Scientific Tracks & Abstracts (Day 1)
Insights of breast cancer epigenetics: An intersection between the endogenous and exogenous systems

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Epigenetics acts as a vital intersect between environmental factors being exogenous and cellular and pathological processes being endogenous. Many studies have suggested that epigenetics alterations manifest to diseases as result of environmental, microbial, UV light exposure, dietary including alcohol consumption and smoking and lifestyle factors increasing the risk of cancer. The reversibility fact of epigenetics effects serve as a fertile platform in oncological and cancer studies, of which DNA methylation, histone modification, microRNA expression and many others widen the doors for biomarker search for early detection, diagnosis, classification along with therapy targets and prevention. Aberrations in DNA methylation pattern and miRNA expression profile are established in breast cancer and exhibit good example of epigenetic effect resulting from the exogenous and exogenous interactions. Herein, this paper will shed light on the predisposition of these exogenous epigenetic effects factors like diet and the potential reversibility and preventive possibilities of breast cancer as endogenous manifestation.

Biography
Manal H Al Khanbashi is currently working as a Lecturer at Applied Science Department of Higher College of Technology, Oman. She has completed her PhD in Medicine, Breast Cancer Genetics and graduated from Sultan Qaboos University and Karolinska Institute, Sweden. She has also worked in breast cancer epigenetics where miRNA, methylation and cancer related studies were covered.

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A metabolomics approach for therapy response in breast cancer

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Due to its broad clinical heterogeneity, the treatment of breast cancer is based on a wide variety of protocols. However, only a fraction of patients will show a beneficial response. The discovery of biomarkers which enable the classification of responders and non-responders patients may have important implications to treatment protocols and outcomes. In this study, we carried out a metabolomic profiling of 46 serum samples of breast cancer patients at diagnostic to identify potential biomarker candidates that can predict response to neoadjuvant chemotherapy. To this end, we analyzed the samples using liquid chromatography couple to high resolution mass spectrometry LC-HRMS and the data matrix obtained was subjected to univariate and multivariate statistical analysis.

Biography

Pedro Sanchez-Rovira has completed his PhD from Sevilla University and Postdoctoral studies from Córdoba University School of Medicine. He is the Director of Oncology Unit in Jaen Hospital. He has published more than 75 papers in reputed journals and has been serving as an Editorial-Board Member of repute.

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Scientific Tracks & Abstracts
(Day 2)
Single-cell molecular analysis reveals a possibility of epithelial to circulating tumor cell transition when a tumor cell enters into the bloodstream

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Circulating tumor cells are important biomarkers function as liquid biopsies for cancer diagnostics and therapeutics. However, traditional analyses of tumor cells and tissues are not suitable for circulating tumor cells due to the limited number of circulating tumor cells and the molecular analyses of a population of tumor cells that may miss crucial information such as single-cell heterogeneity. Therefore, we have developed an automatic device that isolates live circulating tumor cells from a breast cancer patient’s blood sample and performs a range of single-cell molecular analyses to determine tumor cell characteristics. The developed automatic device isolates live circulating tumor cells from patients’ blood samples. This device is useful for the positive enrichment, negative enrichment or different combinations of negative and positive enrichment of circulating tumor cells. Up to 100 gene expression analyses were performed on the isolated single circulating tumor cells with the profile of the 100 genes showing great heterogeneity at the single-cell level on housekeeping genes expression and the molecular signatures of apoptosis, stem cell, transition, etc. About 1/3 of the analyzed CTCs lost housekeeping genes, suggests that these CTCs were already dead or lost the ability to continue growing. There is also a large portion of CTCs that either does not express or have low levels of mesenchymal cell signatures, suggesting the current EMT hypothesis only happened in limited numbers of CTCs. Our single-cell molecular analysis results on breast cancer patients’ CTCs reveals that there is a strong possibility that when an epithelial cell enters the bloodstream, its first transition will be epithelial to circulating tumor cell transition (ECT), followed by the CTCs performing the circulating to mesenchymal cell transition (CMT) and finally the mesenchymal to epithelial cell transition (MET). Our results also suggest that the ECT transition may be very important for the survival of early CTCs in the bloodstream and may lead to more investigations about the survival ability and metastatic possibility of tumor cells at the DNA and RNA level.

Biography
Glenn Deng has completed his PhD from Tokyo University in Marine Science and Technology and Postdoctoral studies from Stanford University. He is the Professor of China Three Gorges University School of Medicine and the Senior Scientist of Stanford University School of Medicine. He has published more than 30 papers in reputed journals.

