INVITED LECTURES ABSTRACTS
AUTOMATION AND WORK-FLOW ANALYSIS IN CLINICAL LABORATORY

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Lean production is a quality process that focuses on adding more value by eliminating activities that are considered “waste.” Any activity or process that wastes resources and/or time without adding value should be viewed or removed from the system. Lean production and Six Sigma Process have been integrated with the quality process in obtaining quality results in clinical and molecular diagnostic laboratories. The development of automation in clinical laboratories has been provided by contribution of vendors developing more flexible and multifunctional systems. Now, automation is not only used to help the laboratory technician in test performance but also to provide processing and transport of samples, loading of samples into automated analyzers, evaluation of the results of the tests made and storage of samples. Thus, automation in clinical laboratories is changing the definition of automation and expanding its scope. The laboratory automation must begin with an assessment mapping the current laboratory workflow from handling the patient samples to completion of testing and reporting of results. The mapping of sample and data flows directly reflects the flow of the process. Ultimately, (1) bottlenecks, (2) staff waste, and (3) potential sources of become illuminated. Workflow mapping can thus better define what steps should be taken in the laboratory for automation. The expected results of the applied automation should be evaluated about 6 months after installation.

Keywords: Laboratory automation, LIS, preanalytical automation, laboratory work-load, laboratory work-flow

ERAD: A NEW PLAYER ON PROSTATE CANCER

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Prostate cancer is the second leading cause of cancer mortality. More than one third of prostate cancer patients developed metastasis and the survival rate is around 33%. Besides their regulation by androgen, it is known that prostate cancer cells are highly secretory. Endoplasmic Reticulum (ER) is the organelle responsible for the synthesis and maturation of proteins that are destined for the secretory pathways. A process called “ER Stress” is triggered due to the accumulation of misfolded proteins in the ER lumen. In response to ER stress, “Unfolded Protein Response (UPR)” is activated and enhances the protein folding capacity of the ER while directing the misfolded proteins to degradation process. Misfolded or unfolded proteins are ubiquitininated and translocated from ER into the cytosol for proteosomal degradation via “ER associated degradation (ERAD).” Therefore, it is important to elucidate the regulation of ERAD and UPR, which are associated with the pathogenesis of various diseases such as diabetes and neurodegenerative diseases. Androgens activate IRE1α signaling pathway of UPR, while coordinately inhibit the PERK pathway; thereby regulating the growth and survival of prostate cancer cells. In our laboratory, we characterized the androgen-mediated regulation of ERAD. The roles of ERAD members on prostate cancer determined by functional analysis. In addition, it was observed that different responses were obtained against ER stress in the presence/absence of androgen in prostate cancer cells. Studies have also been conducted to elucidate the potential activity of ERAD inhibitors on prostate cancer. All these data suggest that UPR and ERAD may be a mechanism that can be targeted in the prevention and/or treatment of prostate cancer.

EFFECTS OF ANGIogenesis AND ANTI-angiogenesis IN THE CANCER

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Cancer is one of the most widespread causes of death in the world, and some cancers are very resistant to drug treatment. Cancer spreads through the blood vessels and lymphatic system. This invasion has been shown to be made easier by angiogenesis. Angiogenesis is the creation of new capillaries from pre-existing blood vessels. Angiogenesis is a physiological process which is beneficial in situations such as the healing of wounds, growth and development, but at the same time it plays a role in tumor growth and metastasis. There are many factors which affect the progress and metastasis of cancer. One of these is the presence of angiogenesis system activators and inhibitors, the balance between which inhibits or activates the progression and spread of cancer. One of the most important activators of the angiogenic system is VEGF. This is a multi-functional molecule with important biological activity. VEGF increases vascular permeability and makes metastasis easier by stimulating secretion of MMP, which is responsible for breaking down the extracellular matrix. Endothelial cells brought into action by VEGF first synthesize MMPs. The MMPs are released and disrupt the structure outside the blood vessels, preparing the ground for angiogenesis. The most important anti-angiogenic agents are endostatin (ES) and thrombospondin (TSP).

In the light of this information, we made a study in stomach cancer cell cultures receiving a treatment dose of CAPE from the standpoint of the factors relating to the effects of matrix proteins. Also, in another study we made a comparison of pre and post-treatment angiogenesis markers in patients with bladder cancer.

