, Alhasan KA, Alsughayir M, Al Shammari M, Mahmoud A, Al-Hassnan ZN, Al-Husain M, Osama Khalil R, Abd El Meguid N, Masri A, Ali R, Ben-Omran T, El Fishway P, Hashish A, Ercan Sencicek A, State M, Alazami AM, Salih MA, Altassan N, Arold ST, Abouelhoda M, Wakil SM, Monies D, Shaheen R, Alkuraya FS. Clinical genomics expands the morbid genome of intellectual disability and offers a high diagnostic yield. Mol Psychiatry. 2016
53	Scott EM, Halees A, Itan Y, Spencer EG, He Y, Azab MA, Gabriel SB, Belkadi A, Boisson B, Abel L, Clark AG; Greater Middle East Variome Consortium, Alkuraya FS, Casanova JL, Gleeson JG. Characterization of Greater Middle Eastern genetic variation for enhanced disease gene discovery. Nat Genet. 2016.
54	Okun JG, Gan-Schreier H, Ben-Omran T, Schmidt KV, Fang-Hoffmann J, Gramer G, Abdoh G, Shahbeck N, Al Rifai H, Al Khal AL, Haege G,Chiang CC, Kasper DC, Wilcken B, Burgard P, Hoffmann GF. Newborn Screening for Vitamin B6 Non-responsive Classical Homocystinuria: Systematical Evaluation of a Two-Tier Strategy. JIMD Rep. 2016.

Past Research Grants

Past Research Grants	Impact on patient care
Qatar National Research Fund (2015-2018): USD$ 822,030 Grant for the project "Novel Therapies for Qatari Patients with Homocytinuria (NPRP 7-355-3-088)".	We proposed several mechanism to repair CBS enzyme activity of the Qatar mutation p.R336C with cysteamine, generate a suitable mouse model for CBS deficiency & develop a safe, non-viral (minicircle) vector-based gene therapy for homocystinuria. Testing efficacy of both therapeutic approaches will be done on patients' cells and on a CBS-deficient mouse model. If cysteamine is proven successful, it could be instantly used in a phase 1 clinical study of Qatari homocystinuria patients
Qatar National Research Fund (2013-2018): $1,049,500.00 USD grant for the project "Exome Sequencing in Patients from Qatar and other Arab Countries to Improve Diagnosis of White Matter Diseases. (NPRP 6 -1463-3-351	We identified 22 novel disease-causing genes and characterized the phenotypic diversity among patients. This information led to an improvement in diagnosis and in some an improvement in therapy as we identified the first potentially treatable form of autism with epilepsy
Qatar Innovation Promotion Award (QIPA) (2015-2016): $ 100,000 USD for the project "Development of Absolute quantification kit for CALR types 1 and 2 mutations for Essential Thrombocythemia (ET) and Primary Myelofibrosis (PMF) patients" QIPA1 no-0908-14039.)	Introducing an absolute quantification kit to measure a new biomarker in MPNs to classify cancer patients and monitor Minimal Residual Disease (MRD). (A prototype MDx kit
Qatar National Research Fund (2012-2015): $1,047,989.00 USD grant for the project "Genetic Basis of Autosomal Recessive Disorders in Qatar (NPRP 4-093-3-035)	Our study highlights the importance of using WES as molecular diagnostic approach for discovery pathogenic gene mutations compared to traditional molecular genetic testing. We showed that the WES was successful to identify causal mutations underlying phenotypically complex disorders in ~46% of our patients. The results of this study will help to establish population-specific diagnostic panels, and improve clinical diagnosis and patient management in the country.

Qatar National Research Fund (2012-2015): $1,048,510.80 USD grant for the project "The Identification of Genetic Causes of Autosomal Recessive Intellectual Disability in Qatar: A collaborative research and training program with Boston Children's Hospital. (NPRP 5-175-3-051)".	We performed homozygosity mapping of Autosomal Recessive (AR)-Intellectual disability (ID) loci by high-density SNP microarray genotyping; & identified novel potential deleterious mutation in causative genes using high-throughput DNA sequencing also conducted functional analyses using animal systems and human disease-specific neurons derived from induced pluripotent stem cells and a database of strong candidate genes associated with ID was generated. This study shows that using a powerful molecular approach for discovery pathogenic gene mutations -especially when traditional molecular genetic screening has failed. With decreasing sequencing costs & improving analysis pipelines, we expect this technology to be in widespread clinical use in the near future. It will provide a cost-effective means of making genetic diagnoses in rare and simplify diagnostic strategies to decrease time and cost to diagnosis, allowing us to focus on appropriate treatment and supportive care.
Qatar National Research Fund (2012-2015): $1,049,984.00 USD grant for the project "Brain growth and Development Genes in Qatar (NPRP 4-099-3-039)".	We collected & phenotypically characterized Microcephaly (MIC) syndromes encountered in Qatar; several causative genes that are unique of (MIC) syndromes were identified & validated and a customized panel of gene for our cohort of patients is proposed to apply in clinical service providing. We have published a paper in the American Journal of Medical Genetics A.2014 164A. Title: Whole genome sequencing identifies a novel occluding mutation in microcephaly with band-like calcification and polymicrogyria that extends the phenotypic spectrum. We have also submitted another paper to Nature Genetics.
Qatar National Research Fund (2012-2014): $543,967.04 USD grant for the project "Marriage and Tradition: Exploring the Foundations of Qatari First Cousin (NPRP 4-086-5-007)".	This study helps to improve Qatar's knowledge about the genetic diseases and the disabilities resulting from the consanguineous marriage. The project produced materials and scientific data about this type of marriage and about the cultural and social framework that reproduces and normalizes consanguineous marriage in the region. Through its ethnographic focus, the study also examined the relations and problems that consanguineous couples face in their daily lives, as well as a data set exploring population attitudes about consanguineous marriage. These data help better inform policy makers on social, educational, and public health initiatives that might mitigate the impact of genetic disease in Qatari society.
Research Award, Medical Research Centre, Hamad Medical Corporation (2011-2014): 250,000 QR ($68,000 USD) grant for the project "Homocystinuria: A Common but Treatable Inborn Error of Metabolism in Qatar Treatment and Pathophysiology)"-GC 1023A.	The project objective is towards optimal therapy of homocystinuria patients in Qatar. Arm A) 8 weeks only methionine restriction followed by 8 weeks methionine restriction plus oral betaine therapy. Arm B) 8 weeks only oral betaine therapy, followed by 8 weeks oral betaine therapy plus methionine restriction. Arm C) 8 weeks only vitamin B12 followed by 8 weeks vitamin B12 plus additionally oral folate. Arm D) 8 weeks only oral folate, followed by 8 weeks oral folate therapy plus vitamin B12

Research Award, Medical Research Centre, Hamad Medical Corporation (2011-2014): 250,000 QR ($68,000 USD) grant for the project "Homocystinuria: A Common but Treatable Inborn Error of Metabolism in Qatar Treatment and Pathophysiology)"-GC 1023A.	The project objective is towards optimal therapy of homocystinuria patients in Qatar. Arm A) 8 weeks only methionine restriction followed by 8 weeks methionine restriction plus oral betaine therapy. Arm B) 8 weeks only oral betaine therapy, followed by 8 weeks oral betaine therapy plus methionine restriction. Arm C) 8 weeks only vitamin B12 followed by 8 weeks vitamin B12 plus additionally oral folate. Arm D) 8 weeks only oral folate, followed by 8 weeks oral folate therapy plus vitamin B12
Research Award, Medical Research Centre, Hamad Medical Corporation (2011-2014): 250,000 QR ($68,000 USD) grant for the project "Using of the Medication Event Monitoring System (MEMS) to estimate Imatinib myslate (IM) compliance in chronic myelocytic leukemia (CML))"-GC 1013A.	Medication compliance is a key factor in the treatment of CML, and one of the most important causes for CML suboptimal response, failure to treatment is noncompliance with IM. In Qatar, 45% of CML patient do fail or resist IM according to European leukemia net (ELN) recommendations, therefore; we are expecting that patients are poorly adherent or noncompliant to IM Our strategy takes advantage of recent advances of utilizing electronic monitoring technology (MEMS caps) versus manual pill count & self-report. We propose to measure CML patient-s adherence to IM using medication electronic monitoring system that records the occurrence and time of each bottle opening along with manual pill count & self-report.

