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Qatar Biomedical Research Institute
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HAMAD BIN KHALIFA UNIVERSITY

Summer Research Program - Projects

Project #1

Title: Developing valuable tools for diagnosis for Parkinson's disease and related disorder

Description: Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide. Currently, no diagnostic test exists to identify sufferers. In order to accurately detect and diagnose the disease there is urgent requirement for tools that can detect and quantify the pathogenic species in a disease. Antibodies play a major part in many phases in diagnosis, drug discovery and development. Antibodies are the gold standard when it comes to the specific detection of the pathogenic molecule in a disease. In this project we will purify and characterize antibodies specific to alpha synuclein post translation modified species using various techniques.

Mentor/s: Dr. Omar M. Ali El-Agnaf, Scientific Director. Email: oelagnaf@hbku.edu.qa
Mr. Nishant N Vaikath, Research Associate. Email: nvaikath@hbku.edu.qa

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Project # 2

Title: Parkinson's disease early diagnosis: a step closer

Description: Parkinson's disease, one of the most devastating neurodegenerative diseases, that lacks not only a treatment but also a reliable diagnostic test. Parkinson's disease is a movement disorder with symptoms ranging from mild tremor to the point where the patient needs wheelchair to move around. In this project, we aim to explore the potential of our novel monoclonal antibodies as diagnostic tools for Parkinson's

Mentor/s: Dr. Omar M. Ali El-Agnaf, Scientific Director. Email: oelagnaf@hbku.edu.qa
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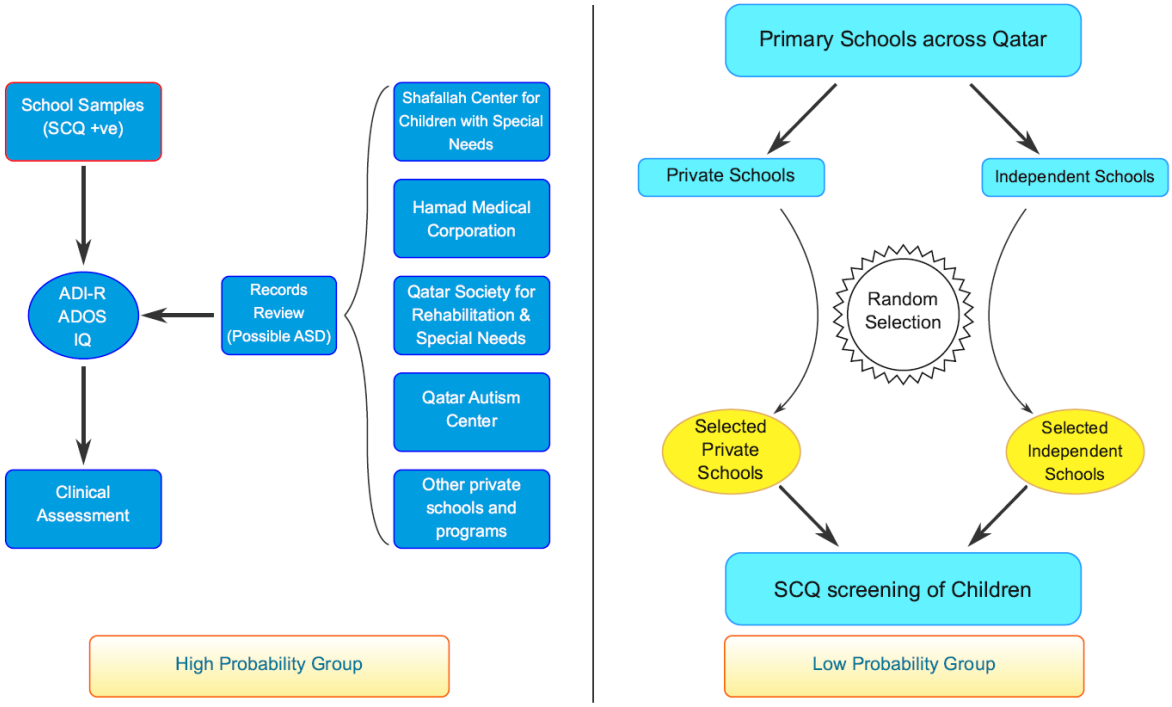
Project # 3

Title: Prevalence of Autism Spectrum Disorder in Qatar

Description: To recruit patients with Autism; through those patients consulting Shafallah center for children with disabilities or Rumailah hospital. Also screening primary school children for this disorder using a special screening questionnaires, known as the Social Communication Questionnaires (SCQ). Those who score above the cut-off point will be examined and checked to see if they have the Autism disorder.



