



# THE

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## KAIMRC HOSTS 11<sup>TH</sup> RESEARCH SUMMER SCHOOL

More than 90 students participated in the six-week clinical research program

KAIMRC hosted its 11<sup>th</sup> research summer school earlier this year, a six-week intensive course on clinical research, in which 91 students gained an insight into how to conduct research theoretically and practically, and how to write a scientific paper that could be accepted for publication in peer-reviewed journals.

“It is a unique programme in Saudi Arabia,” says Ibraheem Bushnak, head of the Research Training and Development Section at KAIMRC. The course was open to students in the fields of medicine, dentistry, pharmacy, nursing and applied medical sciences.

Bushnak believes that developing medicine in Saudi Arabia can only happen if research is conducted locally and on the Saudi genetics. He explains that treatment coming from Western communities is not always effective since the genetic make-up of the community is different. “To advance we need to conduct research, not just be consumers of what is given to us from outside,” he explains.

Bushnak says the research skills taught on the programme will not only advance Saudi medicine, but will also further the students’ careers, as they will be more focused on Saudi-specific problems and specialise in much-needed areas.

The course also exposes students to core skills like communication, teaching them how to present research ideas to scientific audiences. “A big part of research is communication,” says Bushnak.

Launched in 2008, the school has since grown in popularity and attracts Saudi students from abroad. “We’re hoping to expand it to international students,” says Bushnak. Social media helps promote the programme, and as soon as the course is opened for registration on the school’s Twitter account, it goes viral.

This year, 1,200 students applied and 91 were selected, resulting in 28 projects across diverse medical research topics. Since the inception of the school, around 35 papers have been published locally and internationally.

Bushnak hopes to introduce a scholarship scheme in the future to open up the programme to gifted students from wider segments of society. The course currently costs SAR 4,000 (\$1,100).

## COMMUNICATION IS KEY DURING A HEALTHCARE CRISIS

Bandar AlKnewy reflects on the lessons learned managing a MERS-CoV outbreak



Bandar AlKnewy, CEO of MNG-HA

Running the King Abdulaziz Medical City in Riyadh, one of the largest and busiest hospitals in Saudi Arabia, is a demanding task even under normal conditions. “We have almost 5,000 clinic visits per day and around 700 emergency room visits,” says Bandar AlKnewy, CEO of the Ministry of National Guard-Health Affairs. But when Riyadh was hit with an outbreak of

Middle East Respiratory Syndrome coronavirus (MERS-CoV) in August 2015, AlKnewy and his colleagues were forced to make difficult choices about how best to serve their patients and protect their staff. The successful response to the outbreak of this deadly virus, however, offers valuable lessons about effective crisis management.

The medical city’s management ultimately elected to close the hospital until the MERS-CoV threat was under control. In a recently published review in *BMJ Leader*, AlKnewy recounted the factors that guided his decision-making process and some of the lessons learned. He recalls that his staff remained committed to caring for their patients even as the number of infections continued to rise, but that the virus soon spread to many members of the hospital’s team. “Around 48 of our staff were infected, and nine of them had to be admitted into the intensive care unit,” he says.

AlKnewy explained in the article that after a flurry of discussion with teams at the medical centre, it became clear that urgent action was needed. Management closed all departments except those providing essential care, such as chemotherapy, and had non-infected patients transferred to other facilities. In parallel, all MERS-exposed hospital staff were monitored to keep track of new cases. Throughout this process, the administration maintained constant communication with their employees, the medical authorities and the media.

AlKnewy believes that such openness was essential to effectively managing this crisis—and is key for any leader aiming to safely navigate around a potential epidemic. “You have to discuss things and take advice to be sure you’ll make the right decision,” he says.

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# NEW PROTOCOL FOR GENOMICS RESEARCH

KAIMRC launched a cutting-edge genetic testing protocol

KAIMRC's Medical Genomics Research Department is set to apply a newly launched genetic testing protocol to address disorders and genomic challenges in the Saudi population.

The launch was marked by a ceremony last July under the auspices of Bandar AlKaway, the CEO of the Ministry of National Guard-Health Affairs (MNGHA), where he recognised the researchers who developed the protocols.

The new protocols include whole genome sequencing — a first in the Middle East, according to Majid Alfadhel, KAIMRC's deputy executive director. This next-generation technology provides insight into all genetic mutations in a patient's DNA by sequencing both protein coding and

non-coding regions of the genome. "It is the most accurate genetic test so far with a maximum diagnostic rate exceeding 45 percent," he says.

The department has also unveiled three perinatal platforms: non-invasive perinatal testing, preimplantation genetic testing for aneuploidy, and preimplantation genetic testing for monogenic disorders. Non-invasive perinatal testing analyses fetal DNA that is released by the placenta and circulates in the mother's blood. It can be done as early as the 10th week of gestation to detect gender, trisomies, and other chromosomal abnormalities, such as the Cri-du-Chat and Jacobsen syndromes.

