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CONFERENCE ABSTRACTS

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The Effect of Ionising Radiation in Cell Lines of the Oral Cavity and Prostate Cancer

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Objectives: This study aimed to examine the effect of ionising radiation (IR) in *apoptosis*, using cell lines of epidermoid carcinoma of the oral cavity (ECOC) and prostate cancer (PC) with mutated or inactive P53 and associate it to the mismatch repair (MMR) system. ***Methods:*** The study was performed in BICR 10 ECOC and LNCaP PC cell lines previously exposed to IR (0–6 Gy). P53 expression, MMR protein and apoptotic markers were analysed using Immuno-cytochemistry. In order to evaluate the cell morphology, May-Grünwald Giemsa staining was performed. ***Results:*** Our results suggest a decrease in proliferation associated with a higher radiation dose in both cell lines. The expression of caspase3 and BAD increased significantly after IR exposure in a dose-dependent manner. An increase in MSH2 and MSH6 expression in BICR10 and LNCaP cell lines was observed, respectively, without statistical significance. A significant positive correlation between caspase 3 and MSH2 protein expression in both cell lines and between MSH2 and PMS2 in BICR 10 cell line was observed. ***Conclusion:*** In both cell lines, our results suggest that the MMR system actively participates in *apoptosis* induction in response to IR in a P53-independent pathway. Moreover, it seems to suggest that MMR-dependent *apoptosis* occurs through the intrinsic pathway and does not result from the participation of the MutLα and MutSα.

The Challenges Faced in the Education of Biomedical Science Curriculum

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The biomedical science curriculum presents a number of educational and professional challenges. This talk will examine how these challenges can be overcome to ensure that biomedical science graduates are fit for the future workplace. It will use the Quality Assurance Agency subject benchmark statement and curriculum frameworks as reference points. It will discuss the curriculum's depth and breadth, different assessment strategies, the challenges of delivering practical classes, and supporting projects. In addition, it will look at the value of practitioners in delivering discipline-specific aspects. From an employer and professional aspect, the challenges of new technology and the changing landscape of pathology will be examined and discussed.

The Role of Biomedical Laboratory Scientists in Health Professions

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Biomedical laboratory scientists (BLS) play essential roles in various settings, from laboratories and clinics providing health and medical care services, to pharmaceutical and academic research laboratories. Technology is changing rapidly and a healthcare revolution is underway to meet the challenges of an ageing population, an increase in chronic diseases and spiralling costs. Tomorrow's patients are well informed, expect choices and high-quality personalised care. To keep pace with these changes, BLS must evolve to participate in, stay on top of and often lead the rapidly changing technologies and new ways of providing healthcare. In addition to core competencies, a strong professional identity developed through ethical reflection and strong core values can support the professionals. IFBLS works to stimulate discussion and raise awareness among the practitioners to ensure that the BLS will continue to bring unique knowledge, competencies and skills to a wide variety of fields, from being person-centred healthcare partner to biotechnology research, meeting the changing needs of the 21st Century.

Updates in the Medical Sciences Profession

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Biomedical sciences (BMS) have evolved significantly over the last years due to unprecedented knowledge increase and technology development. From the fundamental areas (such as haematology, blood banking, clinical biochemistry, microbiology, immunohistochemistry, cytopathology and public health) to a molecular era (such as molecular biology, proteomics and all omics, genetic profiles, among others), BMS are now fully available for diagnosis, treatment and monitoring of diseases. With a rapid translation from research to bench, the conjunction of science and technology allowed BMS to be one of the fastest and most adaptive professions worldwide. The miniaturisation of equipment, point-of-care testing, online connection, wearable devices, higher patient levels of literacy, the integration of big-data, virtualisation (health 4.0), all contributes to higher knowledge demands

at education levels for the future biomedical scientists and their continuous professional development and access to post-graduate education. Regarding patient safety, these health professionals have to fulfil determined minimum standards and rules to enter the regulated profession. The future will bring new challenges for biomedical scientists including being recognised as a full diagnostic partner capable of getting out of the laboratory and actively contributing to clinical decisions, improving the health service and the output for the patient. In the near future, all biomedical scientists with the right level of knowledge, skills and competencies should be able to become laboratory directors. The challenges ahead for this profession are vast, but biomedical sciences' future can only be bright.

Oral Presentations

Genomic and Expression Analyses Define MUC17 and PCNX1 as Predictors of Chemotherapy Response in Breast Cancer

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Objectives: Poorer prognosis breast cancers are treated with cytotoxic chemotherapy, but predictive markers are not currently available. Treatment failure (recurrence) is relatively common. We aimed to identify predictive markers and resistance pathways. The hypothesis was that tumour cells remaining after neoadjuvant chemotherapy (NAC) contain somatic variants causing therapy resistance, while variants present pre-NAC but lost post-NAC cause sensitivity. ***Methods:*** Whole exome sequencing was performed on matched pre- and post-NAC cancer cells (isolated by laser microdissection) (n = 6). Somatic variants selected for/against by NAC were identified. Candidates were screened *in vitro* using knockdowns. Expression was tested for predictive value in cohorts of chemotherapy-treated breast cancers (n = 53 and n = 303). ***Results:*** Somatic variant diversity was reduced after therapy (P <0.05). MUC17 variants were identified in three tumours and were selected against by NAC, while PCNX1 variants were identified in two tumours and were selected for by NAC. *In vitro* knockdown of MUC17 or PCNX1 were associated with increased or decreased chemotherapy sensitivity respectively (P <0.05). Kaplan-Meier analyses revealed that low MUC17 expression was significantly associated with longer survival after chemotherapy, while low PCNX1 was significantly associated with reduced survival. ***Conclusion:*** Therapy-driven selection of somatic variants allows identification of chemotherapy response genes. MUC17 and PCNX1 are mediators of chemotherapy response.

β-caryophyllene Induces *Apoptosis* and Inhibits Angiogenesis in Human Colorectal Cancer Xenografts *In Vivo*

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Objectives: β-caryophyllene (β-C), bicyclic sesquiterpene, is one of the major terpenes found in several essential oil plants. Previously, we have reported the anticancer properties of β-C by employing a series of *in vitro* antitumour-promoting assays using colorectal cancer cells. β-C is the lead compound of a relatively new class of vascular disrupting agents that target existing tumour blood vessels. In this regard, the present study was designed to investigate the anti-tumour activity of β-C against xenograft tumour models (ectopic and orthotopic) of human colorectal cancer and the associated mechanisms by which it inhibits angiogenesis and induces *apoptosis*. ***Methods:*** The effect of β-C on apoptotic morphological changes of colorectal cancer HCT-116 was investigated using human antibody apoptotic array and transmission electron microscopy (TEM). On the other hand, an orthotopically implanted human colorectal cancer cells (HCT-116) into xenograft nude mice model were used to investigate the effects of β-C on tumour growth; the tumour volume was determined by fluorescence molecular tomography. ***Results:*** Results of human antibody apoptotic array study demonstrated that β-C downregulates the cell survival proteins Survivin, HSPs and XIAP and at the same time upregulates the pro-*apoptosis* marker p21. β-C was also strongly antiangiogenic by inhibiting endothelial cell migration, tube formation, sprouting of rat aorta microvessels and suppressing the vascular endothelial growth factor. In the tumour xenograft model, β-C showed a remarkable reduction in all treated animals' tumour size, in a dose-dependent manner. Tumour histology revealed a clear reduction of the density of vascularisation. ***Conclusion:*** Overall, it can be concluded that β-C exhibits strong inhibitory activity against colorectal tumour growth through a mechanism that appears to involve *apoptosis* induction and angiogenesis suppression.

Sigma2 Receptor/Pgrmc1 is a Potential Modulator of Epidermal Growth Factor Receptor Expression in Human Gastric Cancer Cell Line

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Objectives: S2R/Pgrmc1 is essential for tumour formation, invasion and metastasis, and is upregulated in different types of tumours including gastric cancer. S2R/Pgrmc1 increases the expression of epidermal growth factor receptor (EGFR) in breast cancer cell lines, indicating that S2R/Pgrmc1 may play a role in the stabilisation trafficking of EGFR to the cell surface. This study aimed to determine whether S2R/Pgrmc1 can be used as an alternative targeted therapy for gastric cancer through EGFR, which was achieved by studying the extent to which S2R/Pgrmc1 affect EGFR expression on gastric cell lines. ***Methods:*** This study was carried out between July 2016 and March 2017 at the Pharmacology Laboratory of the Sultan Qaboos University in Muscat, Oman. In the present study, we have treated gastric cancer cell line (AGS) with increased concentration of S2R/Pgrmc1 inhibitor (AG-205) and the samples were analysed for viability and protein expression of EGFR and S2R/Pgrmc1. ***Results:*** S2R/Pgrmc1 inhibition reduced gastric cell line viability significantly (P <0.05). S2R/Pgrmc1 and EGFR levels decreased significantly with the treatment.