Our purpose was to find an alternative way related to these changes which would be less toxic to normal cells while causing the greatest damage to cancer cells and thus provide not only an effective treatment but also a better quality of life. At the same time this will provide the possibility of finding the development of new and more effective methods in the future on the effects of angiogenic of antiangiogenic factors in the treatment of cancer patients.

CALCULATIONS OF LOD, LOQ AND LINEARITY IN METHOD VALIDATION

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It is crucial that analytical methods used in diagnosis, prognosis and treatment of diseases produce accurate, reproducible and reliable results. According to international regulations issued by regulatory agencies such as FDA, Eurachem, ICH, USP, “analytical sensitivity, linearity, measurement range, accuracy, precision, Limit of detection and limit of quantification” are accepted as mandatory validation parameters. In this presentation, the definition, validation and application examples of Linearity, LOD and LOQ parameters will be presented. Linearity is defined as the ability of a method to respond directly and proportionally to changes in the concentration of the analyte, and it can be determined directly by diluting the stock standard having a given concentration or indirectly determined by analyzing components of the test substance separately. Linearity determination analyzes are performed in duplicate or triplicate at a minimum of five different concentrations. Evaluations are carried out both visually and computationally. Among the validation concepts: LOD and LOQ are the most important analytical parameters to be determined. Depending on whether the procedure is performed manually or instrumentally, various approaches are used to detect LOD and LOQ. These include: A. Visual evaluation, B. Evaluation according to signal-to-noise ratios, C. Evaluation by slope and standard deviation analysis. While the slope estimate is performed using the calibration data, the standard deviation estimates can be made in different ways: -Through the appropriate number of blank readings and repetitions; -Through the residual standard deviation of the regression line; -Through the standard deviation of the regression line intercept; can be calculated. Where LOD and LOQ tests are performed by calculation or extrapolation; These estimates should then be verified by analyzing of samples with appropriate concentrations.
DIABETES PROGRAM IN TURKEY AND HEALTHY LIVING CENTERS
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The World Health Organization's Global Diabetes Report released on World Health Day on April 7, 2016 announced that the prevalence of diabetes increased from 4.5% to 8.5%, doubling between 1980 and 2014. The adult diabetes population increased fourfold to 422 million from 108 million. Diabetes increases throughout the world, but in developed countries, this increase is associated with aging of the population. As a matter of fact, it is determined that the prevalence of diabetes is not increased when standardization is made according to age. In countries with low and middle income groups, in addition to the prolongation of the average life span, obesity also increases and the prevalence of diabetes increases much more rapidly.

On the one hand, the prevalence of diabetes in our country has rapidly increased due to the aging of the surviving population on the one hand, and the lifestyle change that leads to inactivity and unhealthy nutrition on the other, and today it has become a serious parallel with the issue involving 15% of the population. There is a significant effect of preventable risk factors in this rapid increase in diabetes mellitus. For this reason, it is very important for the primary care to take an active role in early recognition of diabetes, effective fighting with risk factors and regular follow-up of treatment.

The Ministry of Health received a decision to launch “Healthy Life Centers” throughout the country with an emphasis on the promotion of health and the importance of primary health care services in the preparation of the 2018-2023 Strategic Plan. These centers are designed as centers that include dieticians, physiotherapists, psychologists, physical activity consultants, and family physicians in this sense. In this context, it is planned to employ 30,000 non-physician health workers at 1,149 Healthy Living Centers. In addition, the preparations are made for employing case managers which will work in full coordination with family physicians and follow chronic patients. Case managers will follow the treatment adaptations of chronic patients through the automation system to be established, organize and remind their appointments, and the rate of treatment compliance of the chronic patients will be increased.

In the presentation, patient journey in diabetes management and the new primary care service model supported by the Healthy Living Centers, the plans and new term objectives of the Ministry of Health’s Diabetes Program will be shared.

THE COMPARISON OF TWO GLUCOSE MEASUREMENTS: POINT-OFF-CARE TESTING GLUCOMETERS AND LABORATORY METHOD
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OBJECTIVES: The glucose meters (glucometers; GMS) are used for two purposes: point-of-care testing and self-monitoring of glucose, both of which are very important in the management of diabetes, hypo-glycemia, or hyperglycemia and in therapeutic decisions. The aim of this study was to determine the test reliability of glucometers and to compare their results with those of clinical laboratory method, since it is mandatory to correctly measure blood glucose concentrations for management of glycemia in emergent situations.