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Notes:
Studying methylation status of p16, p14, MLH1, APC and UNC5C in the plasma as diagnostic biomarkers of colorectal cancer

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Colorectal cancer, in spite of different screening strategies is detected in late stages in Iranians patients. Hence, we aimed to study if different epigenetic markers could be helpful in detecting colorectal cancer in any stages. We studied 50 patients (25 males and 25 females) affected with colorectal cancer. Plasma of patients was extracted before any surgical operations. After extraction of free DNA in the plasma, the methylation status of P16, P14, MLH1, APC and UNC5C in the plasma of these patients in comparison with the plasma of normal controls was studied by High Resolution Melting Curve Analysis technique. It was shown that P14, P16 and MLH1 were not methylated in the palms of these patients. Three sites in CpG islands of P14, P16 and MLH1 were studied by this technique. Three sites of UNC5C were studied by HRM. It was shown that 15%, 32.5% and 12.5% of DNA plasma samples in patients with colorectal cancer were methylated from 12.5% to 75%. Also, three sites of APC gene were studied in these patients. In addition, three sites of APC gene were studied by HRM. In 50%, 75% and 70% of patients, APC was methylated in plasma samples. Plasma samples of normal controls was studied too and it was shown that none of the genes in the plasma samples of normal controls was methylated. This study shows that UNC5C and APC methylation can be considered as good candidates for diagnosis of colorectal cancer though more studies are needed before considering them as markers.

Biography

Ladan Teimoori-Toolabi has completed her MD, PhD and Postdoctoral studies from Pasteur Institute of Iran. She is an Associate Professor in Molecular Medicine Department of Pasteur Institute of Iran. She has published more than 35 papers in reputed journals in ISI and has been serving as an Editorial-Board Member of two journals.

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Notes:
Predictive biomarker discovery of treatment response in lung cancer: A metabolomic approach

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Although the broad range of chemotherapeutic agents approved in the late years, it is a challenge for oncologists to choose which drug or combination of drugs will represent the best option for each individual, since only a portion of patients will respond properly. In this regard a biomarker approach to predict patient response to treatment may be very helpful in the making decision process. Metabolomics, the unbiased identification and quantification of small molecule metabolites in biological samples, is particularly promising for biomarker development because altered metabolism is considered a hallmark of cancer. In this work, we have investigated the metabolome of 115 plasma samples from lung cancer patients by mean of liquid chromatography high resolution mass spectrometry. The obtained data matrix was analyzed according the clinical response to each therapy (Neoadjuvant and Immunotherapy) in order to search for a predictive molecular signature in each group of patients.

Biography

Jose Perez Del Palacio is a Scientist with 18 years of industrial experience in a leading pharmaceutical research company (Merck Sharp & Dohme), working mainly in biochemistry and drug discovery. He has broad knowledge of bioanalysis technologies and metabolomics. He has additional experience and specialization in analytical methods development for HPLC, LC/MS/MS, GC and GC/MS systems. He is the author of several papers, scientific posters and presentations at international conferences and congresses.

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Validity of prostate health index and percentage of [-2]pro-prostate-specific antigen as novel biomarkers in the diagnosis of prostate cancer first reported Omani tertiary hospitals experience

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Statement of the Problem: Prostate cancer is the leading cancer in older men. When prostate cancer is detected early (organ defined), it is potentially curable by radical prostatectomy. As per the Ministry of Health (MOH) Oman Cancer Incidence Registry, cancer of prostate is the second most common cancer (in males) and seventh most common cancer (in both males and females), with 57 cases were diagnosed in 2011. Therefore, early detection is important and prostate-specific antigen (PSA) is widely used as a laboratory test for this purpose. However, despite its wide use, its value in screening men particularly asymptomatic is controversial particularly in term of risks and benefits of early detection.

Methods: This is an observational prospective study that included 136 male patients aged (mean±SD: 67±8.89; range 45-90) who were scheduled for prostate biopsy in two different tertiary care teaching hospitals in Muscat, Oman. Blood specimens from these patients were collected at the same setting before obtaining the prostatic biopsy; the sera were stored at -200 °C until analysis. Laboratory measurements of the three prostate specific antigen (PSA) markers (tPSA, fPSA and [-2]proPSA) were processed using UniCell DxI 600 Access Immunoassay System (Beckman Coulter, USA). Calculation of Prostate Health Index (phi) using Access Hybritech phi® software was performed too. The histopathological report of the prostatic biopsy for each patient was obtained from the histopathology laboratory of the concerned hospital along with the clinical and laboratory data through the Hospital Information System (HIS).

