

2 Unlocking the secrets of MERS

3 A local solution for life sciences labs

4 KAIMRC's cutting-edge core labs

8 Stem cell research takes centre stage



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A Biotech Bolster

Local and international scientists agree it's a pivotal time for Saudi Arabia to convert to a knowledge-driven economy.

7th Annual Forum
For Medical Research
المنتدى السنوي للبحوث الطبية
مركز الملك عبد الله العالمي للأبحاث الطبية
King Abdulrah International Medical Research Center

Saudi Arabia's latest economic diversification plan, Saudi Vision 2030, aims to steer the kingdom toward a prosperous economy that is less dependent on oil. This new vision underpins KAIMRC's strategy and activities, said Dr Ahmed Alaskar, the centre's executive director, at the opening ceremony of the 7th Annual Forum for Medical Research held last December in Riyadh.

KAIMRC's strategy focuses on investing in education and training. Alaskar said it hopes its investment in medical and innovative research will have a positive impact on health and on the national economy.

"KAIMRC is a national bastion of knowl-

edge. It's a collaborator with scientific research centres around the world in the race to be part of the knowledge revolution," added Dr Bandar Al Knawy, chief executive officer of the Ministry of the National Guard-Health Affairs and president of King Saud bin Abdulaziz University for Health Sciences.

Boosting innovation does not come without challenges, Al Knawy emphasized. These include translating research investment into competitive new products, and stimulating growth and employment by encouraging collaborations between small and large companies, universities, and national laboratories.

The "7th Annual Forum for Medical Research: Impact of Medical Research on Knowledge Economy" was held in Riyadh from 13 to 15 December, with 4,000 participants from the Middle East, the US, UK, France, Germany and Belgium.

The forum addressed the kingdom's strengths and challenges in conducting biomedical research of international standard and in creating real impact on health and the economy. Participants heard about the latest research developments from local and international scientists who specialize in KAIMRC's strategic focus areas: infectious diseases, diabetes, cancer and cardiovascular diseases.

UNLOCKING THE SECRETS OF MERS

A full genome analysis of the virus causing MERS may help track the spread of the virus and halt it.

KAIMRC is expected to make great strides in the fight against Middle East respiratory syndrome (MERS). First diagnosed in Saudi Arabia during a flu outbreak in 2012, the disease has reached many other countries, including the US and the United Kingdom. South Korea suffered a major outbreak in 2015, sparking worldwide concern.

MERS symptoms include diarrhoea, fever, cough, and shortness of breath. The disease is caused by a single-stranded RNA virus, which was isolated for the first time in 2012. It is believed to spread through direct and indirect contact with infected camels as well as between human patients. However, the exact mechanism for its transmission remains unclear. This has hindered efforts to find a suitable vaccine or treatment.

To get a better handle on this infection, a team, led by Hanan Balkhy and Mahmoud Aly from KAIMRC's Infectious Diseases Research Department, has undertaken the painstaking task of solving the virus structure by RNA sequencing. This full genome analysis will provide a means to track MERS outbreaks and pinpoint sources of infection.

The team's approach will establish evolutionary relationships, or phylogenies, between various virus strains based on their physical and genetic similarities and differences. According to Aly, this will help identify the phylogenetic clustering — the co-occurrence of closely related nucleic acid sequences — for genes of

interest, such as the spike protein that facilitates viral attachment to the target receptor.

"These sequences may explain the phylogeny of the MERS outbreak that occurred in the hospitals of King Abdulaziz Medical City in Riyadh in 2015."

The researchers generated complementary DNA sequences using viral RNA extracted from MERS patients and amplified them for sequencing. Despite only having started in October, Aly says their preliminary data show promising outcomes. They have submitted initial partial sequences to the US-based National Center for Biotechnology Information. "These

sequences may explain the phylogeny of the MERS outbreak that occurred in the hospitals of King Abdulaziz Medical City in Riyadh in 2015," he adds.

"Collaboration is crucial," says Aly. The team is working on an agreement with Malik Peiris from Hong Kong University for next-generation sequencing — an expedient but costly technique that can cover the entire pathogen genome within a single run.

In addition to continuing this full genome analysis, the researchers are evaluating genetic variations within the Saudi population that may promote this infection and the environmental factors that contribute to its spread within the Kingdom and the Arabian Peninsula. They are also investigating virus survival in intensive care units.