Mentor/s: Dr. Fouad A Wahab Al Shaban, Senior Scientist, Email: falshaban@hbku.edu.qa
Mrs. Iman Ghazal, Senior Research Associate. Email: ighazal@hbku.edu.qa

Note: Please note that there is no bench work involved

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Project # 4

Title: Completing clinical case report manuscripts

Description: Dr. Zahir's work has generated a few clinical results that need to be written up for publication. They are the products of whole genome sequencing and chromosomal microarray studies conducted in Canada. We have found causative genetic defects in children with Intellectual Disability and Autism that we are now certain are pathogenic. We require to publish our findings as a clinical manuscript.

Mentor: Dr. Farah Zahir, Scientist. Email: fzahir@hbku.edu.qa

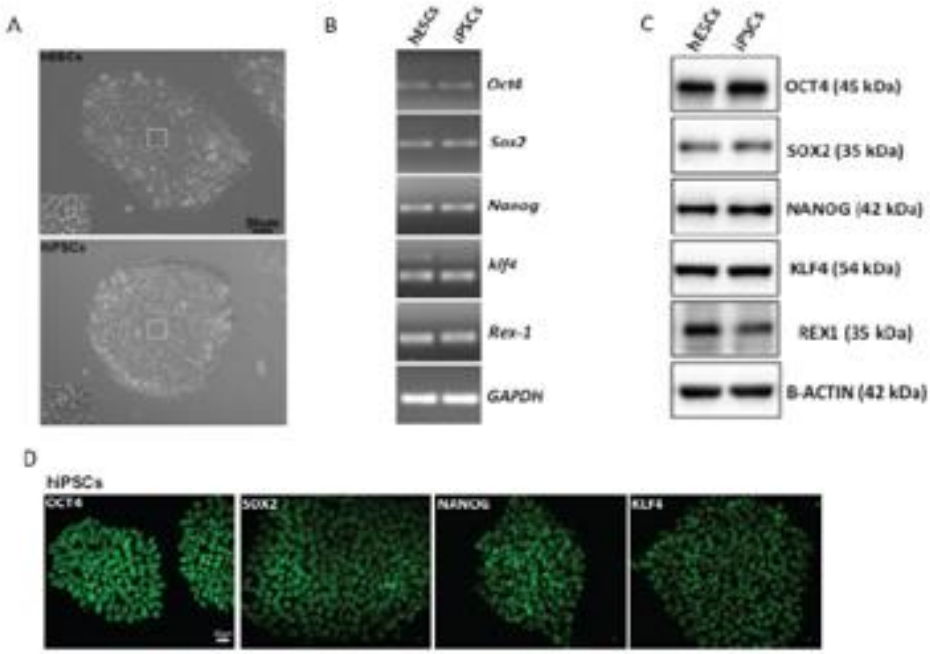
Note: Please note that there is no bench work involved

Project # 5

Title: Effect of stress on pluripotent stem cells self-renewal and neuronal differentiation: A step forward towards better model to study neurological disorders

Description: Pluripotent stem cells are highly sensitive to oxidative stress, indicating the importance of the stress response program in regulating stem cell fate. Stress Granules (SGs) are ribonucleoprotein aggregates, which had been previously observed in different types of cells subjected to environmental stresses such as oxidative stress and heat shock. In this project we will determine the effect of oxidative and thermal stresses on SG formation in pluripotent stem cells to eventually establish whether these granules play role in regulating self-renewal and neuronal differentiation. This will help to develop a reliable stem cell based model to study the pathogenesis neurological disorders.

Mentor: Dr. Mohamed M. Emara, Scientist Email: memara@hbku.edu.qa



Characterization of hiPSCs. (A) hiPSCs (lower panel) showed typical colony morphology of hESCs (upper panel). hiPSCs expresses pluripotent markers as detected by (B) PCR, (C) Western Blot analysis and (D) Immunofluorescence.