Preimplantation genetic testing for aneuploidy is performed to determine subtle chro-

somal abnormalities in embryos produced through in vitro fertilization, especially in cases of recurrent pregnancy loss and implantation failure. Finally, preimplantation genetic testing for monogenic disorders, such as sickle cell anemia and spinal muscular atrophy, provides

**"It is the most accurate genetic test so far with a maximum diagnostic rate exceeding 45 percent."**

a means to alert a couple carrying a specific genetic defect of the possibility of having a baby with a similar condition. It screens for a specific familial genetic defect within embryos and identifies unaffected embryos.

Alfadhel explains that these preimplantation tests require an initial workup that lasts up to three months depending on the complexity of the genetic condition. "We have to custom-make the tests for each individual couple," he says. "We are also forming an international collaboration in therapeutic genomics to translate the research from bench to bed and take it to the search for treatments."

# NEW APPOINTMENTS AT KAIMRC

Five experts have joined KAIMRC's team



Khalid Alsayegh



Naif Al Harbi

KAIMRC has appointed five experts to key positions in the management of several departments, projects and facilities. Majed Alghoribi as the chairman of the Infectious Diseases Research Department (IDRD). Salleh Ehaideb joins KAIMRC as the director of the Animal Research Facilities and associate research scientist for medical genomics. Naif Al Harbi will manage the newly formed Safety Office, and Khaled Alsayegh was appointed as the associate director of Biomedical Research for KAIMRC-Western Region. Jahad Alghamdi was also appointed as the head of the Saudi Biobank.

Alghoribi will replace Hanan Balkhy, World Health Organization assistant director-general for antimicrobial resistance, who is leaving the department with a track record of successful and outstanding research projects after 10 years of leadership.

After earning a PhD on the molecular epidemiology of antimicrobial resistance at the University of Manchester, UK, Alghoribi went on to research multi-drug resistant pathogens through cutting-edge bioinformatics and microbial genomics approaches at Public Health England. Since joining KAIMRC in 2008, the epidemiologist has developed a national antimicrobial resistance reference laboratory and a surveillance programme to reduce the threat of emerging infectious diseases in the Arabian Peninsula. He will manage research teams conducting projects on clinical infectious diseases and public health. "My ultimate goal is to build capabilities and infrastruc-

ture for translational research to tackle the existing burden in infectious diseases and facilitate antimicrobial drug discovery," he says.

Ehaideb will oversee three state-of-the-art animal facilities in three

different regions in the kingdom, of which the largest facility in the country is still under construction in Riyadh. The facilities will house rodents, larger animals such as sheep, and aquatic animals such as zebrafish, for KAIMRC as well as other Saudi universities and research centres. After receiving his bachelor's degree in pharmaceutical sciences, Ehaideb earned a PhD in neurogenetics and electrophysiology from the University of Iowa, where he worked extensively with several types of animals. "What sets me apart is my expertise in working with drosophila fruit flies," he says, noting that these flies are easy to use, very cheap to maintain, and have short life cycles. There are also no ethical regulations governing the use of fruit flies in research, which makes them attractive animal models for human cancer studies, one of KAIMRC's strategic projects.

Alsayegh will supervise all research activities of the Western centre in Jeddah. He will also ensure that the scientists work under optimal conditions to maximize productivity and that all projects performed in the Western region

uphold KAIMRC's vision and strategic plan. He explains that this role is highly challenging because many essentials are missing from this recently established centre and biomedical research is relatively new in this part of the world. To address these issues, KAIMRC has established close collaborations with more established institutes in the western region of the kingdom, such as KAUST and King Abdulaziz University.

An associate research scientist at the National Guard hospital, Alsayegh received his PhD from the Medical College of Virginia, specializing in human and molecular genetics, and strengthened his expertise in stem cell biology and gene editing at Tokyo Women's Medical University.

Alghamdi will oversee the Saudi Biobank, which serves as a repository of all biological samples collected from any approved research project within KAIMRC and aims to enrol more than 200,000 participants across the kingdom. His team will ensure that these specimens and their associated data are stored and organised systematically while maintaining participants' privacy and confidentiality. "The expertise that I acquired through my post-graduate studies has enriched my understanding of the key steps in establishing, maintaining and accessing Biobank resources," says Alghamdi, who extensively used biological materials and analysed data from Generation Scotland, the Scottish Biobank project, during his PhD in genetics, genomics and systemic medicine at the University of Glasgow. As head of the project, he believes that the Saudi Biobank will transform healthcare practices and biomedical research while engaging participants as active partners.