INHERITED METABOLIC DISORDERS? THERE'S AN APP FOR THAT!



A new smartphone app developed by a Saudi paediatrician is helping hundreds of people with rare metabolic disorders manage their medications.

The app is designed to assist those with inborn errors of metabolism (IEM), a generic term for a group of more than 500 genetic diseases that affect an estimated one out of every 600 babies born in Saudi Arabia. These disorders are caused by inherited mutations that impair the body's ability to effectively turn food into energy.

There are dozens of medications available to treat these congenital disorders, but it's often a challenge for patients and their caregivers to know which drugs are best for which disease and at which dose. A few years ago, Majid Alfadhel, a paediatric geneticist at KAIMRC and King Saud Bin Abdulaziz University for Health Sciences, scoured the scientific literature in search of reliable reports on appropriate medication dosages for managing inborn errors of metabolism.

His exhaustive survey turned up 83 drugs, a list of which Alfadhel published, along with their respective dosages, in the journal *Archives of Disease in Childhood*.

That paper serves as a reference for clinicians but such an academic article is not the most accessible way for patients to glean the information they need. So Alfadhel wanted to develop a smartphone app that would "serve as a quick and easy way for patients with inborn errors of metabolism to know what medications are prescribed and how to use them."

For each medication included in the app, called IEM Drugs, it lists the diseases it can treat, the form in which it comes, the suggested dose, the route of administration, known side effects and the level of scientific evidence that supports its use. In the future, Alfadhel also plans to include protocols for emergency management of IEM, as well as add medical foods, dietary supplements and other nutritional interventions.

To make these improvements, Alfadhel needs to secure more funding. Until this point the app has been a labour of love for Alfadhel, who worked on it in his free time. He is now seeking partners who can help fund further development and refinement.



Biotech Park Project: A Local Solution for Life Sciences Labs (UFC)

A local startup company seeks to fulfill Saudi Arabia's growing hunger for research reagents and material.

A young biotechnology company based in Riyadh aims to overcome a perennial supply problem for the kingdom's growing life sciences and molecular biology sector. The company, UFC Biotech, provides materials and reagents for the regional market, meeting the needs of researchers in Saudi Arabia. "We're basically a solutions company," says founder and CEO Bayram Arman.

Established in late 2012, UFC Biotech is a joint venture between New York-based UFC Biotechnology and KAIMRC to provide solutions and reagents for research and diagnostics in labs across the kingdom and beyond. The company manufactures a wide range of products locally, from growth media and supplements to electrophoresis buffers, and distributes products such as antibodies, human proteins and complementary DNA clones.

The company initially faced difficulties bringing raw materials into the country. Extensive and labyrinthine regulations delayed logistics, leading to spoilage of the material. "But we learned," says Arman. "Working together with KAIMRC, we can now bring in raw materials in one or two weeks and satisfy the needs of researchers much faster." These lessons have enabled the company to deliver products to its customers quickly and inexpensively, saving them the time and cost of importing expensive reagents from abroad.

This year, UFC Biotech will move into the new KAIMRC building and Arman expects the proximity will lead to closer collaboration with KAIMRC and other MNG-HA researchers and clinical staff.

The company is gearing up to produce various media used in hospital diagnostics. This year, UFC Biotech will also start producing stem cell culture media, and aims to broaden its product line to include higher value, proprietary solutions. "We're expanding organically, adding products where we see demand in the market," says Arman.



A CUTTING-EDGE CORE

KAIMRC core labs to offer researchers across the Middle East access to cutting-edge equipment to further their research.

Scientific progress often happens in tandem with technological progress. But as research projects at KAIMRC become ever more sophisticated, not all scientists have the technical prowess to master all the latest cutting-edge instrumentation and techniques.

The Medical Research Core Facility and Platforms Department has 12 staff members available, for a reasonable fee, to help with running the most cutting-edge molecular analyses, cellular characterizations and clinical work-ups; all from laboratory spaces equipped with the latest research platforms.

Launched in 2014, the department is committed to enhancing and expanding the capabilities of any investigator at KAIMRC, King Saud bin Abdulaziz University for Health

Sciences and the Ministry of National Guard—Health Affairs.

