Medical Biochemistry

Integrative pipeline to identify potential long non coding RNA-Associated competing endogenous RNA and its implication in hepatocellular carcinoma cells
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Background: Circulating transcriptome plays a crucial role in hepatocellular carcinoma (HCC) development and progression.
Method: First, utilizing bioinformatics tools, we selected an HCC-specific RNA-based biomarker panel including; glucose autophagy-associated (SOGA1) mRNA with long non-coding RNA antisense for X-inactive-specific transcript (lncRNA-TSIX) and microRNA-548-a-3p. Second, we attempted to validate these biomarkers using the sera of HCC versus control by qPCR.
Results: The RNA-based biomarker panel exhibited excellent sensitivity and specificity in differentiating HCC patients from controls.
Conclusion: The chosen circulatory RNA-based biomarker panel has potential role in HCC pathogenesis.

CRISPR: a promising tool for treatment of cancer
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CRISPR (clustered regularly interspaced short palindromic repeats) are specific repeated bacterial DNA sequences that originally identified in bacteria and archaea. CRISPR systems are involved in bacterial adaptive immunity against invading viruses. Natural and engineered CRISPR systems are recently utilized as gene-editing tools. Based on CRISPR RNA/target DNA interaction, it is highly-specific, flexible gene-editing tool. In addition, it is relatively fast and cheap and does not require special expertise. Optimizing of several technical parameters including custom design of guide RNA and delivery method of the system is, however, essential for increasing the efficiency of CRISPR system and solving the notable limitation of off-target DNA cut.

Promising CRISPR application’s list is rapidly expanding including but not limited to performing cutting-edge biomedical research, treatment of genetic diseases, and treatment of cancers. There is an actively running clinical trial for treatment of lung cancer in China and a US-approved clinical trial for treatment of multiple myeloma, sarcoma and melanoma to be conducted soon during early 2018.

There is an urgent need to establish and regularly update the legal and ethical standards for basic and preclinical CRISPR-based research on the expression of human genes, and the use of the technique in somatic cells for clinical applications; and with some restrictions, in germ-line cells or embryos, at least until adequate information would be available on its safety.

Applied bioinformatics in medical research
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Large and fast steps had been moved on through the area of Bioinformatics “the use of computers to collect, analyze, and interpret biological information at the molecular level”. In this presentation, we will focus on how to use bioinformatics tools to develop a project for Medical research, based on an integrative approach of using several bioinformatics resources together with experimental laboratory validations of the interplay of the genomic information. We will learn How to retrieve Disease related genes and their regulatory noncoding-RNAs from different databases, which represent an organized collection of tremendous amount of stored sequence information accumulating worldwide. Such in silico data; is based on previous microarray studies that integrated both the information gained from microarray gene expression profiling of protein-coding genes and the noncoding RNAs profiling.

The presentation is concerned of Liver cancer which represents nearly 6% of the global cancer incidence and represents the second most common cause of cancer related death worldwide. Novel accurate strategies for early detection of hepatocellular carcinoma (HCC) and hence better treatment are strongly needed. This could rely on studying the cancer transcriptome (coding and non-coding) which plays a critical role in HCC.

First, we will retrieve HCC related genes from different data bases as; Oncogenic database of HCC, OncoDB.HCC, CellminerHCC are databases of microarray expression profiles of different HCC cell lines. To enhance the data reliability, we will verify the expression of the chosen gene in HCC by searching the Cancer Genetic web, The Cancer Genome Atlas (TCGA), Gene Atlas, Protein Atlas and Gene atlas databases.

This will be followed by a pathway enrichment analysis of the chosen genes using the Reactome Pathway database, the KEGG pathway and the Genemania database to explore the role of the target gene in special biological process categories involved in carcinogenesis, e.g. enrichment for cell cycle, angiogenesis, apoptosis, cell proliferation and cell adhesion.

Finally, we will start to identify the target gene and its regulatory noncoding RNAs association, first, miRNA-Target interactions; by retrieving data from mirRNA.org - Targets and Expression, mir2disease.org and mirWalk databases. As regard the identification of lncRNAs that act as epigenetic regulator of the Target gene we will access the database of lnc-RNA acting as competing endogenous RNA (lncedb), lncRNA and disease database and for more verification we will search the lncRNome knowledge database. Furthermore, for circular RNAs associated with the chosen gene we will go through the CircInteractome database and Cancer specific circular RNA data base: a database for cancer-specific circular RNAs.
Many training and education online courses have been developed and held by H3Africa/H3ABioNet as IBT and eGenomic Medicine. They aimed to train different categories of trainees: Bioinformaticians, Data scientists, and Medical professionals on several Bioinformatics fields and related aspects. We can use such online platforms to design professional and specified courses for Medical Researchers.