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Project # 7

Title: Effect of Glucagon-like peptide-1analog on modulating metabolic stress: Possible role of heat shock response

Description: Insulin resistance (IR) and b-cell failure are the two core metabolic defects that lead to type 2 diabetes (T2D) (Ref). These defects occur as a consequence of chronic metabolic stress that includes chronic low-grade inflammation, imbalance in the redox system, persistent ER stress. Failure of the heat shock response (HSR) to mitigate these various forms of metabolic stress is an early event that precedes IR as manifested by impaired expression of heat shock proteins (Hsps) (Ref.). Developing strategies that mitigate metabolic stress or restore the HSR hold the promise to improve insulin sensitivity and prevent b-cell failure in individuals at high risk, thereby, preventing the epidemic spread of T2D.

Although the current oral anti-diabetic drugs showed a clear beneficial effect to control and manage T2D, they have some undesirable side effects such as weight gain, digestive problem, CVD, risk of hypoglycemia & certain cancers, that may limit their use (Ref. Nathan 2009). In addition, they failed to show efficacy to preserve b-cell integrity and function. Recently, a new class of anti-diabetic drugs referred to as, Incretin hormones have become available and they showed efficacy with a higher therapeutic index (Ref. Drucker). Incretin hormones are made by the gastrointestinal tract system and they consist of Glucagon-like peptide (GLP-1) and Gastric inhibitory polypeptide (GIP) (Ref.). They exert important actions that contribute to glucose homeostasis by stimulating insulin secretion by b-cell and improving its sensitivity at target tissues, reducing central satiety, promoting weight loss and mitigating metabolic stress (Ref.). However, their effect on the heat shock response has never been investigated. In this investigation we will explore the in vitro effect of Exendin-4, a GLP-1 analog that mimics GLP-1 action on: 1) The expression of key components of the heat shock response (Hsp-40/DNAJB3, Hsp-25 and Hsp-72) in skeletal muscle, adipocyes, hepatocytes and pancretaic cells and 2- Investigate whether Exendin-4 effect is mediated by the activation of heat shock factor-1 “HSF-1”. The outcomes of this invesigation will be related to glucose uptake and changes in the inflammation, oxidative stress and ER stress.

In this study, we will carry out a series of cell related experiments “western blot, transient gene transfer, luciferase activity, glucose uptake…”.

If successful, this will be the first demonstration that GLP-1 analogs exert a beneficial effect by modulating the HSR. It will also complement our in vivo study that we plan to conduct on Qatari patients.

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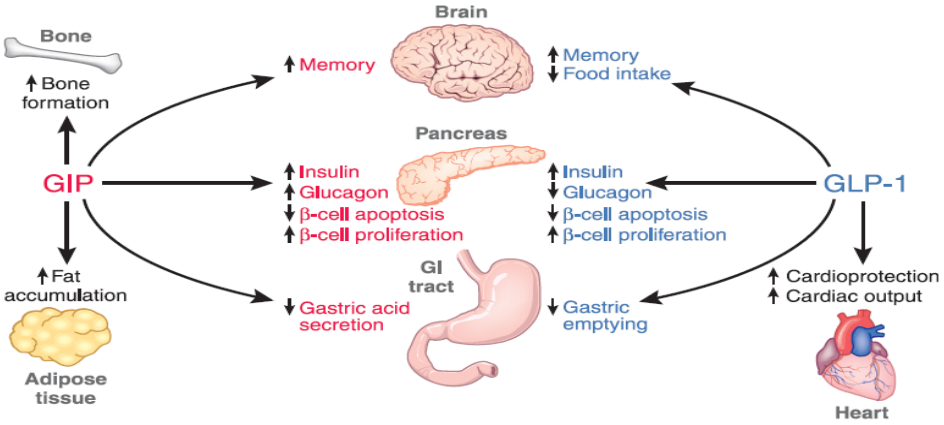

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Project # 8

Title: Role of the heat shock response on pathophysiology of insulin resistance and type 2 diabetes