Conclusion: The results demonstrate that S2R/Pgrmc1 is a potential therapeutic target for gastric cancer and can solve many problems associated with targeting EGFR.

Boswellic Acid Sensitises Gastric Cancer Cells to Cisplatin-Induced *Apoptosis* via p53-Mediated Pathway

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Objectives: Gastric cancer (GC) is the fourth most common cancer worldwide and the fifth in Oman. Although cis-diamminedichloridoplatinum (CDDP) is an effective chemotherapeutic agent for treating GC, most cases develop resistance against it. Such resistance occurs when CDDP fails to induce *apoptosis* by either activating pro- (i.e. p53) or inhibiting anti-apoptotic (i.e. Akt and NFkB) proteins. CDDP-resistance is a multifactorial process that can be partially overcome by additional agents with anticancer properties, one of which is AKBA (acetyl-keto-beta boswellic acid) has shown promising anticancer effects in certain types of cancer. However, its role in enhancing CDDP-induced *apoptosis* in gastric cancer and the underlying molecular mechanisms has not been studied. Therefore, this study aimed to examine the effectiveness of AKBA on p53-mediated, CDDP-induced *apoptosis* in GC cells. ***Methods:*** AGS and NCI-N87 gastric cancer cells were treated with different CDDP concentrations (0, 50, 100 μM) and AKBA (0, 25, 50, 100 μM). *Apoptosis* and expression of p53, Akt and NFkB proteins were assessed using flow cytometry and Western blot, respectively, while the role of p53 was determined by inhibiting its function through siRNA. ***Results:*** In NCI-N87 cells, both CDDP and AKBA significantly induced *apoptosis* in a dose-dependent manner (P = 0.004 and P <0.001 at 50 μM, respectively). Decreased Akt and NFkB expression with loss of p53 expression. In AGS cells, a similar effect of both drugs was seen in *apoptosis* induction and Akt and NFkB expression except for p53 protein, which was increased. P53 down-regulation affected *apoptosis* induction by both drugs, suggesting its role in their mechanisms' of action. ***Conclusion:*** Altogether, our findings suggested, for the first time, that AKBA enhances GC cell sensitivity to CDDP-induced *apoptosis* via a p53-mediated pathway.

Characterisation of Congenital Von Willebrand Disease Types by Von Willebrand Factor Multimer Analysis in Oman

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Objectives: Von Willebrand disease (VWD) is the most common inherited bleeding disorder. It is caused by quantitative (type 1 and type 3) or qualitative (type 2) defects of Von Willebrand factor (VWF). The study aimed to perform the VWF multimeric analysis on known diagnosed Omani VWD patients and subclassify them into appropriate types. ***Methods:*** In this study, a cohort of 40 historically diagnosed and classified VWD patients at Sultan Qaboos University Hospital was investigated by VWF multimer analysis using sodium dodecyl sulphate agarose gel electrophoresis and capillary blotting. The phenotyping test results and the clinical history of the patients were used to assist the classification process. ***Results:*** Overall, VWF multimer analysis results matched in 38 out of 40 cases of historically diagnosed VWD patients. Of which, 11 cases (type 1) showed normal multimer structure to a mild reduction in the intensity of the multimer bands. Multimer analysis of type 2 VWD showed abnormal multimers in six cases and normal multimers in 14 cases. The total absence of all multimers was observed in seven cases (type 3). The analysis of VWF multimer was not informative in two cases of studied VWD. ***Conclusion:*** The analysis of VWF multimers was successfully used to classify VWD types and flagged potential misdiagnosis of some type 1 and one type 2 VWD that require follow-up investigations. The VWF multimeric assay helped classify the different VWD cohort subtypes with the incorporation of clinical history and quantitative laboratory tests.

National Registry of Red Blood Cell Phenotypes for the Blood Donors in Oman: *What is Next?*

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Objectives: This study aimed to determine the characteristics of red blood cell (RBC) antigen phenotypes among the blood donors in Oman and create a centralised RBC donor phenotype registry. This registry helps improve the transfusion management and outcome of many sickle cell disease (SCD) patients by providing a phenotype matched RBC. ***Methods:*** A total of 610 blood donors attending the Department of the Blood Banks Services were randomly included from January 2018 to July 2019 and were tested by ID-gel column techniques for ABO/Rhesus (Rh) (D) and the other blood group antigens. ***Results:*** The most common ABO blood group was group O with a frequency of (51.5%) followed by group A, group B and lastly group AB. The majority of the blood donors are RhD positive, representing 89%. R1r is the most common among the Rh phenotype (32.6%), whereas R2R2 is the least (2.5%). Kell system (K-k+ 92.1%, K+k- 0.5%), Kidd (Jk(a+b+) 49 %, Jk(a-b+) 16.4%. MNS (MSs 23.3%, Ns 0.2%). Fy(a-b-) 71.8%, Fy(a+b+) 5.9%. Le(a-b+) 64%, Le(a+b+) 0.5%. Lu(a-b+) 97%, Lu(a-b-) 0.3%. ***Conclusion:*** Blood donor RBC phenotype registry is crucial to ensure phenotype-matched blood to multi-transfused patients, including SCD. This study also showed the differences in the RBC antigens among blood donors in Oman compared to other ethnic groups. Building up a national database of phenotyped RBC is ongoing, labour-intensive and requires continuous updating to ensure blood availability for all patients, including patients who need support with rare blood types.

Comparative Analysis Between the Manual Gel Card and Automated Technique for ABO and Rh Grouping

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Objectives: The ABO and Rhesus (Rh) groups are the most important systems in blood transfusion. Different methods are used to assess the ABO and Rh groups, including the manual gel card and the automated IH-1000 instrument. This study aimed to assess the agreements between the manual gel card method and the automated IH-1000 technique for assessing ABO and Rh blood groups using routine blood samples. ***Methods:*** This cross-sectional study performed at Sultan Qaboos University Hospital from September to November 2018. All blood samples received at the blood bank unit for ABO and Rh typing were tested by the manual gel card and the automated IH-1000 methods. In addition, some blood samples were tested for antibody screening. The clinical information for each participant was taken from the SQUH database. Chi-square test was used to compare the data. ***Results:*** A total of 1,419 samples were screened for ABO and Rh groups using both methods. Among these samples, 143 cases were also tested for antibody screening. The mean age of the study population was 30 ± 16 years and 51.6% were female. No statistically significant differences were found between the two methods for ABO and Rh typing ($P = 0.99$). However, five cases (0.35%) showed discrepancies in ABO typing. Similarly, discrepancies were observed in 18 cases (12.5%) for antibody screening. ***Conclusion:*** Overall, a good-to-excellent agreement was evidenced between the manual gel card and IH-1000 automated instrument methods, but some discrepancies were also noticed.

SOCS3 Gene is not Epigenetically Silenced by CpG Methylation in Gastric Cancer

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Objectives: Gastric cancer is a life-threatening disease considered the fifth most diagnosed cancer and the third cause-related death. A complex heterogeneity characterises it with no early specific signs and symptoms associated with its onset and progression. Suppressor of cytokine signalling (SOCS) family is an essential negative regulator of the cytokine signalling mediated by the JAK/STAT pathway. Loss of *SOCS3* expression was reported in gastric cancer, suggesting its tumour suppressor role. This study aimed to identify the methylation status of the *SOCS3* gene using patients' tissues and a large cohort of GC TCGA database. ***Methods:*** In this study, we analysed 44 patient's tissues using gene panel exome sequencing along with a larger cohort of 118 patients found on TCGA public databases to examine the question of whether the *SOCS3* gene was silenced by methylation mechanism(s). Kaplan Mayer curve was used to examine the effect of *SOCS3* methylated and unmethylated cases on survival. ***Results:*** Thirteen out of forty-four (29.5%) patients showed methylation suggesting gastric cancer's epigenetic role. The Cancer Genome Atlas database (TCGA; NCI) was used to validate the hypothesis that *SOCS3* expression is silenced by CpG methylation. A negative correlation ($r = -0.82$) was found between *SOCS3* expression and the methylation status estimated by β-values. Moreover, moderate methylation ($\beta < 0.4$) and high methylation ($\beta > 0.4$) did not affect free survival. ***Conclusion:*** Silencing the *SOCS3* gene is likely to be regulated by other mechanisms such as miRNA and lncRNA rather than methylation.