Future directions

1. Developing genetics and genomics capabilities, because these technologies are becoming increasingly affordable, already having a major impact on PM and transforming the management of genetic and metabolic diseases. In PM, genomic technologies enable more precise diagnoses or prediction of diseases and response to therapy, so patients can be treated in a more individualized way. Genomic technologies alone will not be enough to deliver precision medicine and public health. Other high throughput molecular diagnostic approaches "omics" and advanced therapies will play an important role in the future of PM.
2. Continue running several basic/translational research projects in our lab in collaboration with well recognized universities and hospitals based on our successful projects, our future research plans are
    - Development of novel therapeutic alternatives, including chaperones and gene therapy approaches for metabolic and genetic diseases.
    - Regenerating Central Nervous System of white matter using induced pluripotent stem cells.
    - Development of Genomic Newborn Screening approach
    - Development of a comprehensive gene panels (Qatar Mendeliome assay)
    - Clinical and molecular genetics characterizations of metabolic and genetic disorders
    - Establish of metabolic and genetic patients' cell lines representing patients' phenotypes
    - Development of innovation techniques/methods for metabolic and genetic patients
    - Participate in International Clinical trials and PI initiating clinical trials for metabolic and genetics
3. Expand the genetic service and implement a development plan for new facilities to ensure a better patient experience across the country as well as to sustain and the delivery of high-quality clinical service to meet increasing patients' needs/demands at the right time and place.
    - Priority 1 –Medical Genetics Service workforce
    - Priority 2 - Wider healthcare workforce
    - Priority 3 – Recruitment and retention of health care system and academic genomics workforce
4. Promote clinical education and translational research within Genetics such that we become a major national centre for education and research in collaboration with our academic partners.
    - Priority 1 - Integrating Current Infrastructure
    - Priority 2 - Information Technology
    - Priority 3 - Clinical Data for Research

References

- Al-Bader, S. B., Alsulaiman, R., Bugrein, H., Omran, T. B., Abbaszadeh, F., Bakheet, N., . . . Ghazouani, H. (2018). Cancer genetics program: Follow-up on clinical genetics and genomic medicine in Qatar. Mol. Genet. Genomic Med., 6(6), 865–872. doi:10.1002/mgg3.534
- Al-Dewik N, Al-Mureikhi M, Shahbeck N, Ali R, Al-Mesaifri F, Mahmoud L, Othman A, AlMulla M, Sulaiman RA, Musa S, Abdoh G, El-Akouri K, Solomon BD, Ben-Omran T. Clinical genetics and genomic medicine in Qatar. Mol Genet Genomic Med. 2018 Sep;6(5):702-712. doi: 10.1002/mgg3.474.
- A. L.-Dewik, N. I., & Qoronfleh, M. W. (2019). Genomics and Precision Medicine: Molecular Diagnostics Innovations Shaping the Future of Healthcare in Qatar. Advances in Public Health, 2019. doi:10.1155/2019/3807032
- Ginsburg GS, F. E., Balatbat C, Flott K, Prestt J, Dzau V. (2016). PRECISION MEDICINE A GLOBAL ACTION PLAN FOR IMPACT.
- Ismail, S., Al Sulaiman, R., Fakhro, K., Yousri, N., Saad, M., Afifi, N., . . . Aleem, A. A. (2020). Genomic and National Databases: Rare Diseases and Precision Medicine Perspectives: Panel Discussion. Hamad bin Khalifa University Press (HBKU Press), 2020(2), 24. doi:10.5339/qproc.2020.NMD.24

Precision Medicine In Clinical Imaging Department

Utilization of Artificial Intelligence techniques in Clinical Imaging Department

Adaption of automated solution and growing trends of Machine Learning is a must to improve the patient care and to deliver the care in productive manner and HMC clinical imaging department-initiated plans on this to align with these Innovative trends. This annual report is to update the current departmental activities on Artificial Intelligence.

Workshop:

The department conducts regular workshops to understand the needs and requirements around Artificial Intelligence projects

Clinical Imaging Precision Medicine and Artificial Intelligence Committee (CIPAC)

A committee is formed specifically with the purpose to provides oversight and acts as Advisory committee. It determines the review strategy, monitors, and helps implementation of PM/AI and provides assurance that the implementation is being properly assessed, controlled, and mitigated.

Educational sessions and Demos

Department arranged multiple educational sessions and demos on Artificial Intelligence. Education sessions helps the team to explore more on Machine Learning algorithm and the possibilities of Artificial Intelligence.

Trial based AI integrated solution

Recently department used two AI application on trial base, and the purpose of integration is to get the radiologist feedback:

1. Siemens AI rad application; mainly for the Chest image analysis and this application still in use. Modalities are integrated to send the Chest CT and X-ray images.
2. Koios US breast Analyzing tool; directly integrated with PACS which helps the radiologist direct launch of AI tool from PACS.

In addition to these two the department has plans to introduce a trial for Koios US Thyroid Analyzing tool.

Research projects

The clinical imaging department conducted several projects in the field of AI. Some of these projects are conducted inside the department by clinical imaging staff and others in collaboration with other departments and facilities. Below you find a table summarizing the projects conducted in 2021:

AI Related Research and Case Studies			
SN	**Category**	**Title**	**Author**
1	Research	Training of AI Algorithm for Mammographic Interpretation	Dr. Mohamad Hajaj, Dr. Hiba Esmayil
2	Research	Development and Evaluation of an Infrastructure to Generate Patient-Scientific Anatomical Holograms to Support Surgical Planning and Education at HMC	Dr. Shidin Balakrishnan
3	Research	Towards Developing a Platform for Fusion of Preoperative CT and Intra-Operative Ultrasound Images for Hepato-biliary Procedures in Interventional Radiology: A Complete Visualization In Augmented Reality	Dr. Sarada Prasad Dakua Academic Research Scientist Department of Surgery, HMC
4	Research	Identifying novel diagnostic and predictive biomarkers for breast cancer in Qatar	Dr. Eyad Elkord (Qatar Biomedical Research Institute, Dr. Salahddin Gehani (HMC Site PI)
5	Case Study	Barriers To Artificial Intelligence In Radiology Practice: The optimism and pessimism.	Dr. Anirudh Venugopalan Nair
6	Research	Smart system for automatic assessment of bioprosthetic heart valve designs for transcatheter aortic valve replacement therapy	Qatar University Lead PI Dr. Huseyin Cagatay Yalcin HMC Heart Hospital Lead PI Dr. A.Rahman Dekhayel M H Alnabti
7	Research	Computer Vision and Machine Learning: Empowering the diagnostic capability of the Radiology Tests for Musculoskeletal Injuries	Dr. Khalid Mukhtar, Specialist Orthopedics Surgeon, #026365

Precision Medicine In Dlmp

Department of Laboratory Medicine and Pathology (DLMP)

DLMP is a large internationally accredited modern medical laboratory with a workforce of close to 1000 personnel comprising pathologists, clinical scientists, technical and support staff. It operates 24/7 and annually performs over 23 million laboratory tests. There are 29 sections (laboratories) across the organization including point of care testing and Blood Bank services supporting HMC and other regional hospitals and clinics in Qatar. The laboratories have maintained compliance to international accreditations standards such as, the Joint Commission International (JCI, since 2006), the College of American Pathologists (CAP, since 2014), and the American Society of Histocompatibility and Immunogenetics (ASHI, since 2019), etc.

Over the past two decades various DLMP laboratories have introduced a wide range of tests either directly related to or in support of precision medicine (PM) services in HMC. The following pages provide a summary of the services that are currently on offer.