Description: The overall focus of our research is to understand the role of DNAJB3, a component of the heat shock response in the pathophysiology of obesity and diabetes. We recently described that obese and diabetic humans displayed impaired expression of DNAJB3 with a concomitant increase in various forms of metabolic stress that are known to contribute to diabetes through the development of insulin resistance (i.e., inflammatory response, oxidative stress, endoplasmic reticulum stress and activation of JNK-stress kinase). We are currently pursing our research activity to elucidate the direct role of DNAJB3 in glucose homeostasis and insulin signaling both in vitro and in vivo. More specifically, we will investigate the effect of DNAJB3 on:

- Glucose uptake
- Protein translocation
- Insulin signaling
- Protein-protein purification
- Inflammatory response/Luciferase assay
- Metabolic stress

We will use an array of modern techniques used in molecular and cellular biology such as transient and stable expression of the clone of interest in transfected cells, transfection of silencing RNA, luciferase assay, glucose uptake, insulin signaling and apoptosis, western blot, RT-PCR

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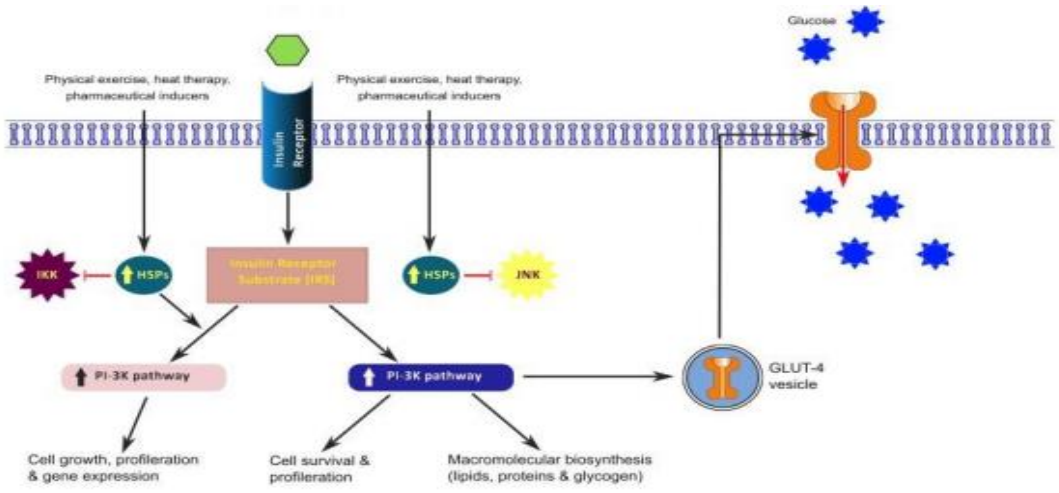

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Project # 9

Title: Mechanisms of transcription factors involved in pluripotency and B cell development

Description: Student will work with recombinant protein production (transcription factors) involved in stem cell pluripotency pathways as well as B cell development. The protein will be used for various protein-protein and protein-DNA interactions assays such as EMSA and ITC to find binding and thermodynamic parameters. Finally protein crystallization and X-ray crystallography will also be used to find a high resolution three-dimensional structure.