Reliability of Carbapenem Inactivation Method and Modified Carbapenem Inactivation Method for Detection of OXA48 and NDM-1

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Objectives: Two phenotypic tests, carbapenem inactivation method and modified carbapenem inactivation method, were recently developed to rapidly detect carbapenemase-producing gram-negative bacilli. In this study, we compared the ability of carbapenem inactivation method (CIM) and modified CIM (mCIM) to differentiate between carbapenemase producers and nonproducers among carbapenem-resistant bacteria. ***Methods:*** Fifty-six carbapenem-resistant organisms (28 each from Oman and India) were identified in various clinical samples. Identification of the isolates and antimicrobial susceptibility testing was performed as per standard guidelines. Genotyping of all strains was performed. CIM, mCIM and Modified Hodge test were performed. ***Results:*** In Oman, most isolates were *Klebsiella pneumoniae* and expressed OXA-48 genotype. In India, the majority of the isolates were *Escherichia coli* and they expressed NDM-1 genotype. Modified Hodge test was positive in all the OXA-48 producers and 57% of the NDM-1 isolates. The sensitivity of CIM in detecting 0XA-48 and NDM-1 carbapenemases were 10% and 89%, respectively. On the other hand, mCIM detected 56% and 57% of 0XA-48 and NDM-1 carbapenemases, respectively. ***Conclusion:*** CIM and mCIM are simple, cheap and easy to perform tests. CIM gave excellent results with NDM1 strains while was relatively poor in predicting OXA-48. Detection of OXA-48 improved to 57% when mCIM was used while NDM1 detection was relatively poor. The two methods' sensitivity appears to vary in different genotypes of carbapenemases and further evaluation is needed.

Determination of the Prevalence of Methicillin-Resistant-*Staphylococcus aureus* in Sultan Qaboos University Hospital Healthcare Workers

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Objectives: This study aimed to detect the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in nasal carriage among healthcare workers in the Sultan Qaboos University Hospital (SQUH) and determine the risk factors possible transmission of MRSA. ***Methods:*** A total of 200 nasal swab samples were collected from the healthcare workers at SQUH from October 2018 to

January 2019. Data on risk factors for MRSA colonisation were also collected. ***Results:*** Forty-one of the 200 screened healthcare workers (20.5%) were found to have nasal carriage of *S. aureus*, of which 63.4% were methicillin-sensitive and 36.6% were methicillin-resistant. MRSA was isolated from 15 of the 200 screened healthcare workers giving a prevalence rate of nasal colonisation with MRSA of 7.5%. We found no association between healthcare worker MRSA nasal colonisation and age, gender, speciality, hand hygiene practices, skin condition, previous MRSA infection or previous exposure to antibiotics. ***Conclusion:*** According to this study, the prevalence of MRSA nasal colonisation in screened healthcare workers at SQUH was 7.5%. This finding is concerning and calls for large scale prevalence studies to determine the true prevalence and guide preventive strategies, including universal and periodic healthcare worker screening.

Whole-Genome Sequencing of Clinical Isolates of *Staphylococcus epidermidis* Identifies Copper Efflux Transporters of the Arginine Catabolic Mobile Element and the Copper and Mercury Resistance

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Objectives: Two mobile genetic elements (MGEs) namely the arginine catabolic mobile element (ACME) and the copper and mercury resistance (COMER) were shown to enhance the fitness by facilitating the survival of methicillin-resistant *Staphylococcus aureus* (MRSA) within the host macrophages. These elements have been closely associated with Staphylococcal chromosomal complex (SCCmec). This study aimed to analyse copper efflux transporters and antimicrobial resistance-conferring genes carried by or on MGEs in *S. epidermidis*; the reservoir for resistance determinans, utilising whole-genome sequencing (WGS). ***Methods:*** ACME and COMER and MLST were investigated by analysing WGS of 24 *S. epidermidis* isolates recovered from bacteremic patients from SQUH using BLAST and Artemis bioinformatics tools. Antimicrobial resistance genes were identified through CARD online tool. Hospital-adapted lineages were studied using whole-genome phylogenetic single nucleotide polymorphism tree. ***Results:*** SCCmec was identified by SCCmecfinder tool in most isolates, mainly type IV (n = 8, ST-2). High variability in ACME subtypes was observed in S. epidermidis isolates with type I being the most prevalent (n = 16), Type II (n = 2), Type III (n = 1), Type IV (n = 1) and Type V (n = 4). By contrast, COMER elements were very similar to copper efflux transporters copB, mco and copA/copZ from core chromosome identified in most isolates. CopR (two strains), and an additional copy of (copA/copZ) in 17 strains were associated with copper resistance in *S. epidermidis*. Disc diffusion assay showed reduced susceptibility to copper in most strains, but none were hyper-resistant. ***Conclusion:*** This study has shed light on WGS contribution to analysing antimicrobial and metal resistance determinants.

Investigating the Role of Sphingosine Kinase in Leishmaniasis

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Objectives: Sphingosine-1-phosphate (S1P1) receptor expression in activated T cells *in vivo* is downregulated by receptor internalisation and degradation. This study aimed to determine the effect of FTY720 and its analogues on the expression of S1P1 receptors on the T cells *in vitro*. Additionally, activating T lymphocytes using OVA technique and studying the effect of FTY720 on activated CD4+ T cells *in vitro*. A new approach has been studied, in which cell line expressing S1P1 was used to analyse the influence of the novel compounds in S1P1 receptor expression and localisation. ***Methods:*** The effect of FTY720 on S1P1 level on T cells from OTII mice *in vivo* was investigated by flow cytometry. A cell line expressing a stable amount of S1P1 was used to examine the effect of FTY720 and FTY720 analogues in the expression level of the receptor by Western blot. ***Results:*** Increasing the incubation time of T cells pulsed with OVA antigen more than 24 hours increases the expression of the S1P1 receptor. FTY720 did not suppress S1P1 in treated T cells. FTY720 treated cell line showed decreased expression of S1P1 receptor. Among the analogues used, compound A showed a remarkable effect in S1P1 protein as several fragments were formed in the treated cell. Fragment formation was suppressed by a proteasomal inhibitor. ***Conclusion:*** The two compounds and FTY720 affected the amount of S1P1 receptor and those compounds can be used for *in vivo* study to investigate their role in inhibiting the egress of T cells in inflammation and infection.

Assessment of Estrogen Receptor, Progesterone Receptor and Human Epidermal Growth Factor Receptor 2 Immunohistochemistry of Breast Cancer Fine-Needle Aspiration Cell Blocks

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Objectives: This study aimed to evaluate the expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) immunohistochemistry in the fine needle aspiration (FNA) cell block (CB) of breast cancer (BC) and correlate the finding with surgical tissue block (TB). ***Methods:*** Immunohistochemistry was performed in 48 FNA CBs diagnosed with BC from 2007 to 2016 at Sultan Qaboos University Hospital. The results were scored and compared with previously made TB results. Sensitivity, specificity, positive predictive value, and negative predictive value were measured. Cohen's kappa (κ) test was used to calculate the degree of agreement between the two methods. ***Results:*** ER results showed 67.7% sensitivity, 94.1% specificity, 95.5% PPV and a moderate agreement (κ = 0.588). PR results showed 50% sensitivity, 90% specificity, 87.5% PPV and a fair agreement (κ = 0.368). HER2 results showed 58.3% sensitivity, 100% specificity, 100% PPV and a moderate agreement (κ = 0.539). ***Conclusion:*** The results of this study confirm the wide variations that occur between immunohistochemistry in CB and TB. Compared with other studies, low sensitivity and high specificity rates for ER, PR and HER2 in FNA CB were reported. More studies are needed.

Expression of Programmed Death-Ligand 1 in Breast Carcinoma with Correlation to Molecular Subtypes and Clinicopathological Parameters in Patients Following at Sultan Qaboos University Hospital

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Objectives: Breast cancer (BC) is the most common cancer among Omani women. Programmed death ligand 1 (PD-L1) protect tumour cells form anti-tumour immunity and promote tumour proliferation. This study aimed to investigate the PD-L1 expression in breast cancer cases presented to Sultan Qaboos University Hospital and correlate it with the molecular subtypes, different clinicopathological parameters and clinical outcome. ***Methods:*** We studied PD-L1 expression in 55 breast carcinoma specimens collected from 2010 to 2016 using immunohistochemistry (IHC) on tissue microarray (TMA) with the use of commercial anti- PD-L1 antibody. The expression was evaluated according to the intensity of the staining in the tumour cells. Chi-square and log-rank tests were used to determine the correlation of PD-L1 expression with the molecular subtypes, clinicopathological parameters and clinical outcomes. ***Results:*** Twenty-seven out of 55 cases (51.9%) showed membranous PD-L1 expression ranging from mild (n = 17) to moderate expression (n = 10). PD-L1 was associated with a positive family history (P = 0.023) and high cellular marker of proliferation Ki-67% (P = 0.04) but was not correlated with clinicopathological parameters, receptor status and molecular subtypes. PD-L1 was associated with better relapse-free survival (RFS) in the overall population (P = 0.028) but was not correlated with overall survival (OS; P = 0.131). ***Conclusion:*** The high positivity rate of PD-L1 may support immunotherapy in the treatment of breast carcinomas. In addition, PD-L1 may be considered as a potential marker for prognosis. Further validation with a larger sample of the population and the use of different antibody types is warranted.