Mohamed Boudjelal, the department's head, came to KAIMRC after more than a decade working in the pharmaceutical industry in the United States and Europe, where he helped establish similar shared-service laboratories. That experience, he says, informed how he designed the KAIMRC facility, which has five units and drug discovery capabilities that are unparalleled in the Arabian Gulf. "Hopefully we will be able to serve the whole region," he says, "or at least the all of Saudi Arabia."

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The facility's cell biology unit maintains cell lines from different model organisms



and humans, and offers technologies for analysing the physical and chemical properties of a cell. The molecular, microbiology and biochemistry unit is equipped to characterize DNA, RNA and other biological molecules. The proteomics unit can do full run-downs of all the proteins in a sample. The bio-imaging division houses sophisticated microscopes for extreme clarity in visualizing specimens. The drug discovery section can screen and validate potential therapeutic candidates.

Since its launch, the core lab has assisted in a number of research projects aimed at understanding and tackling cancer, asthma, MERS and various other threats to the health of Saudi Arabians. These efforts have led to many scientific papers and patents, with many more to come.

THE CHALLENGE OF COUNTERFEIT AND SUBSTANDARD MEDICINES



In a new book published by the UK's Royal Society of Chemistry, a KAIMRC medicines expert assesses the global problem of fake and substandard medication.

Badr Aljohani, team leader at KAIMRC's translational research unit, has contributed a chapter to a book collating international expertise on substandard and counterfeit medicines, a major concern for medics, governments and crime agencies worldwide. "The counterfeit market is worth more than US\$150 billion each year," says Aljohani, highlighting the considerable risks to patients.

Aljohani's interest in this issue started while working with researchers in pharmacology and bioanalysis during his masters and doctoral studies at the Queen Mary University

of London's School of Medicine and Dentistry. With colleagues, he developed a method to analyze the immunosuppressant drug ciclosporin, and detected significant impurities and contaminants in many brands.

"I found I was looking at the tip of an iceberg," says Aljohani. By digging deeper into the field he gained the expertise that led to the invitation to write his chapter.

His work at KAIMRC includes developing a clinical trials unit, analyzing generic drugs, and surveying patient views on use of generic drugs rather than their branded counterparts. Legitimate generic drugs can offer significant cost advantages, but the generic market does increase the opportunity for substandard and even fake products.

In his chapter, Aljohani reveals incidents responsible for thousands of deaths, including those due to fake vaccines used in Nigeria, contaminated paracetamol in India and Haiti,

and counterfeit anti-malarial drugs in Cambodia.

He also considers the key factors that allow the circulation of counterfeit and substandard medicines, including weak regulatory structures in many countries and limited availability of genuine products. Also, legitimate and good quality drugs can become substandard if incorrectly stored. Although most prevalent in developing nations, significant problems also exist in the developed world. The US Food and Drug Administration estimates that, globally, 10% of medications are counterfeit.

International cooperation is key to tackling the issues more effectively. This could include better 'track and trace' technology that might incorporate radio-frequency ID chips in legitimate packaging.

Aljohani expresses particular concern about evidence that the profits from drug counterfeiting can be channelled into organized crime and terrorism. "Governments and health authorities worldwide really must come together to stem the flow of funds to such activities," he says.

A PHYSICIAN DIGGING FOR CURES



A medical doctor who turned to research has found an ideal environment for her work at KAIMRC.

when Sihem Aouabdi was working as a medical doctor in Algiers, she treated many patients with challenging medical conditions. The limitations of what she could offer to help pushed her toward a career change, eventually taking her to KAIMRC in Jeddah.

"As a doctor, I was considering how I could improve the situation of patients like those I met and offer them better health. The only answer I could see was to move into research," says Aouabdi.

This led her to the University of Surrey in the United Kingdom to

undertake a master's degree in clinical biochemistry and molecular biology, followed by PhD in molecular biology and toxicology. She then held research posts in industry for seven years, where she acquired a wide range of skills, most specifically in stem cells and their application in regenerative medicine.

