In April 2016, the Saudi Arabian government, under the leadership of King Salman bin Abdulaziz Al Saud, released Saudi Vision 2030, a diversification blueprint to boost non-oil-based revenues; tapping into other natural resources such as gold, copper, uranium and aluminium; enhancing the role and contributions of small- and medium-sized enterprises; and increasing dependence on and investment in renewable energy sources, among others.

The kingdom seems well on its way to an economic transformation, now ranking 29 on the Global Competitiveness Index 2016/2017, which looks at the drivers of different economies’ productivity and prosperity. It also ranks third among all the countries of the Arab world (see graph on page 8).

In the areas of health and higher education, training, technological readiness, and innovation King Abdullah International Medical Research Center (KAIMRC), the research institute of the Ministry of National Guard–Health Affairs (MNG–HA), steps in.

“The main aim [of Saudi Vision 2030] is encapsulated by KAIMRC’s strategy and activities,” explained Ahmed Alaskar, KAIMRC’s executive director.

MNG–HA’s strategy focuses on investing in education and training to support the ambitions and potential of Saudis. “It is also to sustainably invest in people’s minds by conducting medical and innovative research guided by a strategy to have a positive impact on people’s health and on the national economy,” adds Alaskar.

KAIMRC’s executives point to it as a source of knowledge and a centre of collaboration with science researchers around the world.

“KAIMRC is keen on adopting new, creative and innovative research that will achieve a paradigm shift in healthcare services,” said Bandar AlKnawy, chief executive officer of MNG–HA and president of King Saud University of Health Sciences. “In this way, we are developing the healthcare sector and the knowledge economy.”
DELVING INTO THE ORIGINS OF INHERITED DISEASES

KAIMRC is making a splash in the understanding of genetic disorders that impact the immune system thanks to Abbas Hawwari, a senior research scientist at KAIMEC and King Saud bin Abdulaziz University for Health Sciences.

Hawwari has devoted his career to elucidating the genetic causes of primary immunodeficiencies in Saudi Arabia, where they are more prevalent than in the rest of the world due to high consanguinity rates. While helping physicians diagnose immunodeficiency diseases, he aims to speed up diagnosis and treatment in affected children and facilitate premarital screening for couples from families with a history of these diseases.

After a Master of Science in immunology and infectious diseases at John Hopkins University in the US, the microbiologist earned a doctoral degree in molecular immunology from the University of Adelaide in Australia. He honed his expertise in this field at Duke University Medical Center before joining the King Faisal Specialist Hospital and Research Centre (KFSH&RC) in Riyadh as head of the transcriptional genetics and immunogenetics sections.

At KFSH&RC, Hawwari’s team discovered and characterized novel genetic defects that are unique to Saudis with immunodeficiencies.

For the first time, the researchers also generated a panel of 264 genes involved in the development of immunodeficiency. Implementing the panel in a next-generation sequencing platform, which can decrypt an entire genome within a single run, provided a money- and time-saving screening system for immunodeficient patients.

“I am proud of this work because we found many genetic defects that were undetectable by conventional methods,” says Hawwari.


Moreover, the researchers devised newborn screening methods for some immunodeficiency diseases. Early disease identification is expected to facilitate a timely intervention that could save the lives of immunodeficient babies. “Very few laboratories around the world have developed such screening methods,” he says.

Hawwari has now expanded his scope of research. His KAIMEC team is investigating a transcription factor called RORgammat, whose absence affects the development of the immune system and, consequently, promotes cancer and autoimmunity. The team is also studying the gene DOCK-B, which triggers severe allergic reaction and death when mutated. The team hopes to identify and create diagnostic tools for the condition along with alternatives to bone marrow transplantation, which is currently the only treatment for the mutation-induced disease.

According to Hawwari, methodologies used to evaluate inherited defects are applicable to other high-priority areas for KAIMEC, such as cardiovascular and endocrine disorders as well as cancer.