Evaluation of a Protective Effect of Aqueous Thymus Extract against Diclofenac Sodium-Induced Hepatocytotoxicity in Mal Syrian Hamster

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Objectives: This study aimed to evaluate the protective effect of aqueous extract of thymus leaves against diclofenac sodium-induced hepatocytotoxicity. ***Methods:*** 32 mal hamsters were used and equally divided into four groups. Group 1 was the control, while group 2 received an oral thymus extract dose (300 mg/kg.b.w) orally daily for five weeks. Groups 3 received diclofenac sodium (6mg/kg.b.w) three times/week also for five weeks. Group 4 received a dose of diclofenac sodium combined with a thymus extract dose in the same concentrations. Blood was taken from each animal and stored until biochemical study. Then, hamsters were sacrificed, autopsied, and liver tissue samples were prepared for histopathology assessment. ***Results:*** Biochemical study showed a significant increase in the levels of ALT, AST enzymes, bilirubin, uric acid, and urea (P <0.001) while albumin level decreased (P <0.001) in the blood serum of group 3 compared to the control and group 2. A significant decrease in all the precedent biochemical parameters (P <0.001) and elevation of albumin have been recorded in the blood serum of group 4. Histopathological study revealed strong indices of injury mediated by diclofenac sodium, especially congestion of liver cells, dilation of the hepatic portal and central veins, cell nucleus disappearance and inflammatory cells infiltration. These indices were greatly ameliorated and activation of liver cells division was recorded in the liver of 4th group animals. ***Conclusion:*** The present results suggest that aqueous extract of thymus leaves could be a potent natural herbal product provide a promising hepatoprotective effect against hepatotoxicity induced by diclofenac sodium.

Neoadjuvant Chemotherapy *in vitro* Models Reveal an Increase in HER-2 and Neuropilin-1 Proteins Conferring Drug Resistance

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Objectives: Locally advanced breast cancer patients usually receive third-generation neoadjuvant chemotherapy (NAC). Although NAC treatment improved overall survival, patients' response varies, some acquire resistance and others exhibit a conversion in their breast cancer molecular subtype. We aimed to identify the molecular changes attributed to NAC resistance attempting to find new therapeutic targets in different breast cancer subtypes. ***Methods:*** We mimicked NAC treatment used in clinical practice and generated resistant cell lines in an *in vitro* model. The resistant cells were generated by consequent treatment with four cycles of adriamycin/cyclophosphamide (4×AC) followed by an additional four cycles of paclitaxel (4×AC + 4×PAC). ***Results:*** Our data revealed distinct mechanisms of resistance depending on breast cancer subtype and drugs used. AC and paclitaxel resistant MDA-MB-231 cells activated NRP1/TNC/Integrin β3/FAK/NF-κBp65 axis and displayed a decrease in breast cancer resistant protein (BCRP/ABCB2). In turn, resistant MCF7 cells to AC (4×AC), induced HER-2 expression which converted MCF7 subtype from being a luminal A to luminal B-HER-2 type, upregulated NRP-1, ER-α, and EGFR and activated PI3K/Akt/NF-κBp65 survival axis. Unlike MDA-MB-231 cells, MCF7 cells upregulated BCRP/ABCG2 in response to paclitaxel resistance. Co-immunoprecipitation demonstrated a novel interaction between HER-2 and NRP-1 which drives the resistance features. ***Conclusion:*** NAC induced a concurrent increase in NRP-1 and HER-2 expression, enhancing breast cancer drug resistance. This translational study suggests that anti-NRP-1 might be useful for treating triple-negative breast cancer and might increase the efficacy of herceptin in treating resistant luminal A overexpressing HER-2 as a result of NAC.

Design, Synthesis and Biological Evaluation of Some New 2-Pyridylquinazoline Derivatives

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Objectives: 2-pyridyl [3H]-quinazolin-4-one derivatives fused or substituted with different oxygen or nitrogen heterocycle

moieties as potential anti-tumour and antimicrobial agents were prepared, characterised and biologically screened synthesise. A novel series of 6-bromo quinazolin-4[3H]-ones linked or fused to other heterocyclic moieties such as pyrazolone, triazole, tetrazole ring systems are evaluated for their antimicrobial and antiproliferative activity in this study. ***Methods:*** The synthesis process started from 5-bromo-2-[pyridin-4-ylcarbonyl]amino]benzoic acid 1 which was converted to the crucial building block 3 via two alternative procedures. Compound 3 underwent halogenation reaction POCl3 and PCl5 to afford compound 4. Various cyclisation reactions were applied to compound 4 to afford the novel compounds 5a,b-10. The newly prepared compounds underwent antimicrobial screening as well as cytotoxicity evaluation against five different cell lines. ***Results:*** Only compound 9 was found to possess selective activity against *Staphylococcus aureus*. This Gram-positive selective activity may be due to the selective targeting of 9 to the thick cell wall of Gram-positive bacteria. Moreover, a toxicological assessment of compound 9 revealed no human cytotoxicity on tested normal and cancer cell lines. Therefore, 9 may serve as a good candidate for further development studies by structure modification in order to optimise its potency. ***Conclusion:*** A new series of 2-pyridyl [3H]-quinazolin-4-one derivatives incorporated into diverse N and O heterocyclic moieties as potential antimicrobial agents were synthesised, characterised and screened for their antimicrobial and cytotoxic activity. Among all new compounds, only compound 9 was found to process selective antibacterial activity against Gram-positive bacteria *S. aureus* (IZ = 26 mm, MIC = 256 µg/ml).

Development of Prolactin Receptor Antagonists

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Objectives: Prolactin (Prl) consists of 200 amino acids and binds to a membrane-bound Prl receptor. A role for Prl in breast, prostate and ovarian cancer is suspected since this growth-promoting hormone can be produced by cancer cells and that the Prl receptor is frequently overexpressed. A specific feature of the Prl receptor is that it is rapidly internalised into cells once it has bound Prl. Due to the suspected cancer relevance of Prl, we have developed antagonists for the Prl receptor and have also initiated attempts to link such antagonists to low molecular weight anticancer drugs. The design, manufacture and bioactivity of these new Prl receptor antagonist are described. ***Methods:*** Plasmid constructs were made for using an *E. coli* expression system to produce a variant of Prl with antagonistic activity. This variant has four amino acid substitution that converts the agonist into an antagonist. The recombinant proteins were tested in Biacore assays and cultured cells. The Prl receptor antagonist was further conjugated to DM1, an anticancer compound, using the so-called Sortase system. Prl receptor binding of the produced compounds was tested using Biacore assays and biological activity was tested in cultured cells by analysing STAT5 phosphorylation. ***Results:*** Systems for recombinant Prl receptor antagonist production can be established in *E. coli*. The Sortase system is an efficient method to achieve site-specific drug conjugation. The recombinant Prl receptor antagonists bind the Prl receptor with equal or higher affinity compared to native Prl. Prl is known to activate STAT5 in cultured cells and our results indicated that Prl receptor antagonists could block this activity. ***Conclusion:*** The first steps to produce Prl receptor antagonists have been taken, which allows for further investigations on the role of Prl in cancer.

Extracellular Vesicles Mediate Development of Renal Cysts

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Objectives: Patients with tuberous sclerosis complex (TSC) experience disease because of developmental and cell growth control abnormalities. The disease can manifest as solid tumours in the kidney, called angiomyolipoma or renal cancer, or fluid-filled lesions called cysts. This latter lesion can be as aggressive and even more devastating than the solid tumours. Mechanism of cyst development in TSC is not known. ***Methods:*** Various models were used to study cyst fluid from Tsc2 deletion in principal cells (Aqp2CreTsc2 mice), Tsc2 deleted cell lines and patients with TSC-renal cysts. ***Results:*** We found, unlike the solid tumours, the cysts do not have a significant burden of cells that have experienced additional mutations, but rather the cysts are composed of genetically healthy cells that are 'instructed to do bad things' by a very small population of genetically mutant cells. We have discovered that these instructions, or communication, between the genetically mutant or 'sick' cells and genetically normal cells occur through structures called extracellular vesicles (EVs). EVs isolated from principle cells and patient's cysts fluid had a mean diameter of 300–400 nm. EVs form Tsc2-null cells had a pH buffering effect. Tsc2 deletion in cells showed increased mTORC1 activity and increased EVs synthesis and release. Recipient cells had higher mTORC1 activity when treated with EVs or EVs-protein/RNA from Tsc2-null cells. These data suggest that disease phenotype is conveyed via EVs from mutant cells to normal cells. Mice with Tsc2 deletion in principal cells (Aqp2CreTsc2 mice) develop renal cyst(s) with age and urine EVs characteristics are similar to above. Aged Aqp2CreTsc2 mice develop renal cell carcinoma, which implicates chronic phenotype spreading via EVs in cellular re-programming. ***Conclusion:*** Extracellular vesicles provide a novel mechanism of developing renal cysts in TSC and may mediate cellular programming into renal cell carcinoma.