1. Precision Medicine Diagnostics Section – Anatomic Pathology

The Precision Medicine Diagnostics Section is heavily involved in cancer diagnosis and management. Immunohistochemistry and in situ hybridization (i.e. two branches of precision medicine diagnostics) are essential modalities involved in tumor biomarkers evaluation and are vital in cancer diagnosis, treatment and prediction of behavior and prognosis. Almost every cancer case specimen undergoes testing by Immunohistochemistry /ISH to make proper and confident diagnosis, to decide which modality of treatment should the patient take, to direct the oncologists toward specific drugs to treat cancer cases and to predict prognosis in some of these patients. Recently we started to play a pivotal role in immunotherapy as a treatment for cancer by introducing the revolutionary testing of (PD-L1).

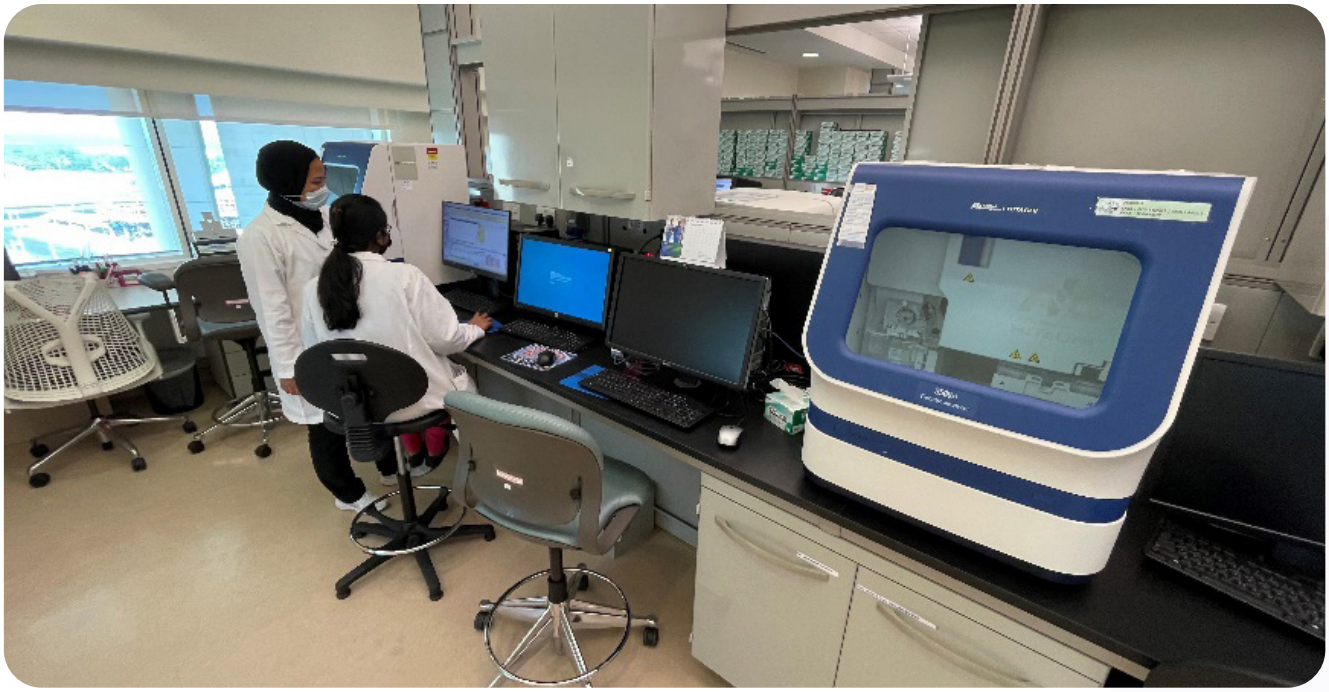
Below are some examples of tests performed at Precision Medicine Diagnostics Section with the corresponding targeted therapy.

Tumor Biomarker	Indication / Tumor type	Drug
Hercep Test pharmDx	Breast cancer GEJ adenocarcinomas	Herceptin trastuzumab
PD-L1 22C3 pharmDx	HNSCC, NSCLC & GEJ adenocarcinomas	Keytruda Pembrolizumab
ALK 5A4	NSCLC	Alectinib, Crizotinib
CD117, c-kit	GIST	Imatinib
MMR/MSI	Colorectal cancers endometrial cancer	Pembrolizumab
CD20	Lymphoma	Imatinib
Estrogens	Breast Cancer	Tamoxifen, Anastrazol

2. Diagnostic Genomic Division (DGD)

The Diagnostic Genomic Division of Department is the 2018 merger of two well-established HMC laboratories; cytogenetics laboratory (established in 1982) and molecular genetics laboratory (established in 2002). The Division offers comprehensive and integrated services in the following five areas of Cytogenetics & Molecular Cytogenetics, Molecular Genetics, Haemato-Oncology, Hereditary Cancers & Rare Diseases, and Solid Tumors. The Division is well equipped with conventional as well as state-of-the-art technologies for DNA and RNA extraction and analysis from blood, CVS, amniotic fluid, soft tissue, bone marrow, and FFPE; tissue culturing; karyotyping; Fluorescent In Situ Hybridization (FISH); array CGH; Real-Time PCR; Fragment Analysis; Sanger Sequencing; and Next Generation Sequencing (NGS). The NGS services are currently for gene panels and the laboratory is in the final stages of introducing whole exome sequencing (WES).

The following DGD sections offer services that are related to Precision Medicine (PM) at HMC. Additionally, the Division is involved in a translational research project in collaboration with Qatar Genome Program and Qatar Biobank, using genome data of 6,000 Qatari nationals to identify the Loss-of-Function variants of this population. So far, we have identified >100 putative pathogenic variants that are of diagnostic value, some of which had not been reported previously.



1. Haemato Oncology Section

Towards Precision Medicine in Blood Cancers

Precision medicine offers a new approach to disease management by identifying genetic subsets of patients to match to treatment strategies that are most likely to be effective. For the clinical management of cancer patients this involves a comprehensive genomic analysis of DNA to identify patient specific biomarkers driving disease that can be therapeutically targeted.

Precision medicine strategies for the management of blood cancers are well embedded in clinical practice at HMC. Genomic profiling reports are routinely incorporated into a multidisciplinary diagnosis of leukemia and allow for rationale therapeutic decisions to be made in relation to the choice of drug prescribed.

Precision Medicine for Blood Cancer at HMC

Genomic profiling of Acute Myeloid Leukemia (AML): AML accounts for 73% of all adult acute leukaemia cases in Qatar. It is a complex dynamic disease demonstrating genotypic and phenotypic diversity which can evolve over time. Until recently the clinical standard of genetic investigation of AML involved conventional cytogenetics however even within cytogenetically defined risk groups AML is highly heterogeneous in clinical behaviour and outcome. Next Generation Sequencing is now offered as part of the routine workup of new AML presentations to provide a comprehensive analysis of 66 myeloid associated genes. Examples of how this information can impact on clinical management are illustrated in the attached poster presented at the 2nd Haematology Symposium in Doha in 2019.

Monitoring minimal residual disease (MRD) in CML: Molecular monitoring of BCR-ABL1 transcript levels following treatment with tyrosine kinase inhibitors (TKIs) is central to the effective clinical management of patients with CML. Evaluation of the depth and durability of response to treatment is assessed using standardized real time quantitative PCR (RT-qPCR) to guide clinical management following best practice recommendations from the National Comprehensive Cancer Network (NCCN) and the European LeukemiaNet expert networks.

Managing patients in this way allows for signs of poor adherence or resistance to treatment to be detected early and allow for effective clinical intervention. Together with the ability to accurately define long term sustainable deep molecular responses the chances of a successful outcome for all patients can be maximized. The clinical impact of MRD monitoring of CML patients at NCCCR is illustrated in the attached poster presented at the MRC annual research day in 2017 when 100 patients had been analysed. The data provides an evidence based framework for the routine use of genomic analysis to support personalized treatment strategies and informed clinical decision making at Hamad Medical Corporation. In 2021 DLMP are now actively monitoring 247 CML patients on targeted therapies. Because CML patients treated with targeted therapies at NCCCR have undergone long term response monitoring there is now the potential to identify patients who may be suitable to stop therapy and be considered as “cured”.

