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Byung Woo Kim et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Anticancer activity of *Osmanthus matsumuranus* extract by inducing G2/M arrest and apoptosis

Byung Woo Kim, Soojung Jin, You Na Oh, and **Hyun Ju Kwon**
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Osmanthus matsumuranus, a species of Oleaceae, is found in East Asia and Southeast Asia. The bioactivities of *O. matsumuranus* have not yet been fully understood. Here, we studied on the molecular mechanisms underlying anticancer effect of ethanol extract of *O. matsumuranus* (EEOM). EEOM showed the cytotoxic activities in a dose-dependent manner in various cancer cell lines, but not in normal cells, and HepG2 cells were most susceptible to EEOM-induced cytotoxicity. EEOM induced G2/M arrest in HepG2 cells associated with decreased expression of cyclin-dependent kinase 1 (CDK1), cyclin A and cylcin B, and increased expression of phospho-checkpoint kinase 2, p53 and CDK inhibitor p21. Immunofluorescence staining showed that EEOM-treated HepG2 increased doublet nuclei and condensed actin, resulting in cell rounding. Furthermore, EEOM-mediated apoptosis was determined by Annexin V staining, chromatin condensation and DNA fragmentation. EEOM caused upregulation of FAS and Bax, activation of caspase-3, -8, -9, and fragmentation of poly ADP ribose polymerase. These results suggest that EEOM efficiently inhibits proliferation of HepG2 cells by inducing both G2/M arrest and apoptosis via intrinsic and extrinsic pathways, and EEOM may be a possible candidate for the anticancer drug development.

Recent Publications:

1. Boutros R, Lobjois V and Ducommun B (2007) CDC25 phosphatases in cancer cells: key player? Good targets? Nat. Rev. Cancer 7: 495-507.
2. Fulda S and Debatin K M (2006) Extrinsic versus intrinsic apoptosis pathways in anticancer chemotherapy. Oncogene. 25: 4798-4811.
3. Singh S, Singh P P, Roberts L R and Sanchez W (2014) Chemopreventive strategies in hepatocellular carcinoma. Nat. Rev. Gastroenterol. Hepatol. 11: 45-54.
4. Stewart Z A, Westfall M D, Pietenpol J A (2003) Cell-cycle dysregulation and anticancer therapy. Trends Pharmacol. Sci. 24: 139-145.
5. Taylor W R and Stark G R (2001) Regulation of the G2/M transition by p53. Oncogene. 20: 1803-1815.

Biography

Byung Woo Kim has completed his PhD in Pharmacology from Busan University, Busan, Republic of Korea. He is currently working as a Professor at Division of Applied Bioengineering, Biopharmaceutical Engineering Major, Dong-Eui University and as the Director of Blue-Bio Industry Regional Innovation Center, Dong-Eui University, Busan, Korea. His research field is Pharmaceutical biotechnology of natural Products.

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Soojung Jin et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Anti-oxidative and anti-cancer activities of *Machaerium cuspidatum* extract

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Machaerium cuspidatum, a canopy liana, is a species of genus legume in the Fabaceae family and contributes to the total species richness in tropical rain forests. In the present study, we investigated the anti-oxidative and anti-cancer effects of *M. cuspidatum* and the molecular mechanisms of its anti-cancer activity in human lung adenocarcinoma A549 cells and human hepatocellular carcinoma HepG2 cells. Methanol extract of *M. cuspidatum* (MEMC) showed significant anti-oxidative activity and the cytotoxic effect in a dose-dependent manner in several cancer cell lines. Annexin V-positive apoptotic cells and apoptotic bodies increased by MEMC treatment. Further investigation showed that MEMC-induced apoptosis was associated with the increase of p53 and Bax expression, and the decrease of Bcl-2 expression. In addition, MEMC treatment led to proteolytic activation of caspase-3, -8, -9 and degradation of poly ADP ribose polymerase (PARP). Taken together, these results suggest that MEMC may exert a beneficial anti-cancer effect by apoptosis induction via both extrinsic and intrinsic pathways in A549 and HepG2 cells.

Recent Publications:

1. Andreas G (2003) Introduction to apoptosis. Apo Review. 2-26.
2. Fulda S (2015) Targeting apoptosis for anticancer therapy. Semin. Cancer Biol. 31:84-88.
3. Fulda S and Debatin K M (2006) Extrinsic versus intrinsic apoptosis pathways in anticancer chemotherapy. Oncogene. 25:4798-4811.
4. Halliwell B H and Gutteridge JMC (1990) Role of free radicals and catalytic metal ions in human disease: an overview. Methods Enzymol. 186:1-85.
5. Newman D J and Cragg G M (2007) Natural products as sources of new drugs over the last 25 years. J. Nat. Prod. 70: 461-477.

Biography

Soojung Jin has completed her PhD in Immunology from Osaka University, Osaka, Japan. She is presently working as an Assistant Professor at Blue-Bio Industry Regional Innovation Center, Dong-Eui University, Busan, Republic of Korea. Her research is focused on bioactive natural products and oncology.

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Antioxidative and anticancer activities of *Julbernardia globiflora* extract

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Julbernardia globiflora, a tropical African tree widespread in Miombo woodland, has been used in folk medicine for the treatment of depression and stomach problems. However, the bioactivities of *J. globiflora* have not yet been fully determined. The objective of this study was to evaluate the antioxidative and anticancer effects of methanol extract of *J. globiflora* (MEJG) and the molecular mechanism of its anticancer activity in human colon carcinoma HT29 cells. MEJG exhibited significant antioxidative activity and cell growth inhibitory effect on HT29 cells in a dose-dependent manner. MEJG induced apoptosis of HT29 cells with the increase of apoptotic cells and apoptotic bodies using Annexin V staining and 4,6-diamidino-2-phenylindole (DAPI) staining, respectively. The MEJG-induced apoptosis was associated with the increase of Fas, a death receptor, and Bax, a pro-apoptotic protein, and the decrease of Bcl-2, an anti-apoptotic protein, resulting in the release of cytochrome c from the mitochondria into the cytosol and activation of caspase-3, -8 and -9. The apoptotic effects of MEJG were confirmed by cleavage of poly (ADP-ribose) polymerase (PARP). Collectively, these results suggest that MEJG may exert the anticancer effect in HT29 cells by inducing apoptosis via both the intrinsic and extrinsic pathways.

Recent Publications:

1. Adam J M and Cory S (2007) The Bcl-2 apoptotic switch in cancer development and therapy. Oncogene. 26: 1324-1337.
2. Fulda S and Debatin K M (2006) Extrinsic versus intrinsic apoptosis pathways in anticancer chemotherapy. Oncogene. 25: 4798-4811.
3. Galluzzi L, Lopez-Soto A, Kumar S and Kroemer G (2016) Caspases connect cell-death signaling to organismal homeostasis. Immunity. 44: 221-231.
4. Li P, Nijhawan D and Wang X (2004) Mitochondrial activation of apoptosis. Cell. 116: 57-59.
5. Riedl S J and Shi Y (2004) Molecular mechanisms of caspase regulation during apoptosis. Nat. Rev. Mol. Cell Biol. 5: 897-907.

Biography

Hyun Ju Kwon has completed her PhD in Bioengineering from Osaka University, Osaka, Japan. She is presently working as a Professor at Division of Applied Bioengineering, Biopharmaceutical Engineering Major, Dong-Eui University and as an Assistant Director of Blue-Bio Industry Regional Innovation Center, Dong-Eui University, Busan, Korea. Her research field is Natural Products and Oncology.

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Antioxidant and Anticancer Activities of *Sorbus rufopilosa* extract in *Human Colon* adenocarcinoma HT29 Cells

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Sorbus rufopilosa, a tsema rowan, is a species of the small ornamental trees in the genus Sorbus and the family Rosaceae found in East Asia. The antioxidant and anticancer effects of *S. rufopilosa* remain unclear. The objective of this study is to evaluate the antioxidant and anticancer effects of ethanol extract of *S. rufopilosa* (EESR) and the molecular mechanism of its anticancer activity in human colon carcinoma HT29 cells. EESR showed significant antioxidant activity and inhibitory effect on HT29 cell growth in a dose-dependent manner. EESR induced cell cycle arrest at G2/M phase in a dose-dependent manner by modulating the expression of cyclin B, cyclin-dependent kinase 1 (CDK1), and CDK inhibitor p21. EESR-induced apoptosis was associated with the upregulation of p53, a death receptor Fas, a pro-apoptotic protein Bax and the activation of caspase 3, 8, and 9, resulting in the degradation of poly ADP ribose polymerase (PARP). These results suggest that EESR efficiently inhibits proliferation of HT29 by inducing both cell cycle arrest and apoptosis, and may be a possible candidate for the anticancer drug development.

Recent Publications:

1. Andreas G (2003) Introduction to apoptosis. ApoReview 2-26.
2. Evan GI, Vousden KH (2001) Proliferation, cell cycle and apoptosis in cancer. Nature 411:342-348.
3. Fulda S (2015) Targeting apoptosis for anticancer therapy. Semin. Cancer Biol. 31:84-88.
4. Fulda S, Debatin KM (2006) Extrinsic versus intrinsic apoptosis pathways in anticancer chemotherapy. Oncogene 25:4798-4811.
5. Udensi UK, Tchounwou PB (2016) Oxidative stress in prostate hyperplasia and carcinogenesis. J. Exp. Clin. Cancer Res. 35:139.

Biography

You Na Oh has completed her Master in Microbiology from Dong-Eui University, Busan, Republic of Korea. She is currently working as a researcher at Blue-Bio Industry Regional Innovation Center, Dong-Eui University. Her research is focused on Bioactive Natural

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Nurhasni Hasan, J Proteomics Bioinform 2017, 10:12(Suppl)
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Surface charge engineering of nitric oxide-releasing polymeric nanoparticles: Adhesion and anti-biofilm efficacy against wound infection associated MRSA biofilm in db/db mice

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Biofilm-associated wound infections have been considered a life-threatening infection that affects millions of people each year and are among the major cause of infectious disease-related mortality and morbidity worldwide. Bacterial biofilms protect bacteria from host immune responses and promote strong resistance to antibiotic treatment which leads to impaired wound healing, hospitalization and amputation particularly in chronic wound such as diabetic foot ulcer. Recently, nitric oxide (NO) has emerged as novel agent in biofilm dispersal and accelerates wound healing. In this study, we investigated the potency of positively charge NO-releasing PLGA/PEI nanoparticles (NO/PPNPs) for adhesion on biofilm surface that elevate biofilm dispersal and wound healing efficacy. Poly (lactic-co-glycolic acid) (PLGA) were used to incorporate polyethyleneimine (PEI)/NO adduct (PEI/NONOate) by an oil-in-water (O/W) emulsion evaporation method to form NO/PPNPs. Adhesion of NO/PPNPs on bacterial biofilm and the progress of *in vivo* biofilm dispersal were performed in biofilm wound and characterized by 3D confocal microscopy. *In vivo* biofilm was prepared by inoculating Methicillin-Resistant Staphylococcus aureus (MRSA) suspension on the surface of wound in db/db mouse (type-2 diabetic). Photographs of the wounds were taken to observe the gross visual wound healing. Furthermore, histological analysis was performed with H&E and Masson trichrome stain to observe the skin morphological and collagen deposition, respectively. Positively charged of NO/PPNPs facilitated the electrostatic binding to the negatively charged biofilm matrix, thereby increasing the biofilm dispersal by NO released from NO/PPNPs. NO/PPNPs treatment a biofilm-challenged diabetic mouse accelerated wound healing as compared to untreated and blank nanoparticles. In addition, histological examination revealed that wounds treated with NO/PPNPs showed increased numbers of fibroblast-like and collagen deposition with healed skin structures close to the normal healthy epidermis. Thus, the NO-releasing polymeric nanoparticles investigated in this study could be a promising approach for the treatment of biofilm-challenged chronic wounds and various skin infections.

Recent Publications:

1. H Nurhasni, J Cao, M Choi, I Kim, B L Lee, Y Jung, J W Yoo (2015) Nitric oxide-releasing poly (lactic-co-glycolic acid)-polyethylenimine nanoparticles for prolonged nitric oxide release, antibacterial efficacy, and *in vivo* wound healing activity, International journal of nanomedicine. 10: 3065.
2. J S Choi, J Cao, M Naeem, J Noh, N Hasan, H K Choi, J W Yoo (2014) Size-controlled biodegradable nanoparticles: Preparation and size-dependent cellular uptake and tumor cell growth inhibition, Colloids and Surfaces B: Biointerfaces.122: 545-551.
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5. J W Yoo, D J Irvine, D E Discher and S Mitragotri (2011) Bio-inspired, bioengineered and biomimetic drug delivery carriers, Nature reviews. Drug discovery. 10: 521.

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Ana Despina Ionescu et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Biotechnological studies on some plant species able to be used for the remediation of pharmaceutical industry's wastewater

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A constructed wetland is an artificial wetland created for the purpose of treating anthropogenic discharge such as municipal or industrial wastewater. It may also be created for land reclamation after mining, refineries, or other ecological disturbances. Constructed wetlands are engineered systems that use natural functions of vegetation to treat different water streams. Plants are often thought of as a treatment pathway. With a plant mono-culture, it is possible to accurately and to model the behavior of a wetland. In additional, a detailed water characterization is necessary to determine explanatory parameters and inventory the constituents in the water. In this paper, we provide our researches carried out in laboratory level, concerning the use of some selected plants in order to be used for the remediation of the wastewater resulted from the pharmaceutical industry. The tested species were the algae *Chlorella vulgaris* and the aquatic plants *Lemna minor* and *Spyrogira sp*. The algae culture was obtained by successive selection works starting from an identified cell and then all plant species were kept on special selected growth media. The 5 tested solutions used as representing some natural waste waters consisted in NH_4NO_3, Pb $(NO_3)_2$, $MgSO_4$, $ZnSO_4$ and NaCl. The ions which were analyzed concerning their concentration's evolution during a period of 72 hours (starting from 1%) were: Pb, NO_3, SO_4, Mg, Zn and Cl. The results indicate a better final situation in the case of those 2 aquatic plants, than in the case of using *Chlorella.*

Recent Publications:

1. Gratão L P et al. (2005) Phytoremediation: green technology for the clean up of toxic metals in the environment. Braz. J. Plant Physiol. 17: 53-64.

Biography

Ana Despina Ionescu has her expertise as the Director of different Romanian Research Projects related to the bioremediation of the industrial waste waters, the use of some biological filtering systems in order to reduce the toxic contaminants of some natural water resources and the establishment of requested parameters in order to use the natural mineral water springs for the public health improvement. She is a PhD in the field of Industrial Biology and she has obtained more Medals at the International Innovation Fairs from Brussels and Geneva during the period 2005-2014. She is working as a Senior Scientific Researcher at the National Chemical-Pharmaceutical for Research and Development Institute, Bucharest, Romania.