Effects of Mobile Phone Electromagnetic Field on the Living Cells: *An In Vivo Study*

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Objectives: This study aimed to examine the effects of electromagnetic waves emitted by mobile phone on gross morphology of the developing chick embryo and the organelles in the liver and heart tissues. ***Methods:*** Forty zero-day fertilised eggs of *Gallus domesticus* were randomly divided into control and experimental groups and placed in an egg incubator. The experimental group was exposed to electromagnetic waves by placing a mobile phone inside the incubator and calling it from outside according to a planned schedule. The control group had no such exposure. Embryos were euthanised at day 10 and day 15. Gross morphology, histology, EM, Hsp 70, mRNA was studied in liver and heart tissues. ***Results:*** Mortality was higher in the exposed group. Cutaneous haemorrhages limb deformities were apparent. Liver revealed fatty change, increase the number of degenerated and

deformed mitochondria and fat-filled vacuoles. Cardiac muscle also revealed a marked increase in the number of elongated and degenerated mitochondria. A significant increase in Hsp 70 mRNA in the experiment group was seen. In the control group, no such abnormities were seen. ***Conclusion:*** The electromagnetic field has caused morphological and intracellular damage to liver and heart in developing chick embryo.

A Non-Invasive Microwave-Based Sensing System for Water Accumulation Abnormality Detection in Lungs

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Objectives: Lungs play an important role in the respiratory system for breathing. Deficiencies in lung operations result due to accumulation of fluid inside the lungs, which is considered a sign of a medical abnormality, for instance heart failure. Current diagnosis techniques are time consuming and relatively unable to monitor, detect or even provide accurate assessment of water accumulation in lungs in terms of water accumulation percentage and related degree of illness. As such, developing low cost mechanism for water accumulation in lungs will provide an alternative yet rapid and accurate enough diagnosis tool for critical conditioned patients. ***Methods:*** Electromagnetic detection mechanism using microwaves is well suited for detecting watery fluid accumulation in the lungs. This is because accumulated water in the lungs has high dielectric constant concentration compared to normal lungs. In this work, we developed a low-cost non-invasive microwave detection system for water accumulation in small-scale lungs. Two low-profile microwave sensors were placed in a front-to-back scenario to capture the amount of electromagnetic field strength as a transfer power strength. This power detector can easily map the amount of power to a reasonable voltage level that then can be processed and displayed in an LCD unit. This study was carried out in a capstone design project in a controlled laboratory room at the Department of Electrical and Computer Engineering at Sultan Qaboos University. ***Results:*** Experimental trials were conducted by changing lungs status through loading it with salty water in different percentages. The detection status was correct in all scenarios. In future work, we aim to integrate the system with more sophisticated algorithms that will provide both qualitative and quantitative measures. ***Conclusion:*** In this abstract, a microwave-based non-invasive detection system was developed for water accumulation abnormality detection in the lungs. Different water accumulation percentages in lungs were detected from all performed scenarios in this study, with correct status display as either normal or abnormal lungs. In the second phase of this research work, the developed detection system shall be integrated with more additional sensing units including capturing heart rate, ensuring accuracy of reading the percentage of water accumulation within the lungs and integrating textile sensors within an easy to carry washable belt.

The Application of Herzberg's Two-Factor Theory of Motivation to Job Satisfaction in Clinical Laboratories in Omani Hospitals

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Objectives: Job satisfaction is an important condition for staff retention in most healthcare organisations. As a concept, job satisfaction is linked to motivation theory. Herzberg's two-factor theory of motivation is used in this study to explore what motivational elements are associated with job satisfaction among medical laboratory professionals (MLPs) in Oman. ***Methods:*** A qualitative methodology was adopted and focus group discussions (FGDs) were used for data collection. The FGDs were conducted in the three main hospitals in Oman: the Royal, Al Nahdha and Khoula Hospitals. Participants included senior and junior staff classified as MLPs. The study was undertaken in 2017 and the data were analysed by directed content analysis. ***Results:*** The MLPs identified the following factors that influenced their job satisfaction: health and safety, recognition and appreciation, salary and promotion, organisational policies, professional training and relationships with coworkers and leaders. Applying Herzberg's theory, participants showed a low motivation level in their jobs. ***Conclusion:*** The job dissatisfaction reported by the participants in each of the three hospitals resulted from the absence of factors that lead to satisfaction. Such factors, referred to as hygiene factors in Herzberg's theory, must be present for this group of health professionals to experience job satisfaction; therefore, hospital managers need to address these factors or actively incorporate satisfiers that increase motivation and improve job satisfaction.

Poster Presentations

Evaluating Ordering Blood Smear Criteria in Haematology Laboratory at Sultan Qaboos University Hospital

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Objectives: This study aimed to evaluate existing blood smear ordering criteria used at Sultan Qaboos University Hospital (SQUH) and obtain the optimal cut-off percentage of immature granulocyte (IG) that should be applied. ***Methods:*** An evaluation study was conducted to evaluate the current cut-off percentage of IG used by the SysmexXN9000 analyser. A total of 118 blood samples were selected randomly within 24 hours of collection from the laboratory. Blood smears were performed, stained using Romanwsky stain and stored. The WBC differential was performed manually using a manual cell counter. For data analysis, Bland and Altman's analysis was used to see the agreement between the two different methods and deciding the optimum cut-off percentage by observing the tendency of the data. ***Results:*** The agreement interval was found using the following equation: 1.96 SD ± mean equal (−0.042, 0.024). At a cut-off (mean) = 3%, the bias was toward the Sysmex IG%. At a cut-off between 4–6%, IG Sysmex IG% > Manual IG%. Outliers for number of patients differed so that Sysmex measured much more IG than manual at a cut-off of nearly 5% and more. However, at a cut-off between 3–7%, Sysmex measured IG% much less than manual. ***Conclusion:*** Ordering blood smear criteria at the SQUH is based on an IG = 10% cut-off point. However, according to the results obtained from this research, using 10% as a cut-off leads to loss of cases. Therefore, ordering criteria cut-off should be set to 3% IG.

Assessing Pro- and Anti-Coagulant Pathways in Early-Onset Preeclampsia

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Objectives: This study aimed to characterise coagulation in patients with early-onset preeclampsia (EOP) and to elucidate the underlying mechanism. ***Methods:*** Patients with EOP (n = 26), normal pregnant controls (PC; n = 21) and non-pregnant controls (n = 16) were recruited at the Rotunda Hospital, Dublin, Ireland. Blood samples were collected into vacutainers containing sodium citrate (contact or intrinsic coagulation pathway not inhibited) or sodium citrate plus corn trypsin inhibitor (contact pathway inhibited) as an anticoagulant. Platelet poor plasma was prepared and coagulation was assessed using calibrated automated thrombography and measurement of D-Dimer, thrombin-antithrombin III (TAT) and tissue factor pathway inhibitor (TFPI) levels. ***Results:*** Compared to PC, EOP patients had comparable tissue factor pathway-dependent thrombin generation profiles when the contact pathway was not inhibited. In contrast, EOP patients were characterised by impaired thrombin generation compared to pregnant controls when the contact pathway was inhibited. This impaired thrombin generation was most apparent in patients with severe EOP. Furthermore, EOP patients had increased sensitivity to activated protein C (APC) anticoagulant activity and endogenously generated APC compared with PC. D-Dimer and TAT levels were not elevated in EOP patients than PC, suggesting that the impaired thrombin generation was not due to an *in vivo* coagulopathy and the consumption of clotting factors. However, TFPI levels were elevated in EOP patients, most significantly in severe cases. Inhibition of TFPI corrected the impaired thrombin generation profile in preeclampsia patients, suggesting that elevated TFPI levels were responsible for this observation. ***Conclusion:*** Thrombin generation is reduced in patients with EOP owing to elevated TFPI levels. This may explain the reduced VTE risk seen in association with preeclampsia patients compared to other inflammatory disorders.

Anti-D Alloimmunisation in RHD+ Sickle Cell Disease Patient

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A 28-year-old woman with SCD was admitted with a history of multiple transfusions and was known to have multiple antibodies with anti-E, anti-C and anti-Kell antibodies. The blood bank investigations showed that the blood group was O RhD + and confirmed the already known antibodies with anti-C, anti-E and anti Kell specificities. However, there were additional reactions observed suspicious of anti-D detected by the enzyme method only. The direct antiglobulin test (DAT) was negative. We report a case of SCD found to have anti-D despite being serologically strong RhD+. Full sequencing of the RhD for the patient revealed that the patient harboured a partial D allele DAU-3 which harboured two mutations V279 and T379M. Given these findings, the transfusion recommendation was to give antigen-negative for D, C, E and Kell and cross-match compatible. Six months later, the patient's sample was sent again as she required transfusion and the antibody identification test confirmed the presence of anti-D in addition to the already identified antibodies with anti-C, anti-E and anti-Kell specificities. The anti-D used for the RhD typing demonstrated that the patient's sample reacted strongly (3+ to 4+). The previous patient's D typing demonstrated the same findings using different RhD typing reagents. Genotyping was performed to explain anti-D's paradoxical findings in the serologically normal RhD positive patient. Analysis of the RhD gene and sequencing revealed that the patient harboured DAU-3 RhD allele (V279M, T379M) described in African ethnic origin. Anti-D immunisation in patients with SCD harbouring partial D alleles is a problem despite giving phenotypically matched blood transfusion as current serological D typing may not detect some partial D variants harbouring some of the DAU alleles. Molecular testing should be considered for patients with SCD on chronic transfusion who develop anti-D even when the RhD typing reacts strongly with the D typing reagents as some partial RhD variant may give normal reaction with RhD typing reagents.