2. Solid Tumor Section

In the current genomic era of medicine, it is possible to offer 'personalized medicine or precision medicine' (PM) by identifying molecular biomarkers for each patient, and accordingly select the most effective targeted therapy. The PM approach has replaced the era of one-size-fits-all approach for treatment selection.

DLMP and, in particular, the Solid Tumor Section of the DGD, offers the most needed services for Qatar's patient population affected with different cancer types. Various molecular biomarkers are used for pre-disposition (likely developing disease), predictive (treatment selection), diagnostics (confirmation of the disease), prognostics (indication of disease development) or monitoring (follow up) purposes. For detection of somatic solid tumor biomarkers, the section utilizes advanced technology such as real-time PCR and Next Generation Sequencing (NGS) for screening over 50 genes. NGS is a high throughput technology for DNA and RNA sequencing in the tumor site for detection of most frequent mutated genes and fusion drivers in a single reaction. We are working to expand the gene number in one panel to cover over 350 genes.

The following are examples of biomarker tests at the Solid Tumor Section:

Cancer Type	Genes	Benefits
Colon	KRAS, NRAS, BRAF	Predictive biomarkers
Lung	EGFR	Predictive for TKI
GIST (Gastrointestinal somatic tumor)	KIT, PDGFRA	Predictive biomarkers
Glioma	IDH1, IDH2	Diagnostic biomarkers

3. Cytogenetic & Molecular Cytogenetic Section

Cytogenetics studies using molecular cytogenetic techniques like FISH provides essential diagnostic, prognostic, and therapeutic information for cancer precision medicine and research. By virtue of its ability to detect drug targets, the FISH technique is a convenient method to support the practice of personalized medicine. Numerous examples can be found in hematological malignancies and solid tumors. In chronic lymphocytic leukemia (CLL), risk stratification can be undertaken by a FISH panel and coupled with determination of IgVH mutation status or expression of ZAP70 and CD38. The presence of del(11q) and del(17p) is often associated with a poor prognosis, del(13q) or a normal karyotype is associated with low-risk disease, and the presence of trisomy 12 may be considered a marker of intermediate risk. Likewise, recent international guidelines recommend a minimum FISH panel for the detection of t(4;14), t(14;16) and del(17p) which recognizes the high risk category in myeloma. The interphase FISH test should be performed on a bone marrow sample for analysis of genetic aberration. First reported in 2007, the EML4- ALK gene fusion is a new molecular aberration in non-small cell lung cancer (NSCLC) and occurs as a result of a small inversion within chromosome 2p.(43) The fusion gene is oncogenic and represents a novel molecular target in NSCLC. Patients tend to be younger, are more likely to be male, have never smoked or are light smokers and are double negative for EGFR and KRAS gene mutations.EML4-ALK fusion may be detected by a dual-colour split-apart FISH probe that targets the ALK gene. Patients harboring EML4-ALK gene fusion are candidates for clinical trials of ALK inhibitor therapy. Below is a list of FISH testing services available In Cytogenetic laboratory, Diagnostic Genomic Division at HMC. These services support clinical decision making in cancer patient care.

FISH testing for cancer in the Cytogenetic Section	
Acute Lymphoblastic Leukemia (B-ALL) - FISH Panel	Acute Lymphoblastic Leukemia (T-ALL) - FISH Panel
Acute Myeloid Leukemia (AML) - FISH Panel	B-Cell Lymphoma
(BCR/ABL(DF) t(9;22)(q34;q11.2	Burkitt Lymphoma (BL) - FISH Panel
Chronic Lymphocytic Leukemia (CLL) - FISH Panel	Chronic Myelogenous Leukemia (CML) - FISH Panel
Diffuse Large B-Cell Lymphoma (DLBCL) - FISH Panel	Extra-nodal MZL - FISH Panel
Follicular Lymphoma (FL) - FISH Panel	Hairy Cell Leukemia (HCL) - FISH Panel
Hyperoeosinophilic Syndrome	Mantle Cell (MCL) - FISH Panel
Marginal Zone - FISH Panel	Marginal Zone of MALT Lymphoma
Multiple Myeloma (MM) - FISH Panel	(Myelodysplasic Syndrome Panel (MDS
Myeloproliferative Neoplasms (MPN) - FISH Panel	PML/RARA(DF) t(15;17)(q22;q21.1)-APL
T-Cell Lymphoma	Transplant Monitoring
Waldenstrom's Macroglobulinemia (WM) - FISH Panel	1p/19q
ALK	FFPE Burkitt Lymphoma
Ewing Sarcoma	HER2
MDM2	Synovial Sarcoma
ROS1 FFPE	

4. Hereditary Cancer and Rare Diseases Section

Pathogenic or likely pathogenic variants in BRCA1 and BRCA2 (together known as BRCA genes) account for most of hereditary breast and ovarian cancer syndromes (HBOC). A woman harboring such BRCA variant has a respective cumulative risk of 45%–66% and 11%–41% for developing breast or ovarian cancer by age 70 years. Pathogenic BRCA genes also confer predisposition to prostate and pancreatic cancers as well as melanoma. Due to the high lifetime risk of developing breast and ovarian cancers in individuals with BRCA pathogenic variants, the early adoption of preventative care and surveillance strategies is very important.

BRCA genes are tumor suppressors that are involved in DNA double-strand breaks repair through a homologous recombination repair (HRR) mechanism. Cells with defective BRCA1 or BRCA2 cannot perform HRR efficiently. PARP inhibitors exploit synthetic lethality by trapping poly (ADP-ribose) polymerase (PARP) on the DNA, creating a double strand break lesion that is repairable through the HRR pathway in BRCA-functioning normal but not in BRCA1- or BRCA2-deficient cells. Approved PARP inhibitor therapy has provided major benefit for newly diagnosed BRCA positive ovarian cancer and improved progression-free survival in advanced ovarian, breast, prostate and pancreatic cancers containing BRCA pathogenic variants.

Diagnostic BRCA analysis is therefore a powerful approach to define the subpopulations that are most likely to benefit from personalized therapeutic interventions. These benefits as well as increased public awareness about breast cancer has led to a continuous increase in BRCA testing over the last two decades.

The Hereditary Cancer and Rare Diseases Section of the DGD has offered diagnostic, predictive, and confirmation BRCA analyses by means of Next Generation Sequencing (NGS) and Sanger sequencing for > 350 patients and their unaffected family members per annum that are referred through Cancer High Risk Clinic at NCCCR, since 2015. To identify the underlying genetic predisposition in BRCA-negative HBOC, we were awarded a research grant titled "Identification of genes predisposing to BRCA1/2- negative hereditary breast and ovarian cancers (HBOC) in Qatar- Towards precision treatment and prevention" by Hamad Hospital's Medical Research Council (MRC).

This section will soon start its diagnostic services for other inherited cancers as well as rare diseases through whole exome sequencing (WES). Until recently, DNA testing for disorders with underlying genetic component was performed by testing for a known single gene or a group of genes that are associated with those disorders. However, when the genetic cause of disease is unknown, but the clinical phenotypes of a patient suggests a Mendelian disorder, or when a disorder is too genetically heterogenous to be tested by a single gene or even gene panel, WES becomes an ideal tool for causative gene discovery. For patients with rare inherited disorders WES provides a diagnosis-predicated precision medicine, which can reduce their diagnostic odyssey and provide vital information to improve their clinical management, in seriously ill newborns, it may be life-saving.

5. Molecular Genetics Section

The Molecular Genetics Section of the Diagnostic Genomic Division is the diagnostic service provider for hereditary conditions prevalent in Qatar's population and offers tests in areas of prenatal (e.g. for beta-thalassemia and sickle cell disease) and postnatal diagnosis (e.g. Fragile X and Y-chromosome microdeletions) as well as premarital genetic screening (e.g. Cystic Fibrosis and Spinal Muscular Atrophy). With rapid technological advances in the field of Precision Medicine (PM) it is now possible to accurately diagnose numerous genetic disorders, for some of which new therapies are being developed. A recent example is Spinal Muscular Atrophy for which gene therapy is now a reality and although not yet curable, management of the symptoms by any of the three FDA approved drugs is highly effective.