Stem cells give rise to all the more specialized types of cells in the body. Unravelling the molecular mechanisms that can coax stem cells into so many different developmental routes is crucial to be able to use them to repair malfunctioning cells that are causing disease. This is the challenge that Aouabdi has been grappling with since moving to King Abdullah University of Science & Technology (KAUST) in 2012, and then to KAIMRC in Jeddah in 2014.

"I hope to combine my clinical knowl-

edge and my research experience to help reach the stage of transplanting stem cells into patients to restore defective tissues or organs," says Aouabdi.

Her current work is focused on developing treatments for diabetes and cardiovascular disease. She has also published research on stem-cell approaches to prostate cancer, and on using nanoparticles to detect breast cancer.

Collaboration is also a vital part of successful science, and Aouabdi has found many experts to work with within KAIMRC and KAUST. Wider collaborations also include researchers at King Saud bin Abdulaziz University in Jeddah and the University of Kuwait.

"I came to KAIMRC because the support and collaborations it can offer for both basic and clinical research build a perfect bridge from the laboratory bench to the patients in hospitals and clinics," says Aouabdi.



STRATEGY MEETINGS FORTIFY KAIMRC'S ROLE IN ADVANCING HEALTH

How KAIMRC is becoming a collaborative hub to boost biomedical research in the kingdom.

A recent series of meetings have been held to discuss initiatives to nurture creativity, improve productivity and develop stronger mechanisms to address critical scientific and medical concerns in the Kingdom of Saudi Arabia.

Last October, a landmark meeting at King Abdulaziz Medical City was led by Dr Bandar Al Knawy, chief executive officer of the Ministry of National Guard—Health Affairs (MNG-HA) and president of King Saud bin Abdulaziz University for Health Sciences (KSAU-HS). Called “Medical Research: Future Planning”, representatives included faculty from the MNG-HA hospitals, KSAU-HS and KAIMRC. Al Knawy shared updates on major infrastructure improvements in Riyadh, Alahsa and Jeddah that aim to improve facilities for researchers. He also stressed

the importance of collaboration to strengthen the kingdom’s innovation capabilities.

KAIMRC’s executive director Dr Ahmed Alaskar presented the centre’s long-term vision and discussed some major projects underway. These include the establishment of a new medical biotechnology park: a cornerstone of KAIMRC’s strategy to exploit the commercial potential of research discoveries.

Also in October, at another strategic planning workshop with an enthusiastic crowd from KSAU-HS, Al Knawy reiterated the importance of biomedical research attaining excellence in healthcare and education. In keeping with the theme of multidisciplinary investigations, he invited faculty members to form creative partnerships to reinforce research and development

across the enterprise. Alaskar highlighted many ongoing collaborative research projects between KAIMRC and KSAU-HS.

A follow-up workshop on KAIMRC’s five-year strategic plan focused on projects and initiatives that will be implemented across the KAIMRC system and across the kingdom to advance the goal of serving humanity through research, knowledge generation, and the commercialization of key life science innovations.

At a KAIMRC general staff meeting in November, eight people received staff performance awards in recognition of their dedication and commitment to KAIMRC’s mission. Those honoured included Lilybeth Doria, Sultan AlHarthy, Mohammed Alarab, Khaled Al Arefi, Thadeo Trivilegio, Lubna AlKhudhairi, Raul Azana and Julie Aleta.



GEARING UP FOR MATTERS OF THE HEART

In line with its efforts to promote and encourage high-impact evidence-based, preventative measures for cardiovascular diseases, KAIMRC gave the Ministry of National Guard—Health Affairs’ (MNG-HA) 2016 Senior Researcher Award to cardiologist Mouaz Al-Mallah.

The selection committee chose Al-Mallah based on his contribution to the scientific community through publications, his ability to generate extramural funds, his role in science publishing as an editorial member and reviewer for scientific journals, and his mentorship activities, says Abdelali Haoudi, head of KAIMRC’s strategy and business development department.

Currently leading KAIMRC’s clinical cardiovascular research program, Al-Mallah has devoted his career to evaluate advanced cardiovascular imaging procedures as prognostic tools and their impact on risk prediction, as well as patient management and outcomes.