The ABO Blood Group Discrepancies among Patients Referred to the Red Cell Reference Laboratory at the Department of Blood Banks Services

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Objectives: The Red Cell Reference Laboratory (RCRL) is considered a reference lab for Oman's blood banks. It provides technical support and transfusion advice for all regional blood banks and resolves difficult immunohaematology cases. This study aimed to provide information on the causes of ABO discrepancies among referred patients to the RCRL from January 2014 to December 2015. ***Methods:*** A retrospective analysis was performed on samples referred to ABO discrepancy between January 2014 and December 2015. Samples referred to RCRL which showed ABO discrepancies were analysed as per the classifications into forward and reverse group discrepancies. Then further classification of causes of each group was done. ***Results:*** One thousand eight hundred sixty-three samples were referred to the RCRL in the study period; 42 patients were found to have ABO discrepancies with an incidence of 2.25%. 60.8% of ABO discrepancies causes were due to reverse ABO group discrepancy and of these, 25.49% was an age-related cause which gives a weak antibody reaction on reverse grouping. Forward group discrepancy was observed in 39.2% of patients and A subgroup was the common cause seen in this group. Three cases showed both reverse and forward group discrepancy. ***Conclusion:*** The incidence of ABO discrepancy among referred patients to RCRL in the study period was found to be 2.25% with the majority (60.8%) of them due to reverse group discrepancy. In order to find compatible blood for recipients, ABO discrepancies must be resolved to prevent ABO hemolytic transfusion reaction.

Association between Vitamin D Binding Protein SNP rs2282679 and the Level of Serum 25-Hydroxyvitamin D

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Objectives: Vitamin D is a secosteroid hormone produced in the skin upon exposure to sunlight. In addition, it can be obtained from food. Vitamin D binding protein (VDBP) is found in plasma and is used to transport 25(OH)D from the liver to the kidneys

and other organs where it is converted to the biologically active vitamin D form, 25(OH)2D. VDBP is highly polymorphic and the plasma concentrations of 25(OH)D depends on different genotypes. Vitamin D deficiency is a high prevalence problem worldwide that leads to different health outcomes such as chronic liver disease, muscle weakness, low creatinine clearance and chronic renal diseases. Investigate whether the VDBP single nucleotide polymorphism (SNP) rs2282679 is associated with the serum level of 25(OH)D in a healthy Omani population. ***Methods:*** 29 DNA samples extracted from blood samples collected from healthy Omani volunteers along with the vitamin D serum levels were available. Polymerase chain reaction (PCR) followed by Sanger sequencing was used to determine each sample's genotype. ***Results:*** Almost 70% of the samples had the homozygous major genotype for the VDBP SNP rs2282679, whereas only 30% were heterozygous. For the vitamin D level classifications, 13 samples had a deficient level (less than 30 nmol/l), two samples had an insufficient level (30–50 nmol/l) and 14 samples had a sufficient level of vitamin D (more than 50 nmol/l). The Chi-square test was used to look for an association between the VDBP SNP and the serum level of 25(OH)D in our samples and the *P* value was 0.652. ***Conclusion:*** There were no significant association between the VDBP SNP rs2282679 and the level of 25(OH)D in the serum among the volunteers in this study. This study should be repeated with a sufficient number of samples to represent the Omani population.

Expression Status of the *Pro-Apoptotic Caspase-3* Gene after Knocking Down *FAT4* Gene in Epithelial Ovarian Cancer

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Objectives: Ovarian cancer (OC) is considered the 7th most common tumour and the 8th most incident neoplasms worldwide. OC is composed of different histological subtypes 90% of which are of epithelial origin. In Oman, the 2013 mortality rate of OC was estimated to 0.4 per 100,000 females, accounting for 4.5% of all cancer cases. In a previous OC related study, we have identified a cross-talk between the E2F5 transcription factor, which is involved in the early set-up of OC and the adhesion molecule *FAT4* gene. The obtained results were validated in MCAS, OVSAHO and OV2008 ovarian cancer cell lines using qRT-PCR. Since E2F5 regulates *FAT4*, we hypothesised that the latter may have a role in OC and operates through *apoptosis* using different effectors, including Caspase-3. This study aimed to monitor the expression of Caspase-3 in MCAS and OVSAHO cell lines treated with siRNA to down-regulate *FAT4* gene expression. ***Methods:*** The change in the expression of Caspase-3 in *FAT4* siRNA treated MCAS and OVSAHO cell lines was examined using the qRT-PCR and delta-delta-Ct method for quantitation. ***Results:*** Significant overexpression of Caspase-3 was found after the *FAT4* gene was knockdown in both cell lines. While MCAS cells express Caspase-3 gene 1.3 fold higher than normal cells, OVSAHO cells express Caspase-3 gene 1.7 fold higher than normal cells. ***Conclusion:*** When *FAT4* is down-regulated, Caspase-3 may have another role than pro-apoptotic effector in epithelial ovarian cancer.

Hyperhomocysteinemia is Associated with N-Homocysteinylated Albumin Formation in Prediabetic Omani Adults

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Objectives: This study aimed to assess homocysteine (HCY) status and the formation of N-homocysteinylated albumin protein in the sera of prediabetic Omani adults. ***Methods:*** One hundred five female Omani college students at Sultan Qaboos University were recruited voluntarily and screened for prediabetes (impaired fasting blood glucose or impaired glucose tolerance). Only 53 study participants were found to be prediabetic and fasting serum samples were collected from this group to measure HCY level and to quantify N-homocysteinylated albumin protein. ***Results:*** It was observed that the study participants had a comparable age (21.5 ± 1.5 years) and were overweight based on their body mass index (BMI, 26.84 ± 1.19 kg/m^2). The measured serum levels of HCY were higher than the normal range (71.25 ± 6.11 µmol/L), suggesting that the prediabetic participants had hyperhomocysteinemia. Proteomic measurements of N-homocysteinylation in serum albumin revealed the formation of N-homocysteinylated albumin in all of the assayed serum samples. Correlation coefficient analysis revealed that the serum HCY was positively correlated with age and BMI. ***Conclusion:*** The results suggest that hyperhomocysteinemia was associated with N-homocysteinylated albumin protein's pathological formation, which might be considered a diagnostic marker for prediabetes before aggravating to type 2 diabetes.

Is a Single Body Site Swab Sufficient to Detect Methicillin-Resistant *Staphylococcus aureus* from a Surveillance Swab Culture?

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Objectives: The economic burden for screening and treating the various infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is challenging worldwide. Early detection of MRSA can reduce further spread of this pathogen in hospital settings. MRSA is detected by either molecular-based methods or culture-based methods. This study aimed to explore the efficiency of culture-based methods in detecting MRSA from three body sites. ***Methods:*** Retrospective data were obtained from electronic patient's records at the Sultan Qaboos University Hospital of all MRSA positive in-patients from 2016 to 2018. The positivity rate of the culture versus molecular methods to detect MRSA was compared. ***Results:*** Of the 199 patients who met the inclusion criteria: 82.9% (n = 165) were MRSA positive from nasal swabs alone. 4.5% (n = 9) showed positive MRSA from the groin, whereas 4% (n = 8) of the total positive MRSA were *axilla* positive. MRSA positivity from two different sites simultaneously (nasal and groin, nasal and *axilla* and *axilla* and groin) were 5%, 2.5% and 1%, respectively. Out of the total MRSA swabs, only 37% were PCR positive, of which 44.8% were nasal positive, 25% had positive *axilla* sample and none had positive groin samples of total 83 PCR positive. Two patients were PCR positive and culture negative. ***Conclusion:*** Collectively, our data have shown that nasal swabs have the highest positivity rate. Moreover, it suggests that multiple site surveillance increases the detection rate of MRSA as opposed to a single site. Molecular testing could be spared to cases when treatment is needed.