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Murtada A Oshi et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Layer-by-layer coated dexamethasone microcrystals for experimental inflammatory bowel disease therapy

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Layer-by-layer (LBL) coating has gained popularity for drug delivery of therapeutic drugs. Herein, we described an approach for enhancing the therapeutic efficiency of the locally administered dexamethasone (Dx) for the treatment of inflammatory bowel disease (IBD). We utilized a LBL-coating technique for alternative coating of Dx microcrystals (DxMCs) with multiple layers of polyelectrolytes composed of poly (allylamine hydrochloride), poly (sodium 4-styrene sulfonate) and Eudragit® S100. The successful deposition of the layers onto DxMCs surfaces were confirmed through zeta potential measurement and confocal laser scanning microscopy, while the surface morphology was investigated through scanning electron microscopy. The drug encapsulation efficiency for LBL-DxMCs was 95% with a mean particle size of 2 μm and negative surface charge of -45 mV. Moreover, *in vitro* drug release studies showed a minimum release of the drug (15%) at an acidic condition during initial first 5 h followed by sustained-release at alkaline condition. For *in vivo* study, LBL-DxMCs were administered orally to male ICR mice suffering from dextran sulfate sodium-induced colitis. LBL-DxMCs was found to substantially enhance anti-inflammatory efficacy of the drug compared to uncoated DxMCs. Macroscopic, histological and biochemical (tumor necrosis factor-α, interleukin-6 and myeloperoxidase) examinations revealed marked improvements of colitis signs in the mice treated with LBL-DxMCs compared with those treated with uncoated DxMCs. Overall, the obtained results demonstrate that LBL-DxMCs are an effective and safe colon-targeted delivery system for the treatment of inflammatory bowel disease.

Recent Publications:

1. Murtada A O, Abdelkarim M A and Huyam A M (2013) The effect of sodium starch glycolate concentration on physical effectiveness of chlorpheniramine tablets. J Pharm Educ Res. 4 (1): 47-53.
2. Muhammad Naeem, Wooseong Kim, Jiafu Cao, Yunjin Jung and Jin-Wook Yoo (2014) Enzyme/pH dual sensitive polymeric nanoparticles for targeted drug delivery to the inflamed colon. Colloids and Surfaces B: Biointerfaces. 123: 271-278.
3. Murtada A O and Abdelkarim M A (2013) Phytochemical screening and evaluation of Monechma ciliatum (black mahlab) seed extracts as antimicrobial agents. Avicenna J Phytomed. 3 (2):126–134.
4. Murtada A O (2013) Evaluation of Physical Effectiveness of Three Brands of Diazepam Tablets Available in Sudanese Retail Pharmacies. Int. J. of Pharm. & Research Sci. 2 (4): 642-651.
5. Muhammad Naeem, Jiafu Cao, Moonjeong Choi, Woo Seong Kim, Hyung Ryong Moon, Bok Luel Lee, Min-Soo Kim, Yunjin Jung and Jin-Wook Yoo (2015) Enhanced therapeutic efficacy of budesonide in experimental colitis with enzyme/pH dual-sensitive polymeric nanoparticles. Int J Nanomedicine. 10: 4565–4580.

Biography

Murtada A Oshi is pursuing his PhD at college of Pharmacy, Pusan National University, South Korea majoring in Manufacturing Pharmacy. His study in the field of colon-specific delivery of nano and microscale drug delivery system for the treatment of inflammatory bowel disease: ulcerative colitis and Crohn's disease. He is mainly focusing on solving out the disadvantages of traditional anti-inflammatory drugs, e.g. systemic side effects, poor targetability etc., used for the treatment of inflammatory bowel disease. Now, he is studying the anti-inflammatory activity of different nano and microscale drug delivery systems loaded with of anti-inflammatory drugs for the treatment of inflammatory bowel disease. He evaluates the anti-inflammatory activity of the formulations both *in vitro* and in *in vivo*. For *in vivo* study of inflammation, he used experimental animal colitis using different models such as dextran sodium sulfate, dinitrobenzene sulfonic acid and trinitrobenzene sulfonic acid.

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Biosynthesis of levan by using the strain *Zymomonas mobilis* ATCC 10988 in static and shaking fermentation

Angela Casarica, Ana Despina Ionescu, Corina Bubueanu, Delia Maria Jitea and **Maria Petrescu**
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Levans are fructose polymers synthesized by a broad range of microorganisms and a limited number of plant species as non-structural storage carbohydrates and they have potential applications in the pharmaceutical, food, and cosmetic industries. The present study shows a comparative analyses of polysaccharide type Levan biosynthesis in static and shaking fermentation by using *Z. mobilis* ATCC 10988 strain. All fermentation processes were carried out in Erlenmeyer flasks presenting a capacity of 500 ml and working volume of 100 ml culture medium, in both fermentation types: static and on the rotary shaker, with stirring of 220 rpm, with the temperature maintenance at 32°C for 72 hours. In figure 1, we can find the results obtained by static fermentation for different initial concentrations of sucrose. The best development of the microbial culture in terms of microbial biomass was seen for the initial concentration of 15% sucrose, due probably to the favorable ratio between the source of C and N. The largest amount of polysaccharide was obtained from the experiment with 40% initial sucrose (8.9 g%), but this value is also similar to the experiment with 25% initial sucrose (8.47 g%). The Figure No. 2 shows the results obtained by the stirred fermentation with the strain *Z. mobilis* ATCC 10988 for different initial concentrations of sucrose. Concerning the content of polysaccharide, if the initial concentration of sucrose in the biosynthesis medium was greater than 20%, the amount of polysaccharide was about 5 g%, without any increase of production in the case of higher concentrations. By comparing the results shown in figures 1 and 2, it can be noticed that the strain *Z. mobilis* ATCC 10988 performs better concerning the polysaccharide biosynthesis in the frame of a static fermentation, which is not a surprise considering that these bacteria are an optional aerobic one.

Recent Publications:

1. Park H-E (2003) Enzymatic synthesis of fructosyl oligosaccharides by levansucrase from *Microbacterium laevaniformans* ATCC 15953. Enzyme Microb. Tech. 32: 820-827.
2. Rairakhwada D (2007) Dietary microbial levan enhances cellular non-specific immunity and survival of common carp (*Cyprinus carpio*) juveniles. Fish Shellfish Immun. 22: 477-486.
3. Gupta S (2008) Microbial levan in the diet of *Labeo rohita* Hamilton juveniles: Effect on nonspecific immunity and histopathological changes after challenge with Aeromonas *hydrophila*. J. Fish Dis. 3: 649-657.
4. Jathore N R (2012) Microbial levan from *Pseudomonas fluorescens*: Characterization and medium optimization for enhanced production. Food Science and Biotechnology. doi:10.1007/s10068-012-0136-8.

Biography

Angela Casarica has her expertise as a Project Responsible of different Romanian Research Projects related to Bacterial Cellulose for pharmaceutical and industrial purposes, studies to obtain an eyewash technology based truffle extract, fungal chitosan: isolation and biological characterization, curdlan-type polysaccharide obtained using a strain of *Agrobacterium rhizogenes*, product of natural origin for ophthalmic treatment and obtaining procedure. This work and experience in biotechnology was attained by approximately 10 biotechnological processes, seven patents and over 50 scientific papers published in specialized journals. She is a PhD in the field of Horticulture and she has obtained more medals at the International innovation fairs from Brussels and Geneva during the period 2008–2014. She is working as a Senior Scientific Researcher at the National Chemical-Pharmaceutical for Research and Development Institute, Bucharest, Romania.

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Corina Bubueanu et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Haemostatic activity of butanol extracts of *Lamium album* and *Lamium purpureum*

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The genus *Lamium* contains about 40 species, distributed in Europe, Asia, and Africa, some of which are used in traditional medicine. Currently, the genus *Lamium* is less studied and much less utilized compared to other members of the Lamiaceae family to which it belongs. *Lamium* album and *Lamium* purpureum are species belonging to the *Lamium* genus. Aerial parts of the two species and roots of *Lamium* album have applications in human and veterinary traditional medicine. Literature data presents as main components of the *Lamium* genus species iridoid glycosides. The active principles have diuretic, anti-inflammatory, anti-diarrheal, astringent, expectorant, vasoconstrictor, antirheumatic, haemostatic and emollient properties. In this paper, haemostatic properties of the *Lamium* species are investigated by two experimental (topical and systemic administration) models: hemostatic test by tail bleeding time detemination and acenocoumarol-carrageenan test. The haemostatic test results by tail bleeding determination topical administration, have demonstrated that both extracts have haemostatic activity. In the acenocoumarol-carrageenan test, systemic administration, only *Lamium album* extract have shown haemostatic activity, comparable with those obtained for administration of vitamin K. Based on the qualitative chemical composition in iridoid glycosides (HPTLC analysis) and the results obtained in experimental tests, there is the possibility that the compound responsible for the haemostatic activity is 8 acetylshanzhiside methyl ester. Both extracts have no toxicity based on an acute toxicity test.

Recent Publications:

1. Bubueanu Corina, Gheorghe Campeanu, Pirvu Lucia, Bubueanu George (2013) Antioxidant activity of butanolic extracts of romanian native species - *Lamium* album and *Lamium* purpureum, Romanian Biotechnological Letters. 18 (6): 8855-8862.
2. Lucia Pirvu, Corina Bubueanu, Minerva Panteli, Lucian Petcu and Dragomir Coprean (2015) Centaurea cyanus L. polysaccharides and polyphenols cooperation in achieving strong rat gastric ulcer protection Open Chemistry. 13: 910–921.
3. Alice Grigore, Lucia Pirvu, Corina Bubueanu, Minerva Panteli and Iuksel Rasit (2015) Influence of chemical composition on the antioxidant and anti-inflammatory activity of Rosmarinus officinalis extracts - Romanian Biotechnological Letters. 20 (1): 10047–10054.
4. Lucia Pirvu, Cristina Hlevca, Ioana Nicu and Corina Bubueanu (2014) Comparative studies on analytical, antioxidant, and antimicrobial activities of a series of vegetal extracts prepared from eight plant species growing in Romania -Journal of Planar Chromatography. 27 (5): 346–356.
5. Corina Bubueanu. Ramona Pavaloiu, Lucia Pirvu (2016) HPTLC profiles and antioxidant activities from leaves to green and roasted beans of coffea arabica. Malaysian Journal of Medical and Biological Research. 3 (1): 31-36.

Biography

Corina Bubueanu is a Biochemist, has completed her PhD in Horticulture (2013) with 15 years' of experience in research in the field of obtaining of new, natural medicines/drugs based on the selective herbal/vegetal, mushrooms extracts, involving both, fundamental research in order to design the most properly phytochemical composition, as well as applicative research concerning the following activities: the isolation of the various selective vegetal extracts enriched in the interest phytochemical compounds; analytical screening of the obtained vegetal extracts and the selection of the most proper ones by using specific, combined methods (spectral and spectrophotometric methods combined with HPTLC); the obtaining of the final pharmacological active product with pharmacological potential by the combination of the most active vegetal extracts; the setting up of the most appropriate and reproducible extractive technologies of these extracts and the correspondingly final active product as to the technological transfer from laboratory to pilot level.

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An accelerator mass spectrometry-enabled micro-tracer study to evaluate the human mass balance of KD101, an anti-obesity drug under development

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In clinical drug development, it is important to understand the absorption, distribution, metabolism and excretion (ADME) properties of a drug in humans. The micro-tracer study based on the accelerator mass spectrometry (AMS) is an ultrasensitive technique to obtain human ADME profiles with a negligible radiation dose. KD101 is a novel compound under development to treat obesity. The aim of this study was to investigate the absorption, metabolism and excretion properties of KD101 in obese subjects. A randomized, open-label, single-dose, one-treatment, one-period, one-sequence study was conducted in six males with a BMI ≥27, who received KD101 at 400 mg with 3.52 μg of [14C]-KD101 (180 nCi) in the fed state. Plasma, urine and feces samples were collected up to 288 hours post-dose for mass balance and metabolite profiling. Plasma concentrations of KD101 were determined using a validated GC method. Total radioactivity in the samples was determined using AMS. Safety and tolerability was evaluated based on vital signs, adverse events, clinical laboratory tests, and electrocardiography. All of the subjects completed the study with no clinically significant safety issue. Mean total recovery rate (range) was 85.21% (75.36-99.01%), consisting of 77.96% (68.31-92.33 %) for urine and 7.26% (5.91-8.51%) for feces, which differed greatly from the pre-clinical data. Oral absorption of [14C]-KD101 was rapid with the peak plasma concentration reaching at 5.83h post dose, which was consistent with the previous report. In the urine radiochromatogram, five large peaks were identified including a peak represented by the parent compound. KD101 is excreted predominantly through the urine in humans. Many of the excreted materials in the urine were considered metabolites. This study demonstrated effectiveness of the micro-tracer study enabled by AMS in humans to investigate the ADME property of KD101, which hugely differed from that seen in the preclinical animals.

Recent Publications:

1. Kim Y K, Kim A, Park S J, Lee H (2017) New tablet formulation of tacrolimus with smaller interindividual variability may become a better treatment option than the conventional capsule formulation in organ transplant patients. Drug Design Dev Ther. (11): 2861-2869.
2. Kim Y, Kim A, Lee S, Choi S H, Lee D Y, Song J S, Lee H, Jang I J, Yu K S (2017) Pharmacokinetics, Safety and Tolerability of Tedizolid Phosphate After Single-Dose Administration in Healthy Korean Male Subjects. Clin Ther. 39 (9): 1849-1857.
3. Lee H, Chung H, Lee S, Lee H, Yang S M, Yoon S h, Cho J Y, Jang I J, Yu K S (2017) LBEC0101, A Proposed Etanercept Biosimilar: Pharmacokinetics, Immunogenicity, and Tolerability Profiles Compared with a Reference Biologic Product in Healthy Male Subjects. BioDrugs. DOI: 10.1007/s40259-017-0230-9.
4. Yi S, Lee H, Jang S B, Byun H M, Yoon S H, Cho J Y, Jang I J and Yu K S (2017) A novel K+ competitive acid blocker, YH4808, sustains inhibition of gastric acid secretion with a faster onset than esomeprazole: randomized clinical study in healthy volunteers. *Aliment Pharmacol Ther*. doi: 10.1111/apt.14148.
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Biography

Howard Lee is the Founder and Director of the Center for Convergence Approaches in Drug Development (CCADD). He serves as a Professor at the Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology, Seoul National University. He is also appointed at Seoul National University College of Medicine and Hospital, affiliated with the Department of Clinical Pharmacology and Therapeutics. He previously served as the Head of Global Strategy and Planning, Clinical Trials Center, SNUH. As of August 2017, he was appointed as Chair of the Graduate Program in Clinical Pharmacology, Seoul National University. He has spearhead the introduction of Accelerator Mass Spectrometry (AMS)-enabled exploratory early clinical drug development studies to the Korean biopharmaceutical R&D sector, which has awarded him two government grants.

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Pedro Almirall et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Mebendazole in *giardiasis*: Systematic review and meta-analysis

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Introduction: At present, 5-nitroimidazole compounds are the pharmacological cornerstone for people with *Giardia* infections. However, treatment failures are increasingly reported. Mebendazole (MBZ), a benzimidazole compound, has received attention in treating patients with giardiasis since beneficial effects have been demonstrated *in vitro* and *in vivo*.

Aim: The aim of this study was to assess in a systematic review and meta-analysis of randomized controlled trials (RCTs) the efficacy of MBZ compared to other antigiardial agents in children.

Methods: RCTs of MBZ for the treatment of *Giardia* infections published in PubMed and EBSCO host were searched. Application of inclusion and exclusion criteria, data extraction, and assessment of methodological quality were independently performed in duplicate. The endpoint was the parasitological response to therapy.

Results: Seven RCTs were found in the systematic review (639 patients) and were included in the meta-analysis. There is not clinical difference in the parasitological cure between MBZ and metronidazole (MTZ). The relative risk (RR) is 0.88 (95% CI 0.70-1.10), with a moderate heterogeneity (I2=66%). The prediction interval expected to cover the results of a new trial is wide enough (0.35-2.21) to support both a parasitological relevant difference favoring MBZ and a parasitological relevant difference favoring MTZ.