Salleh Ehaideb



Jahad Alghamdi



Majed Alghoribi

# A SHOWCASE OF CLINICAL EXCELLENCE

The 8<sup>th</sup> Annual Research Day brought together 275 participants

King Abdullah International Research Center-Eastern Region (KAIMRC-ER) held its 8th Annual Research Day at King Saud bin Abdulaziz University for Health Sciences in Al-Ahsa under the theme “Bridging the gap between basic science and clinical practice.”

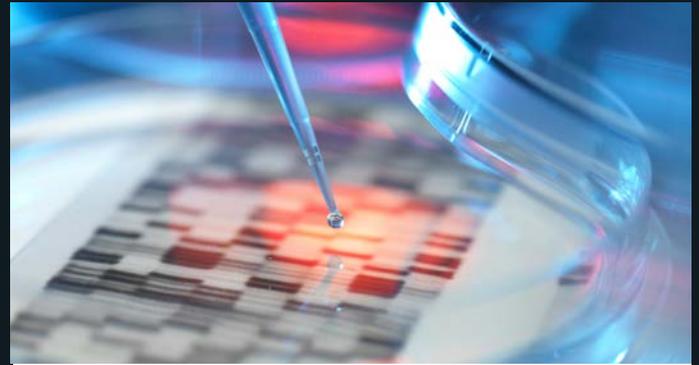
The event brought together 275 participants, including key people at the Ministry of National Guard-Health Affairs in the Eastern Region (MNGHA-ER), researchers, clinicians, and healthcare providers from around the kingdom to discuss ways to help translate scientific research into clinical practice.

Ali Al-Qarni, the head of KAIMRC-ER, gave an opening address, followed by a keynote from Majid Alfadhel, the deputy executive director of KAIMRC, on rare genetic disorders in the kingdom. Alfadhel highlighted the need to motivate medical staff throughout the kingdom, adding that excellence and progress rely on individual and organizational commitment to pursue their goals. Ahmed Al Arfaj, executive regional director of the MNGHA-ER, praised the role of KAIMRC-ER in advancing research in the region.

Clinicians, researchers, and students gave presentations on topics ranging from disease genetics and cell biology to organ donation and knee surgery. Two workshops offered participants training on writing scientific manuscripts and preparing grant proposals.

During the lunch break, Abdulaziz Al Osaimi, operations director of KAIMRC-ER, took Alfadhel and other guests on a tour of the new state-of-the-art vivarium. The new facility has two rooms for rats and four for mice, along with a range of equipment, including an anesthesia vapouriser and surgical microscopes.

With 12 talks and nearly 80 posters, the event combined presentations about basic science with discussions of clinical medicine to offer valuable insights to the diverse audience. A follow-up survey rated the event favourably, with more than 90 percent of respondents saying they would recommend it to others.



## KAIMRC ACES SFDA INSPECTION

KAIMRC-ER trial site received a zero-finding report from the SFDA

The King Abdullah International Medical Research Center – Eastern Region (KAIMRC-ER) passed its first inspection by the Saudi Food and Drug Authority (SFDA) with flying colours — an essential accomplishment for the biomedical research centre. The SFDA is tasked with ensuring that any centre conducting a clinical trial in the kingdom meets the standards established by the ‘Good Clinical Practice’ framework.

The KAIMRC-ER trial site received a zero-finding report from the SFDA, indicating that the site met or exceeded all the standards set for Good Clinical Practice guidelines. “The final meeting was just a lot of praise for our team, and especially the trial coordinators,” says Mohammad Al Arab, clinical research coordinator at KAIMRC. He notes that this represents the first time any site in the kingdom has received a zero-finding report since 2011, making this a particular milestone. “We’re all very proud of our work,” says Al Arab. “This is an achievement for KAIMRC as a whole, not just the Eastern Region.”

The SFDA guidelines govern all the aspects of the trials, from the welfare of human subjects to the conditions of the research site and handling of the data generated. According to Al Arab the SFDA inspection team only gives trial sites limited notice, which means that everything needs to be running smoothly well before the agency schedules its visit. “They will just inform you, we are coming in two weeks, so prepare yourself,” says Al Arab.

SFDA scheduled its visit towards the conclusion of a Merck-sponsored clinical trial investigating the use of a combination of two drugs, sitagliptin and metformin, for the treatment of children with type 2 diabetes. This was the first time that KAIMRC-ER had ever undergone such an inspection, and Al Arab’s team had limited information to work with in advance of the SFDA team’s arrival. “We got a lot of instructions and guidance from the trial sponsor,” he says. “But we didn’t know from experience how they do things and what they might ask for.”



# A TOP YEAR FOR GENETICS RESEARCH

A review of five high-impact papers published by KAIMRC researchers

From developing techniques to identify disease-associated gene mutations to discovering several new genetic causes for various diseases, KAIMRC researchers have published several high-impact papers in the field of rare diseases and medical genetics, a key area at KAIMRC.