MATERIALS-METHODS: Five different glucometers, used for hospitalized patients, were included in the study. The capillary and venous specimen of the same patient was concurrently obtained. The former was analyzed in glucometer, and the latter in laboratory analyzer. The analytical performances of each device were monthly followed, and its results were compared with those of laboratory analyzer. The results of any glucometer were included if the error was ±20%, and excluded if >20%.

RESULTS: From a total of 1,837 GMS read-outs, 1,748 capillary and venous comparisons were evaluated. The majority of the glucometer measurements were within acceptable limits.

The error percentage distribution of GMSs indicated that the accuracy of GMSs is higher in the prediabetic/diabetic measurement range than at normo-/hypoglycemic levels.

CONCLUSIONS: A compatibility of glucometers and laboratory method was observed in general. However, the health care professionals and the diabetic patients, in the case of self-monitoring, should be alert in evaluation of the glucometer results, and they should make cross-check, as frequently as possible, with laboratory determinations.

Keywords: Glucose meter, glucometer, glucose monitoring system, diabetes P0CT

SREBP PATHWAY AND LIPID METABOLISM
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SREBP-1 and -2 are transcription factors regulating cholesterol and triglyceride metabolism in mammals. Drosophila has only one homolog of SREBP and it is involved in triglyceride metabolism. SREBP-GAL4 reporter was generated by replacing nuclear part with GAL4 so that upon activation, with UAS-GFP responder, it can be observed where it is activated normally and upon different interrogations. We have determined the effect of some other genes on the activation of the pathway by crossing flies carrying the GAL4 driver and GFP responder with different RNAi strains. Genes known to affect SREBP pathway from mammalian studies have been tested by knocking dawn them with RNAi, and this has confirmed the validity and relevance of our assay. After identifying new genes in a pilot screen, we performed genome-wide RNAi screen for about 4000 genes. Upon general introduction about Srebp pathway our results will be presented.

RELATION OF OBESITY AND METABOLIC DISEASES WITH HIGHGLUCOSE -FRUCTOSE SYRUP OBTAINED FROM CORN STARCH
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OBJECTIVES: Consumption of high glucose fructose syrup obtained from corn starch (HGFCS) is increased dramatically at last 50 years. Our aim is to discuss of HGFCS consumption is giving damage to body with which metabolic pathways.

MATERIALS-METHODS: HGFCS was started to be produced through isomerase enzym at the years of 1960 s and after that its usage was extremely increased.

RESULTS: During production of HGFCS, mercury and carbonyl compounds are contaminated. Just this fact is also a sufficient reason why this product to be used. Besides consumption of HGFCS creates an anarchy in the metabollism and so a lot of diseases are triggered. The results of this anarchy are increased fat deposition, metabolic increase of high uric acid levels, atherosclerosis syndrome, some side DM and extention of carsinogenesis process due to increase of some products.

CONCLUSIONS: HGFCS must extiation be an avoided contamination, and genetically modified corn that is HGFCS consumption metabolism especially and so a lot of diseases creates of are triggered renal diseases, carsinogenesis product an anarchy like due is not hypertension, process due to toxic substance used in its production in the carbohydrate high uric acid levels, obesity, DM, hypertension in the childhood period. HGFCS (nearly added to every food product) Countries producing to the whole world prohibit its usage in their boundaries almost completely. Restrict or prohibit of this product in our country is vital importance for our future. As a consumer to investigate the product ingredients very carefully shows how we care to our health.

Keywords: Corn starch, glucose-fructose syrups, metabolism
THE USE AND IMPORTANCE OF CLINICAL DECISION LIMITS IN CLINICAL DIAGNOSIS

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While reference intervals (RIs) describe health and physiology and are derived from a reference distribution, clinical decision limits (CDLs) focus on disease and pathology and are based on the diagnostic question. CDLs are obtained from specific clinical studies to define the probability of the presence of a certain disease or a different outcome, published professional recommendations and consensus values. These limits lead to the decisions of how individuals with values above or below the decision limit should be treated. The clinical sensitivity and specificity of the diagnostic test, relative distribution of individuals between the two subgroups and the clinical costs of mis-classification are the basic requirements of CDLs. Lipids such as total-LDL cholesterol, glucose and Hba1c are good examples which have well-defined CDLs. The rationale of this kind of CDL is based on outcome studies that have demonstrated different levels of survival or incidence of complications for patients with concentrations above or below the limit. There are several CDLs that can be applied to Hba1c; (1) 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0%