Conclusions: This study synthesized available evidence on (and documented) the efficacy of MBZ in treating *Giardia* infection in children. There is no difference in efficacy between MBZ and MTZ regarding parasitological cure. Hence, the decision to support any of the competing treatments should be based nit in efficacy but, in other characteristics such as tolerance with the treatment or associated costs. Although our results suggest that MBZ may be an effective treatment option for children with *Giardia* infection, they should be interpreted and translated into clinical practice with caution, as the meta-analysis was based on a limited number of heterogeneous RCTs.

Recent Publications:

1. Escobedo A A, Almirall P, Cimerman S and Rodríguez-Morales A J (2016) Sequelae of giardiasis: an emerging public-health concern. International Journal of Infectious Diseases. 49: 202-203.
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3. Escobedo A A, Cimerman S and Almirall P (2011) An old drug against giardiasis: mebendazole as a treatment option. Infectious Disorders - Drug Targets. 11: 94-95.
4. Escobedo A A, Lalle M, Hrastnik N I, Rodríguez-Morales A J, Castro-Sánchez E, Cimerman S, Almirall P and Jones J (2016) Combination therapy in the management of giardiasis: what laboratory and clinical studies tell us so far. Acta Tropica. 162: 196-205.
5. Escobedo A A, Ballesteros J, González-Fraile E and Almirall P (2016) A meta-analysis of the efficacy of albendazole compared with tinidazole as treatments for *Giardia* infections in children. Acta Tropica. 153 (2): 120–127

Biography

Pedro Almirall has his expertise giardiasis pharmacotherapy and public health. He has been working for years as a Clinical Epidemiologist and has experience in research, evaluation, and teaching, both in Cuban hospitals and education institutions. He has published his research in international scientific journals and currently, he is pursuing his PhD.

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Hyun A Lee et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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A Physiologically-based pharmacokinetic model adequately predicted the human pharmacokinetic profiles of YH4808, a novel potassium-competitive acid blocker, to treat gastric acid related diseases

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YH4808 is a highly potent, selective and reversible potassium-competitive acid blocker on H+/K+-ATPase under development for the treatment of gastric acid related diseases. The objectives of this study were to develop a human PBPK model optimized by human pharmacokinetic (PK) data, to predict the PK profiles of YH4808 using the PBPK model in various settings and to mechanistically understand the main factor of clinically observed nonlinear PK of YH4808 by exploring various drug-drug interactions (DDIs). A PBPK model was developed using SimCYP® based on the physicochemical properties, preclinical *in vitro* and clinical data of YH4808 (Figure 1), which was further refined using human plasma concentrations obtained from a single-dose ascending phase I clinical trial of YH4808. The absorption of YH4808 was described by the advanced dissolution, absorption and metabolism model. The Vmax and Km values for each CYP isozyme involved in the metabolism of YH4808 were determined from the *in vitro* Ki values using a graphical method (GraphPad Prism7, GraphPad Software, Inc., USA). The DDI potential for YH4808 with other co-administered drugs was predicted using the PBPK model by calculating the geometric mean ratio of the model-predicted and observed for the area under the concentration-time curve (AUC). The PBPK model adequately predicted the observed concentrations of YH4808 after a single and repeated oral administration at 100 mg (Figure 1 (b), Figure 2 (a)). However, the simulated plasma concentration profiles after repeated oral administration at 200 and 400 mg were not in line with the observed concentrations, particularly toward the terminal phase, showing some sort of non-linear accumulation (Figure 2 (b) & (c)). The PBPK model-based simulated AUC of YH4808 increased by 2.08-2.90 times when co-administered with phenacetin, mephenytoin and dextromethorphan, respectively, suggesting the metabolism of YH4808 may involve CYP1A2, 2C19 and 2D6, which was confirmed by *in vitro* DDI studies. These metabolic pathways can be saturated at a higher dose of YH4808 at >200 mg, resulting in a non-linear PK profile. A PBPK model adequately predicted observed concentrations of YH4808 in humans after a single and repeated oral administration. The saturation of liver metabolism by CYP1A2, 2C19 and 2D6 appears to be associated with the nonlinear PK characteristics of YH4808 after multiple oral administration. The PBPK model can be used to predict the PK profiles of YH4808 in various clinical settings.

Recent Publications:

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2. Lee H A, Leavens T L, Mason S E, Monteiro-Riviere N A, Riviere J E (2009) Comparison of quantum dot biodistribution with a blood-flow-limited physiologically based pharmacokinetic model. Nano Letters. 9 (2): 794-9.
3. Lee H A, Imran M, Monteiro-Riviere N A, Colvin V L, Yu W W, Riviere J E (2007) Biodistribution of quantum dot nanoparticles in perfused skin: evidence of coating dependency and periodicity in arterial extraction. Nano Letters. 7 (9): 2865-70.

Biography

Hyun A Lee is a PhD student at the Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology, Seoul National University in South Korea. She is also a trainee in clinical pharmacology at the Department of Clinical Pharmacology and Therapeutics, Seoul National University College of Medicine and Hospital. She has graduated from North Carolina State University (NCSU) in the USA with a Master's degree in Biomathematics (2010). Prior to that, she went to the University of Alabama (2001-2004), where she received a Bachelor's degree in Biology and Mathematics. After completing her undergraduate course, she worked as a Research Scientist at the Center for Chemical Toxicology Research and Pharmacokinetics (CCTRP) in NCSU. Her research area is physiologically based pharmacokinetic (PBPK) modeling and simulation to optimize new drug development. She has a lot of experience in PBPK modeling and simulation with new drugs.

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Roxana Madalina Stoica et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Studies on extraction and utilization of biologically active compounds from Capsicum genus in the pharmaceutical industry

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Bioactive compounds existing in the Capsicum genus, particularly capsaicinoids, provide many therapeutically uses due to its anti-inflammatory properties, to treat chronic pain, such as rheumatoid arthritis and neuralgia, and due to its anticancer, antimicrobial and antioxidant activity. The pungent metabolites in the fruits of Capsicum species are called capsaicinoids, and among the most abundant of these components are capsaicin and dihydrocapsaicin, which are responsible for about 90% of total pungency. Other important components resulting from the extraction of oleoresins are carotenoids (mainly capsanthin and capsorubin), which are widely used in the food industry, both because of their coloring and their antioxidant characteristics. The amount of capsaicinoids in peppers varies depending on the stage of maturity, variety used, cultivation conditions, nutrients soil and water stress. The capsaicinoids begin to accumulate in the early stages of fruit development and they reach a maximum rate as the fruit matures. The main objective of this study had involved the extraction of capsaicinoids from three Capsicum varieties, such as Guindilla Larga Roja, Fresno and Congo Trinidad, in order to obtain a pharmaceutical product for topical use. The realization of a topical formulation containing capsaicin, known for its analgesic action and local vasodilator, is a viable alternative in pain therapy. Capsaicinoids were identified in all extracts with concentration ranging from 0.3 to 0.7% (dry weight) and the best results were obtained with 96% ethanol as solvent comparing with methanol and acetonitrile, using Soxhlet extraction.

Recent Publications:

1. Dang Y Y, Zhang H and Xiu Z L (2014) Three -liquid-phase extraction and separation of capsanthin and capsaicin from *Capsicum annuum* L. Czech J. Food Sci. 32: 109-114.
2. Anwar E F and Ramadon D H (2014) Formulation and evaluation of gel and emulgel of chili extract (*Capsicum frutescens L.*) as topical dosage forms. International Journal of Pharmacy and Pharmaceutical Sciences. 6: 13-16.
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5. Sganzerla M, Janclei P C, Tavares de Melo A M and Godoy H T (2014) Fast method for capsaicinoids analysis from *Capsicum* Chinese fruits. Food Research International. 64: 718-725

Biography

Roxana Madalina Stoica is a Researcher at the National Institute for Chemical-Pharmaceutical Research and Development-ICCF, Bucharest, Romania, in the Pharmaceutical Biotechnology Department. She has obtained her PhD in the field of Biotechnology and her research was focusing on the obtaining of biologically active principles from vegetal sources.

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Georgiana Gabriela Iordache et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Comparative study on the growth and consumption curves of *Zymomonas mobilis* NCIB 1163 and *Z. mobilis* ATCC 10988, levan producer

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Levans are fructose polymers synthesized by a broad range of microorganisms and a limited number of plant species as non-structural storage carbohydrates and they have potential applications in the pharmaceutical, food, and cosmetic industries (1-5). This study presents a comparative analysis of the growth and consumption curves of *Z. mobilis* NCIB 1163 and *Z. mobilis* ATCC 10988, levan producing microorganisms. The growth and consumption curves were performed in a liquid medium with a concentration of 5% sucrose and 5% glucose. Thus, the bacterial cells in the exponential growth phase were centrifuged at 12.000 g and the pellet was washed twice with a sterile 0.9% NaCl solution. Finally, the cells were resuspended in 1 ml of physiological saline and they were used as inoculum in 5% liquid medium, which was monitored concerning the fermentable carbohydrate consumption and the growth. The consumption curves were performed under anaerobic conditions (the culture medium was coated with a layer of sterile paraffin oil) by periodical weighing of the medium seeded with different bacterial strains of *Z. mobilis* and by the graphical representation of weight loss (due to release of carbon dioxide). Exponentially growing cells were used as the inoculum, made at approximately 107 cells/ml. Cell growth was assayed turbidimetrically at a wavelength of 600 nm. The consumption curves of *Z. mobilis* NCIB 11163 and *Z. mobilis* ATCC 10988 bacterial strains on complete sucrose substrate medium, 5% under anaerobic conditions (Figure 1) revealed that strains NCIB 11163 and ATCC 10988 exhibit a similarly kinetics of consumption's substrate. The consumption curves of *Z. mobilis* NCIB 11163 and *Z. mobilis* ATCC 10988 bacterial strains on complete glucose substrate medium, 5% under anaerobic conditions (Figure 2) show that glycolysis is more intense than hydrolysis of sucrose. From the curves profile it is observed that the strain ATCC 10988 shows a curve having a more pronounced linear decrease.

Recent Publications:

1. Park H-E, (2003) Enzymatic synthesis of fructosyl oligosaccharides by levansucrase from Microbacterium laevaniformans ATCC 15953. Enzyme Microb. Tech. 32: 820-827.
2. Rairakhwada D, (2007) Dietary microbial levan enhances cellular non-specific immunity and survival of common carp (Cyprinus carpio) juveniles. Fish Shellfish Immun. 22: 477-486.
3. Gupta S, (2008) Microbial levan in the diet of Labeo rohita Hamilton juveniles: Effect on nonspecific immunity and histopathological changes after challenge with Aeromonas hydrophila. J. Fish Dis. 3: 649-657.
4. Kang SA, (2009) Levan: Applications and perspectives. pp. 145-161. In: Microbial Production of Biopolymers and Polymer Precursors. Rehm BHA (ed). Caister Academic Press, Norfolk, UK.
5. Jathore, N. R., (2012) Microbial levan from Pseudomonas fluorescens: Characterization and medium optimization for enhanced production. Food Science and Biotechnology, 21(4), 1045–1053. doi:10.1007/s10068-012-0136-8.

Biography

Georgiana Gabriela Iordache has her expertise as a Project Responsible of different Romanian Research Projects related to Heparin Sodium for pharmaceutical and industrial purposes. This work and experience in biotechnology was attained by approximately 10 biotechnological processes, 2 patents and over 3 scientific papers published in specialized journals. She is a PhD student in the field of Biotechnology. She is working as a junior researcher at the National Chemical-Pharmaceutical for Research and Development Institute, Bucharest, Romania.

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Samantha A Byrnes et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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A framework for selecting analytical biomarkers: A first principles approach

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Biomarkers are objective indications of a medical state that can be measured accurately and reproducibly. Traditional biomarkers enable diagnosis of disease through detection of disease-specific molecular signatures or distinct physiological or anatomical signatures. Appropriate selection of biomarkers with innovative test design can transform patient care by providing earlier diagnosis, treatment monitoring, and ultimately reduced burden of disease. These results will be best achieved through collaborations between researchers, device designers, and clinicians to drive test development for addressing clinical questions. We developed a framework for selecting biomarkers that are most likely to provide useful information about a patient's disease state. This framework describes the trade-offs between biomarkers' sensitivity/specificity for a disease-causing agent, the complexity of detection, and how this knowledge can be applied to the development of diagnostic tests. This report also details assessment criteria for successful tests. Our framework aims to assist stakeholders from test developers to clinicians by focusing on validating biomarker selection for an explicit clinical question (e.g., direct correlation with pathogenesis) followed by test development expediency (e.g., ease of detection). There are few, if any, ideal biomarkers due to trade-offs based on performance, cost, and usability. It is important to consider how and where a test will be used in order to select an appropriate biomarker. Our framework is intended to help assess these trade-offs to design new systems and enhance those that are already available.

Biography

Samantha A Byrnes completed her PhD in Bioengineering and MPH in Global Health Metrics at the University of Washington, Seattle. She has lived and worked in developing settings which has included the testing of a nucleic acid purification and storage prototype in Nicaragua and she is helping to develop an assessment framework for a vaccination campaign in Bangladesh. Currently, she works for Intellectual Ventures Laboratory focusing on development of products for rapid disease diagnosis and biomarker selection.

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Notes:

James Hall, J Proteomics Bioinform 2017, 10:12(Suppl)
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Blood-based biomarkers of neuropsychiatric symptoms in Alzheimer's: Inflammation, vascular risks, gender and APOEε4 status

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Background: The presence of neuropsychiatric symptoms (NPS) in Alzheimer's disease (AD) is frequent, difficult to treat, the largest risk for nursing home placement and a primary source of caregiver stress. This research is directed toward identifying blood-based biomarkers that could be useful in identifying those individuals with Alzheimer's who are at greater risk for developing NPS.

Methods: Data were analyzed on 300 AD participants from the TARC cohort. Blood-based markers of cardiovascular risk, inflammation and microvascular pathology were assayed. NPS were assessed using NPI-Q and the Geriatric Depression Scale.

Results: Total cholesterol and homocysteine were positively related to NPS. Cholesterol was a positive marker for total NPS and symptoms of hyperactivity, psychosis, affective and apathy among men. IL-15 and IL-1ra were negatively associated with neuropsychiatric symptoms and homocysteine positively associated for females. Total cholesterol was related to NPS in males regardless of APOEε4 status. IL15 was found to be negatively and significantly related to NPS for female APOEε4 carriers only. High TC in males was related to number and type of NPS. Lower MIF was a strong predictor of depression and TNFα predicted apathy. For females MIF, ICAM and CRP and TNFα were significant.

Conclusions: Elevated cholesterol is a primary risk for NPS in males and inflammatory processes and oxidative stress primary for females. Findings indicate the biomarkers of NPS are related to both gender and APOE4 status and these variables need to be taken in account in the identification and treatment of AD patients at risk for NPS.

Biography

James Hall is a Professor of Psychiatry and Medicine in the Center for Alzheimer's and Neurodegenerative Disease at the University of North Texas Health Science Center. He had published over 100 peer reviewed articles and presents internationally at scientific meetings on Alzheimer's disease and biomarkers. He is Director of the Proteomics Laboratory and Director of the Memory Disorders Clinic at the University of North Texas Health Science Center.

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Notes:

Dawn Sloane et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Expression of PD-L1 in relation to Human Papillomavirus (HPV) and p16 INK4a protein in primary and metastatic Squamous Cell Carcinomas of the Head and Neck (SCCHN)

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University of Arizona in Tucson, USA

Background: It is known that HPV plays an important role in the etiology of a subset of SCCHN. The degree of PD-L1 expression has been reported to be increased in those patients with HPV-positive disease. Recent clinical studies having shown efficacy of various therapies targeting the PD-1/PD-L1 pathway for patients diagnosed with SCCHN tumors. The determination of primary and/or metastatic tumors having HPV origins could be used in the identification of patients who may benefit from these more targeted treatment modalities.