Al-Mallah’s appointment at King Abdulaziz Cardiac Center in Riyadh as a consultant cardiologist and the division head of advanced cardiac imaging led to the first dedicated cardiac positron emission tomography (PET) unit in the Middle East that routinely performs myocardial perfusion tests and coronary flow reserve measurements. These assessments are pivotal for detecting and characterizing the progress of coronary artery disease, a serious condition that encompasses angina, myocardial infarction, and sudden cardiac death. Since its inception, the unit has facilitated more than 6,000 procedures.

Under Al-Mallah’s supervision, Riyadh is expected to host the largest dedicated cardiac imaging centre in the Middle East, which will act as a clinical, research, and educational hub at national and regional levels.



Making Light Do Work

A pioneering photochemist builds light-sensitive molecules that could become micro-engines for medicine and industry.

Rabih Al-Kaysi makes light work, literally. The chemist creates organic molecules that respond to light by changing shape, making photochemical engines that convert weightless photons into physical work.

Al-Kaysi hopes that his fundamental research program will ultimately lead to useful ‘microrobots’ that may, for example, be injected to release a drug cargo in the body in response to a precisely targeted light pulse.

On learning of the late King Abdullah’s initiative to develop nanotechnology in Saudi Arabia, Al-Kaysi was attracted by a mixture of scientific opportunity and Arab patriotism to accept a position as associate professor of chemistry at King Saud Bin Abdulaziz University for Health Sciences. He attaches great importance to his teaching duties and role as a PhD mentor, in addition to the research that continues to push forward the frontiers of photochemical nanotechnology.

With a dedicated research team and international collaborators, Al-Kaysi publishes a steady stream of papers describing the synthesis of a wide variety of organic crystals that can be induced to expand, bend, coil, twist or peel when bathed in the energy of visible or ultra-violet light. In one dramatic video, crystalline rods can be seen wiggling and dancing like chemical performers in the spotlight.

Creating such materials demands the building of molecules that will move as required and coaxing them to combine into sufficiently large crystals to make their behaviour potentially useful. One of Al-Kaysi’s most recent developments is crystalline microcapsules that could be loaded with a water-soluble drug. A light pulse penetrating diseased tissue might then induce the capsule to open and release the drug.

Fundamental research tends to reveal unexpected outcomes, and sure enough other medical possibilities are emerging: “Some of our photochemically-active molecules have also shown anti-cancer activity,” says Al-Kaysi. To investigate and develop these and other medical opportunities, Al-Kaysi collaborates closely with the nanomedicine and drug discovery/medicinal chemistry units at KAIMRC. Some time in the future his shape-shifting molecules may be dancing in the spotlight to help patients with serious illnesses.

STEM CELL RESEARCH TAKES CENTRE STAGE

A stem cell conference showcasing domestic and international research highlights new horizons for organ repair and regeneration.

KAIMRC is expected to increase its status in stem cell research locally and internationally after hosting its third conference in this field. Held between 19 and 21 September 2016, the conference was associated with the fourth International Placenta Stem Cell Society (IPLASS) meeting. IPLASS is an international scientific organization founded in 2009 to promote research related to placenta-derived stem cells. The event was evidence of the international scientific community's regard for the quality of KAIMRC's stem cell research, according to organizer and stem cell and regenerative medicine department director, Mohamed Abumaree.

Along with globally recognized experts, the conference attracted junior researchers and students from 17 countries including Germany, China and Qatar, offering a great opportunity to introduce KAIMRC to top scientists, as well as build networks and collaborations. Pointing to the large number and diversity of attendees, Abumaree added that the organizing committee received very positive feedback.

"We focused on the latest advances in the basic science of stem cells, cord blood banking, stem cell



transplantation, disease modelling, tissue bioengineering and bone marrow donor registry," says Abumaree.

By facilitating organ repair and regeneration without the need for replacement, mesenchymal stem cells could revolutionize the treatment of inflammatory and immunological diseases such as multiple sclerosis, cancer and diabetes. However these cells, which differentiate into bone, fat, muscle and cartilage cells, are typically isolated from human bone marrow.

As an alternative to this invasive procedure, the human placenta has recently proven a sustainable and accessible stem cell source. In their quest for therapeutic applications of these placental cells, Abumaree's team discovered that different immune responses were elicited when these cells were derived from the fetal or maternal portion of the placenta. "These cells will soon be used in preclinical and clinical studies to develop effective anti-cancer therapies at KAIMRC," adds Abumaree.