Molecular Docking Studies for Discovery of Plant-Derived Urease Inhibitors

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Objectives: A series of natural compounds were isolated from different medicinal plants and characterised using advanced spectroscopic techniques. In order to identify urease inhibitors, 15 natural compounds were screened including alkaloids, carotenoids, flavonoid, lignans and terpenoids. Molecular docking study was performed to understand the binding modes of the active compound into the active site of urease enzyme. This study aimed to evaluate the *Helicobacter pylori* urease inhibitory activity of isolated natural compounds for gastric ulcers therapy. ***Methods:*** Urease activity, through indophenols method, was measured by the production of ammonia, as described by Weatherburn. Thiourea was used as the standard inhibitor of urease. Finally, the results were processed by the softwares SoftMax Pro (Molecular Devices, CA, USA), MS-Excel and Ez-fit. Docking was conducted on MOE docking suite (MOEv2014.09). Three-dimensional structure of urease in complex with inhibitor (acetohydroxamic acid) (PDB code 4UBP, resolution 1.55Å) was retrieved from RCSB Protein databank. ***Results:*** On this assay, camptothecin exhibited promising inhibition with IC50 value = 130.4 ± 7.884 µM. Moreover, Emetine Hydrochloride, Curcumin, Karanjin, Hypophyllanthine and Callophyllolide also showed reduced activity with 98.7 ± 2.251, 26.5 ± 0.262, 21.8 ± 1.081, 18.9 ± 0.619 and 17.5 ± 0.218 µM respectively. ***Conclusion:*** Many natural compounds were isolated and evaluated as novel urease inhibitors and found that camptothecin showed more inhibition and was the most active urease inhibitor. Furthermore, the proposed scaffold of urease inhibitor offers convenient further modifications and extensions that could give rise to the structures with improved inhibitory activity against urease enzyme.

Epidemiology and Genotyping of Human Papillomavirus among Omani Women Attending Sultan Qaboos University Hospital and the Royal Hospital

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Objectives: Persistent infection with high-risk (HR) HPV genotypes has been associated with cervical cancer. It is the third most common cancer affecting women in Oman with a crude incidence rate of 4.7 and mortality rate of 2.5. No data on the prevalence of HPV infection or its risk factors have been reported in Oman. This study aimed to assess the prevalence and genotype distribution of HPV and the risk factors among Omani women. ***Methods:*** Cervical samples (n = 258) obtained from Omani women aged 18–68 years, attending two tertiary hospitals in Oman between September 2014 and April 2015. HPV genotyping were done using a multiplex real time-polymerase chain reaction (RT-PCR) assay. ***Results:*** 22 different HPV genotypes were detected in 46 women (17.8%) and included 15 HR and 7 LR genotypes. Human immunodeficiency virus (HIV) patients (P = 0.052) and oral contraceptives users (P = 0.016) showed significant association with HPV infection. ***Conclusion:*** The most frequently observed HPV types were HR HPV 82 and LR HPV 54. These findings indicate that the predominant HPV genotypes in Oman are different from those seen in worldwide studies. This finding is baseline data to determine the potential impact of preventive measures including using new vaccines to reduce the burden of cervical cancer.

A Substitute to Xylene in Deparaffinisation and Clearing Prior to Coverslipping in Histopathology

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Objectives: Deparaffinisation and clearing before coverslipping are important steps in all staining methods in histopathology. Xylene is the most commonly used agent worldwide. However, xylene is toxic. We evaluated safer alternative dewaxing and clearing agents prior to coverslipping in a histopathology laboratory. ***Methods:*** Thirteen different fresh surgical tissues were cut into two halves. One half processed using xylene and the other half processed using UltraClear™. Five groups were designed. For each A, B, C and D group, 100 slides were cut from xylene-processed blocks. For group E, 100 slides were cut from UltraClear™-processed blocks. Group A is the standard method. Group B evaluates UltraClear™ as a dewaxing agent only. Group C evaluates UltraClear™ as a clearing agent before coverslipping only. Group D evaluates UltraClear™ as both dewaxing and clearing agents before coverslipping. Group E evaluates UltraClear™ as both dewaxing and clearing agents before coverslipping. Six parameters were evaluated: nuclear staining, cytoplasmic staining, cell morphology, clarity of staining, uniformity of staining and cost. ***Results:*** groups B, C, and D showed 79% (P = 0.054), 83% (P = 0.221), and 80% (P = 0.079) adequacy when compared with group A (89%), respectively. However, group E showed only 76% (P = 0.016) adequacy. UltraClear™ is more expensive than xylene. ***Conclusion:*** UltraClear™ is a promising dewaxing agent. It is also a good clearing agent for use before coverslipping in the histopathology laboratory. The cost-benefit balance between laboratory workers' safety, good quality staining and cost-effective strategy needs to be further studied.

The Effect of Calpain Activation on Cisplatin-Induced *Apoptosis* in Triple-Negative Breast Cancer Cells

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Objectives: Globally, breast cancer is the most prevalent type of cancer among women. Triple-negative breast cancer is an aggressive sub-type in which the primary treatment approach is chemotherapy. Cisplatin is a commonly used chemotherapeutic agent that induces *apoptosis* through several pathways; ER-dependent pathway. However, it is associated with adverse side effects. In order to reduce its side effects, it is usually administrated with other drugs. In the current study, the effect of cyclopiazonic acid (CPA), which is a mycotoxin, on cisplatin-mediated calpain activation, and *apoptosis* induction in triple-negative breast cancer cells, was investigated. ***Methods:*** Upon cisplatin treatment, endoplasmic reticulum (ER) related protein expression was measured

using the Western blotting method. Moreover, *apoptosis* induction in triple-negative breast cancer MDA-MB-231 cell line was detected by Hoechst stain 33258. ***Results:*** This study demonstrated that CPA increases intracellular calcium concentration (Ca+2); as indicated by calmodulin induction in a concentration-dependent manner. In addition, CPA alone was shown to induce ER-stress (indicated by an increase in glucose-regulatory protein 78 (GRP 78) expression compared to the control). GRP 78 is a molecular chaperone, located on the ER, and used as an ER stress indicator. As for calpain expression, CPA was able to activate calpain and this activation was detected by the cleavage of alpha (α)-fodrin, which is one of its downstream effectors. Like GRP 78, caspase-12 (a cysteine protease located in the ER) cleavage indicates ER-stress. Cisplatin significantly induced *apoptosis* (P <0.05) and showed similar trends to CPA regarding the ER-related proteins, except for calpain activation which was not consistent. There was no further effect of CPA on CDDP-induced *apoptosis*. ***Conclusion:*** CPA was able to induce ER stress due to increased calcium influx, activate calpain and eventually lead to *apoptosis*. Hence, CPA might be used in combination with CDDP in the treatment of TNBC.

Detection of E2F1 and Akt1 Interaction in Triple-Negative Breast Cancer Cells

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Objectives: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer that is unresponsive to hormonal and targeted therapy. It can be treated using platinum-based chemotherapy such as cisplatin. However, most patients are at first responsive, eventually relapse and become resistant to additional treatment. Many theories were suggested to identify chemoresistance mechanisms and one of them is inhibition of *apoptosis* by survival proteins. E2F1 is a transcription factor overexpressed in response to DNA damage to induce cell death. It is suggested that overexpression of E2F1 following the genotoxic effect of chemotherapy might activate AKT1, a survival protein. The current study aimed to detect the interaction between E2F1 and AKT1 in TNBC and examine cisplatin's effect on their expression. ***Methods:*** MDA-MB123 cell line (TNBC cell line) was used. Cells were treated with varying cisplatin concentrations. Cisplatin's effect on E2F1 and AKT1 expression was detected by western blot and immunofluorescence staining (IF). IF was also used with immunoprecipitation to assess the interaction between the two proteins. IP was used as a confirmatory experiment for the interaction. ***Results:*** Western blot and IF showed an increase in E2F1 expression and decreased AKT1 expression as cisplatin concentration increases. IF and IP results suggested a successful interaction between the two proteins. ***Conclusion:*** The findings confirmed the role of cisplatin on E2F1 and detected its effect on AKT1. It also suggested an interaction between E2F1 and AKT1, which might be enhanced by cisplatin and involved in the development of chemoresistance in TNBC cells.

Prolactin Receptor Expression in Cyotomegalovirus Positive Ovarian Cancer

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Objectives: Ovarian cancer (OC) is considered the second most common gynaecological cancer with increased morbidity and mortality in women worldwide. High serum level of prolactin (PRL) is found in OCs patients, although it is not yet considered a clinical biomarker for OC. Human cytomegalovirus (HCMV) proteins are frequently detected in OC tissue specimens, but the potential impact of HCMV infection on the PRL/PRL receptor (PRLR) system has so far not been investigated. ***Methods:*** In this study, HCMVs effects on PRLR expression were assessed in infected ovarian cancer cells (SKOV3) by PCR and Western blot techniques. Expression of HCMV proteins (-IE, -pp65) and PRLR in paraffin-embedded OC tissue sections, obtained from patients with OC who underwent surgery, was assessed by immunohistochemistry. ***Results:*** We found that HCMV infection enhances the expression of PRLR and induces the production of PRL in OC cells compared to uninfected control cells. We also found an association between extensive PRLR levels and extensive HCMV protein expression levels in tissue specimens obtained from OC patients positive for CMV. ***Conclusion:*** Infectious activity of HCMV can stimulate the activation of local growth factors, including the PRL/PRLR system. HCMV induces PRL and PRLR transcripts and proteins in HCMV infected ovarian cancer cells. Extensive expression of PRLR found in HCMV infected OC may provide another mechanism by which HCMV can promote OC's pathogenesis. Future studies devoted to blocking HCMV infection and PRLR may offer new treatment possibilities for ovarian cancer patients.