Key words: Clinical decision limits, Reference intervals, postanalytic quality

UNDERGRADUATE AND POSTGRADUATE BIOCHEMISTRY EDUCATION AND SPECIALISATION IN MEDICAL BIOCHEMISTRY IN TURKEY

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Higher education is regulated by the Higher Education Law, legislation no: 2547, in Turkey. Biochemistry education is mandatory for undergraduate education of medicine, pharmacy, dentistry, veterinary, chemistry, biology, and engineering (agriculture, food, environment and forestry). There are main science departments of biochemistry in the medicine, pharmacy, science (chemistry), and veterinary faculties. Additionally, there are few associate, undergraduate and postgraduate biochemist education programs. Currently, there are 84 medical faculties, 34 pharmacy faculties, 72 chemistry departments and 28 veterinary faculties in Turkey. Postgraduate biochemistry education, including master and doctorate programs is governed by health sciences institutes within universities. Problem based learning has become widespread since the second half of 1990s. The reform process in higher education starting with the Bologna Declaration in Europe,1999, has been adopted by Turkey in 2001. In this connection, “Regulation on Academic Evaluation and Quality Development in Higher Education Institutions” has been published in 2005 and thus the accreditation process has been started. Finally, “Regulation on Quality Assurance in Higher Education” has been published in 2015 and the Higher Education Quality Board has been established. Based on this regulation, the establishment of quality boards has become mandatory in all higher education institutions.

Medical biochemistry and medical microbiology education have been given in the medical specialisation area. The name of the education is medical biochemistry. The education is given by medical faculties and the training and research hospitals of the Ministry of Health (TRMHH). Currently, TRMHs are affiliated to Health Sciences University. The number of medical faculties and TRMHs giving medical biochemistry competency are 55 and 14, respectively. Period of assistance is 4 years and physicians, pharmacists, chemists and veterinarians can take the central examinations. The Core Curriculum of Medical Biochemistry was accepted in September 2016. There are external rotations of internal diseases (4 months), pediatrics (2 months) and medical microbiology (1 month) during the period of 4 years training and education. The central board examinations are not currently established.

FLOW CYTOMETRY IN HEMATO-ONCOLOGIC DISEASES: RECENT IMPROVEMENTS AND CHALLENGES

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Clinical decision limits avoid confusion, the C28-A3 recommended reporting decision limits with a clear postanalytic quality, it is important that RIs are not confused with CDLs. To reach consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0%, and it is important that RIs are not confused with CDLs. To reach consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0%

Conclusion: While cloning of this isoenzyme was performed using restriction enzymes in the literature, it was obtained in one step by TA cloning method in our study. Through the SUMO protein in the vector that we used here, the solubility of the expressed protein was increased.

Keywords: Carbonic anhydrase, pET SUMO vector, TA cloning method

FINANCIAL SUPPORT AND IMPORTANCE

ZARDA

There are several CDLs that can be applied to Hba1c; (1) 7.0% vs. 8.0% to change diabetic management, (2) ≥6.5% for diabetes diagnosis and (3) ≥5.5% to assess cardiovascular risk. An example of a CDL based on consensus is an upper reference limit for thyroid-stimulating hormone (TSH) of 7.0% vs. 8.0%

Objective: In recent years, recombinant protein production is increasing rapidly using molecular biological methods. Carbonic anhydrase, a member of the family of metalloenzymes, catalyzes the conversion of CO2 to HCO3-. Using Zn metal as cofactor. In this study, this enzyme with vital precursor was recombinantly produced with the fusion protein by the TA cloning method using the pET SUMO vector. This method was used as part of Deryanur Kilis’s PhD work under my supervision to determine the function of amino acid present in the active region of the recombinant carbonic anhydrase II enzyme by replacing single amino acid.

Materials and Methods: For the recombinant enzyme production, the sequence region encoding the hCA II isoenzyme was first identified using the NCBI database. Specific primers were designed using the Primer3 program for this sequence. The portion encoding the hCA II isoenzyme was amplified by PCR with the primers designed using the human pancreatic cDNA library. Recombinant DNA was then obtained by TA cloning using the pET SUMO vector. The resulting recombinant DNA was transformed into competent OneShot Mach1 E. coli cells by heat-shock method. Plasmid isolation was performed from positive transformants that were identified by colony PCR. The resulting recombinant plasmid sequence analysis was performed with vector primers.

Findings: The PCR product made with the primers designed specifically for the sequence region encoding the hCA II isoenzyme was carried out on an agarose gel and the band observed at the desired site. E. coli cells harboring recombinant DNA were selected for LB agar containing kanamycin. Sequence analysis result of the plasmid DNA isolated from positive transformants was blasted with hCA II sequence. As a result, it was found to be 100% similar.