The section is also involved in a translational research project in collaboration with Qatar Genome Program (QGP) and Qatar BioBank (QBB), using genome data of 6,000 Qatari nationals to identify the Loss-of-Function (LOF) variants of this population. So far, we have identified >100 putative pathogenic variants that are of diagnostic value some of which had not been reported previously.

In order to increase its capacity for molecular diagnosis of a large number of diseases, the Section is also collaborating with Qatar Genome Program and Qatar BioBank to develop QChipPMv2, which is a SNP array for detection of > 50,000 known pathogenic variants associated with a wide variety of genetic disorders. QChipPMv2 is currently undergoing clinical validation and once in service, it will be used as the first-tier testing of pediatric and adult patients prior to whole exome sequencing.

3. Hematopathology Division

The hematopathology division plays a crucial role in the diagnosis and management of various haematological neoplasms. Flow cytometry is a multiparametric data-gathering state-of-the-art technology that can simultaneously analyse several characteristics of the cells and thus can determine the biomarker signature of the individual cell. This places the flow cytometry as an important tool in precision medicine through:

1. Early and quick diagnosis of the hematological neoplasm including leukemia, lymphoma and plasma cell neoplasm. This will determine the treatment course that is tailored for each patient according to the diagnosis.
2. Detection of druggable CD markers: Detection of specific CD markers (antigen) on the cells will direct the use of the appropriate specific monoclonal antibody for treatment (targeted immunotherapy). An example of these CD markers that are processed in our flow cytometry laboratory are CD20, CD79b, CD38, CD22, CD33.
3. Detection of prognostic markers that predict response to treatment and prognosis (ex CD49d, CD38).
4. Monitoring of response to therapy and in detection of residual disease

4. Histocompatibility & Immunogenetics Section

The goal of most of our testing is to stratify the immunological risk associated with any given donor recipient pairs which guides the rigor of pharmacologic immunosuppression as well as different modalities of management.

The tests currently on offer are:

- HLA Flow Crossmatch tests: HLA Flow Crossmatch-Recipient and HLA Flow Crossmatch-Donor tests
- HLA Donor Specific Antibodies test
- HLA-B*5701 test
- Any other HLA disease association hypersensitivity test
- STR Chimerism Post BMT test
- cfDNA test (under validation process)

5. Transfusion Medicine Section

In Transfusion Medicine Section applies Precision Medicine through selecting specific donor phenotypes for the Rh and Kell system to a specific category of patients who may need frequent transfusions; to prevent the formation of Alloantibodies.

The patient categories in which specific donor phenotypes are matched include:

1. Females of child bearing age (pregnant and not pregnant).
2. All Sickle cell disease and Thalassaemia patients.
3. All patients with Haematopoietic neoplasms including Leukaemia, Lymphoma, Myelodysplastic states, Myeloproliferative states (Polycythemia vera, Thrombocythemia, Myeloid neoplasms/Myelofibrosis). In addition to Aplastic anaemia and Congenital anaemias.
4. Haematpoietic stem cell Transplant recipients.

The specific Rh and Kell phenotypes that we match are to select:

1. R1R1 packed RBC for R1R1 patients.
2. rr Packed RBC for rr patients.
3. E negative Packed RBC for R1r patients.
4. K negative for K negative patients.

6. Metabolic Medicine Section

The Metabolic Medicine Section is the service provider for the National Newborn Screening (NBS) Program which involves screening each newborn infant for more than 80 metabolic, endocrine, hematologic and other genetic disorders for early detection and intervention in the State of Qatar. This service has greatly improved the lives of hundreds of affected children (both Qatari and non-Qatari). Screening is performed by pricking infant's heel to get blood on a filter paper called Guthrie card (also known as dried blood spot/DBS) in healthcare facilities.

Recent advances in Laboratory Medicine and Metabolomics with tandem Mass Spectrometry (MS/MS) has revolutionized the NBS screen to test for an array of biochemical metabolites from a 3.2 mm DBS punch. With advanced technology and research, it has been possible to extract DNA from Guthrie cards. DNA testing has been primarily used as second tier test on DBS for conditions such as Cystic Fibrosis, Sickle Cell Disease and has been expanded as part of diagnostic work up for other genetic disorders diagnosed through NBS.

In HMC, both the Metabolic Laboratory and Genomics Laboratory are working collaboratively in adapting new methodologies and performing biochemical and genetic correlation in genetic disorders. There is ongoing research worldwide to see whether whole genome or exome sequencing for healthy newborns has a place in NBS programs. With decrease in costs for DNA testing, there is debate whether metabolic NBS should be replaced by genomic NBS in the future. While genomic NBS as part of Precision Medicine can increase the number of disorders identified in Newborns, the generalization of its practice raises a number of important ethical issues as well that will need to be addressed.

7. Virology Section

Virology has developed from a point where there were few if any effective antiviral drugs to the present time where antiviral agents and monoclonal antibody therapies coupled with test directed immune modulation are now available for a wide range of viral infections. While there are no specific companion diagnostics in virology, the service provides molecular and serology diagnostics for a wide range of viral and atypical bacterial infections that help initiate intervention in a number of clinical scenarios. For example, in the transplant setting antiviral prophylaxis and pre-emptive therapy options are available to prevent CMV infections and treatment options are also available where breakthrough infections take place. Post transplant monitoring for BKV viraemia helps guide interventions to reduce immune suppression and to sustain renal graft function. Confirming EBV loads in Post Transplant Lymphoproliferative Disorder likewise direct therapeutic immune modulation and therapeutic options for recovery. In Qatar the incidence of brucellosis is high by international standards and a complete array of antibodies are available for acute, past and atypical presentations.

The HMC Virology laboratory is also a WHO National Influenza Center and provides a surveillance screening service for seasonal and novel influenza viruses. In collaboration with the Crick Institute in London viruses are sequenced to provide phylogenetic typing for strain selection and vaccine manufacture. This facility also provides diagnostic services for a broad range of respiratory viruses including the new SARS-CoV-2 coronavirus. During the pandemic virology has worked with Qatar Biobank and Qatar University to provide a variant sequencing service to monitor the spread of SARS-CoV-2 viral strains in the country.

For these services Virology provides a range of Quantitative Realtime Polymerase Chain Reaction (qRT-PCT) assays – both singleplex and multiplex, and a range of antibody assays including IgG and IgM ELISAs, as well as Western Blot and avidity antibody assays for patient management.

Sequence Based Services

These are being developed for delivery within HMC and will use the Oxford Nanopore MinIon and Illumina next generation sequencing platforms. Currently services are provided though collaborations with a number of institutes including - the Mayo Clinic, Qatar University and The Crick Institute in London. The services provided include HIV genotyping, Influenza phylogenetic typing; SARS-CoV-2 variant genotyping; antiviral resistance typing.

Examples of assays available in Virology Section

Transplant Monitoring	Vaccine Preventable Infections	Human Immunodeficiency Virus
Cytomegalovirus DNA qRT-PCR	Mumps - IgG and IgM assays, qRT-PCR	HIV RNA qRT-PCR, Western Blots, Genotyping
Epstein-Barr virus DNA qRT-PCR	Measles - IgG and IgM assays, qRT-PCR	
Adenovirus DNA qRT-PCR	Rubella - IgG and IgM assays, qRT-PCR	
BK virus DNA qRT-PCR		
HHV6 DNA qRT-PCR		

Precision Medicine In Pharmacology

Pharmacogenetic And Precision Medicine in Pharmacy

The role of pharmacy in Precision Medicine mainly in three domains:

A. Pharmacogenomics
B. Targeted Therapy
C. Gene Therapy

A. Pharmacogenomics Existing and Proposed Projects 2020:2025

Lead PI: Dr. Moza Al Hail (Executive Director of Pharmacy-HMC)

Projects being conducted in collaboration with **"The Qatar Genome Programmed (QGP)"**:

1. Personalization of Clopidogrel Antiplatelet Therapy in Patients undergoing

Percutaneous Coronary Intervention in Qatar

- Timeline: October 2020- Dec 2023
- Initiation of a pilot clinical research projects along with Qatar genome and Qatar university
- Pilot Study Done On 300 patients from 2016-2020, project completed
- study proposal submitted to MRC
- Collaboration with Heart hospital, Qatar genome and Qatar biobank (QBB)
- Partial funding by QGP

2. Influence of Pharmacogenetics on The Clinical Outcome of Qatari Patients

Breast Cancer Treated with Anthracycline/Cyclophosphamide-Based Chemotherapy.