Silybum marianum Hydroalcoholic Extract as New Herbal Drug to Reduce Intra-Abdominal Adhesions

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Objectives: Adhesions usually begin to form after surgery during repair of intra-abdominal injured sites. The main cause of adhesion formation is the lack of balance between the formation and destruction of fibrin. In the present study, we examined the Silymarin effect on intra-abdominal adhesion. ***Methods:*** Thirty Wistar rats were divided into three groups. Groups A and B received 1% and 5% concentrations of the *S. marianum* extract, and group C (control group) received distilled water. After anaesthesia, the abdominal wall was opened and three shallow, longitudinal and transverse 2 cm incisions were made on abdomen right wall. A 4 cm^2 piece was removed from the peritoneal surface on the left side. 3 mL of *S. marianum* extract or distilled water were administered into the abdominal cavity. After two weeks of adhesion degrees, histopathological factors, phenolic and flavonoids were determined and analysed by SPSS version 16. ***Results:*** The adhesion degree in groups A and B were significantly lower than control (P <0.05; P = 0.023). In the histopathological examination, significant differences were observed between control and extract-treated groups in histopathological markers (P <0.05). The total phenolic content of *S. marianum* was 109.7 mg/g gallic acid equivalent; its total flavonoid and flavonol contents were 9 and 5 mg/g rutin equivalent/g. The antioxidant activity of the *S. marianum* extract was 35% of β-carotene. ***Conclusion:*** This new drug that contains *S. marianum* extract has preventive effects on post-laparotomy intra-abdominal adhesion both in macroscopic and microscopic scores. Therefore, through further clinical studies, *S. marianum* extract and its derived compounds might be used in humans as a new herbal drug.

Antifibrotic Effect of Extracted Natural Products from Date Palm Fruit (*Phoenix Dactylifera L.*)

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Objectives: Since ancient time, plants were used as a medicine for many diseases. More than half of the world's population is still using plants for their medical uses as it is a traditionally trusted source. Previous studies reported several biological activities of date palm fruit including antioxidant, anti-inflammatory, antibacterial and anticancer activity due to the phytochemical composition. ***Methods:*** Natural products have been extracted from date fruit using the maceration method in different solvents (water, ethanol, acetone and ethyl acetate). These four extracts have been investigated for their biological activities in pancreatic stellate cells (PSCs) stimulated with tumour necrosis factor. Ethyl acetate extract was isolated into nine fractions using column chromatography based on their polarity behaviour. ***Results:*** Ethyl acetate extract significantly reduced fibrosis compared to the control and other date fruit extracts. Ethanol, acetone and ethyl acetate extracts suppressed the cells' proliferation while water extract had almost no effect on proliferation of the activated PSCs. ***Conclusion:*** These findings showed that date fruit has active compound/s which can transform PSCs from active to a quiescent state by suppressing the secretion of α-SMA. Hence, these active compounds may be useful for treating pancreatic fibrosis which would probably boost the effect of known anticancer drugs.

Computational Investigations of the Binding of Common Cystic Fibrosis Drugs to the Atomic Structure of CFTR

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Objectives: Cystic fibrosis (CF) is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR). We aimed to identify potential binding sites of CFTR pharmacological modulators and explain differences in drug potency and mechanisms of action. ***Methods:*** The binding of VX770, VX809, VX661, quercetin and GLPG2222 to human CFTR (PDB:6MSM) using structural docking was investigated. The structures were prepared using Pymol and ChemDraw software. The SwissDock server was used to predict binding parameters and visualised them using UCSF Chimera. The change in Gibbs free energy (ΔG) and the number of H-bonds were employed as drug-binding strength indicators. ***Results:*** All drugs formed a higher number of H-bonds with clusters predicted at the interface between the two nucleotide-binding domains (NBDs) or between the NBDs and the membrane-spanning domains (MSDs). Quercetin was the best binder at the NBDs interface forming 3.75 H-bonds. VX809 binds best at the NBDs/MSDs interface with 1.8 average H-bonds and ΔG of -14.8 kcal/mol. Notably, its structural analogue VX661 formed more H-bonds at these pockets. GLPG2222 binds best at the NBDs/MSDs interface. VX770 was the weakest binder to the NBDs and fitted well in clusters at the MSDs. ***Conclusion:*** We were able to identify potential binding clusters of the studied molecules. Notably, our findings of the binding of quercetin and VX809 fitted well with published experimental data. The better formation of H-bond by VX661 when compared to VX809 might explain the differences in drug potency. These results inform drug design strategies for CF treatment.

An Overview of ECG Analysis by Wavelet Transforms

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Objectives: Electrocardiogram (ECG) plays an indispensable role in the primary diagnosis, prognosis and survival analysis of heart diseases. In ECG, most useful clinical information is derived from the onset and offset of P, QTS and T waves and their amplitudes. Detection of such waves in an ECG is difficult due to the time-varying morphology of the signal and the presence of various noise factors. ECG signals' key characteristic is its non-linear dynamic behaviour and that the non-linear component changes conspicuously between normal and abnormal conditions compared to the linear component. In this direction, a relatively recent tool *viz*, the Wavelet transform gains great importance in analysing ECGs by the suitability of its excellent time-frequency localisation characteristics, unlike the traditional Fourier analysis. This review aimed to highlight the significance of Wavelet analysis, their offshoots and their ability in ECG signal enhancement studies and different denoising techniques besides highlighting its elegance for the evaluation of various pathological conditions. It may be mentioned here that the choice and criteria of mother wavelet also ensure desired results such studies. ***Methods:*** This work summarises the salient and significant outcomes of Wavelet transform applications and its offshoots to ECG analyses available in the literature. A different approach of denoising ECG signal and algorithms for detecting weak constituent waves in ECG and their onset and offset are discussed. ***Results:*** Among comprehensive studies on the wavelet transform in ECG signals, it has a prominent influence of precise location of P, QRS and T waves. It is superior in denoising ECG than other existing methods. Criteria for choice of mother wavelets in such studies are also highlighted. ***Conclusion:*** ECG signals' key characteristic is its non-linear dynamic behaviour and that the non-linear component changes conspicuously between normal and abnormal conditions than the linear component. We can conclude that the wavelet transform is a valuable tool and highly reliable for analysing ECG signals.

Applications of Fractals for Feature Extraction in EEG Signals: *An Overview*

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Objectives: Fractal structure, being a relatively a recent tool, is gaining great importance in studying non-linear signals such as electroencephalogram (EEG). Several algorithms are in vogue to estimate the fractal dimension of EEG signals. The three prevalent techniques that estimate these signals' fractal dimension are the box-counting method, Katz's algorithm and Higuchi's algorithm. This study aimed to provide an overview of the analysis of EEG signals which are useful to identify and distinguish different states of physiological function of the brain. ***Methods:*** This work reviews the main result of studies in the literature regarding the fractal dimension estimation in EEG signals by Higuchi's algorithm and other non-linear methods. Furthermore, a brief review of Higuchi's

fractal dimension application's benefits and drawbacks was provided from the medical context. ***Results:*** Among the vast number of studies and discussions on the fractal dimension estimation of EEG signals, an accurate result based on direct approach with Higuchi's algorithm paves the way for extracting a few known disorders associated with the human brain. ***Conclusion:*** Non-linear methods like fractal dimension are more appropriate for analysing the EEG signals for feature extraction and characterisation than the linear methods. Computing the fractal dimension of EEG signals with Higuchi's algorithm are very useful since it gives more accurate results compared to the other methods. In contrast, this method showed some drawbacks in some cases of application. There is always a need for enhancement to overcome these drawbacks.

Myocardial Bridging of Left Anterior Descending Coronary Artery and its Clinical Implication

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Objectives: Myocardial bridge (MB) is defined as the muscle overlying the intramural segment of a major epicardial coronary artery, mainly the mid-portion of the left anterior descending coronary artery. MB has been associated with angina, arrhythmia, depressed left ventricular function, myocardial stunning, early death after cardiac transplantation and sudden death. The objectives understudy validate the prevalence and segments of coronaries with MB, length and diameter of bridging segments and the relationship between the presence of bridges and their clinical relevance. ***Methods:*** Seventy-eight formalin-fixed cadaveric heart specimens irrespective of age, gender, and race were collected and serially numbered from 1 to 78. The left coronary artery (LCA) was dissected out carefully avoiding damage to the small branches and the number of terminal branches of the main trunk at a subepicardial level was noted. The location, type, number and direction of MB's were noted. With digital callipers' help, the length of MB was measured, noted and photographs were taken. ***Results:*** Out of the total 78 dissected hearts 68 showed MB in at least one coronary artery or one of its significant branches. The overall prevalence was 87.17%. The maximum length of MB was 5.1 cm. ***Conclusion:*** The present study adds up the information regarding MB's prevalence and relationship to coronary arteries. Knowledge of MB's morphology and morphometric details facilitates cardiologists in diagnosis, planning therapeutic strategies and prognostic predictions.