Conclusion: While cloning of this isoenzyme was performed using restriction enzymes in the literature, it was obtained in one step by TA cloning method in our study. Through the SUMO protein in the vector that we used here, the solubility of the expressed protein was increased.

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THE STATUS AND ROLE OF NON-INVASIVE METHODS TO DETERMINE FETAL HEALTH IN LABORATORY MEDICINE

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The advance of technology and knowledge in the past two decades has made significant contributions to the development of non-invasive methods used in monitoring and detecting fetal health. Nowadays, blood tests are performed in thousands of pregnant women in order to screen and determine fetal anomalies. However, cell-free nucleic acids (cfNA) have been used as an important tool in many pathophysiological conditions such as cancer, transplantation, autoimmune disease, trauma, infectious disease and cardiovascular disease to provide new opportunities for more effective clinical management. There are three important evidences which prove that the placenta is the main source of fetal DNA in maternal plasma. First of the three evidences is that in anembryonic pregnancy only consisting of placenta, fetal DNA is found in the maternal plasma in typical concentration. Second evidence is, placenta carrying the same methylation markers with the fetal DNA in the maternal plasma and thirdly, in cases where placenta carries a distinctive cytogenetics signature, the same signature is found in the maternal plasma. As, in 1997, Lo et al. revealed that the gene sequences belonging to the fetus in maternal plasma can be amplified, and beginning from 2012, cell-free fetal DNA (cfDNA) entering the clinical practice created new exciting applications for the methods of non-invasive prenatal test (NIPT). Also, invasive diagnostic methods needing fetal tissue sampling such as amniocentesis, cordocentesis and chorionic villus sampling, increase the mortality and morbidity of the fetus. Therefore, prenatal diagnosis practitioners should improve the usage and accessibility of non-invasive diagnostic methods. Today, non-invasive prenatal diagnosis, which achieves the complete genetic information of the fetus and minimizes the fetal risks, is taking steady steps to become a must. Therefore, prenatal diagnosis practitioners should improve the usage and accessibility of non-invasive diagnostic methods. NIPT can detect aneuploids, fetal Rh incompatibility, sex chromosomal disorders and fetus sex using fetal DNA. As it was reported in 2012 that NIPT in high-risk pregnancies can detect trisomy 21, 18 and 13 with about 98% accuracy, and under 0.5% false positives. Ongoing researches committed to expanding the diversity of conditions that can be tested noninvasively to include microdeletion/duplication syndromes and common Mendelian genetic disorders. Also, NIPT has been used to diagnose various autosomal dominant conditions that occur paternally or de novo, including torsion dystonia and achondroplasia. In addition, NIPT has been used to exclude the father’s mutation in autosomal recessive diseases, such as beta thalassemia when parents carry different mutations. The emergence of new technologies such as next generation sequencing and digital PCR broadens this perspective. As a result, a major challenge for the medical community is the speed of development and clinical presentation of non-invasive tests. The decision to include into routine laboratory parameters of a new NIPT is given by the clinician, not by the laboratory. It is often difficult to distinguish commercial promotional statements from objective test performance evaluations. Examination of the tests must be previously done by partners through the existence of any professional guidelines and proficiency testing. In this case, test providers should supply comprehensive details on their websites for a good evaluation of the service. Lastly, it must be kept in mind that assisting patients on present test stitions and effects it has its own difficulties. Counseling is often necessary based on very limited data on individuals who will be given non-invasive testing and pregnant women.

Keywords: Non-invasive methods, fetal health, laboratory medicine.

Molecular Mechanisms of Memory in Imprinting

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Visual imprinting is a learning process through which young, visually naïve animals come to recognize a visual stimulus by being exposed to it (training) and subsequently approach the object in preference to other objects. As a model this phenomenon offers a number of important advantages for the study of molecular and cellular mechanisms of learning and memory. From these advantages we will outline only two: (i) a region of the brain, the forebrain, has been identified as being of crucial importance for the learning and memory process of imprinting.