Mentor/s: Dr. Prasanna R. Kolatkar, Senior Scientist. Email: pkolatkar@hbku.edu.qa
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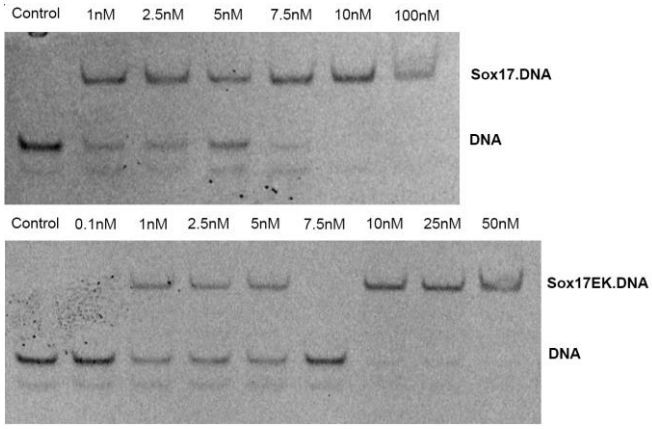
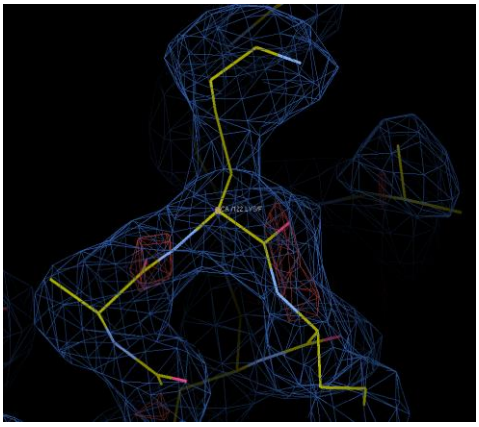
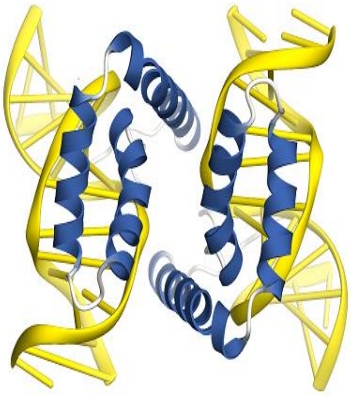
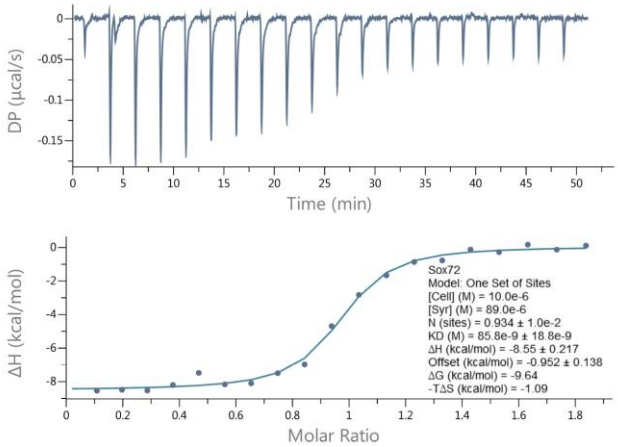
Mr. Mohamed Abdalla A. Eldaw, Research Associate. meldaw@hbku.edu.qa









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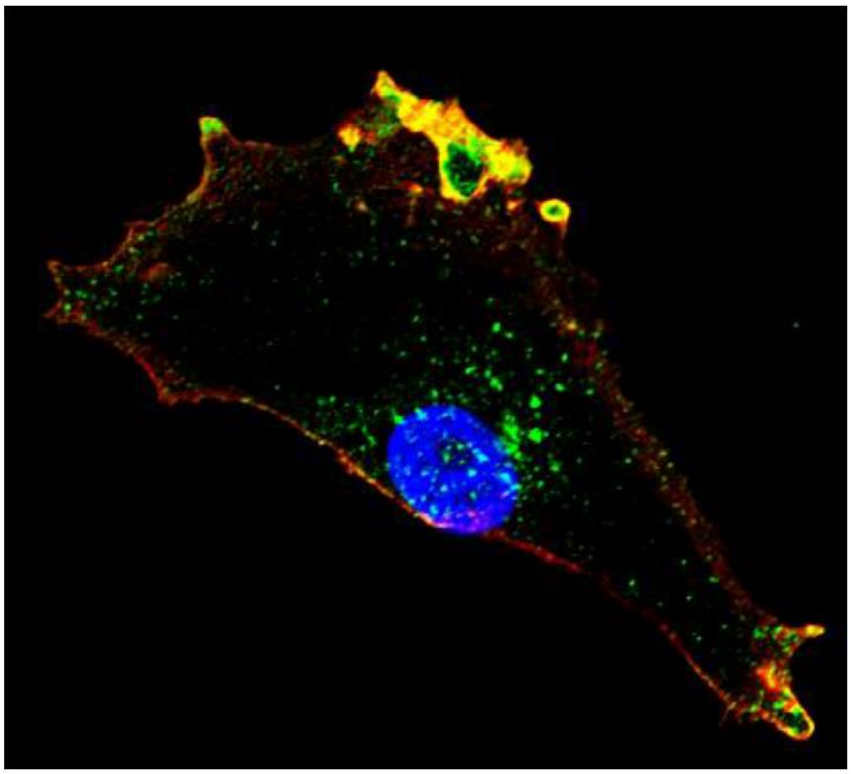
Project # 10