Results: The study showed that Phi has the best validity markers as compared with other prostate markers. It gave sensitivity and specificity of 82.1% and 80.6%, respectively with AUC of 0.81 at cutoff value of 41.88. The remaining prostate markers showed sensitivities and specificities of 78.6% and 25.9% for tPSA; 35.7% and 92.6% for %fPSA; 64.3% and 82.4% for %p2PSA: and 75% and 35.2% for age-adjusted tPSA, respectively. Their AUCs at the best cutoff values were 0.67 at 10.1 µg/L for tPSA; 0.70 at 11.6% for %fPSA; 0.55 at 1.4% for %p2PSA and 0.50 for age-adjusted tPSA.

Conclusion: The study has proved the usefulness of Phi and its component assays in predicting the diagnosis and prognosis in men who are suspected of having prostate cancer. The use of Phi outperforms other conventional prostate markers; tPSA and fPSA, when used alone or in combination. Phi appears to be more accurate than tPSA and fPSA in terms of excluding prostate cancer before biopsy; hence it helps the physicians to avoid unnecessary biopsies, particularly in patients with gray zone tPSA level. Phi is the strongest marker that also correlates proportionally with Gleason Score and therefore it is also useful in predicting the aggressiveness of the disease.

Biography
Safana Salim Al Saidi is a Chemical Pathologist and Specialist, working at the Directorate General of Quality Assurance Centre, Ministry of Health, Oman. She has graduated from Medical College, Sultan Qaboos University, Oman in 2003 as a Medical Doctor and completed her Residency training program in Clinical Biochemistry by Oman Medical Specialty Board (OMSB) in 2014. Presently she is a Fellow of the Royal College of Pathologist, UK. She has three publications to her credit and has great interest in conducting researches which are of help to the patients.

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Notes:
EGF induces paradoxical growth arresting via the up-regulation of PTEN by activating Ref-1/Egr-1 in human NSCLC cells

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Epidermal growth factor receptor (EGFR) signaling promotes cell proliferation and survival in several types of cancer. Here, however, we showed that EGF inhibits proliferation and promotes apoptosis in non-small cell lung cancer (NSCLC) cells. In A549 cells, EGF increased redox factor-1 (Ref-1) expression and the association of Ref-1 with zinc finger-containing transcriptional regulator (EGR1) via activation of p22phox, RAC1 and an NOX subunit. EGF increased p22phox and RAC1 expression through activation of purinergic receptors (P2Y). Elevated Ref-1/EGR1 levels increased phosphatase and PTEN levels, leading to inhibition of the Akt pathway. EGF-induced PTEN up-regulation increased apoptosis and autophagy-induced damage in A549 cells, whereas Ref-1 knockdown blocked EGF-induced PTEN up-regulation in an NOX -p22phox subunit-independent manner. In addition, p22phox knockdown restored EGF-induced effects, implying that changes in P2Y activity caused by EGF, which activates NOX via RAC1, influenced Ref-1-mediated redox regulation. Finally, EGF similarly attenuated cell proliferation and promoted autophagy and apoptosis in vivo in a xenograft model using A549 cells. These findings reveal that EGF-induced redox signaling is linked to Ref-1-induced death in NSCLC cells.

Biography
In-Hye Jung has completed her MSc from University of Ulsan College of Medicine. She is the Fellow in Department of Radiation Oncology of Asan Medical Center.

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Notes:
DNA methylation of microRNA genes in gastric carcinoma and its clinicopathological association

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Background & Aim: To explore the role of epigenetic mechanisms in the down-regulation of miRNA genes, we examined the presence of DNA methylation-associated silencing of miRNAs in gastric carcinoma and observed that aberrant methylation of these miRNAs is associated with expression of target gene products.

Materials & Methods: The extent of promoter methylation of has-miR-9-1, has-miR-9-3, has-miR-129-2 and has-miR-137 was assessed using methylation-specific polymerase chain reaction in 100 gastric carcinoma tissues and corresponding non-tumor tissues. The potential target gene products of miRNAs were studied by immunohistochemistry and the relationship between methylation profiles of miRNAs.

Results: Methylation of the has-miR-9-3 and has-miR-137 CpG island was frequently observed in tumor tissues (89% and 86%, respectively) and non-tumor tissues in 100 gastric carcinoma patients (70% and 78%). However, methylation level of the has-miR-129-2 did not show a significant difference in tumor tissues (97%) compared with non-tumor tissues (90%) and normal gastric tissues (90%). Expression of NF-κB and SOX4 protein, which are has-miR-9 and has-miR-129-2 potential target respectively, were inversely correlated with methylation level of miRNAs.

Conclusion: The results suggest that specific miRNAs methylation in gastric carcinoma could be an important molecular mechanism causing loss of control of its target and it may be correlated with the high transcriptional activity of target gene. Epigenetic silencing of some miRNAs may involve in the early stage of gastric carcinogenesis.

Biography
Ho Gun Kim is a Professor in the Department of Surgery and Pathology at Chonnam National University Medical School, Gwangju, South Korea.

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