# 2020 IN REVIEW

A snapshot of key developments at AKU-CRM



THE AGA KHAN UNIVERSITY CENTRE FOR REGENERATIVE MEDICINE AND STEM CELL RESEARCH



# **FIRST PRIMARY CANCER CELL LINES** Developed at AKU in Pakistan

Under the broader umbrella of cancer stem cell research at CRM, PhD studies of two students led to developing the first primary cancer cell lines. Both students conducted their PhD research under the supervision of Professor El-Nasir Lalani, Founding Director, CRM.



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### DR NAZIA RIAZ

Dr Riaz's doctoral research investigated the expression of androgen receptor (AR) and cancer stem cell markers in a cohort of Pakistani breast cancer patients. Her results showed that AR was frequently expressed in both luminal and non-luminal breast cancer subtypes and its expression provided a survival advantage even in patients with cancer stem cell-like traits. She developed a unique AR expressing metaplastic cancer cell line from a Pakistani patient.



### **DR SHEERIEN RAJPUT**

Dr Rajput's PhD research evaluated the potential crosstalk between Mucin 1 (MUC1) and X-Box binding protein 1 (XBP1) in multiple myeloma, a type of blood cancer. Her study also examined the effect of this crosstalk on cellular proliferation and function. Dr Rajput derived, established and characterised a unique myeloma cell line from a Pakistani patient.

#### Research in Progress



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### **GROWING ORGANOIDS** To understand neural diseases and disorders

For the first time at CRM, Dr Jahan Salma grew 3D cerebral cortex organoids, a particular part of the brain, using Induced Pluripotent Stem Cells (iPSC). Brain organoids mimic features of the embryonic development of the brain creating a new possibility for modelling neural diseases and disorders in the lab.

Dr Salma is using these organoids to investigate the function of a specific family of genes in the development of the embryonic human cortex and their potential role in neurodevelopmental disorders such as Autism Spectrum Disorder.

Overall, her research aims to examine the emergence of human-specific neural cell types, cortical features and molecular mechanisms that regulate embryonic development of the cortical brain.

# **IN SEARCH OF NEW TREATMENTS** For blood diseases and disorders



#### Dr Afsar Mian, Assistant Professor

Dr Mian is working on developing novel drugs and treatment approaches for treatmentresistant Leukaemia, a type of blood cancer. His current focus is on designing a cell and peptide-based method for treating Philadelphia-positive Leukaemia. It is expected that, unlike the existing treatment methods, the new therapy wouldn't require repetitive administration, hence, reducing treatment cost and drug manipulation risks.



#### Dr Hammad Hassan, Assistant Professor

Dr Hassan and his team are developing *in vitro* systems to generate red blood cells (RBCs) from different stem cell sources including adult, cord blood and iPS cells. While the research is at a very early stage, the team's ultimate goal is to make RBCs available as a shelf product for transfusion therapies in patients suffering from anaemia, sickle cell disease and thalassemia.

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# **PUBLICATIONS** In peer-reviewed journals

Our faculty including Professor El-Nasir Lalani and Drs Afsar Mian, Mohammed Yusuf, Jahan Salma contributed to several publications in peer-reviewed and high impact journals. Here are some of the articles published in Nature, Accountability in Research, Policies and Quality Assurance, Frontiers in Oncology, Journal of Synchrotron Radiation and Biophysical Reviews.



### Enhancing Research Facilities





### **IPSC TECHNOLOGY** Brought to AKU for the first time

CRM took the lead in introducing the Induced Pluripotent Stem Cells (iPSC) technology at AKU in Pakistan. Dr Jahan Salma led the development of an iPSC Core facility at CRM.

The facility offers a great opportunity to reprogramme cells from any origin to their embryonic-like state. These embryonic-like cells are called induced pluripotent stem cells (iPSC). Researchers can differentiate the iPS cells into any cell type such as brain, heart, liver or muscle cells in the laboratory.

Using this facility, our researchers are developing different cell lines to model disease and explore the potential therapeutic benefits of stem cells.

### Enhancing Research Facilities



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# MOLECULAR CYTOGENETICS CORE

With a newly established Molecular Cytogenetics Core facility, CRM now provides state-of-the-art chromosome analysis for in-house research on a range of samples such as cell lines, peripheral or cord blood and bone marrow cells.

The core also carries out Multicolor FISH analysis, a powerful 24-colour, whole-chromosome genome-wide painting assay that can detect complex rearrangements, translocations, large deletions, duplications and aneuploidy.

Overall, it assesses numerical and structural chromosome abnormalities and chromosomal instability in cells.

Dr Mohammed Yusuf and his team led the development of the facility.

### Enhancing Research Facilities



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# **3D BIOPRINTER** To support cuttingedge research

We added a 3D bioprinting facility to our extensive research portfolio at CRM. This addition is an effort to build on the Centre's vision for cutting edge research in regenerative medicine.

The 3D bioprinter is an advanced additive manufacturing technology. It is used for evaluating drugs, developing 3D cell culture and fabricating organ-on-a-chip models and tissues.

Researchers at CRM are using the printer facility to develop 3D cell culture for biological assessment and exploring the effect of different biomaterials and scaffolds on the growth and differentiation of stem cells. The 3D culture is also being used to assess how cancer cells spread in the body.

# **ONLINE GUEST LECTURES**

### For stem cell and regenerative medicine researchers

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Building capacity of researchers is one of our strategic objectives. In addition to 25 in-house learning sessions, we invited renowned and early career researchers to share their knowledge and expertise through online presentations at CRM.