“Studying the underlying genetic defects of these diseases is of primary importance to KAIMEC,” he adds.
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<td><em>European Heart Journal</em></td>
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<td>Permissive underfeeding or standard enteral feeding in high and low nutritional risk critically ill adults: Post-hoc analysis of the permit trial</td>
<td><em>American Journal of Critical Care Medicine</em></td>
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<td>10</td>
<td>Rapid molecular diagnostics of severe primary immunodeficiency determined by using targeted next-generation sequencing</td>
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HELPING DRUGS WORK

A laboratory service at King Abdullah International Medical Research Center is bringing tailored monitoring of drug dosage to Saudi Arabia and beyond.

Powerful drugs are becoming more effective and safer in the treatment of disease thanks to an initiative that monitors patients’ medication levels during treatment, allowing precise adjustment according to an individual’s specific needs. Treatment usually involves swallowing a pill then forgetting about it until the next dose. Some medical conditions, however, demand that the concentration of a drug at its target area in the body be maintained at a narrow, optimum range. The dose must be sufficiently high to work, but not so high as to cause dangerous side effects. This is especially true of powerful medicines used to treat cancer.

King Abdullah International Medical Research Center (KAIMRC) is responding to this challenge by offering a therapeutic drug monitoring (TDM) service. As the KAICMR team develops its expertise, it is bringing refinements in drug dosage not previously available in Saudi Arabia, and there are plans to extend its reach across other countries in the region.

Salman Alfadhel, the researcher leading the TDM service, says the initiative grew from a decision to tackle the wider issue of weaknesses in biochemical capabilities in Saudi Arabia. “In 2009, a KAICMR committee wanted to address concerns about the quality of generic drugs produced in Saudi Arabia, and to find ways to maximize the use of home-produced generic drugs while ensuring optimum benefits for patients,” he explains. This led to the establishment of a new KAICMR bioanalytical lab in 2013, with the provision of TDM services as part of its remit.

TDM involves monitoring drug levels in blood or plasma to ensure optimal concentrations in specific target tissues. The chemical analysis procedures required to check drug levels depend on sophisticated equipment. The KAICMR laboratories are kitted out with facilities to perform refined state-of-the-art identification and quantification. The team already provides TDM services for all the Ministry of National Guard - Health Affairs (MNGHA) hospitals across the kingdom.

They are currently working to optimize TDM methods for drugs used to treat cancer, fungal infections and tissue rejection following transplant surgery. They are also working with clinical specialists in epilepsy to explore the possibilities for monitoring a range of anti-epileptic drugs. People can vary markedly in the level of drugs that most effectively control epileptic seizures, making epilepsy an obvious target for the TDM approach.

TDM is a growing aspect of the KAICMR bioanalytical work, both in terms of increasing staff numbers and widening reach. “Eventually we want to expand beyond MNG-HA hospitals and Saudi Arabia and into all the Gulf Cooperation Council countries,” says Alfadhel.

LEADING THE WAY IN MERS RESEARCH

Tackling MERS will require an international multi-pronged approach, and KAICMR is an integral part of this.

In September 2012, the world was introduced to an unknown virus that causes severe respiratory symptoms and can lead to organ failure and death. First identified in Saudi Arabia, Middle East respiratory syndrome (MERS) is caused by a coronavirus called MERS-CoV.

There have been more than 1800 reported cases of MERS in 27 countries with an average mortality rate of about 35%, said KAICMR virologist Naif AlHarbi. More than 1400 of those cases were reported in Saudi Arabia.

Since the discovery of the disease, KAICMR has worked actively to study it and develop treatments and a vaccine to stop its spread.

“All peaks in [MERS-CoV] activity are dominated by hospital outbreaks,” said Maria Van Kerkhove, the head of the outbreak-investigation task force at Institut Pasteur’s Center for Global Health in France. These outbreaks could be contained, she said, because they’re mainly caused by slow isolation of suspected patients, overcrowding in emergency departments, inadequate basic infection prevention and control measures, and cultural differences in seeking out medical attention.

Countries need to raise awareness of MERS, especially those with close ties to Saudi Arabia, so that healthcare systems can identify and isolate patients early. More consistent testing of close contacts is also crucial, especially for healthcare workers and hospital cleaners. Finally, the role of asymptomatic healthcare workers in the transmission of the disease should be studied and communication should be improved between hospitals and the public.