Methods: Immunohistochemistry (IHC) and in situ hybridization (ISH) assays on the VENTANA BenchMark ULTRA instrument were used to determine the HPV and p16INK4a status as well as the PD-L1 expression level in 30 cases of SCCHN, with matching primary and metastatic resections. The VENTANA PD-L1 (SP263) assay was used to determine tumor cell expression of PD-L1. HPV status of the tissues was determined using the INFORM HPV III Family 16 Probe (B) product while the detection of the p16INK4a protein was completed using the CINtec p16 Histology assay.

Results: Evaluation of samples from the primary as well as the metastatic resections from each of the 30 cases (60 samples total) for percent expression of PD-L1 in tumor cells, HPV status and p16INK4a status was completed. The PD-L1 expression level for this sample set ranged from 0% to 75%. Of the 30 cases represented 17 cases show indication of HPV infection. The resulting data were analyzed using a t-test of the log of the PD-L1 expression level (natural log scale) and was found to be marginally and positively associated with evidence of HPV infection (Diff. of means = 1.363: 95%Cl: [-0.176;2.902]; p-value=0.077). However, a larger sample set would be needed to validate these findings.

Conclusion: While the results from this small contingent are far from conclusive, the initial results show that a diagnostic approach including these three assays may lead to a better understanding of the tumor origin and thus aid in the determination of treatment options for SCCHN patients.

Biography

Dawn Sloane has completed her studies in Molecular and Cellular Biology from the University of Arizona in Tucson, Arizona and holds certification as Technologist in Molecular Biology from the American Society of Clinical Pathology. She is currently a Scientist at Ventana Medical Systems, Inc., a member of Roche Molecular Solutions division of Roche Ltd. Basel, Switzerland. Her current assignment is in the development of diagnostic assays for cancer immunotherapeutic treatments. Previously, she led the Molecular Diagnostics division of a local healthcare system's clinical laboratory including fellowship and residency training for pathologists in cooperation with the University of Arizona College of Medicine.

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Notes:

Andrei V Ivanov, J Proteomics Bioinform 2017, 10:12(Suppl)
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The fluctuations in homocysteine level caused by various combinations of folic acid cycle genes SNP alleles as a factor in the course of pregnancy violation

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Female reproductive system disorders are the classic example of the multifactorial diseases. One of its violation factors including habitual miscarriage and pre-eclampsia is of the pathological alleles of single nucleotide polymorphisms (SNP) of the folic acid cycle genes presence in the genome. The realizing mechanism for this genetic predisposition is homocysteine level increasing in the blood named hyperhomocysteinemia. However, the lack of direct correlation between the genotype of the four most clinically significant SNPs and the blood homocysteine level detected is in some contradiction with the literature data. This study presenting an attempt to find the relationship between the genotype for the four SNPs of the three folate cycle genes - C677T and A1298C of the MTHFR gene, A2756G of the MTR gene and the A66G of the MTRR gene and the homocysteine level in the blood of women with impaired pregnancy. In total there were 131 patients: European population, reproductive age and residents of the North-West region of Russia. As a result no direct correlation was found between homocysteine level and folic acid cycle genotype in patients and control group. But it was found a statistically significant interlation between the presence of pathological alleles of the studied SNP and the mean square deviation (σ) of the homocysteine level fluctuations over time. For the polymorphism C677T of the MTHFR gene σ of the homocysteine blood level fluctuation is increased up to four times in women with a homozygous pathological state TT compared with the normal homozygotes CC. The clinical importance of monitoring the homocysteine blood level has been shown especially for women with folate cycle genes pathological alleles presence that would help this recognition.

Recent Publications:

1. Uvarova M A, Ivanov A V, Dedul A G, Sheveleva T S and Komlichenko E V (2015) The effect of single nucleotide genetic polymorphisms of folic acid cycle on the female reproductive system disorders. Gynecological Endocrinology. 31 (1): 34-38.
2. Ivanov A V, Dedul A G, Fedotov Y N and Komlichenko E V (2016) Toward optimal set of single nucleotide polymorphism investigation before IVF. Gynecological Endocrinology. 32 (2): 11-18.
3. Uvarova M A, Ivanov A V (2016) Three folic acid cycle genes single nucleotide polymorphisms as hereditary factors for female reproductive system disorders development. Terra Medica. 4 (86): 22-28.

Biography

Andrei V Ivanov is the Head of Department of Human Genetics. He has a PhD in Cell Biology and specialization in Clinical Laboratory Diagnostics. One of his most productive researches is the influence of genetic part of multifactorial diseases such as female reproductive system disorders, irritable bowel syndrome, and metabolic syndrome. His interests are metabolomics (especially steroid profiling), cell therapy of diabetic foot syndrome and biobanking. He considers his main task to be the introduction of results of the biological research into broad medical practice.

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Notes:

Paola B Castro Garcia, J Proteomics Bioinform 2017, 10:12(Suppl)
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Cancer stem cells as the target: Early detection for therapy

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Gliomas, like other types of cancer, are composed of a heterogeneous mixture of neoplastic cells, the great diversity between tumor cells, makes them the center for different studies *in vitro* and *in vivo* for their ability to grow, an intimately related property with the differentiation state of the cell. However there are cells that do not differentiate, regularly in a quiescent state, which are called cancer stem cells (CSC`s) with great tumorigenic potential due to the ability of self-renewal that is characteristic of a stem cell. Their proliferation by external stimuli or their own niche, gives rise to the offspring of multiple lineages, among them to progenitors that later differentiate to a more specific cell. These quiescent cells can be a fundamental therapeutic target, since currently cancer treatments are cytotoxic to most proliferating tumor cells, but do not destroy the compartment of CSCs, allowing these cells to survive and give rise to tumor recurrence. However, the identity and origin of CSCs remains unknown. In this paper we analyze the study of glioma cells and the implications of the CSC hypothesis for the development of future therapies for brain tumors.

Biography

Paola B Castro Garcia has completed her PhD from Castilla-La Mancha University and Post-doctoral studies from Hokkaido University School of Medicine. She is a Research Professor in University of Guadalajara, México.

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Notes:

Ashlin Ninibeth Lara Holguin et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Characterization of a microRNA expression signature associated with recurrence in oral cavity cancer patients

Ashlin Ninibeth Lara Holguin, Joaquín Manzo Merino, Roberto Herrera Goephert and **Marcela Lizano Soberón**
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Oral cavity cancer is one of the most prevalent and lethal cancers worldwide. In this type of cancer the local, regional and distal recurrence develops in up to 76% of the cases. This is associated with treatment failure, as well as high mortality rates. Therefore, there is a need to identify biomarkers that allow the recognition of patients at high risk of developing cancer recurrence. MicroRNA (miRNAs) are short single stranded RNA molecules, which regulate genetic expression at the post-transcriptional level. Changes in the expression profiles of miRNAs have been associated with diagnosis and prognosis in different types of cancer. Since miRNAs can be recovered from paraffin embedded biopsies, they could have a potential as biomarkers to understand the course of the disease. Hence, the aim of this work is to characterize a microRNA expression signature associated with recurrence, in oral cavity cancer patients. A total of 40 paraffin-embedded biopsies from patients with oral cavity cancer were analyzed. These biopsies were separated in groups of recurrence (n=16, <1 year) and no recurrence (n=24, >4 years). Total RNA was extracted and quantified for microRNA microarrays analysis (GeneChip® miRNA 4.0, Affymetrix). The data are being analyzed to determine the differentially expressed miRNAs between the groups, which will be validated in public databases, and by qRT-PCR. In addition, the expression levels of some targets at the level of mRNA and protein will be determined by qRT-PCR and immunohistochemistry.

Biography

Ashlin Ninibeth Lara Holguin has completed her Bachelor's Degree from the Faculty of Superior Studies Iztacala in Universidad Nacional Autónoma de México, where she obtained Honorific Mention. She is currently studying her Master's Degree in Biochemical Sciences from National Cancerology Institute, México in Universidad Nacional Autónoma de México.

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Notes:

Radka Vaclavikova et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Gene expression profiling reveals novel candidate genetic biomarkers of ovarian carcinoma prognosis and metastasis

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Epithelial ovarian cancer (EOC) has the highest mortality among gynecological carcinomas. Given the diversity in responses to the therapy, there is a need for identification of reliable biomarkers of prognosis, progression and prediction of EOC therapy outcome. The aim of our study was (i) to explore differences in expression of 94-gene panel connected to drug transport (ABC, SLC transporters), metabolism and cell cycle regulation in a set of primary EOC tissues (n=60), intraperitoneal metastases (n=29) and control ovarian tissues (n=14) as well as in a validation set of EOCs (n=57) using quantitative real-time PCR; (ii) to investigate associations of gene expression level with prognosis, development of metastasis and progression-free survival of EOC patients. Different gene expression profiles were found in ovarian carcinomas when compared with controls. Expression of ABCA7 significantly increased and that of ESR2 decreased in the order control ovarian tissues - primary EOCs – EOC metastases. The most important associations between gene expression and clinicopathological data were found for membrane transporters (*ABCA2/9/10, ABCG2, SLC16A14*) and cell cycle regulators (*PLK1, CIT, PRC1*). Transporters from the ABCA family, ABCG2 and ESR2 are involved mainly in lipid metabolism, membrane transport and cell proliferation. These processes are thus probably important for EOC progression. In conclusion, we have proposed novel genetic biomarkers of ovarian carcinoma prognosis and progression potentially useful as therapeutic targets.

Biography

Radka Vaclavikova has completed her PhD from Charles University in Prague, CZ and conducted her Post-doctoral studies in cooperation with Faculty of Medicine, University of Oslo, Norway. She is a Principal Investigator in Toxicogenomics Unit, National Institute of Public Health in Prague, CZ and in Laboratory of Pharmacogenomics, Biomedical Center in Pilsen, CZ. She has published 34 papers in impacted journals (450 citations, H Index 12) and serves as a Mentor of doctoral studies under Faculty of Medicine, Charles University in Prague.

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Cardiac troponins and their predictive value of myocardial injury on model of chronic anthracycline cardiomyopathy

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Cardiac troponins (cTn) seem to be more sensitive for the detection of anthracycline cardiotoxicity than the currently recommended method of monitoring LV systolic function. However, the optimal timing of blood sampling remains unknown. Hence, the aims of the present study were to determine the diagnostic window for cTns during the development of chronic anthracycline cardiotoxicity and to evaluate their predictive value. Cardiotoxicity was induced in rabbits with daunorubicin (3 mg/kg, weekly, for 8 weeks). Blood samples were collected 2-168 hrs after 1st, 5th and 8th drug administration, and concentrations of cTns were determined using highly sensitive assays: hs cTnT (Roche) and hs cTnI (Abbott). The plasma levels of cTns progressively increased with the rising number of chemotherapy cycles. While only a mild non-significant increase in both cTn levels occurred after the 1st daunorubicin dose, a significant rise was observed after the 5th and 8th administrations. Two hours after these administrations, a significant increase occurred with a peak between 4-6 hrs and a decline until 24 hrs. While greater variability of cTn levels was observed around the peak concentrations, the values did not correspond well with the severity of LV systolic dysfunction. Unlike AMI in cardiotoxicity, cTn elevations may be better associated with cumulative dose and AUC than cmax. Very strong correlation between dP/dtmax and AUCtotal5-10 (calculated from the 5th till the 10th week) for both cTnI and cTnT ($R=-0.857$, $p<0.01$ and $R=-0.833$, $p<0.01$; respectively) and LV FS ($R=-0.810$, $p<0.01$ and $R=-0.833$, $p<0.01$; respectively) were found.

Biography

Michaela Adamcova is an expert in cardiovascular toxicity markers. Her research activities have been focused mainly on cardiac troponins as translational markers for evaluation of cardiotoxic and potentially cardioprotective effects of new drugs in oncology. She has published 84 scientific papers, including several invited reviews, e.g. "Troponin as a marker of myocardial damage in drug-induced cardiotoxicity" for the journal *Expert Opinion on Drug Safety*, commentary "Troponins in children and neonates" for *Acta Paediatrica* and "Cardiac troponins – translational biomarkers in cardiology: Theory and practice of cardiac troponin high assays" for BioFactors.

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RhoGDI3 and the novel role in carcinogenesis: Pancreatic Ductal Adenocarcinoma (PDAC)

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RhoGDI proteins have been described as small GTPases negative regulators, sequestering GTPases in cytosol avoiding their activation; nevertheless, there is evidence about their implication in cancer, particularly RhoGDI1 and RhoGDI2 but not in RhoGDI3. In our group, we have reported an imbalance among the RhoGDI3 protein and three different staging cells, from non-cancerous to highly aggressive cancerous pancreatic cells; normal and low expression levels respectively. To elucidate the possible functions of RhoGDI3 in this pathology process, we performed reconstitution assays in the cancerous pancreatic cell line (PANC-1), which let us know that, normal levels of RhoGDI3 protein produces a smaller tumor compared with the cells not reconstituted and that the different levels of RhoGDI3 regulated gene expression, such as TRIO, EPHA2, RHEB, KLF10, EGFR, all of them implicated in cancerous process and tumor maintenance. There are very few proofs about the RhoGDI3 and the correlation with cancer, specifically PDAC, and our findings open up a gap to expand knowledge, from the RhoGDI3 as a negative regulator, the classical function, to a RhoGDI3 protein with novel role, decreasing the malignant behavior in PDAC.

Biography

Rocío Thompson Bonilla has completed her Bachelor's Degree at UNAM and her MSc and PhD from ENCB-IPN in the Dept. of Immunology and PhD in Rutgers University in 2010. She served as Director of Research in ISSSTE, the second public health institution in Mexico. She won the national price of Biomedicine in 2015 and has been working with infection diseases and with developing molecular platforms to find new markers in cancer and hereditary diseases.

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Serum EGF in non-small cell lung cancer: The biomarker value & the role of platelets

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Background: The CIMAvax-EGF® is a promising Cuban therapeutic vaccine for advanced non-small cell lung cancer (NSCLC), targeted to the potent mitogen epidermal growth factor (EGF). Retrospective studies of serum EGF concentrations ([sEGF]) in NSCLC patients treated with this vaccine, have revealed the predictive value of the sEGF levels for this immunotherapy. However, its putative diagnostic value, although studied is not conclusive because of the lack of standardized methodologies for quantitation. This study was aimed first at the estimation of the possible diagnostic value of [sEGF], using a previously standardized quantification procedure, controlling the crucial factors that influence [sEGF].

Methods: The [sEGF] of 25 patients were determined by ELISA, before/after the first-line-therapy, in sera collected 1h and 4h after phlebotomy. The contribution of platelets was considered analyzing their counts and through the normalization of some other variables by platelets counts.

Results: The variables [EGF]1h, [EGF]4h and [EGF]4h/platelets/L were not discriminatory (AUC=0.6464, p=0.07590; AUC=0.5267, p=0.7490 and AUC=0.6125, p=0.2424, respectively). There were significant differences between patients and controls by variables r=[EGF]4h/$[EGF]_{1h}$ (AUC=0.7075, p=0.01281), d=$[EGF]_{4h}$-$[EGF]_{1h}$ (AUC=0.6962, p=0.02038), Platelets/L (AUC=0.8253, p=0.0006588), $[EGF]_{1h}$/platelets/L (AUC=0.7440, p=0.01061), and d/platelets/L (AUC=0.8653, p=0.0001487).