Title: Investigation of the combined impact of GLP-1 and Oxyntomodulin on glucose handling by liver and skeletal muscle: towards the understanding of the remission of T2D following bariatric surgery

Description: Many studies have demonstrated that a large percentage of obese diabetics witness remission of their type 2 diabetes after bariatric surgery. Strikingly, the observed normalization of glycaemia occurs before any significant weight loss is achieved, suggesting that the mechanisms underlying the remission are weight loss-independent. Changes in levels of gut hormones, known for their role in glucose homeostasis, have been suggested to explain T2D remission but the mechanisms are still equivocal. The present proposal will investigate the impact of the concerted action of two gut hormones, GLP-1 and oxyntomodulin, on glucose handling by skeletal muscle and liver cells.

Mentor: Dr. Abdelilah Arredouani, Scientist. Email: aarredouani@hbku.edu.qa

C2C12 cells transfected with HA-Glut4-GFP



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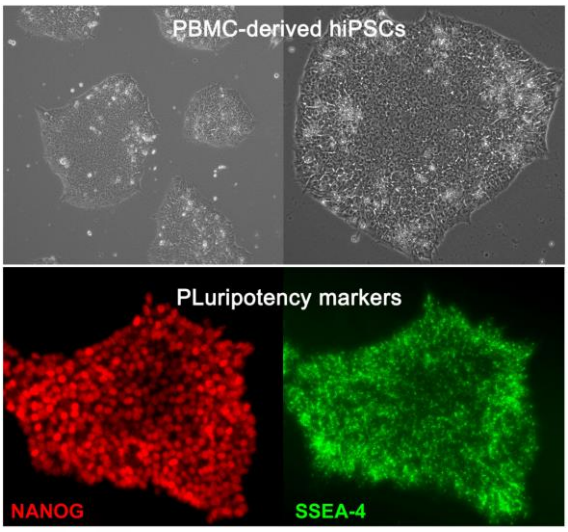
Project # 11

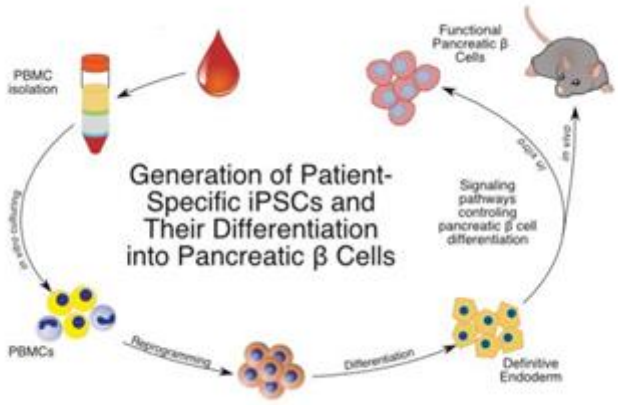
Title: Differentiation of pluripotent stem cells (hESCs/ hiPSCs) into pancreatic progenitors

Description: This project is designed to provide participants with a solid understanding of the basic biology of pluripotent stem cells (hESCs/ hiPSCs) with a specific focus on pancreatic lineage differentiation. It will equip participants with hands-on experience in the following areas:

- Culture, expansion, and maintain hESCs/hiPSCs using feeder-free system.
- Examine the pluripotency and differentiation markers in undifferentiated and differentiated hESCs/hiPSCs using different techniques
- Differentiation of hESCs/hiPSCs into definitive endoderm.
- Differentiation of hESCs/hiPSCs into pancreatic progenitors and pancreatic endocrine cells expressing specific markers.