Much research is underway to develop drugs and vaccines against the virus. One potential target, explains Matthew Fenton, director of the division of extramural activities at the US National Institute of Allergy and Infectious Diseases, is a gene sequence that is responsible for producing a protease enzyme essential for the virus’s replication.

Investigations are also targeting a part of the MERS-CoV genome that produces a ‘spike’ protein, which protrudes from the virus’s surface and binds to a receptor called DPP4 on human cells. The sequence of DNA nucleotides in the DPP4 receptor determines which hosts MERS-CoV is able to infect.

Mice and ferrets, for example, cannot be infected with the virus unless the nucleotide sequence of their DPP4 receptor is modified to become similar to that of humans. Mice models with humanized DPP4 receptors are being used for the rapid assessment of MERS therapeutics.

Vaccinologist Sarah Gilbert, of the University of Oxford’s Jenner Institute and her group are in the process of developing a vaccine, which could potentially be used to prevent MERS in camels and in humans.

It’s an extension of the institute’s previous work in developing ‘adenovirus vaccine vectors’. In these vaccines, one virus, made safe for humans, carries a part of another virus — the one being vaccinated against — in order to stimulate a T-cell response in the vaccinated person or animal. The Jenner Institute developed an adenovirus vector from ChAdOx1, a safe inactivated form of a common cold virus. This vector is being used to develop vaccines against diseases like malaria, tuberculosis, Ebola, and prostate cancer. Preparations are currently underway to manufacture a ChAdOx1-based vaccine against MERS for use in clinical trials in 2017. Phase 1b of the vaccine trials will be conducted in collaboration with KAICMR in Saudi Arabia. KAICMR will also be conducting camel research trials.

KAICMR is also in the process of developing an easily applied and rapid diagnostic test for MERS-CoV, announced the centre’s executive director, Ahmed Alaskar, during the 7th Annual Forum for Medical Research held last December.
More than 100 awareness campaigns conducted around the kingdom have led to an increase in the number of samples available at KAIMRC’s Stem Cell Donor Registry. Established in 2011, the registry aims to find compatible stem cells for patients diagnosed with conditions such as leukaemia and multiple myeloma. The registry currently includes donations from 46,000 people, more than half of whom are women. Eleven stem cell donations have already been used to treat patients in Saudi Arabia and abroad.

KAIMRC SCIENCE DAYS

Promoting research, exploring new opportunities.

A series of science days in the KAIMRC auditorium will promote KAIMRC’s strategic areas in disease throughout 2017. The first day, focused on cancer research, took place on March 5. It will be followed by events devoted to diabetes and cardiovascular, infectious and neurological diseases.

“We hope these days will allow us to explore new opportunities for collaboration, help us to move basic research into clinical trials and generally support our specific strategic research and development programs,” says Abdelali Haoudi, KAIMRC’s head of strategy and development.

The science days are open to researchers and clinicians from any institution, with no invitation required. Each day includes a series of presentations followed by a panel discussion with members of the audience encouraged to contribute. “The day about cancer R&D proved to be very interactive,” says Haoudi, emphasizing that networking to make new contacts and explore new opportunities is one of the days’ primary aims.

STEM CELL REGISTRY GETS LARGER

More than 100 awareness campaigns conducted around the kingdom have led to an increase in the number of samples available at KAIMRC’s Stem Cell Donor Registry. Established in 2011, the registry aims to find compatible stem cells for patients diagnosed with conditions such as leukaemia and multiple myeloma. The registry currently includes donations from 46,000 people, more than half of whom are women. Eleven stem cell donations have already been used to treat patients in Saudi Arabia and abroad.

GLOBAL COMPETITIVENESS INDEX 2016/2017

Saudi Arabia ranked 29 out of 138 states on the Global Competitiveness Index for 2016/2017, only surpassed by two other Arab states. The report, produced by the World Economic Forum, recognized the kingdom’s efforts to diversify its economy through Saudi Vision 2030.