Conclusions: The absolute [sEGF] had no diagnostic capacity, which was better achieved by variables normalized by platelet counts. The comprehension of the role of platelets in the measured EGF levels should allow a better interpretation of the assessed values, to judge about the dependence of the tumors from EGF. This knowledge should also impact the clinical management of patients and the individualization of their therapies.

Biography

Idania González Pérez has completed her BSc in Physics from the Faculty of Physics, Moscow State University, Russia (1985-1990) and Master of Science in Physics and Mathematics from Faculty of Physics, Moscow State University, Russia. She is now involved in a PhD program at the University School of Medicine in Havana. She is a Senior Researcher at the Center for Molecular Immunology in Havana, Systems Biology Department, Biomarkers Group. She has published more than 15 papers in reputed journals and has been serving as a Reviewer in Medical Science Monitor, Journal of Hospital and Clinical Pharmacy and International Blood Research & Reviews.

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Sevgi Yardim Akaydin et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Investigation of GGT5 and GGT7 mRNA expressions in patients with breast cancer

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An increased risk of breast cancer has been reported in individuals with elevated levels of gamma-glutamyltransferase (GGT) recently or in literature. Genome research indicated that besides GGT1, the human genome contains additional related genes or sequences. From the perspective of amino acid sequences, genes with substantial (GGT5 and GGT7) similarity to GGT1 have been identified. The aim of this study was to evaluate the association of gene expression of GGT5 and GGT7 with the breast cancer. For that purpose, tissue and serum samples were taken from 58 patients diagnosed with breast cancer. As controls, 8 healthy persons admitted to the clinic for breast reduction surgery were also included to the study. mRNA expressions of GGT5 and GGT7 in matched-normal and tumor tissues of breast cancer patients and normal tissues of healthy controls were measured by qRT-PCR method. In addition, GGT activity and glutathione (GSH) levels in serum samples were measured by spectrophotometric and ELISA methods, respectively. In the patient cohort, mRNA expressions of GGT5 and GGT7 were increased in tumor tissues than those in matched-normal tissues of the same patients ($p<0.0001$ and $p<0.001$, respectively). 52% and 62% of the patients had shown higher GGT5 and GGT7 gene expression respectively, in tumors compared to matched-normal tissues. Also, GGT enzyme activity was significantly higher in patients than those in controls ($p<0.05$) and it was positively correlated with GSH levels in both controls and patients ($p<0.05$ and $p<0.0001$, respectively). However, we could not find any correlation between neither GGT nor GSH and GGT genes. As far as we know, this is the first study showing GGT5 and GGT7 mRNA expression levels in the patients with breast cancer. Higher expressions in tumor tissues indicated the importance of these genes in the breast carcinogenesis. Our studies on protein expressions and then possible functions of these genes are ongoing in our lab.

Biography

Sevgi Akaydın is currently Professor of Gazi University Faculty of Pharmacy Department of Biochemistry. She earned her MD and PhD degree at Gazi University Faculty of Pharmacy Department of Biochemistry. She focused on cardiovascular disease, oxidative stress and oxidative biomarkers. Her current research focuses on DNA repair mechanism in molecular subtypes of breast cancer. She has 35 refereed publications and her h-index is 13. Her published works deal with cardiovascular disease, oxidative stress, oxidative biomarkers and related proteins in cancer.

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Investigation of expression levels of DNA repair genes in molecular subtypes of breast cancer

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Tip60 histone acetyltransferase (HAT) is critical importance for activation of DNA repair as well as plays role in chromatin remodeling and histone acetylation. After DNA damage, Tip60 acetyltransferase rapidly acetylates and activates ataxia-telangiectasia mutated (ATM) kinase which activates other proteins, such as p53, Chk2, BRCA1, H2AX etc., involved cell-cycle checkpoints and DNA repair. This mechanism may affect radiotherapy sensitivities of the cancer patients. The aim of this study is was to evaluate the status of Tip60-ATM complex in molecular subtypes (Luminal A and B, Her2+, and Triple-) of breast cancer. For this purpose, firstly, mRNA expression levels of Tip60, ATM, p53, BRCA1, Chk2 and H2AX measured by qRT-PCR in normal and tumor tissues of breast cancer patients and normal tissues of healthy individuals. When we compared mRNA expressions in normal tissues of total patients with healthy controls, we did not find statistically significant differences ($p>0.05$). In the total patient group, Tip60, ATM, and BRCA1 expressions decreased ($p=0.08$, $p=0.01$, and $p=0.017$, respectively) and p53, Chk2 increased ($p=0.048$ and $p=0.130$, respectively) in tumor tissues than those in normal tissues in the same patients. According to the subtypes, 47% of Lum A patients, 16.7% of Lum B patients, 56.3% of Triple- patients and 27.3% of Her2+ patients had shown higher Tip60 mRNA expression levels in tumor tissues than in their normal tissues. Similar results were obtained for the other genes and statistically significant differences were observed in normal tissue expressions of almost all genes between Lum B with Lum A and Triple (-) groups. Also, there are significantly positive correlations among genes in the total group, and subtypes, especially in Lum A and Lum B groups. In conclusion, results obtained in this study suggest that patients with higher gene expression ratios in tumor tissues than in normal tissues may have lower radio therapy sensitivities due to the role of Tip60 complex in the repair of DNA damage. Inhibition of Tip60 could be used as a novel radiosensitizing target for breast cancer patients.

Biography

Ece Salihoğlu attended primary, secondary and high school in Ankara. She graduated from the Department of Biology Education of Hacettepe University in 2007. She earned her Master's Degree in Biochemistry from Gazi University, Faculty of Pharmacy in 2011. Then she started her PhD program at the same department and will finish on January. She is currently working on DNA repair mechanism in breast cancer.

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Parisa Sahranavardfard, J Proteomics Bioinform 2017, 10:12(Suppl)
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MicroRNA-9, microRNA-15b and microRNA-205 as biomarkers and metastasis regulators related to BRAF pathway genes in malignant melanoma

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MicroRNAs are involved in the regulation of processes leading to tumorigenesis such as EMT in a variety of cancers and also they are appropriate option for the diagnosis and treatment of malignancies. Moreover, microRNAs can regulate BRAF expression which has very prevalent mutation in melanoma and involved in tumor metastasis. In order to determine expression levels of EMT and BRAF related microRNAs, we investigated the expression of 18 microRNAs in the patient samples with melanoma. To identify the microRNAs related to EMT process and BRAF pathway, we analyzed a publicly available data set for microRNA expression by using bioinformatics databases (miRTarBase, targetscan, miRWalk, and miRCancer). Then we focused on the ones which have differential expression in malignant melanoma. Subsequently we analyzed the expression levels of 18 selected microRNAs in patient biopsies (N=20) and tumor adjacent normal and evaluated six of them in patients' serum (N=10) by quantitative qRT-PCR. The expression levels of six microRNAs were significantly different in samples ($p<0.05$). MiR-205, miR-141, miR-203 and miR-15b showed significant down-regulation and miR-9 and miR-21 were up-regulated in tumor samples compared to normal adjacent tissues. Based on machine learning analysis and integrative bioinformatics analysis in the context of gene regulatory networks, we selected miR-15b and miR-205 as key regulator of healthy and malignant statue. Serum expression of mir-9, miR-15b and miR-205 were significantly different. The expression pattern of miR-205 and -9 was the same as tumor samples but miR-15b in contrast with tumor samples was up-regulated. The data presented at this study suggested that the expression pattern of microRNAs has potential for the use of them as diagnostic and predictive biomarkers in cancers.

Biography

Parisa Sahranavardfard received her MSc in Animal Physiology from Tehran University in 2009. Currently, she is a PhD student in Animal Physiology in Royan Institute and working on her PhD thesis "Manipulation of microRNAs expression involved in EMT process in human melanoma" under the supervision of Dr. Marzieh Ebrahimi.

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Nahid Kianmehr et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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The relationship of adiponectin, vitamin D, copper and zinc serum levels with rheumatoid arthritis

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Iran University of Medical Sciences, Iran

Aim: To compare the serum levels of adiponectin, vitamin D, copper and zinc in rheumatoid arthritis (RA) patients and to investigate the relationship between these factors and disease severity.

Method: Ninety patients with RA and 30 healthy individuals were participated in this study according to the ACR/EULAR criteria for RA. Serum concentrations of adiponectin were determined by ELISA, copper and zinc by colorimetric spectrophotometry and vitamin D by HPLC methods.

Results: Serum adiponectin and vitamin D were increased and decreased in RA patients, respectively. Adiponectin and disease severity are positively correlated, whereas vitamin D and disease severity are negatively correlated. Adiponectin negatively correlate with vitamin D and positively correlated with disease activity score (DAS). Copper and zinc showed no significant difference between two groups.

Conclusion: The definitive roles of adiponectin, vitamin D, copper and zinc is not completely determined. More investigations are needed to deeply explore the impact of them on RA pathophysiology. Finally, we suggest these serum factors as promising diagnostic and therapeutic biomarkers.

Biography

Nahid Kianmehr is a member of Faculty of Iran University of Medical Sciences since 2000. His research interests include Internal Medicine and Rheumatology. He is a Fellow of Emergency Medicine from George Washington University.

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UMELISA EGF®: The companion kit for CIMAvax-EGF® vaccine

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Background: CIMAvax-EGF® is a Cuban therapeutic vaccine approved for treatment of advanced non-small cell lung cáncer (NSCLC). By inducing antibodies vs. epidermal growth factor (EGF), it prevents binding of endogenous EGF to its receptor, thereby reducing tumor size and/or its progression. Phase II and III clinical trials carried out in Cuban patients revealed the pre-treatment predictive value of serum EGF concentrations ([sEGF]) for CIMAvax-EGF® efficacy. Therefore, it makes sense to identify the subset of patients which will be really benefitted with the use of the vaccine, through its stratification by [sEGF] (personalized medicine). The aim of this work was to develop and validate the UMELISA EGF® kit, the future companion diagnostic kit of CIMAvax-EGF® vaccine.

Methods: The ultra micro analytical system technology (Immunoassay Center, Cuba) was used. The system includes the plate washer and instrumentation for automatic reading, quantification, validation and interpretation of results.

Results: A simple sandwich-type ultramicroELISA assay UMELISA EGF®, based on the advantages of high affinity reaction between streptavidin and biotin, was developed for the measurement of [sEGF]. The best performance was achieved with: plates coated with mAb CBEGF-1 at 6 µg/mL, biotinylated mAb CBEGF-2 at 0.5 µg/mL, incubation time for sandwich formation of 18-20 hours at 37 °C and sample volumes of 30 uL.

Conclusions: The UMELISA EGF® kit exhibited similar characteristics to other commercially available assays, in terms of precision, accuracy and dynamic range. Regression analysis showed a good correlation with the commercially available Human EGF Immunoassay Quantikine® ELISA kit (n=130, Pearson r=0.92, p<0.01) (R&D Systems, USA).

Biography

Idania González Pérez has completed her BSc in Physics from the Faculty of Physics, Moscow State University, Russia (1985-1990) and Master of Science in Physics and Mathematics from Faculty of Physics, Moscow State University, Russia. She is now involved in a PhD program at the University School of Medicine in Havana. She is a Senior Researcher at the Center for Molecular Immunology in Havana, Systems Biology Department, Biomarkers Group. She has published more than 15 papers in reputed journals and has been serving as a Reviewer in *Medical Science Monitor, Journal of Hospital and Clinical Pharmacy and International Blood Research & Reviews*.

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Siao Syun Guan et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Fluorescence-conjugated CD166 anti-peptide for detecting colorectal cancer stem-like tumor *in vivo*

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Cancer stem cells (CSCs) possess characteristics associated with normal stem cells and may generate tumors through the stem cell processes of self-renewal and differentiation into multiple cell types. They involved in drug resistance, metastasis and relapse of cancers can significantly affect tumor therapy. Therefore, it is important to develop specific therapies targeted probe at CSCs for improvement of survival and quality of life of cancer patients. Studies have indicated that the CD166 protein has been considered as a specific marker for colorectal CSCs detection. In addition to monoclonal antibodies, small molecules such as anti-peptides could provide more advantages for CSCs detection *in vivo*. Here, we attended to design the CD166 anti-peptide (CD166ap) to detecting the CSCs *in vitro* and *in vivo*. To obtain CSCs, the human colorectal cancer cells (HCT-15) were seeded into selection media (DMEM/F12, 0.4% bovine serum albumin, 2% B27, 5 μg/mL bovine insulin, 4 μg/mL heparin, 20 ng/mL fibroblast growth factor 2, and 20 ng/mL epidermal growth factor) at a density of 1000 cells per mL. Under these conditions, only CSCs and early progenitor cells survive and proliferate, whereas differentiated cells die. Next, we designed a CD166ap (amino acid: KDSEGYESYNGNLGSQC {It is known that human CD6 proteins have the ability to bind the human CD166 proteins specifically (Chappell PE et al., Structure. 2015, 23:1426-1436). Depending on the two proteins binding sites, we designed the amino acid sequence of CD166 anti-peptide. However, the N- and C-terminal amino acid (lysine and cysteine) were added for conjugating with fluorescence, nuclear medicine chelator and Polyethylene glycol (PEG).} and conjugated with fluorescence for CSCs binding assay by flow cytometry and immunofluorescence stain. For *in vivo* imaging detection, the media-induced CSCs (2×106) were subcutaneous inoculated into the right flank of nude mice (n=5 per each group) and grew for one week. Then, the fluorescence conjugated CD166ap was IV injected into animal model for *in vivo* imaging system and biodistribution assay. The primary spheres that derived from HCT-15 cells under serum-free conditions and which are highly enriched for CSCs at 48 hours. These induced CSCs overexpressed the reprogramming factors such as OCT4, c-myc, Nanog and anti-apoptosis factor (Survivin). Moreover, they also showed the characteristic of drug resistance compared with cancer cells. In CSCs targeted probe binding assay, the CD166ap and antibody revealed the quite binding capability in CSCs. The *in vivo* imaging assay, we found that CD166ap specifically targeted to CSCs-induced xenograft model and accumulated in tumor area. In conclusion, we designed a specific probe for CSCs detection *in vivo* successfully. In addition, the CD166ap may label radioisotope for nuclear medicine imaging and conjugate drug for CSCs therapy in clinical.

Biography

Siao Syun Guan received his PhD Degree from the National Taiwan University, College of Medicine Graduate Institute of Toxicology in 2015. His research interests include biomarker discovery and drug development for tumor diagnosis by nuclear medical imaging. He is a Deputy Engineer in Division of Isotope Application, Institute of Nuclear Energy Research in Taiwan. The programs he has participated in includes: Nuclear Medicine in Diagnosis of Central Nervous Diseases (2008-2009), Development of Gastric Cancer Detection Kit (2010-2013), Colorectal Cancer Capsule Endoscopy (2012), Peptide-Based Tumor Target Probe (2014) and Radioactive Protein Labeling Technology (2015-2016). He is currently the Co-Program Manager for Tumortheranostics Drug Development (2017).