**Evaluation of nephroblastoma overexpressed gene, a transcriptional target of forkhead box protein O1 in type 2 diabetes mellitus**

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**Background:** Type 2 diabetes mellitus (DM) is a chronic metabolic disease. The aim of this study was to evaluate the expression of FOXO1 and its target CCN3 in patients with type 2DM in a trial to explore the molecular mechanism underlying β cell failure and to correlate the relationship between the two gene expressions, to each other, to the different clinico-pathological factors and to complications of T2DM. Study design The expression of FOXO1 and CCN3 genes was evaluated by quantitative real time polymerase chain reaction (qPCR) in blood of 60 diabetics and 20 control.

**Results:** A high significant correlation was found between the studied groups regarding fold change of FOXO1 and CCN3 expression (P < 0.001). There was significant correlation between FOXO1 and CCN3 expression and many of the anthropometric measures or clinico-pathological factors among the studied groups.

**Conclusion:** The Results demonstrated the crucial role of FOXO1 and CCN3 in type 2 DM.

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**Recent guidelines of metabolic surgery**

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The accelerating pandemic of diabetes is recognized as one of the greatest global public health threats of our time. Given the micro-vascular and macrovascular complications associated with this disease, as well as the resulting morbidity and mortality, the personal, medical, and societal costs are enormous. In addition, despite continuing advances in diabetes pharmacotherapy, fewer than half of adults with type 2 diabetes mellitus (T2D) achieve therapeutic goals that would reduce long-term risks of complications. It is proved that in about half the cases medical care and lifestyle interventions are disappointing in the long term. In May 2016 a landmark consensus statement has been published in "Diabetes Care." It incorporates Bariatric/Metabolic Surgery in the treatment algorithm of T2D.

Rubino et al. (8) reported new evidence-based guidelines for surgical treatment of T2D, writing on behalf of 48 voting delegates (75% are nonsurgeons) of the 2nd Diabetes Surgery Summit (DSS-II), an international consensus conference organized in collaboration with major diabetes organizations.

These recommendations, endorsed thus far by 45 international professional societies reflect a large body of evidence demonstrating that several gastrointestinal (GI) operations initially designed to promote weight loss (bariatric surgery) can improve glucose homeostasis more effectively than any known pharmaceutical or behavioral approach, causing durable remission in many patients with T2D.

The new guidelines are formally recognized an unprecedented group of societies representing diverse medical and surgical specialties from around the world, these new guidelines can serve as a global reference for the use and study of GI surgery as an intentional treatment option for T2D (“metabolic surgery”).

**The clinical relevance of noncoding RNA in colorectal cancer**

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**Background:** The competing endogenous RNA plays a pivotal role in cancer. Novel proper strategies for early detection of colorectal cancer (CRC) are strongly needed.

**Patients and Methods:** We chose a CRC-specific RNA based biomarker panel based on the integration of differential lethal 3 malignant brain tumor like1 (L3MBTL1) gene expression with its selected epigenetic regulators using in silico data analysis. This was followed by RT-qPCR validation in serum of 70 patients with CRC, 40 patients with benign colorectal neoplasm infection and 40 healthy controls. Moreover, in ten of the 70 CRC cases involved in the study; we examined the expression of RNA based biomarker network in both CRC and adjacent non-tumor tissues and investigated their correlation with the serum level of this network.

**Results:** The 3 RNA based biomarker network [long non-coding intergenic RNA - (lncRNA RP11-909B2.1), hsa- microRNA-595 (hsa-miRNA-595), and L3MBTL1], had high sensitivity and specificity for discriminating CRC from healthy controls and also from benign colorectal neoplasm. Among these 3 RNAs serum lncRNA RP11-909B2.1 is independent prognostic factors.

**Conclusion:** The circulatory RNA based biomarker panel can act as a potential biomarker for CRC diagnosis and prognosis.

**Key points:**
- The circulating transcriptome has been revealed as a novel class of non-invasive biomarker with high specificity and stability for early detection of CRC.
- We proposed an integrative approach between differential L3MBTL1 gene expression with the selected epigenetic regulators.
- This approach has generated an interesting biomarker panel (lncRNA RP11-909B2.1, hsa-miRNA-595, and L3MBTL1 mRNA) for CRC diagnosis and prognosis.

**Role of microRNA-133 in rats with diabetic cardiovascular complications**

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**Background:** Diabetes is one of the most common health problems globally with a serious impact on morbidity, mortality &