- Timeline: March 2020- Dec 2023
- Finalizing research study and submitted to MRC
- Collaboration with NCCCR, Qatar genome (QGP) and Qatar biobank (QBB)
- Submitted to MRC IRGC-07-JI-20-753
- To be funded by HMC Research center

3. Personalized Warfarin Pharmacogenetics therapy

Clinical implementation of pharmacogenetic genotype-guided dosing of warfarin in patients with heart valve replacement in Qatar

- Timeline: Dec 2020- Dec 2023
- Initiation of a pilot clinical research projects along with Qatar genome and Qatar university
- study proposal in the submitting phase to MRC
- Collaboration with Heart hospital, Qatar genome (QGP) and Qatar biobank (QBB)
- Pilot Study Done On 300 patients from 2016-2020
- Partial funding by QGP

4. **Preemptive Genetic Testing for Statin Personalized Prescription: Potential in the Prevention of Statin-Related Myopathy)**
   - Timeline: Dec 2020- Dec 2023
   - Finalizing research proposal
   - Collaboration with HMC, Qatar genome and Qatar biobank (QBB)
   - To be submitted to MRC
   - Partial funding by QGP

5. **Assessment of healthcare professionals' knowledge, attitudes, and barriers of clinical pharmacogenetic implementation in HMC, Qatar**
   - Timeline: November 2020: Dec 2021
   - Finalized research proposal
   - Submitted to MRC
   - To be funded by HMC Research center

6. **Assessment of Patient Perceptions of pharmacogenetic Testing in Qatar**
   - Timeline: November 2020: Dec 2021
   - Writing the research proposal
   - To be funded by HMC Research center

Projects being conducted in collaboration with Hamad Bin Khalifa University (HBKU):

1. **Pharmacogenetic of anti-depressant and antipsychotic medications**

"The impact of antidepressant pharmacogenetics on clinical outcome of Qatari patients with depression and anxiety disorders"

- Finalizing research study and submitted to MRC
- Collaboration with Mental health hospital, HBKU and Qatar genome
- Submitted to MRC IRGC-07-JI-20-753
- To be funded by HMC Research center

In collaboration with Qatar university:

1. **Personalized care for Qatari patients with genetic predisposition to hypercholesterolemia: better prediction, diagnosis and management**
   - Timeline: Dec: Dec 2023
   - Awarded by PPM, QGP
   - Submitted and approved by MRC MRC-03-20-852
2. **The Impact of CYP2C19 Genetic Mutation and Non-Genetic Factors on the Incidence of Bleeding in patients treated with Clopidogrel in Qatar**
   - Timeline: 2014-2020
   - Status: published
3. **The effect of genetic and nongenetic factors on warfarin dose variability in Qatari population Pharmacy department and Qatar university**
   - Timeline: 2014-2020
   - Status published

D. Targeted Therapy

Implementation of Personalized Medicine in Cancer patients in NCCCR:

- Application of Personalized Medicine by treating patient with more than 30 targeted Drug therapies in NCCCR
- Some examples of Cancer types that are treated with targeted therapy in HMC:

1. Breast cancer: HER2 -neu, PI3K, ER, PR, PD-L (in T-cell), BRCA genes
2. Chronic myeloid leukemia (CML): BCR-ABL.
3. Colorectal cancer: EGFR, KRAS gene wild type, VEGF, Mismatch Repair (MMR) Proteins and BRAF gene,
4. Lung cancer: EGFR, ALK and ROS genes.
5. Melanoma: BRAF gene
6. Ovarian Cancer: BRCA genes

October 2020 Implementation of Breast cancer Pharmacy Led Clinic

Publications in targeted thereby precision medicine:

1. Elazzazy S, Gul Zar A, "Cetuximab induced acute cardiotoxicity, a rare but severe side effect". Journal of Case Reports in Practice (JCRP) 2013; 3: 73- 75
2. Aasir M. Suliman, Shaza A. Bek, Mohamed S. Elkhatim, Ahmed A. Husain, Ahmad Y. Mismar, M. Z. Sharaf Eldean, Zsolt Lengyel, Shereen Elazzazy, Kakil I. Rasul ;Nabil E. Omar. "Tuberculosis following programmed cell death receptor-1 (PD-1) inhibitor in a patient with non-small cell lung cancer. Case report and literature review". Cancer Immunology, Immunotherapy, Oct. 2020. doi.org/10.1007/s00262-020-02726-1
3. Omar NE, El-Fass KA, Abushouk AI, Elbaghdady N, Barakat AEM, Noreldin AE, Johar D, Yassin M, Hamad A, Elazzazy S, Dermime S. "Diagnosis and Management of Hematological Adverse Events Induced by Immune Checkpoint Inhibitors: A Systematic Review". Front. Immunol. Oct. 2020. 11:1354. doi: 10.3389/fimmu.2020.01354
4. Elmalik H.H, Elazzazy S, Salem K.S, Bujassoum S, "A Grave Outcome of Posterior Reversible Encephalopathy Syndrome in a Patient Receiving Avastin (Bevacizumab) for Metastatic High-Grade Serous Ovarian Cancer", Case Rep Oncol 2015; 8:290-294, doi: 10.1159/000435805
5. K. Rasul, A. Elessam, S. Elazzazy, R. Ghasoub, A. Gulied "Can we use Sorafenib for advanced Hepatocellular Carcinoma (HCC) Child Pugh B?", The Gulf Journal of Oncology, issue 17, Jan 2015. PubMed ID: 25682457
6. Salih F, Calaud F, Rasul K, Elmistiri M, Elhadi N, et al. Oncotype DX RS correlation with clinic pathologic risk factors and chemotherapy. Retrospective study in early-stage ER positive breast cancer. Ann Breast Cancer. 2018; 1: 1005.
7. Mudawi D, Kassem N, Yassin MA, Abdulqadir N, (2018) Cutaneous manifestations of Nilotinib. Int J Hematol Blo Dis 3(1).13.
8. R Ghasoub , A Albattah, S Elazzazy , R Alokka, A Nemir, I Alhijji, R Taha, "Ibrutinib-associated sever skin toxicity: A case of multiple inflamed skin lesions and cellulitis in a 68-year-old male patient with relapsed chronic lymphocytic leukemia – Case report and literature review", J Oncol Pharm Practice 0(0) 1–5, (2019), DOI: 10.1177/1078155219856422.
9. El-Hadi Omar, N., Nasser, S., Gasim, M., Khanna, M., Nashwan, A. J., Feilchenfeldt, J. W., Rasul, K., & Hamad, A. (2019). CLO19-045: Safety of Immune Checkpoint Inhibitors in Cancer Patients with Microsatellite Instability-High (MSI-H) Status: An Experience from Qatar, Journal of the National Comprehensive Cancer Network J Natl Compr Canc Netw, 17(3.5), CLO19-045-CLO19-045. Retrieved Dec 15, 2019, from

https://jnccn.org/view/journals/jnccn/17/3.5/article-pCLO19-045.xml.

C. Role of pharmacy department in personalized medicine in rare diseases (Gene Therapy)

Gene therapy mediations reviewed by the pharmacy Executive office SPINRAZA® (nusinersen): used to treat spinal muscular atrophy (SMA) in pediatric and adult patients.