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Biomarker of breast cancer using SVM algorithm based on WXS data

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Many researches have been done to confirm the relationship between genetic information and disease. However, since there is too much genetic information, only partial information of genome has been analyzed, which is not enough to be applied to clinical application. Also, it was difficult to identify the relationship between whole WXS data and disease. Therefore, we extract genetic mutations from WXS data and define the significance of each mutation. Then, we determine the set of mutations according to defined significance. Also, the disease and normal samples are learned through SVM algorithm, and blind samples are tested to verify the accuracy of the classification criteria which is the biomarker. We downloaded 550 WXS data related to breast cancer provided by NIH's TCGA and applied proposed method. First, we extracted mutations (SNP, insertion and deletion) from 500 learning samples (250 primary tumors and 250 blood derived normals) by using GATK. After that, we calculated significance of each mutation which is defined as the difference between disease and normal. We generated the set of mutations by varying significance values, and 500 samples were learned using SVM algorithms for each set of mutations. Finally, classification accuracy was confirmed by applying the biomarker derived from SVM learning to 50 (25 primary tumors and 25 blood derived normals) test samples. The maximum classification probability is 80%, which is obtained when significance value is 0.56 and the size of mutation set is 848. This value means relatively high accuracy compared to existing biomarker.

Biography

Gyu-Bum Han has completed his Master's degree at School of Electrical Engineering in KAIST in 2015. Currently, he is a PhD student at School of Electrical Engineering in KAIST. His research area of interest is Bioinformatics.

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Measurement of serum EGF levels, a methodological approach: Learning what means low-/high concentration of EGF in serum - Clinical implications

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Background: Although the contribution of platelets to the measured serum epidermal growth factor (EGF) concentrations ([sEGF]) was reported since 1983, most of reports in healthy donors or patients do not control clotting times. This results in a variation of the notified values, additionally to that caused by the functional polymorphism of the gene. Both issues platelets and SNP make the conventional stratification by absolute sEGF levels not suitable. Within this study we evaluated the [sEGF] in 105 healthy Cuban donors, balanced by gender and age (18-78 years). As a result, a new methodology of stratification of individuals was proposed.

Methods: Sera were collected at two clotting times: 1h and 4h. Comparisons between groups by [sEGF] were carried out. The estimations normalized through the calculation of its ratios r=[EGF]1h/[EGF]4h were used for the stratification.

Results: Differences were found by age ([EGF]4h, p=0.0083) and gender ([EGF]1h, p=0.0167), and between [EGF]1h and [EGF]4h ($p<0.0001$). While 38 out of 105 individuals ranked different in 1h and 4h conventional stratifications, the methodology using ratios yielded a unique score for each individual.

Conclusions: The proposed methodology of stratification by ratios, in contrast to the conventional approach, allows for a proper comparison between EGF levels and individuals. Thus, it should have an impact on diseases for which the association of EGF with the illness has been established, aiding to clarify the connection of the molecule with the disease. This work might be of value to clinicians, scientists, and the healthcare community in general, conducting research regarding the role of EGF as a biomarker.

Biography

Idania González Pérez has completed her BSc in Physics from the Faculty of Physics, Moscow State University, Russia (1985-1990) and Master of Science in Physics and Mathematics from Faculty of Physics, Moscow State University, Russia. She is now involved in a PhD program at the University School of Medicine in Havana. She is a Senior Researcher at the Center for Molecular Immunology in Havana, Systems Biology Department, Biomarkers Group. She has published more than 15 papers in reputed journals and has been serving as a Reviewer in Medical Science Monitor, Journal of Hospital and Clinical Pharmacy and International Blood Research & Reviews.

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Microdosing/microtracing clinical trials using accelerated mass spectrometry in clinical drug development

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Microtracing/microdosing is an innovative technology that can revolutionize the current paradigm of clinical drug development. Typically, a very small amount of the drug, i.e., 'microdose', which is less than 100 micrograms (or 30 nmoles for proteins), is administered to humans. Since this is much smaller than 1/100 of the pharmacologically active dose, microtracing/microdosing technology can be employed at a very early stage of clinical drug development even when there is limited animal toxicology data. Furthermore, in order to trace minute doses, an accelerator mass spectrometer (AMS) is required and the compound should be labeled, typically with 14C. The microtracing/microdosing study allows clinical drug development scientists for generating the intravenous pharmacokinetics, mass balance, metabolite profiling, and absolute bioavailability data much easier, faster, and at a significantly lower cost. Based on this understanding, this study investigated the current status and employment of AMS-based microtracing/microdosing studies in actual drug development. To achieve this objective, we performed an extensive search of the literature and public information, Delphi focus group interviews, surveys, and personal communications with the key players in the field. The number of the clinical studies that used 14C and AMS dramatically increased from only 3 in 2001-2005 to 59 in 2011-2015. The survey showed that 31.6% of new drug development scientists were planning to perform microtracing/microdosing studies. Furthermore, 73.7% of survey responders replied that they would consider AMS-based microtracing/microdosing studies if there is a well-established service provider. This study confirmed that the frequency of AMS-based microtracing/microdosing studies for drug development has been in a steady increase for the past decade or so. This increase was partly because several issues of AMS application in the previous era, such as dose-linearity, sample pre-processing, and high cost, have been adequately addressed. In conclusion, AMS-based microtracing/microdosing studies have been steadily employed in actual drug development, which is expected to increase further in the future.

Recent Publications

1. Kim YK, Kim A, Park SJ, Lee H. New tablet formulation of tacrolimus with smaller interindividual variability may become a better treatment option than the conventional capsule formulation in organ transplant patients. Drug Design Dev Ther. 2017 (11): 2861-2869
2. Kim Y, Kim A, Lee S, Choi SH, Lee DY, Song JS, Lee H, Jang IJ, Yu KS. Pharmacokinetics, Safety and Tolerability of Tedizolid Phosphate After Single-Dose Administration in Healthy Korean Male Subjects. Clin Ther. 2017. Sep;39(9): 1849-1857
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Biography

Howard Lee is the Founder and Director of the Center for Convergence Approaches in Drug Development (CCADD). Dr. Lee serves as a Professor at the Department of Transdisciplinary Studies, Graduate School of Convergence Science and Technology, Seoul National University. Dr. Lee is also appointed at Seoul National University College of Medicine and Hospital, affiliated with the Department of Clinical Pharmacology and Therapeutics. Dr. Lee previously served as Head of Global Strategy and Planning, Clinical Trials Center, SNUH. As of August 2017, Dr. Lee was appointed Chair of the Graduate Program in Clinical Pharmacology, Seoul National University. Dr. Lee has spearhead the introduction of Accelerator Mass Spectrometry (AMS)-enabled exploratory early clinical drug development studies to the Korean biopharmaceutical R&D sector, which has awarded Dr. Lee 2 government grants.

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Accelerator mass spectrometry-enabled microtracer study to evaluate the human mass balance of KD101: Method challenges for analysis of a volatile oil

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The large majority of drugs and not volatile and amenable to standard analytical techniques. Volatile compounds pose a different set of challenges, requiring changes to the total sample preparation procedure and often analytical method. We encountered such situation during a human microtracer study (180 nCi human oral dose) of compound KD101, a single isomeric oil, (-)α-Cedrene (206.23 g/mol). A total of 6 subjects were administered 400 mg of unlabeled KD101 admixed with 180 nCi of radiolabeled drug as a tracer. Detection of the radiolabel was performed using graphite based Accelerator Mass Spectrometry (AMS), with support from Liquid Scintillation Counting (LSC) for early urinary time-points. Post-administration, cumulative urine and fecal voids were collected for 288 hr post-dose. Serial blood collections were taken frequently post-administration and then daily for the duration of the study. Preliminary work showed the KD101 could be completely removed under vacuum concentration in the absence of any trapping agent or biological matrix. This problem was exacerbated by the AMS processing method where samples are also evacuated under vacuum for torch-sealing inside quartz combustion (oxidation to gaseous carbon dioxide, prior to reduction to graphite). We found an acceptable technique to limit volatility losses through the pretreatment of all samples with an excess of tributyrin prior to concentration. The tributyrin served thus as both a carbon source and a chemical trapping agent. Sucrose was also tested but showed little ability to "capture" the compound during dry-down. We showed that parent compound recovery could be improved from <10 to 89% recovery using 2.0 mg of tributyrin per sample or LC fraction, and a minimum dry-down time (20 min). The overall results of the study validated the dilution method. Mean mass balance recovery was 85.21% (77.96% in urine, 7.26% feces). This is considered a good mass balance recovery given the fact that it was difficult to control for losses due to compound volatility. The concentration decay in the plasma was largely bi-exponential after the absorption period, with a wandering baseline out to 288 hr post-dose, with occasional "jumps" in concentration, which was attributed to the displacement of compound in fat depots. Metabolite radiochromatograms from urine and plasma showed intact parent in plasma with metabolites exclusively explaining the urinary components. In summary, we achieved satisfactory results for the mass balance and metabolism of a volatile oil using a chemical trapping agent. The detriment was a lowering of overall detection sensitivity (e.g. 0.88 dpm/mL of plasma vs. 0.05 dpm/mL of unmodified plasma), but sensitivity was still sufficient to achieve mass balance and perform metabolite profiling using highly sensitive AMS detection.

Recent Publications

1. Kim YK, Kim A, Park SJ, Lee H. New tablet formulation of tacrolimus with smaller interindividual variability may become a better treatment option than the conventional capsule formulation in organ transplant patients. Drug Design Dev Ther. 2017 (11): 2861-2869
2. Kim Y, Kim A, Lee S, Choi SH, Lee DY, Song JS, Lee H, Jang IJ, Yu KS. Pharmacokinetics, Safety and Tolerability of Tedizolid Phosphate After Single-Dose Administration in Healthy Korean Male Subjects. Clin Ther. 2017. Sep;39(9): 1849-1857

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Ewa Skarżyńska et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Ceruloplasmin, lactoferrin and myeloperoxidase in serum of healthy pregnant women

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Introduction & Aim: Maintaining homeostasis in terms of redox status determines the suitable environment for the development of pregnancy. Metalloproteins: ceruloplasmin (CP), lactoferrin (LF), myeloperoxidase (MPO) modulate oxidative stress. The aim of the study was to determine the dynamics of changes in the concentrations of these proteins and the relationship between them.

Methods: The concentrations of proteins were measured in serum (n=113) in subsequent trimesters, postpartum (n=28) and in non-pregnant women (n=17) using immunoturbidimetric assay (CP) and ELISA kits (LF, MPO).

Results: CP [mg/dl] (mean±SD) in trimesters; first (33.0±8.7), second (43.1±6.2), third (44.5±5.8), postpartum (42.39±6.4), non-pregnant (24.12±7.4) revealed the largest increase between the first and remaining trimesters (approximately 35%). LF and MPO [μg/ml] (mean±SD respectively) in trimesters; first (6.19±4.54; 0.17±0.12), secend (5.68±4.4; 0.14±0.08), third (6.34±6.98; 0.17±0.14), postpartum (4.86±3.64; 0.25±0.4), non-pregnant (3.9±2.56; 0.14±0.05) were no significant differences. Significant correlations were found ($p<0.05$) between LF vs MPO in all groups as well between CP vs LF and CP vs LF/MPO ratio in the first trimester and in non-pregnant women respectively.

Conclusions: CP synthesized in the liver exhibits tends to increase during pregnancy, unlike neutrophil proteins: LF, MPO. Significant statistical correlations between CP, LF, MPO indicate involvement of these proteins during pregnancy, particular in the first trimester.

Biography

Ewa Skarżyńska is an university Lecturer and Researcher at Medical University of Warsaw. She received her PhD in Pharmacy Sciences from the same Medical University. At present she is working on protein biomarkers, particularly involved in maintaining systemic homeostasis including oxidative-reducing equilibrium.

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H Filiz Ayyildiz et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Development of a new humic acid based- stationary phases for separation and identification of different types of pharmaceuticals using central components analysis

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S**tatement of the Problem:** High performance liquid chromatography (HPLC, including UHPLC) is one of the most powerful separation techniques capable of providing analysis difficult or impossible with other separation approaches. Thus, chromatographers give particular importance to the design of new efficient stationary phases for HPLC. New trends in chromatographic separations have been directed towards the use of multi-modal stationary phases (MM-SPs) which are high resolution, high selectivity, high loading capacity, high speed, minimal solvent consumption compared with single-modal stationary phases (SM-SPs).

Methodology & Theoretical Orientation: A humic acid based stationary phase was prepared by immobilizing humic acid onto aminopropyl silica via an amide linkage formation and used for the separation and quantification of three different drugs. Besides, a central composite design with three factors (% ACN, flow rate, and pH of mobile phase) and five levels was used to optimize the separation of drugs and to assist the development of better understanding of interactions between several factors affecting on the separation.

Findings: The main effects, interaction effects, and quadratic effects were optimized and evaluated in this design. In the evaluation of the design; retention time (tR), resolution (RS) and capacity factor values (k') are taken into consideration. In this context, optimum conditions for good separation of six different drugs were selected as in follows: ACN %: 44.8; pH: 7.5 and flow rate: 1.75 mL/min and the baseline separation of six different drugs were achieved in 10 min. For real application of the developed method, the selected six drugs were also analyzed on the human plasma.

Conclusion & Significance: The developed EC-ImHA-APS stationary phase has good chromatographic properties with high efficiency, excellent resolution, and symmetrical peaks for each drug compound. So, it can be used as a stationary phase which is alternative to commercial ones.

Recent Publications

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Biography

H Filiz Ayyildiz works at Selcuk University as Associate Professor. Her Doctorate thesis was improvement of oil analysis methods by automated flow injection systems. She also works in various fields and has quite a lot of experience. Her working subjects are as follows: Chromatographic separation for food, pharmaceuticals etc., Membrane technology and removal of some ions from aqueous solution by membrane systems, investigation of humic acid properties and its metal sorption capacity: both batch and continuous systems, investigation of continuous solid phase extraction systems for metal ion concentration and removal of them, voltammetric and polarographic assays of electrochemical properties of some organic substances, improvement of flow injection analysis (FIA) techniques for edible oil analysis.

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The possibility of employing micronucleus test for the diagnosis of doubt cases in screening for the determination of breast cancer

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Introduction & Objectives: The aim of this study is to check the possibility to use the test with micronuclei (MN) in saliva for doubt cases (BI-RADS 3) detected in screening for breast cancer.

Material & Methods: It has been an executed bibliographic search in free text and with the cross referring on PubMed for articles published from Jan 1, 2000 to Dec 31, 2016, for the keywords: "micronuclei in exfoliated buccal cells in breast cancer" and also executed preliminary tests on seven patients and, BI-RADS 3 and BI-RADS 2 to evaluate the difference in the score concerning the presence of micronuclei in the two groups. For the small number of patients, these results are not statistically reliable but can still sufficiently show a very indicative trend.

Results: The bibliographic references show as the micronuclei scoring can be used as a biomarker on fine needle aspiration cytology smears of breast cancer, while the tests in peripheral blood lymphocytes have known reproducibility problem. Also, the bibliography show in breast cancer, an increase of MN in exfoliated buccal mucosa. Five studies show that the buccal cells in breast cancer and the amount of MN are significantly higher compared to benign cases as in six studies for the detection of micronuclei in needle aspiration in ductal carcinoma. Contrasting results are for MN in peripheral blood lymphocytes. On concerning our preliminary test in buccal cells, three patients of the group BI-RADS 3 show to have micronuclei, while no positive findings were found in BI-RADS 2.

Conclusions: May be interesting to apply the MN scoring in cases of doubt, according to functional BI-RADS category 3 (probably benign), and which are sent to a successive control.

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Biography

Menicagli Roberto has completed his PhD from Milan University and Post-doctoral studies in Biochemistry and Molecular Genetics, at the Faculty of Biology at Milan University, where he has been a Contract Professor for two years. He is the Director of Roma Biomed Research Lab, Italy a Private Medical Service Organization. He has published more than 20 papers in reputed journals, some also with impact factor; he is also the principal author of 4 international patents in the field of environment and of the biomarkers applications. He has been serving as an Editorial Board Member of two magazines concerning the medical sciences.