This region is the intermediate and medial mesopallium (IMM); (ii) it is possible to measure the strength of learning and memory and correlate molecular changes with this parameter. Special criteria for inferring learning-relatedness of molecular changes after training were formulated. Taking advantage of this knowledge, we have demonstrated a number of molecular changes which could be divided in early, intermediate and late changes. The early changes involve predominantly post-transcriptional modifications of proteins and synthesis of immediate early gene products, whereas the late changes are associated with a number of molecular pathways, including cell adhesion, stability of synaptic structures, release of neurotransmitters, mitochrondrial dynamics and many others. Proteomic, RNA-SEQ, epigenetic and micro-RNA profiling studies 24h after training revealed additional biochemical processes involved in the long-term memory of visual imprinting. The results indicate the progression from transient/labile to trophic synaptic modifications culminating in stable recognition memory.

SWITCHING FROM SERUM TO PLASMA WITHOUT TEARS!

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Laboratories in the Netherlands have a history of adusting the latest technologies, and have embraced plasma ensuring the fastest sample testing and a way to standardise the samples used for both emergency and routine testing. Until recently the EMC had not utilised plasma because of the logistics in place at that time, which allowed for ample clotting time of the serum tubes. With the transition to a new hospital, almost 95% of transport of blood samples is going to be facilitated by an extensive pneumatic tube network allowing for a continuous and fast supply of blood tubes to the clinical laboratory. With this fast supply it is to be expected that there is an increase of latent clotting after centrifugation. The pre-emptive conversion to plasma would tackle this problem. There were many concerns with the conversion to plasma but with the support of BD and their hospital partners the laboratory of the EMC was able to transition from a predominant serum-with-gel workflow to a ligh-herpanin plasma workflow using the new BD Bartric® tube for most of the routine 24/7 chemistry and immunochemistry tests. Completing, in parallel, all of the necessary steps in its move to plasma (i.e. analytical compatibility & validation, LIS updates & hospital wide training).

LABORATORY APPROACH TO INHERITED METABOLIC DISEASES

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Inherited metabolic diseases are a complex pathogenetic group of diseases that can occur with specific or nonspecific findings. These diseases, usually seen in neonatal period or childhood, occur with severe clinical signs and can lead to permanent mental retardation, physiological defects and death. Early diagnosis is important for success in treatment and prevention of permanent sequelae. For this purpose, expanded newborn screening programs are being carried out all over the world. Inherited metabolic diseases can occur both in newborn and childhood as well as in older ages and the greatest difficulty in diagnosing diseases is due to the fact that early signs and symptoms are not specific to these diseases. In the case of Inherited metabolic diseases, it should never be forgotten that the metabolites accumulate especially at the time of attack. The most important step in the diagnosis is to make emergency examinations. For unexamined investigations, samples should be taken at the moment of attack and stored passively.

Due to the large number of consanguineous marriages in our country, the incidence of inherited metabolic diseases is high. Small molecules such as inorganic ions, amino acids, organic acids, carbohydrates, simple lipids, purines, pyrimidines, vitamins, small peptides and oligosaccharides are frequently used in the diagnosis. Complex molecules such as glycolipids, sphingolipids, plasmalogens, glycyogen, mucosylsaccharides and a large number of molecules are important in the diagnosis of inherited metabolic diseases. Complex molecules are usually localized in the membranes and their amounts in body fluids such as blood, urine are very small. Complex molecules can usually be measured using advanced techniques. Determination of metabolites by NMR spectroscopy, measurement of free carnitine, acylcarnitines and amino acids by tandem mass spectrometry, organic
acidity analysis by gas chromatography - mass spectrometry (GC-MS), quantitative amino acid analysis of blood, urine and CSF, biogenic amines, carbohydrate deficient transferrin, purine, pyrimidine bases, very long-chain fatty acid determinations, analysis of bile acids by GC-MS or LC-MS / MS, enzyme analyzes, metabolomics are frequently used for the diagnosis of inherited metabolic diseases.

Definitive diagnosis of inherited metabolic diseases should be made by enzyme analysis in fibroblast culture, leucocyte, lymphocyte, erythrocyte, tissue samples such as liver, muscle, and molecular genetic analysis in DNA. Inherited metabolic diseases. There are characteristic increases / decreases in enzyme activities, metabolomics are frequently used for the diagnosis of these diseases. Further analyzes with metabolomics, proteomics, and next generation DNA sequencing techniques are current methods used to diagnose inherited metabolic diseases. As a result, early diagnosis is the most important step for successful treatment. The missed diagnosis can lead to life-long permanent sequelae and death.