A. Precision medicine in the last the last 7 years in the HMC Pharmacy Department

May 2018: with attending of Dr Asama Al Thani and Dr Moza AL HAIL Establishment of HMC pharmacy department /QGP, Pharmacogenetics Working Group:

- Regular meetings are held to establish the pharmacogenetic in HMC
- Provide the list of most prescribed medications in Qatar to help in establishment the pharmacogenetic CHIP (QCHIP3)

April 2014 collaboration of HMC pharmacy department and College of Pharmacy Qatar university in establishment the pharmacogenetic research

The main objective was to initiate a pharmacogenetic research in antithrombotic therapy (warfarin and clopidogrel) Publications:

The effect of genetic and nongenetic factors on warfarin dose variability in Qatari population L Bader, A Mahfouz, M Kasem, S Mohammed, S Alsaadi, O Abdelsamad,..

The Pharmacogenomics Journal 20 (2), 277-284

The impact of CYP2C19 genetic mutation and non-genetic factors on the incidence of major adverse cardiovascular events in patients treated with clopidogrel in Qatar Z Ali, L Bader, D Al-Masri, M Ali, S Arafa, A Arabi, S Mohammed, N Rizk, ..

JOURNAL OF THROMBOSIS AND THROMBOLYSIS 47 (4), 609-609

B. The Pharmacist's Role in Clinical Pharmacogenomics:

- Pharmacists with specialized education, training, or experience in pharmacogenomics should also assume the following additional functions:
- Serving as an expert consultant on a clinical pharmacogenomics service
- Developing and planning pharmacogenomic-specific advanced training opportunities for pharmacists and other health care professionals
- Designing and conducting pharmacogenomic research.
- Developing pharmacogenomic-specific clinical decision support tools in electronic health record systems that guide prescribers on the appropriate use and dosing of medicines based on a patient's pharmacogenomic profile
- Developing a process, including patient-specific educational materials, to explain to patients the importance and significance of the pharmacogenomic test results, not only in the short term but also over the patient's lifetime.
- Developing institutional guidelines and processes for implementation of a clinical pharmacogenomic service.
- Developing processes to document improved patient outcomes and economic benefits resulting from clinical pharmacogenomics
- Promoting collaborative relationships with other health care professionals and departments involved in drug therapy to encourage the development and appropriate use of pharmacogenomic principles in patient care

C. Pharmacy can participate through:

1. Pharmacy informatics team: under the executive pharmacy department the informatics team can help in implementation of the pharmacogenetic testing and results in CERNER and correlating this with the proper medication doses adjustment.
2. CPPD unit it is providing an American College of Clinical Pharmacy (ACCP) accredited program, we will incorporate the pharmacogenetics courses in the CPPD program with coloration with Qatar university.
3. ASHP post graduate residency program: we will implement pharmacogenetic and personalized medicine in the core rotations
4. Pharmacy quality unit: we are reporting all the adverse drug reactions (ADR) in all HMC hospitals and that data can be used in the future to correlate with the pharmacogenetics of medications and the ADR.

D. Education and Training:

Timeline: January 2021-Dec 2025

Objectives:

- Extending the number of pharmacogenetic pharmacy specialists in HMC to interpret and utilize pharmacogenomic results.
- Preparing the clinical pharmacist staff to be able to lead the pharmacogenetic clinic like our experience with the anticoagulation clinic

Through:

- Initiate a collaboration with expert international pharmacy institutions for example: currently in USA there are two residency programs of pharmacogenetic one in Mayo Clinic and the second one in Florida
- Currently we have An ASHP Postgraduate Year One (PGY1) Pharmacy Residency Programs so we can currently we can incorporate special pharmacogenetic course in this program
- In the future we can extend to establish a PGY2 pharmacogenetic residency programs

Precision Medicine In Radiology

Clinical Imaging and Precision Medicine (PM)

1. Nuclear Medicine

a. Introduction:

- Current practice of imaging and treatment of patients with confirmed or suspected malignancies is based on tumor biology, genetic status, and biochemical phenotype, rather than histopathology, size, and location only. The options for imaging and treatment would need to be modified at every stage of the management because many tumors progress to poor differentiation with the course of time.
- PET/CT molecular imaging & Nuclear Medicine (MINM) plays a very important role in precision medicine by precisely localizing the tumor and to choose the right treatment. In other instances, specific radiotracers are employed to visualize the spectrum of the disease. In addition, hybrid molecular imaging provides important parameters to monitor the response to treatment. Those parameters include affinity for specific radiopharmaceuticals, tumor volume and tumor activity.
- Radiotracer therapies target the tumor with low toxicities and side effects. Most of the treatments are offered on outpatient/day care basis. First ever specific treatment for a cancer was I-131 therapy for thyroid cancer about 75 years ago. Targeting bone metastatic disease has been in practice for over 50 years. Now there are several new radiopharmaceuticals and tracers which are routinely used in the specific conditions to pinpoint the disease and then for treatment.

b. Current Status at HMC: At HMC, the following pharmaceuticals are used to image specific conditions and adding to the Precision medicine practice:

- FDG PET/CT is available for clinical studies, now for almost a decade.
- Breast PET/PEM FDG (project in progress)
- Cardiac PET/CT ((project in progress)
- Fluorine 18 PSMA scan – to stage and restage prostate cancer
- Gallium 68 labeled DOTATATE is used to stage and restage patient with Neuroendocrine disease.
- I-131 to stage well differentiated thyroid cancer post total thyroidectomy.

c. Current options for precise treatment at HMC are:

- Treating hepatocellular carcinoma and metastatic liver disease using Y90 labeled microspheres.
- Treating hyperthyroid conditions with I-131.
- Treating Thyroid cancer on outpatient basis using limited dose I-131.

d. Future Options for Precision Medicine at HMC need support from the institute for new project:

- **Diagnosis/Imaging:**

1. Fluorine 18 Estrogen imaging in identifying the patients with hormone positive disease.
2. To utilize radiolabeled markers for tumor necrosis, hypoxia, cell proliferation and apoptosis to understand the tumor biology and guide right treatment.
3. Brain amyloid and Tau imaging to diagnosis Alzheimer dementia.
4. I-124 PET imaging for thyroid cancer dosimetry.

- **Radiotracer Therapy:**

1. Treat metastatic prostate cancer using Lu177 PSMA, RA223 chloride.
2. Treat patients with metastatic neuroendocrine tumor using Lu177 and Y 90 labeled DOTATE.
3. I-131 high dose therapy for thyroid cancer on inpatient basis.

- **Technology:**

1. PET MR now has established role for treatment planning, complete initial staging in prostate cancer and pediatric malignancies.
2. In patient facility for I-131 high dose therapy in thyroid cancer.

2. MSK

1. US guided soft tissue biopsy: the access, positioning, needles size and number of obtained cores has been variable according to the size of the mass lesion, location and nature of the expected pathology.
2. Aspiration for cytology or culture has been added to the biopsy as per needs at the time of radiological assessment.
3. US guided shoulder barbotage: the target to be achieved for this therapeutic procedures has been adjusted as per the sonographic assessment of each patient considering the age of the calcifications with different follow up injection plans as per needs.
4. Fluoroscopy guided shoulder hydrodilatation for treatment of frozen shoulder. This procedure has been also tailored to achieve the maximum therapeutic benefit as per patient tolerance and level of glenohumeral capsular restriction.
5. US guided dry needling as a treatment for tennis elbow. The duration of the procedure is guided by sonographic imaging changes of specific parameters.

3. Breast

1. DBT (digital breast tomosynthesis) and ultrasound for higher detection rate.
2. MRI to evaluate the tumor stage and loco-regional staging, furthermore, evaluating neoadjuvant chemotherapy response which is comparable to pathology response.
3. CESM (contrast enhanced mammography), right now we perform these exams instead of MRI (in patients who have contraindications to MRI),however, this technique will be helpful in one stop clinic to evaluate symptomatic patients as it is fast procedure (8 - 10 minutes compared to complementary ultrasound scan 20 minutes and MRI 25 - 35 minutes) with high sensitivity comparable to MRI.
4. PEM (positron emission mammography) is considered and we shall commence soon.
5. Computer Aided Detection (CAD) - is used to interpret mammographic images and check for the presence of breast abnormality. CAD system puts a mammogram into digital form and then computer software searches for abnormal areas of density, mass or calcification.
6. Digital Breast Tomosynthesis- is an advanced type of mammography that takes multiple images of the breast in a 3-dimensional (3D) image.
7. Digital Breast Tomosynthesis Guided Vacuum Assisted Biopsy- Tomosynthesis guided biopsy is important because tomosynthesis detected cancer can be difficult to biopsy using ultrasound, especially architectural distortion.
8. Contrast Enhanced Spectral Mammography- combines the benefits of full field digital mammography with iodinated contrast media to assess tumor neovascularity similar to MRI.
9. Breast Elastography- is a sonographic imaging technique that provide evaluation of a stiffness of a lesion.