The first of these studies involved the development of a high-throughput technique for confirming associations between single genes and diseases. Deputy Executive of KAIMRC Majid Alfadhel contributed to the study, which was published in *Genetics in Medicine*. The research team exploited a phenomenon known as autozygosity, in which people carry two identical copies of some genes because their parents are blood relatives. Autozygosity allows identification of disease-causing genes, and the researchers exploited this to speed up confirmation of causal links between specific genes and diseases. The faster verification of gene–disease rela-

tionships could improve genetic diagnosis.

Alfadhel has also contributed to three other important genetic studies published in 2019. In the first of these, published in *Frontiers in Genetics*, Alfadhel led a team that involved several KAIMRC researchers to discover a novel mutation as a cause of congenital vertebral malformation, a developmental abnormality of the spinal column. The study of two siblings revealed mutations in the *Delta Like-1* gene, which encodes a component of a pathway involved in skeletal development. The mutation caused altered expression of multiple proteins related to this pathway, and computer modelling indicated that the mutation was the cause of vertebral malformations. Further studies will determine exactly how the mutation leads to abnormal vertebral development.

In another study, also published in *Frontiers in Genetics*, Alfadhel worked with Muhammad

Umair at the KAIMRC Medical Genomics Research Department, and colleagues from China and Pakistan, to identify a novel mutation as the cause of the rare muscle-wasting disease limb girdle muscular dystrophy. Genetic sequencing in an 11-year-old boy from Pakistan with the condition identified a previously unseen mutation in the *SGCD* gene, which encodes a structural protein in muscle cells. The mutation cuts the gene short, leading to production of a non-functional protein.

In a study published in *Human Mutation*, Alfadhel was part of a large international team that identified several novel mutations in a gene associated with mitochondrial dysfunction, hypertrophic cardiomyopathy and lactic acidosis. The gene encodes a protein called *ELAC2*, which is involved in processing mitochondrial RNA. Seven mutations in the gene had been previously identified, but the researchers identified 16 more, providing insight into how the mutations alter the structure of the *ELAC2* protein.

Finally, Sabine Matou-Nasri from the KAIMRC Medical Genomics Research Department was involved in a study published in *Scientific Reports* that identified links between gene variants and hepatitis B virus (HBV) infection. Two variants in the gene that encodes interleukin-37, an anti-inflammatory protein, were associated with an increased risk of HBV infection and two were associated with progression to severe liver disease. However, six variants were associated with easier clearance of HBV. The researchers say that sequencing of the gene in patients with HBV infection could help predict how the disease will progress.

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# MAWHIBA FOSTERS FUTURE SCIENTIFIC LEADERS

KAIMRC held a three-week training programme for high school students

KAIMRC hosted its third three-week High School Training Program (Mawhiba) last June in Riyadh, in collaboration with King Abdul Aziz and His Companions Foundation for Giftedness and Creativity. The program is designed to nurture exceptionally talented students with an interest in science.

"Here at KAIMRC, we feel it is very important to give back to society by educating these brilliant students, and KAIMRC will also benefit from this," says Ibraheem Bushnak, head of the Research Training and Development Section and the Mawhiba program director.

Bushnak explains that Saudi youth would typically aspire to careers in mainly four areas: medicine, engineering, military, and aviation. Now, there is a national effort supported by institutes like KAIMRC to open students up to alternatives. "The purpose of this [program] is to give students exposure to different careers in science to let them know the importance of research and how it leads to develop our nation and move it forward," he explains. "We are creating the leaders of the future."

The High School Training Program supports



this goal by targeting female and male students, alternating annually. This year's 36 male participants were divided into nine groups based on their preferences, and each group was assigned to a lab and a supervisor in fields like genomics and nano-medicine.

The program was structured around scientific and social topics to enrich students' experiences. "In science, you need to formulate teams and you need to keep those teams intact

until your research is done. That requires a lot of social skills," Bushnak says. Hiking, for example, encourages socialisation and teamwork to achieve a goal. "All of these social aspects can impact their scientific careers greatly and we encourage that."

Morning sessions included scientific lectures on topics like introduction to genomics, that aim to prepare students for their afternoon lab sessions. These lectures were followed by an hour of social activities, discussing topics like protocol or animation. The afternoon was dedicated to practical lab sessions where students learned and practiced common lab techniques.

On student presentation day, groups were encouraged to showcase their work creatively. The winning group enacted a crime scene using forensic techniques they had learned in the lab. "The theatrical presentation that the students did was amazing and unexpected," Bushnak says. "They showed us that science can be communicated through art forms."

Bushnak says students stay in contact with KAIMRC. He welcomes them to practice their ideas at any time and believes it is a fruitful relationship. "Investing in the future generation means the continuity of our scientific community here. We have to focus on that group to lead us forward in the future," he adds.





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