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Kirolos Raafat et al., J Proteomics Bioinform 2017, 10:12(Suppl)
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Combination of Pulsatile and Sustained Effects in Multi-Layer Tablet

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The main objective of the present study is to formulate and evaluate a multi-layer pulsatile drug delivery system (MPDDS) for time dependent release. Based on the utilization of different types of polymers in different ratios. The MPDDS was designed to deliver a rapid pulse of drug after a lag time when it is most needed to patients and another quantity of drug delivered over prolonged period for maintenance dose. The model drug, Etodolac, was incorporated in two separate layers. Sodium starch glycolate (SSG) polymer was incorporated in the fast release (FR) layer. Eudragit RSPO and HPMC K15M polymers were blended with the drug in the sustained release (SR) layer. The two layers were compressed into bilayer tablet using a single-punch tablet machine. Three successive polymer layers of OpadryII, HPMC E5/K4M and Surelease were spray coated using a conventional pan coating processes to provide a lag time before drug release. Bilayer tablets were evaluated for pre- and post-compression parameters. Tablet optimization was performed based on in-vitro dissolution behavior. Addition of 6.67% SSG polymer in the FR layer showed 85.02±0.50% release in 10 min, which is beneficial in the manufacture of fast and pulsatile release tablets. Polymer mixture of Eudragit RSPO and HPMC K15M (2.5:1) resulted in 72.44±0.44% in 12 hours which directly influence the prolongation of drug release. Accession of HPMC K4M to that of E5 (1:80) lengthens the lag time from 2 to 4 hours. Bilayer tablets of etodolac were successfully formulated which achieved a desirable lag time followed by controlled drug release.

Biography

Kirolos Raafat is researching in the field of modified drug delivery systerms. He started his studies testing different techniques of drug delivery, then currently he is trying the combination of multiple techniques to reach optimized techniques for various drugs. He is currently working in medical healthcare institution and he is working on the enhancement of the clinical pharmacy practice in Egypt. He is targeting to enter the field of long-term treatment modification in his next researches.

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Notes:

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Biotechnology and people's health: The infectious diseases and phytonutraceuticals factor

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Phytonutraceuticals generally promises to have greater impacts on health delivery and its management ranging from drug discovery and disease diagnosis. Phytonutraceuticals in both developed and developing countries are alive with rare species that possess pharmacologically active constituents for possible cure of many chronic diseases such as cancer, Tuberculosis, HIV/AIDs, sickle cell anaemia, neurological disorders, and many metabolic diseases. Phytonutraceuticals is a mixture of compounds such as carotenoids, flavonoids and Isoflavonoids (Polyphenols), Phytates (Inositol phosphates), Lignans, Isothiocynates and Indoles, Phenols, Sulphides and Thiols, Terpenes and thus serves as antioxidants, enhance immune response, enhance cell-cell communication, alter estogen metabolism, repair DNA damage caused by smoking and other toxin exposures, others. The Phytonutraceuticals revolution began in the 1980s as a result of substantial evidence to support increase in life expectancy after its administration directly or as foods. The high cost of orthodox medicine pave way for the emergency of Phytonutraceuticals in countries like US, EU and JAPAN. Most African countries rural dwellers depend on Phytonutraceuticals. Literature have it that, most of these plants from savannah and tropical rainforest bio accumulates such Phytonutraceuticals in minute's quantities that are not enough to characterise it and biotechnology is right now the rapidly advancing frontier of science. It has illuminated more deeply and more extensively many genetic, chemical, physiological, and mathematical processes which can be used to mass produce biologically active Phytonutraceuticals in plants. The main objective of the study is to bring to fore the advance in evolution of biotechnology techniques as it affects Phytonutraceuticals development. This will further strengthen research collaboration involving botanist, biotechnologist and chemist etc to further strengthening better health care management.

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Potassium and zinc increase tolerance to salt stress in wheat (*Triticum aestivum* L.)

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Potassium and zinc are essential elements in plant growth and metabolism and plays a vital role in salt stress tolerance. To investigate the physiological mechanism of salt stress tolerance, a pot experiment was conducted. Potassium and zinc significantly minimize the oxidative stress and increase root, shoot and spike length in wheat varieties. Fresh and dry biomass was significantly increased by potassium followed by zinc as compared to control C. The photosynthetic pigment and osmolyte regulator (proline, total phenolic, and total carbohydrate) were significantly enhanced by potassium and zinc. Salt stress increase MDA content in wheat varieties while potassium and zinc counteract the adverse effect of salinity and significantly increased membrane stability index. Salt stress decrease the activities of antioxidant enzymes (superoxide dismutase, catalase and ascorbate peroxidase) while the exogenous application of potassium and zinc significantly enhanced the activities of this enzyme. Significant positive correlation was found of spike length with proline (R2=0.966 ***), phenolic (R2=0.741*) and chlorophyll (R2=0.853**). The MDA content showed significant negative correlation (R2=0.983***) with MSI. It is concluded that potassium and zinc reduced toxic effect of salinity while its combine application showed synergetic effect and significantly enhanced salt tolerance.

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Topical application of aqueous fraction of *Moringa oleifera* modulates the expression of inflammatory markers and vascular endothelial growth factor (VEGF) during wound healing in diabetic rats

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Diabetic wound is a complication which affects significant number of people with diabetes. Its treatment is often very difficult and the available treatments are insufficient with limited success in addition to non-affordability. *Moringa oleifera* Lam (*M. oleifera*) from the family Moringaceae (genus Moringa) commonly called "*Drumstick tree*" is a plant traditionally employed in treatment of many ailments and has been scientifically proven to possess hepatoprotective, anti-inflammatory, antioxidant and hypoglycemic action. The present study was conducted to evaluate the effect of aqueous fraction of *M. oleifera* on expression level of some selected inflammatory markers during wound healing in an animal model of diabetes. The study involved topical application of formulated bioactive fraction of *M. oleifera* using full thickness excision wound model in Streptozotocin (STZ) and Nicotinamide (NAD) induced diabetic rats. Thirty-six healthy adult male Wistar were divided into six groups: Two groups of normal and diabetic controls, three groups of 0.5%, 1% and 2% w/w aqueous fraction treated and one group of positive control that received 1% w/w silver sulfadiazine standard drug. Treatments were applied topically in cream form to the skin wounded area for 21 days. Cytokines analyses were performed using ELISA, Western blotting and immunohistochemistry techniques. The three doses (0.5%, 1% and 2%) of bioactive aqueous fractions were found to be significantly effective in enhancing diabetic wound healing through up regulation of Vascular endothelial growth factor (VEGF) protein and down regulation of inflammatory mediators (TNF-α, IL1-β, IL-6, iNOS and COX-2) in diabetic treated animals compared to untreated diabetic control ($p<0.05$). The downregulation of inflammatory mediators and upregulation of VEGF by aqueous fraction facilitated overall wound healing and closure in diabetic condition. These findings suggest that, topical administration of bioactive aqueous fraction of M. oleifera may accelerate wound healing in hyperglycemic condition. M. oleifera, inflammatory markers, upregulation, downregulation, diabetic wound.

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Acetylcholinesterase inhibiting activity of compounds isolated from *bauhinia rufescens*

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This study has tested the *in vitro* anti-acetylcholinesterase activity of compounds isolated from the stem bark of *Bauhinia rufescens* by employing TLC bioautographic and Ellman's spectrophotometric methods. Among the compounds oxepin (IC50, 516.63 μM), seqouyitol (IC50, 463.77 μM) and α-amyrin acetate (IC50, 832.80 μM) which exhibited a significant acetylcholinesterase inhibitory activity in comparison with a positive control, the galantamine hydrobromide (IC50, 2.92 μM). The phytochemicals isolated from the stem bark of B. rufescens had demonstrated a potent anti-cholinesterase inhibition.

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Silibinin downregulates E-cadherin expression in MKN-45 human gastric cancer cells

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Gastric cancer is currently known as one of the most important causes of cancer-driven death, all over the world. In patients with gastric cancer, a significant proportion of deaths occur due to metastasis. On the other hand, down modulated E-cadherin level has been reported as an important contributor to tumor cell invasion and metastasis. In this regard, the present work was aimed to evaluate the impact of silibinin, a flavonolignan with established anti-tumor efficacy, on cell viability and E-cadherin expression in a gastric cancer cell line; MKN-45. To determine cell viability, MTT assay was performed 48 hours after silibinin treatment (at concentrations of 100, 200 and 400 μM). In addition, quantitative real-time PCR was done following total RNA extraction and cDNA synthesis, to assess E-cadherin level in cells treated with silibinin. The MTT results showed a silibinin concentration-dependent reducing effect on the viability of MKN-45 cells. The findings of quantitative real-time PCR analysis demonstrated upregulated E-cadherin expression in cells treated with silibinin (significantly at concentration of 200 μM) compared to control cells. The current study suggests that silibinin may exert anti migratory/invasive effects on gastric cancer cells by enhancing E-cadherin expression, which need to be further investigated.

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A comparison between biopharmaceuticals and pharmaceuticals in cancer treatment

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Undoubtedly, cancer is one of the main causes of morbidity and mortality around the world. Common treatments of cancer such as surgery, radiotherapy and chemotherapy are effective in curing cancer at early disease stages; however, they cannot completely eradicate it in metastatic condition. For example, the success of chemotherapy has been diminished due to loss of its selectivity and specificity, thereby the administration of dose to patients should be limited because of the toxicity to normal cells. Thus, utilizing targeted anticancer biopharmaceuticals (monoclonal antibodies, non-antibody proteins and small molecules) can be effective in controlling the progression of cancer, having less side effects and survival of cancerous patients. Biopharmaceuticals are macro molecules-based therapeutic drugs which are manufactured in or extracted from biological sources. They are 200-1000 times larger than traditional small molecule drugs. Furthermore, they do not arise from simple chemical processes like traditional pharmaceuticals. So, it makes much greater complexity in their structure than the latter. On the other hand, pharmaceuticals, known as medicine or drug, are a principal component of traditional medicine and include a broad spectrum of medicines. They come from chemicals. In fact, they make up over 90% of the drugs on the market. Biopharmaceuticals and pharmaceuticals differ not only in terms of size, but also in the methods of processing, behavior and type of action in the body and so on. In this paper, features of biopharmaceuticals and pharmaceuticals for the treatment of cancer are explained and compared. These items include safety and efficacy (immunogenic response), bioactivity, side effects, cost, dosage rate and access rate. Having knowledge about effective pharmaceutical methods for the treatment of cancer can be very helpful in choosing an efficient method and its results can be more productive and accurate than conventional methods of cancer treatment.

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Hormonal regulation of fructan content of wheat seedlings during severe drought stress and recovery

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Fructans as a major store of carbohydrates in wheat are involved in the protection of plants during drought. phytohormone extensively interact with each other and might counteract the negative effects of water stress exerted on carbohydrate metabolism and promote the whole plant growth. In the present study the relationship between fructan content and phytohormones was evaluated in 4-day old seedlings of a drought-tolerant (Sirvan) and a drought-sensitive (Marvdasht) wheat cultivar exposed to seven days water cessation and subsequent re-watering. In comparison with sensitive cultivar, the tolerant one accumulated more fructan (3.56±0.3 mg/g FW). Analysis of phytohormon contents showed that drought stress remarkably increased the level of abscisic acid (ABA) of tolerant cultivar (~ 7 fold) higher than of sensitive one. Under water cessation, the level of gibberellic acid (GA) content decreased in both cultivars, while the extents in tolerant one was lower. After drought stress the content of indole acetic acid (IAA) did not show significant change in both cultivars. All together, the results suggest a close relation between the dynamics of phtytohormones (ABA, IAA, GA) and fructan synthesis plays a crucial role in the tolerance of wheat seedling against drought stress conditions.

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DPPH and superoxide anion assay and isolation of the antioxidant compound from the methanolic extract from the leaves of *Costus Afer* Ker-Gwal

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Costus Afer Ker Gwal is traditionally used in African traditional medicine to treat and manage broad spectrum of infectious tropical disease. Apart from the medicinal uses of the plant, it has significant cultural uses such as wrapping of indigenous food items, mat making, and feed to small ruminants. The leaves of *C. Afer* were collected from the Nigeria Natural Medicine Development Agency, Lagos Nigeria. The leaves were dried and extracted separately with methanol and hexane. The extracts were evaluated for antioxidant activity using DPPH and Superoxide Anion radical scavenging assays method. The methanol extract was subjected to column chromatography eluted with dichloromethane-methanol system. The DPPH % RSA value for the methanol and hexane are 84.71 and 18.88 respectively. The methanol extracts has Superoxide Anion value of 28.15. Then harmine was isolated for the first time from the methanol extract with the following spectroscopic data, the molecular formula $C_{13}H_{12}ON_2$, MZ 212.1 $(M+H)^+$ on the basis of its LRMS. 1H- NMR: δ 8.10 (1H, d, J=5.5 Hz), δ 7.99 (1H, d, J=8.5Hz), δ 7.80 (1H, d, J=5.5Hz), δ 7.04(1H, d, J=2.0 Hz), δ 6.87 (1H, dd, J=8.5,2.0 Hz), δ 3.91(3H, s), δ 2.76 (3H,s) and ^{13}C-NMR : δ 162, 144, 142, 138, 122, 114, 112, 96, 56, 29, 29, 24, 20. Literature report indicated harmine to have broad spectrum of biological activities, this tend to validate the extensive use of *Costus Afer* in many traditional medicine.

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Merkel cell carcinoma in an 82-year-old Filipino male: A case report and literature review

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Merkel cell carcinoma (MCC) is an uncommon, highly aggressive skin malignancy that develops usually in sun-exposed areas, most common on the head and neck area (55%). MCC is mainly a malignancy of UV-exposed and fair-skinned elderly Caucasians. We report the case of an 82-year-old Filipino male who presented with progressive left leg swelling with multiple nodules of varying sizes. The nodules were excised and pathologic diagnosis revealed MCC. The patient underwent chemotherapy however expired due to acute respiratory failure type 1 secondary to acute kidney injury as a complication of tumor lysis syndrome. MCC carries a poor prognosis hence early detection is warranted and vital for patient's survival.