MULTI-TARGET-DIRECTED LIGANDS IN ALZHEIMER’S DISEASE TREATMENT
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Alzheimer’s Disease (AD) is a progressive neurodegenerative disease whose multifactorial pathophysiology arise from cholinesterase enzymes, amyloid precursor protein, amyloid Aβ, tau, -synuclein, apoe4 and oxidative stress. Complex and unsolved mechanism of AD directed researchers towards multi targeted drug design recently.

A large part of current treatment approaches are inhibitors of the enzyme acetylcholinesterase, which has been regarded as one of the main targets of AD since 1970. This approach aims to increase the reduced cholinergic transmission observed in AD. Specific AChE inhibitors tacrine, donepezil, galanthamine and a dual cholinesterase inhibitor rivastigmine have been approved by the FDA. But donepezil is the most prescribed drug in AD. For this reason, its analogues and derivatives have recently been evaluated.

Amyloid beta peptide (Aβ) accumulation in the brain is one of the characteristic findings of AD. This accumulation causes a number of events such as neurofibrillary tangle formation, neuroinflammation, and apoptosis, leading to neuronal death. Although several drug candidates targeting Aβ have been developed, clinical phase studies have shown that monotherapeutic approaches are not sufficient.

Following to epidemiologic studies that have shown nonsteroidal antiinflammatory drugs (NSAIDs) may be protective against AD, cyclooxygenase enzymes (COX) have also become drug targets for AD. Antiinflammatory drugs (NSAIDs) may be protective against AD, following to epidemiologic studies that have shown nonsteroidal antiinflammatory drugs (NSAIDs) may be protective against AD, cyclooxygenase enzymes (COX) have also become drug targets for AD.

Mitochondrial and Multidose-directed ligands are developed, clinical phase studies have shown that monotherapeutic approaches are not sufficient.

INHERITED METABOLIC DISEASES
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Mitochondrial diseases are a clinically heterogeneous group of disorders that arise as a result of dysfunction of the mitochondrial respiratory chain due to the inherited or spontaneous mutations in mDNA or nDNA. Mitochondrial diseases are characterized by multi -systemic involvement; especially tissues with high aerobic demands such as brain tissue, heart and skeletal muscle are usually affected severely. Therefore heterogeneous clinical presentations such as developmental delays, muscle weakness, encephalomyopathy, gastrointestinal, ophthalmic or myocardial symptoms can be observed in patients. Elevation in the blood levels of lactate, pyruvate and creatine kinase is usually observed in laboratory testing. For example, skeletal muscle is essential for the histochemical and biochemical analysis of Respiratory Chain Complex (RCC) defects. Molecular genetic testing should be undertaken after detailed clinical, biochemical and histochromic examination.

Muscle biopsies were received from pediatric patients with suspected myocardial myopathy between 2015 - 2017 and analyzed for mitochondrial RCC deficiency. RCC deficiency was observed in 72% of muscle biopsy samples. Complex IV deficiency was the most common (45%), followed by Complex I (34%) and Complex II-III (26%) deficiency. Isolated deficiency was present in 33% of the patients; 16% Complex I, 18% Complex II-III and 56% Complex IV. Decreased I/CS, Complex II-III/CS and Complex IV/CS ratio was observed in 34%, 40% and 40%, respectively. Multiple complex deficiencies were present in 47% of the muscle biopsies; 13% for Complex I+II-III, 55% for Complex IV, 32% for Complex II-III+IV.

Inherited metabolic disorders, single complex deficiency was the most common (53%), followed by double complex (30%) and triple complex deficiency (17%). Complex IV deficiency, either isolated or accompanied by other complex deficiencies, was the most common in our patient groups. At present, there is no definite cure for mitochondrial disorders, supportive pharmacological treatments are directed towards relieving the symptoms.

Key words: Mitochondria, respiratory chain, complex activity

MUCOPOIDIS VS. SIMPLE SKIN
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Mucopolysaccharidoses are a group of genetically determined disorders with progressive and often life-threatening features, including dysmorphia, skeletal, cardiac, and neurologic abnormalities. The most common form is mucopolysaccharidosis type I or Hurler syndrome. The disease is due to a genetic deficiency in the activity of the enzyme α(1-3)-fucosyltransferase, which is responsible for the synthesis of the core structure of the GAG dermatan sulfate.

The diagnosis of mucopolysaccharidoses is not always straightforward as some of the clinical symptoms may overlap with other conditions. Therefore, molecular genetic analysis of the affected genes is necessary for a definite diagnosis. The enzymes involved in the synthesis and degradation of GAGs are frequently mutated in inherited metabolic diseases.