Mentor: Dr. Essam M. Abdelalim, Scientist. Email: emohamed@hbku.edu.qa
Ms. Idil Ahmed, Research Associate
Mrs. Yasmin Abu Aqel, Research Assistant





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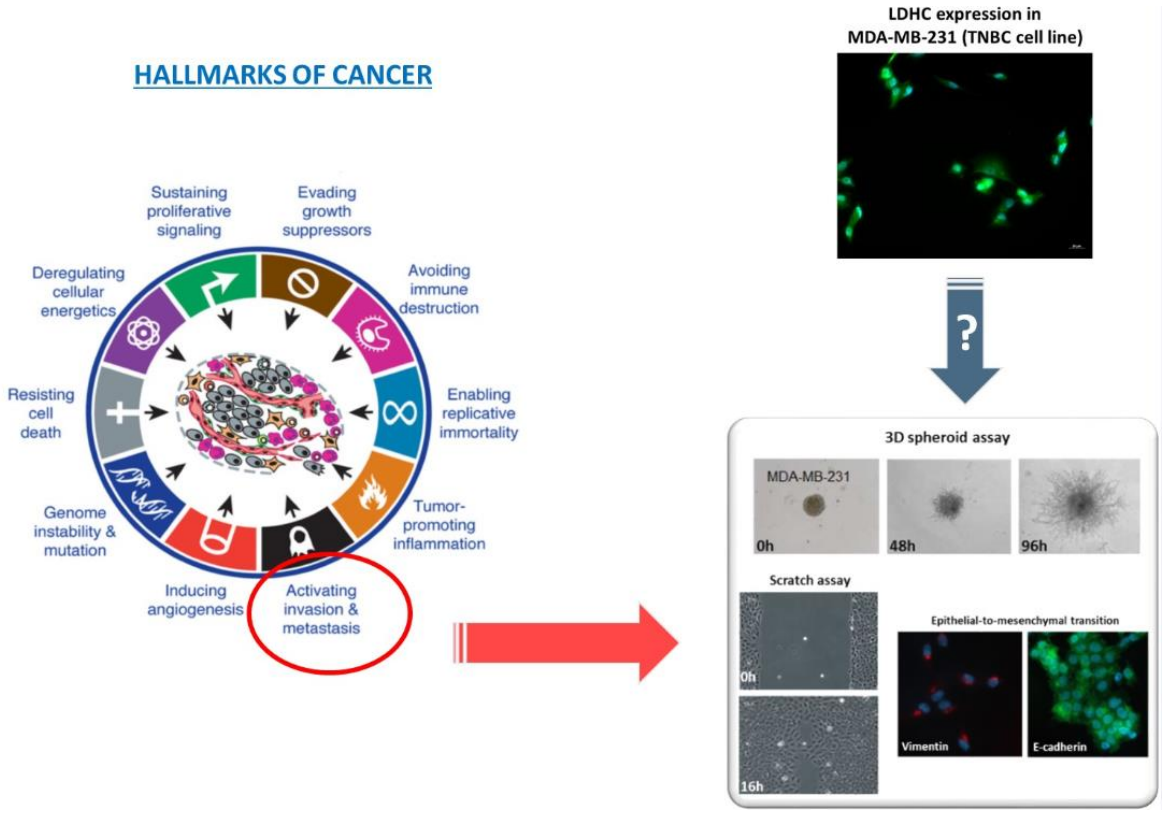
Project # 12

Title: Lactate Dehydrogenase C (LDHC), cell motility and invasion in triple negative breast cancer.

Description: Triple negative breast cancer (TNBC) accounts for one third of all breast cancer-related deaths and is defined by the absence of estrogen, progesterone and Her2 receptor expression. Most patients will relapse over time and face poor survival rates. This project aims to study the role of lactate dehydrogenase C (LDHC) in the acquisition of migratory/invasive capabilities of tumor cells. LDHC expression is restricted to normal germ cells and malignant cells. Preliminary work in our group suggests that LDHC is expressed in breast cancer and might be involved in increasing cancer cell motility, thereby facilitating tumor cells to invade and disseminate.