4. Interventional Radiology:

An approach to interventional radiology that addresses genetic, environmental and societal factors in addition to a patient's current health status.

"The future state of radiology will no longer be just interpreting images, but creating the entire phenotypic picture of a patient,"

a. Genomics:

1. Currently we assist in image guided biopsy. In cancer patients these samples can be used to gain knowledge about the genomics of the tumour.
2. In future with fusion imaging, AI and robotics we may improve the accuracy of the biopsies that we take.
3. In the future we can closely collaborate with the genetics specialists to get the correct size / location / tissue type to give them maximum information.
4. There may be a reduction in the need for biopsy with improved imaging and fusion imaging to give more diagnostic information.

b. Personalized Medicine- current practice:

1. IR is precision medicine - using imaging to plan procedures - catheters / wires are selected according to a patient's anatomy.
2. Planning device usage according to the size of the patient measured on CT. e.g length of ureteric stent, diameter of vascular stent, size of an embolic.
3. Interventional oncology:
   - Different treatments according to the size location of the tumour tailored to the patient e.g liver - ablation / chemoembolisation / radioembolisation.
   - Ablation - amending the thermal energy input to get a diameter that covers the tumour
   - Dosing of radio-embolisation according to the location and volume of the tumour.

c. Future practices

1. AI and augmented reality to improve the planning of procedures
2. Computational modelling to be able to give accurate outcomes from a treatment using big data.
3. Manipulatable catheters / robotics to assist in patients with tortuous anatomy.
4. IVUS in vascular cases to understand better plaques / occlusions and to choose the appropriate balloon or stent.
5. 3D printing
   - Models created to plan interventions - giving a better understanding of a patient's anatomy.
   - devices made to the exact size for a patient e.g vascular stents.
6. When reviewing a case it will become normal to gain knowledge about a patient's genetics
7. Fusion software for CT and ultrasound image
8. Real- time fluoroscopic needle guidance for I guide
9. CT- based 3d needle guidance for percutaneous needle biopsy lesions.
10. Needle I pilot
11. Embolization guidance

5. Computed tomography:

The below are the available software within the CT scan clinical imaging section that 3D images / SSD detects any type of fracture of the area covered.

1. All the vascular post processing software (periphery angiography neck angiography) can detect any artery pathology, stenosis...)
2. Stroke software: perfusion post processing and angiography detect stroke in early stages.
3. Lung nodule software detect and precise the size of any nodule.
4. Calcium scoring to detect the calcification in the coronary artery.
5. Liver volume /kidney volume for donation purpose.
6. Liver analysis: liver segmentation, vessel segmentation, provide also virtual planning.
7. Kidney stone characteristic define the type of the stone.
8. CT body perfusion.
9. CT bone reading specific for bone lesion.
10. The CT scan machine it is also a great tool for intervention procedure diagnostic or treatment (aspiration, drainage, FNA, radiofrequency ablation, microwave ablation for some lesion CT nerves injection).
11. CT scanogram help in detecting the length of Lower limb.
12. CT anteversion and tibia torsion detect the angle that help the orthopedic doctor.
13. CT brain lab guide the doctor in them surgery.
14. CT Robotic technique guide the surgeon in knee joint surgery.
15. Fat measurement in abdomen (CT canon).
16. CT Colonoscopy post processing the fly through that can detect any abnormality.
17. CT air way post processing detect any abnormality.

6. Cardiac Imaging Post Processing At Clinical Imaging Heart Hospital.

These are embedded with AI .

1. Tissue Characterisation
2. Quantitive Perfusion
3. STRAIN (Tissue Tracking)
4. Automatic coronary artery tree visualisation
5. Calcium scoring detection

7. Ultrasound

Please find below some of the advanced softwares in ultrasound that assists in precision medicine:

Advances	Application
(Liver elastography (strain & sheerwave	Assessing liver tissue stiffness
(Breast elastography (strain & sheerwave	Characterizing breast lesions as benign or malignant
(Superb microvascular imaging (SMI	For visualization of low velocity microvascular flow that cannot be assessed with regular color or power doppler
B flow	Non doppler technique for assessing normal and pathological vascular structures
(Contrast enhanced ultrasound (CEUS	Improve the detection and characterization of focal liver lesions
Volume navigation and fusion	For guiding interventional procedures
3D and 4D imaging	To assess uterine and fetal anomalies
Auto-follicle count	For follicular monitoring during hormonal treatment for infertility

References

1. Ministry of public health: data on cancer. [Online]. Available at: https://phs.moph.gov.qa/data/cancer/ [Accessed 24 April, 2019]
2. Achieving excellence in cancer care: A vision for 2022. [Online]. Available at: https://www.moph.gov.qa/publications/Documents/Health%20Publications/National%20Cancer%20Framework%20English.pdf [Accessed 24 April, 2019]
3. The Personalized Medicine Report, 2020, Opportunity, challenges and the future, Precision Medicine Coalition
4. Bujassoum, S., Alsulaiman, R., et al. (2018). Cancer genetics program: Follow-up on clinical genetics and genomic medicine in Qatar. Molecular genetics and genomic medicine 6(6): 865–872 doi: 10.1002/mgg3.534
5. Bujassoum, S., Bugrein, H., & Al-Sulaiman, R. (2017). Genotype and phenotype correlation of breast cancer in BRCA mutation carriers and noncarriers. Journal of Cancer Science and Therapy, 9(2), 358–364.
6. Bujassoum, S., Bugrein, H., Al-Sulaiman, R., & Ghazouani, H. (2016). Qatar's experience with hereditary breast and ovarian cancer and high-risk clinic: A retrospective study 2013–2016. International Journal of Research, 5(10), 184–196.
7. Lee Schwartzberg, et al. 2017. Precision Oncology: Who, How, What, When, and When Not? ASCO EDUCATIONAL BOOK | asco.org/e-book
8. Subha Madhavan, PhD et.al .2018 Art and Challenges of Precision Medicine: Interpreting and Integrating Genomic Data into Clinical Practice. ASCO EDUCATIONAL BOOK | asco.org/e-book
9. Bertier et al. Genome Medicine (2016) 8:108
10. Integrating precision cancer medicine into healthcare—policy, practice, and research challenges
11. Ann Hoeben et.al 2021, 13, 242. https://doi.org/10.3390/cancers13020242
12. Personalized Medicine: Recent Progress in Cancer Therapy /
13. Chandrajit Lahiri1 et.al Precis Cancer Med 2019; 2:33 | http://dx.doi.org/10.21037/pcm.2019.09.01 Precision medicine and future of cancer treatment.
14. . Lennon et al. Genome Medicine (2016) 8:112
15. Technological considerations for genome guided diagnosis and management of cancer
16. Esfahani et al Vol. 27, Supp. 2, April 2020 © 2020 Multimed Inc. A review of cancer immunotherapy: from the past, to the present, to the future.
17. Agur et.al ,2020, CLINICAL PHARMACOLOGY & THERAPEUTICS | VOLUME 108 NUMBER 3 | September 2020
18. Accelerating the Development of Personalized Cancer Immunotherapy by Integrating Molecular Patients' Profiles with Dynamic Mathematical Models.
19. Á. Rodríguez Pérez1, et.al 2020, Clinical and Translational Oncology (2020) 22:1923–1937 Cellular immunotherapy: a clinical state of the art of a new paradigm for cancer treatment