In addition to enzyme deficiencies, there are also cases of enzyme deficiencies involving the synthesis of the GAG turnover. The diagnosis of these disorders is based on the demonstration of the deficiency of the enzyme involved in the synthesis of the GAG turnover. The diagnosis of these disorders is based on the demonstration of the deficiency of the enzyme involved in the synthesis of the GAG turnover. The diagnosis of these disorders is based on the demonstration of the deficiency of the enzyme involved in the synthesis of the GAG turnover.
In addition to all these improvements, in the last 15 years, with the electrospray ionisation (ESI) method especially for large molecules, mass spectrometry finds places. Molecules with the same nominal mass can be distinguished by high resolution mass analyzers. The advantage of high resolution mass analyzers is that they can accurately detect the molecular weight of the substance up to three or four decimal places. Molecules with the same nominal mass can be distinguished by high resolution mass analyzers by measuring their mass-to-charge ratio. For example, nortriptyline, mirtazapine, amitriptyline and imipramine have a molecular weight of 285 Daltons and differ in their decimal parts (Figure). Detection of the decimal parts can be done through the measuring of broad range analytes. Development of the mass spectrometry (MS) techniques became an useful tool for measuring of broad range analytes. Therefore, in the clinical laboratory, high resolution mass spectrometry devices have been used in our clinical laboratory since 2011. Both devices are our instruments, owned by our University therefore we do not have any reagent cost. The cost of LC-MS/MS system was 210000 $, GC-MS system was 64000 $. Both systems require regular maintenance. The cost of analysis is also of critical importance, which is closely related to the number of samples analyzed. The cost of test is lower than other methods for high throughput experiments. For laboratory analysis of urine samples, the cost is much less than the commercial available kits. Net income of the analysis from the devices is about 150000 $ so far. Development of analytical techniques is always expensive, time-consuming and needs expertise. However MS instruments are powerful tools and can be cost-effective after 1-2 years in clinical laboratories. In our department more than 10 postgraduate theses has been made with MS system. Nearly 20 of analytes method validation process have been completed. We organized 2 courses on clinical applications of MS in our clinic.
BIOCHEMISTRY OF METASTASIS

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Cancer constitute the second most common cause of death, aftercardiovascular disease. A neoplasm refers to any abnormal new growth of tissue. It may be benign or malignant in nature. Metastasis is not limited to the passive spread of cells from the primary tumor to other organs via blood and lymphatic vessels. Metastasis beeds to changes in biochemistry, morphology and migration capabilities of tumor cells, emergence of surface receptors that mediated directed migration to target organs; formation of the specific environment in the target organ that facilitates survival and multiplication of metastatic cells. Cancer metastasis progresses through a stepwise cascade of events, including tumor growth, angiogenesis, stromal invasion, intravasation, extravasation, and colonization at secondary sites within the body.

OBESITY: CURRENT KNOWLEDGE AND NEW DEVELOPMENTS

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Obesity has a multifactorial nature resulting from genetic, physiological, behavioral, sociocultural, and environmental factors that lead to imbalance between energy intake and expenditure. Current lifestyle trends, characterized by high calorie diets and lack of physical activity, have increased the incidence of obesity. It is known that obesity is a risk factor for several diseases such as insulin resistance, type 2 diabetes, cardiovascular diseases and some cancers. Many mechanisms such as ectopic lipid toxicity, chronic and mild systemic inflammation in hormonal resistance (insulin and leptin) and bacterial changes in the gastrointestinal system are thought to play a role in the development of obesity. Increased expression of inflammatory mediators has also been observed in fat tissue of obese humans. These cytokines have been shown to disrupt insulin signalling and altered adipokine production (such as adiponectin, leptin, and rezistin) and aberrant fatty acids release. For the management of obesity, lifestyle changes, dietary modifications, increased physical activity, and medications have been suggested and it is shown that the patients will lose weight through these methods. However, the recent researches clearly show that approximately 80% of the patients in which weight loss initially successful do not maintain this weight loss and subsequently regain weight. In addition, the metabolic complications may relapse in 12 months. Dysbiosis which is compositional and functional intestinal microbiomes alterations has been suggested to contribute to the pathogenesis of remaining weight. In recent years, bariatric surgery has rapidly become an option of treatment for severe obesity. The studies regarding to the weight loss after these surgeries show that bariatric surgery improves glucose tolerance and insulin sensitivity in humans. This phenomenon caused these surgeries to be categorized under the metabolic surgery.