#### PROFESSOR OLIVER OTTMANN

Head, Haematology Department, Cardiff University, School of Medicine, UK

shared his exciting work about the development of Tyrosine Kinase Inhibitors (TKIs) and their potential in managing Ph+ ALL Leukemia. Based on several clinical trials, Professor Ottmann suggested that TKIs should be used after stem cell transplant either to prevent the disease or to treat minimal residual disease.

#### **PROFESSOR SUSAN FISHER** Department of Obstetrics, Gynecology and Reproductive Sciences, UCSF, USA

presented insights from her research on the placental genome. She spoke about the role of external modifications to the DNA of placental cells during gestation. Professor Fisher's work showed an unusual genome-scale pattern of alterations in the abundance of histone modifications over the lifetime of the placenta.

# **ONLINE GUEST LECTURES**

### For stem cell and regenerative medicine researchers

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#### SULTAN KHETANI

PhD Candidate, Biomedical Engineering, University of Calgary, Canada

talked about the role and use of biosensors in the care of central nervous system (CNS) injuries. Mr Khetani also shared his experience of developing biosensor integrated organ-on-a-chip models to care for the CNS injuries.

#### DR KHALIL RAWJI

Postdoctoral Fellow, Cambridge Stem Cell Institute, University of Cambridge, UK

presented his research about overcoming the lesion microenvironment to promote regeneration in the ageing central nervous system (CNS). Dr Rawji also discussed how investigators are trying to find novel regenerative strategies for treating CNS diseases.

### Building Capacity of Researchers

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CRM at AKU offers the ideal platform for conducting research that meets international standards. It has given me opportunities to engage with and learn from national and international researchers. For beginners like me, CRM provides an enabling environment to grow and build a promising career in stem cell research.

Sarah Yousuf Research Associate



# **CONTINUING EDUCATION OF CRM RESEARCHERS**

# CRM researchers participated in the ISSCR annual meeting

Our faculty and researchers participated in a five-day annual meeting of the International Society for Stem Cell Research (ISSCR).

They joined scientists, clinicians, business leaders, ethicists, educators, and stem cell professionals to learn about the latest stem cell research and its application. Renowned scientists presented their work and discussed the prospects and challenges of stem cell research.

ISSCR is an independent renowned nonprofit organisation that provides a platform for stem cell research community to connect, learn and share their research.

The annual meeting, which usually takes place in-person, was organised virtually this year due to the COVID-19 pandemic.



### MetaSystem FISH Workshop

Dr Mohammed Yusuf and his team attended the MetaSystem FISH and Systems workshop in Dubai held in early 2020. They applied their learning from this workshop to establish FISH analysis services in the Molecular Cytogenetics Core facility at CRM. FISH (fluorescence in situ hybridization) is a molecular cytogenetic technique that helps researchers to visualise and map genetic material in cells.

### Building Capacity of Researchers

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The environment at CRM and the skills of critical thinking developed through Professor Lalani's continuous and contagious spirit of adventure in science have left a strong imprint not only on my research career but also as a human being. Thank you for being an incredible mentor!

Sheerien Rajput PhD Supervisee, now a Postdoctoral Fellow at CRM



# AKU ETHICS THINKING GROUP

## Diversifying the stem cell ethics debate to include Muslim perspectives

AKU convened a thinking group in 2019 to examine the scientific underpinnings and the clinical, ethical, legal, and social implications of using human stem cells and genome-editing technologies in biomedical research and medicine. The group included an esteemed panel of experts in stem cell research and regenerative medicine, theology, law and ethics.

Members of the thinking group participated in the joint international symposium on stem cell ethics organised by AKU and the NOVA University in Portugal. The forum identified the need to diversify the future discourse by including Muslim perspectives. Following up, the thinking group is currently mapping ethical issues in stem cell research in Muslim contexts. It is working on academic publications to unpack the state of stem cell science, ethics, policy and law in these contexts to inform and improve standards of research and practice. Led by Dr Bashir Jiwani and Professor Lalani, the group is in the process of engaging writing partners and diverse Muslim voices to facilitate a pluralistic debate on stem cell research ethics.





Members of the thinking group include scholars and experts from the USA, Canada, United Kingdom, Portugal, Turkey, Spain, Jordan, Qatar, UAE and Pakistan.

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### Leading in Crisis

# PROVIDING LEADERSHIP IN THE COVID-19 CRISIS

The Global AKDN COVID-19 Task Force appointed Professor El-Nasir Lalani, Founding Director, AKU-CRM as the Chair of its testing committee. With support from the task force and operational teams on the ground, the committee has played a vital role in providing trustworthy testing facilities in countries and regions where AKDN operates.

Professor Lalani is also a member of the vaccines and therapeutics' committee that serves as an advisory body to the task force.



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Established in 2016, the Centre for Regenerative Medicine and Stem Cell Research at AKU aims to design novel therapies for major diseases by developing a deeper understanding of disease processes through functional basic science research. We have a small, passionate team of researchers working with our international collaborators at the University of Calfornia, San Francisco and other universities on exciting research programmes. Most of these programmes are in their exploratory phase. For more information, visit our <u>website</u>.



### THE AGA KHAN UNIVERSITY

### CENTRE FOR REGENERATIVE MEDICINE AND STEM CELL RESEARCH

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