Mentor/s: Dr.Julie Decock, Scientist. Email: jdecock@hbku.edu.qa
Dr. Remy Thomas, Senior Research Associate. Email:remthomas@hbku.edu.qa



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Project # 13

Title: Mechanisms of breast cancer escape from Natural Killer (NK)-mediated anti-tumor immunity

Description: Natural Killer (NK) cells are lymphocytes of the innate immune system that play an important role in preventing and controlling tumor growth and metastasis. NK cells induce the elimination of tumor cells either by directly killing cancer cells or by secreting cytokines, which participate in cancer elimination by several mechanisms including activation of the adaptive immune system. During tumor development and progression, cancer cells develop mechanisms to escape NK surveillance. However, these mechanisms are still unclear.
Our aim is to study NK cell immune surveillance and immune escape in breast cancer which is the most common cancer and second leading cause of death among women in Qatar and worldwide. Understanding these mechanisms may lead to the development of new NK-based approaches to prevent and/or treat breast cancer.

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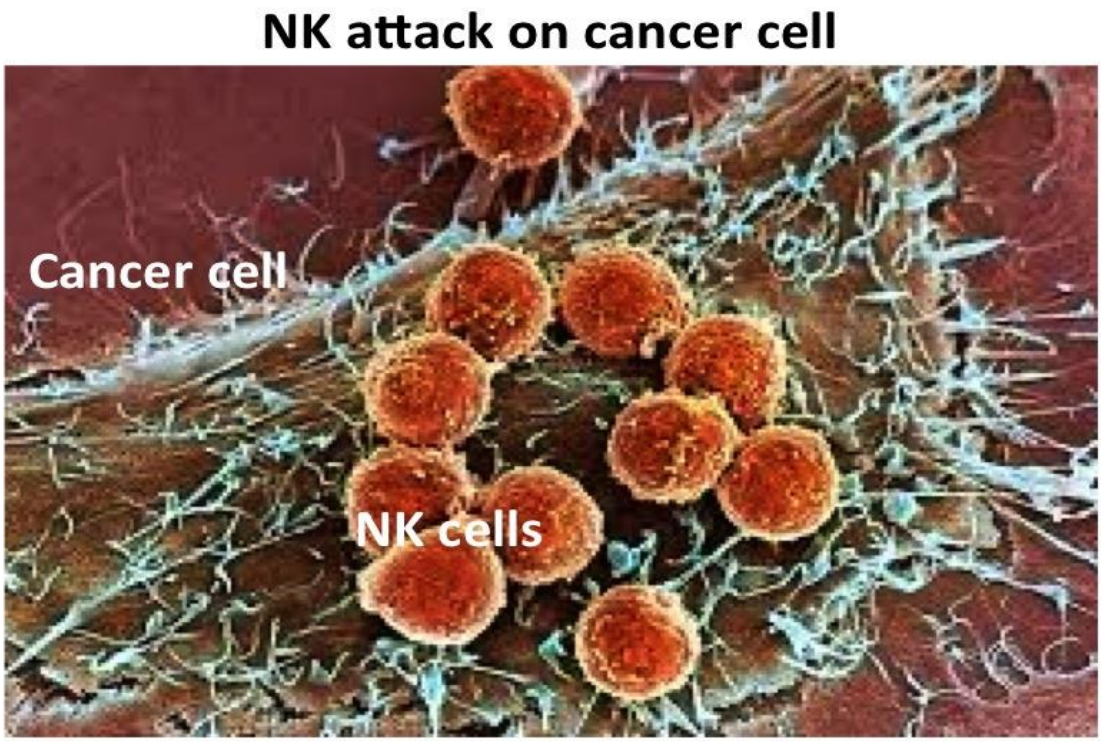
Ms. Ghina M.Taouk, Research Assistant. Email: gtaouk@hbku.edu.qa



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Project # 14

Title: Producing new R-script applications for VisRseq software.

Description: The extensive amount of genome-wide data generated by Next-Generation Sequencing (NGS) technologies in recent years, including "epigenomics" data, necessitates the complementary development of flexible and feature-rich yet user-friendly integrative analysis tools with the capacity for efficient and comprehensive interpretation of these data. To address this need, over the last three years, we developed an R-based visual framework prototype for the analysis of sequencing data called VisRseq (visrseq.github.io). The VisRseq architecture is in the form of a wrapper framework that provides an easy-to-use auto-generated Graphical User Interface (GUI) for existing packages available in the R statistical programming environment and repositories such as Bioconductor on a desktop platform. Our aim is to enrich this software by adding more Bioconductor applications for NGS data analysis.

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Note: Please note that there is no bench work involved