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Merkel cell carcinoma in an 82-year-old Filipino male: A case report and literature review

Hydelene B Dominguez
SLU-Hospital of the Sacred Heart, PhilippinesDevelopment of composition and technology of vincristine nanoparticles using high-molecular carbohydrates of plant origin

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Despite the continuous improvement of cancer fighting strategies, it still remains the main cause of mortality worldwide. The rise of cancer worldwide on the one hand is a major obstacle to human well-being and on the other hand to economies of even the developed and rich countries. In 2010, the total annual cost of cancer was estimated to reach approximately 1.16 trillion dollars. Current cancer therapy strategies are based on surgery, radiotherapy and chemotherapy. The problems associated with chemotherapy are one of the biggest challenges for clinical medicine. These include: low specificity, broad spectrum of side effects, toxicity and development of cellular resistance. Therefore, anti-cancer drugs need to be develop urgently. Particularly, in order to increase efficiency of anti-cancer drugs and reduce their side effects, scientists work on formulation of nano-drugs, using nanotechnology and natural excipients. The objective of this study was to develop composition and technology of vincristine nanoparticles using high-molecular carbohydrates of plant origin. Due to the theory that by target metabolism of glucose, it is possible to develop selective mechanism against cancer we have used plant polysaccharides, particularly, soy bean seed polysaccharides, flaxseed polysaccharides, citrus pectin, gum Arabic, sodium alginate. Based on biopharmaceutical research series vincristine containing nanoparticle formulations were prepared. High-energy emulsification and solvent evaporation methods were used for preparation of nanosystems. Polysorbat 80, polysorbat 60, sodium dodecyl sulfate, glycerol, PVA were used in compositions as emulsifying agent and stabilizer of the system. The ratio of API and polysaccharides, also the type of the stabilizing and emulsifying agents is very effective on the particle size of the final product. The influence of preparation technology, type and concentration of stabilizing agents on the properties of nanoparticles were evaluated. For the next stage of research nanosystems were characterized. Physiochemical characterization of nanoparticles: their size, shape, distribution was performed using AFM (atomic force microscope) and SEM (scanning electron microscope). The present study explored the possibility of production of NPs using plant polysaccharides. Optimal ratio of API and plant polysaccharides, the best stabilizer and emulsifying agent was determined. SEM showed that nanoparticles were spherical in shape. The average range of nanoparticles was visualized by SEM.

lamziraebralidze@gmail.comin malignancy that develops usually in sun-exposed areas, most common on the head and neck area (55%). MCC is mainly a malignancy of UV-exposed and fair-skinned elderly Caucasians. We report the case of an 82-year-old Filipino male who presented with progressive left leg swelling with multiple nodules of varying sizes. The nodules were excised and pathologic diagnosis revealed MCC. The patient underwent chemotherapy however expired due to acute respiratory failure type 1 secondary to acute kidney injury as a complication of tumor lysis syndrome. MCC carries a poor prognosis hence early detection is warranted and vital for patient's survival.

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A study on chemical composition and antifungal activity of essential oil from *Thymus caramanicus, Thymus daenensis* and *Ziziphora clinopodiaides*

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Background: Essential oils (EOS) possess a wide range of significant properties including antiphlogistic, spasmolytic and antinociceptive effects. In this study, we use essential oils (Eos) from *Thymus daenensis, Thymus caramanicus* and *Ziziphora clinopodiodes*. The context and purpose of the study: this study attempts to determine the growth inhibition level of the essential oils of three plants against Aspergillus flavus and Aspergillus parasiticus for 14 days.

Results: The highest rate of inhibition was observed in *Thymus daenensis* in concentration above 7 µL in 100 mL of PDA medium in which no growth was observed during 14 days.

The Main Findings: Among the three essential oils, *T. daenensis* contains the highest level of thymol (77.62%). *Zizipora clinopodioides* contains pulegone (31.21%), menth-3-en-8-0l (23.82%), menthol (7.21%), borneol (2.25%), carvacrol (5.38%) and piperitone (5.55%). Only a concentration of 9 µL of essential oils of *Z. clinopodioides* can prevent mycelium growth of both fungi for 7 days. Thymus caramanicus contains carvacrol (65.52%), p-cymene (13.21%), gamma-terpinene (4.44%), thymol (4.14%) and linalool (2.63%).

Conclusion: Although *T. caramanicus* contains 65.52% carvacrol, its inhibition growth ability does not reach 100% in all concentrations and it is capable of inhibiting fungal growth completely (100%) at 7 and 9 µL concentrations for one day. This indicates that compound thymol is more effective than carvacrol in prevent of growth fungi.

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Discovery and validation of biomarkers for allergy for use in dietary intervention studies

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Non-communicable diseases (NCDs) are becoming a real global problem and it is seen that allergies early in life are one of the first signals of development of immune related disorders later in life. Therefore there is a substantial need to identify and validate early, more specific, better and predictive and/or diagnostic biomarkers for allergy early in life. We have assessed the validity and the predictive value for disease severity and/or response to treatment of the known biomarkers in clinical samples and found differences in allergy-related biomarkers in atopic dermatitis, food allergy, asthma/rhinitis and eosinophilic esophagitis. To this date, no single or specific biomarker for allergy has been identified. Since allergy is not one disease, but a collection of a number of allergic conditions, it is therefore not very plausible that one marker would fit all, and probably a more holistic approach using a combination of clinical history, clinical read-outs and diagnostic markers will be needed. The search for new and reliable biomarker will continue and the evolution in biomarker discovery has resulted in an 'omics' approach, in which hundreds of biomarkers in the field of genomics, transcriptomics, proteomics, and metabolomics can be simultaneously studied. A first attempt to identify new biomarkers for allergy in matched serum and saliva samples of infants with atopic dermatitis versus healthy infants resulted in several potentially interesting new markers which now have to be validated in upcoming studies.

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A novel sparse coding algorithm for classification of tumors based on gene expression

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High-dimensional genomic and proteomic data play an important role in many applications in medicine such as prognosis of diseases, diagnosis, prevention and molecular biology, to name a few. Classifying such data is a challenging task due to the various issues such as curse of dimensionality, noise and redundancy. Recently, some researchers have used the sparse representation (SR) techniques to analyze high-dimensional biological data in various applications in classification of cancer patients based on gene expression datasets. A common problem with all SR-based biological data classification methods is that they cannot utilize the topological (geometrical) structure of data. More precisely, these methods transfer the data into sparse feature space without preserving the local structure of data points. In this paper, we proposed a novel SR-based cancer classification algorithm based on gene expression data that takes into account the geometrical information of all data. Precisely speaking, we incorporate the local linear embedding algorithm into the sparse coding framework, by which we can preserve the geometrical structure of all data. For performance comparison, we applied our algorithm on six tumor gene expression datasets, by which we demonstrate that the proposed method achieves higher classification accuracy than state-of-the-art SR-based tumor classification algorithms.

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Raphia australis polyphenols for cancer treatment

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Cancer, the second cause of death in the world, has been treated with the use of several synthetic drugs. Some of the chemotherapeutic drugs used in orthodox medicine include vinblastine, topotecan, irinotecan and silvestrol. All these drugs come with their side effects like anemia, tiredness, mouth soreness, nausea, hair loss, loss of appetite, skin changes, pain, and infertility. The major anticancer secondary metabolites are saponins, tannins and flavonoids. Due to the low toxicity, and given the fact that there has been no literature report on polyphenols present in the genus *Raphia*, this work therefore looks into the use of *Raphia australis* ethanol extract in cancer chemotherapy. Extraction was done on the dried pulp of *Raphia* australis by steeping in ethanol after extracting and concentrating, thin layer chromatography (TLC) analysis was carried out using ethanol-ethyl acetate-ammonia solvent system in the ratio 5:3:2 respectively. Gravity column chromatography was run using this solvent system. Similar fractions were combined together for further analysis using liquid chromatography-mass spectrometry (LC-MS). Three flavonoids and three tannins were identified which are: afzelechin epicatechin (m/z=561.1397), catechin (m/z=289.0712), protocatechuic acid (m/z=153.0182), umbelliferone also known as 7-hydroxycoumarin (m/z=353.0873), anthocyanidin, and quinic acid (m/z=191.0556). These phenolics all showed anticancer activity. Due to the ubiquitous application of these polyphenols in the treatment of various forms of cancer, this work therefore suggests the use of ethanol extract of the pulp of *Raphia australis* in the treatment of various forms of cancer. The biological evaluation will be done using MTTS assay.

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Epigenomic hard drive (EHD) imprinting: A hidden code within cancer cell to survive beyond the biological death of a tumor patient

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Several genetic and epigenetic theories have been proposed to explain the intricacies of life and death. However, several questions are still remaining unsettled with reference to the death event particularly of the living tissue in case of cancer patients such as destination of cancer cells after the biological death of patients. Cancer can display the intent to communicate with the external environment after the biological death of patient. Do they carry some special information in the form of coding that helps them to survive? To explain such queries in cancer field, we hypothesize epigenomic hard drive (EHD) as a recording and storage of global epigenetic events in cancerous and non-cancerous tissue of cancer patients. This mini-review presents the novel concept of EHD reinforced with the existing knowledge of and genetic and epigenetic events in cancer. In conclusion, revealing such questions will help to understand the tumor community as well as its role in pre and post death events. We propose that cancer cells being a part of human cellular community may carry some encrypted coded message in the form of EHD and could be used beyond the death decoding purpose about the individual life time any events, acts and activities. In future perspectives, state of the art tools and techniques to decipher epigenetic landscape may provide answers to above proposed concept and could pave the way of better understating of cancer, cellular death and human body death. The authors suggest that epigenetic tools based method such as assessment of DNA methylation, histone code signature, small signaling messengers as miRNA could be performed on cancerous and non-cancerous tissue during and after biological death of cancer patients. In this paper, we summarize the EHD understanding may impart huge potential and interest for basic and clinical scientists to unravel mechanisms of carcinogenesis, therapeutic markers and differential drug responses.

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Erythrocyte membrane disorganization: Potent and cost-effective biomarker in early diagnosis of cervical cancer

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Cervical cancer is the fifth most common cancer of the world, and poses a major public health problem. This paper explores a de novo observation that cervical cancer induced oxidative stress is responsible for erythrocyte membrane disorganization in the patients of advanced stage of clinical progression of the disease. The study of carbonyl content, antioxidant enzymes, lipid peroxidation, membrane fluidity and SDS-PAGE of erythrocyte membrane protein has been conducted on 94 adult cervical cancer patients and an equal number of age and sex matched normal subjects. Lipid peroxidation of erythrocyte membrane is observed to be enhanced and antioxidant enzyme activity alters significantly in the pathologic samples. Increased membrane fluidity is indicated by analysis of fluorescence depolarization using 1,6 diphenyl-1,3,5 hexatriene compared to healthy controls. The transition temperature of membrane lipids from gel to sol phase transition is observed to be shifted from 35°C (control subjects) to 25°C (cervical cancer patients). Degradation of the spectrin band is evidenced in SDS-PAGE of the membrane protein profile of the diseased subjects. It can be elucidated that cervical cancer induces oxidative stress in erythrocytes which finally results in increased erythrocyte membrane fluidity, altered phase transition temperature and modified protein profile. This is an original work on the importance of the protein profile of RBC membrane. These findings can be used as a characteristic signature of the red blood cell membranes and may be used for the diagnosis of cervical cancer.

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Screening of proteins targeting circulating miRNAs for improved diagnosis of multiple myeloma using computational methods

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Multiple myeloma is a B-cell malignancy, which is characterized by the expansion of clonal plasma cells in the bone marrow, thereby leading to abnormal accumulation of monoclonal antibodies in circulation. The condition arises from an asymptomatic multiplication of plasma cells, called MGUS (Monoclonal gammopathy of undetermined significance) which eventually progresses to Myeloma. Till date, there are no explicit assays that can discriminate between the premalignant and malignant stages. Circulating miRNAs are deregulated in MM cells and bone marrow. Their differential expression profiles in various body fluids can be quantified and used for the diagnosis of MM. The study focuses on identification of such a protein which would show exclusive affinity for a selected panel of circulating miRNAs reported to be deregulated in MM. A few human RNA binding proteins were selected based on their RNA binding domains and their interacting probabilities with the panel of miRNAs. The 3D structure of miRNAs and proteins were modelled and validated. Molecular Docking was performed for determining the protein-miRNA interaction using AutoDock Vina. Out of the selected proteins, DKC1 showed good binding affinity values of -17.4 kcal/mol with miRNA-720, -16 kcal/mol with miRNA-1246 and -16.9 kcal/mol with miRNA-1308. It also showed some significant hydrogen bonding. miRNA 26 was used as an internal control for docking as it is a circulating miRNA without any significant relation to MM. This protein-miRNA interaction could be used as an economical and reliable ELISA based method for the improved diagnosis of Multiple Myeloma patients.

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Antibodies with functionality as a new generation of translational tools to monitor, predict and prevent demyelination

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Abs against myelin basic protein/MBP endowing with proteolytic activity (Ab-proteases with functionality) is of great value to monitor demyelination to illustrate the evolution of multiple sclerosis (MS). Anti-MBP autoAbs from MS patients and mice with EAE exhibited specific proteolytic cleavage of MBP which, in turn, markedly differed between: (i) MS patients and healthy controls; (ii) different clinical MS courses; (iii) EDSS scales of demyelination to correlate with the disability of MS patients to predict the transformation prior to changes of the clinical course. Ab-mediated proteolysis of MBP was shown to be sequence-specific whilst demonstrating five sites of preferential proteolysis to be located within the immunodominant regions of MBP and to fall inside into 5 sequences fixed. Some of the latter (with the highest encephalitogenic properties) were proved to act as a specific inducer of EAE and to be attacked by the MBP-targeted Ab-proteases in MS patients with the most severe (progradient) clinical courses. The other ones whilst being less immunogenic happened to be EAE inducers very rare but were shown to be attacked by Ab-proteases in MS patients with moderate (remission-type) clinical courses. The activity of Ab-proteases was first registered at the subclinical stages 1-2 years prior to the clinical illness. About 24% of the direct MS-related relatives were seropositive for low-active Ab-proteases from which 22% of the seropositive relatives established were being monitored for 2 years whilst demonstrating a stable growth of the Ab-associated proteolytic activity. Moreover, some of the low-active Ab-proteases in persons at MS-related risks (at subclinical stages of MS), and primary clinical and MRT manifestations observed were coincided with the activity to have its mid-level reached. Registration in the evolution of highly immunogenic Ab-proteases would illustrate either risks of transformation of subclinical stages into clinical ones, or risks of exacerbations to develop. The activity of Ab-proteases in combination with the sequence-specificity would confirm a high subclinical and predictive (translational) value of the tools as applicable for personalized monitoring protocols. Ab-proteases can be programmed and re-programmed to suit the needs of the body metabolism or could be designed for the development of principally new catalysts with no natural counterparts. Further studies on targeted Ab-mediated proteolysis may provide a translational tool for predicting demyelination and thus the disability of the MS patients.

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Plant macromolecule from different species of *Boraginaceae* family and its anticancer efficacy

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A new series of linear and regular 3-arylglyceric acid-derived polyether, namely poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA) was isolated and identified in the water-soluble, high-molecular weight fractions obtained from extracts of different species of comfrey *Symphytum asperum, S.caucasicum, S.officinale, S.grandiflorum* and bugloss *Anchusa italica*. According to data of ^{13}C, 1H NMR, APT, 2D $^{1}H/^{13}C$ HSQC, 1D NOE and 2D DOSY experiments the polyoxyethylene chain is the backbone of the polymer molecule. 3,4-Dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of this regular polymer is 3-(3, 4-dihydroxyphenyl) glyceric acid residue. This compound is a first representative of a new class of natural polyethers. Then the racemic monomer 2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid (DDPPA) and its virtually pure enantiomers (+)-(2R,3S)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid and (-)-(2S,3R)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid were synthesized for the first time via Sharpless asymmetric dihydroxylation of trans-caffeic acid derivatives using an osmium catalyst, a stoichiometric oxidant N-methylmorpholine-N-oxide and enantiocomplementary catalysts cinchona alkaloid derivatives (DHQ)2-PHAL and (DHQD)2-PHA as chiral auxiliaries. It is well known that epoxides are valuable synthons in organic synthesis and have been introduced into pharmaceutical applications, such as in the synthesis of antitumor drugs. Subsequently, the building block for the production of derivatives of PDPGA, methyl 3-(3,4-dimethoxyphenyl) glycidate was synthesized based on the Darzen reaction or by oxidation with oxone in order to produce in future derivatives of synthetic analogue of natural polymer through ring-opening polymerization of 2,3-disubstituted oxirane. PDPGA is endowed with intriguing pharmacological properties as anticomplementary, antioxidant, anti-inflammatory, burn and wound healing and anticancer properties. PDPGA and DPGA exerted anticancer activity *in vitro* and *in vivo* against human prostate cancer (PCA) cells. However, anticancer efficacy of PDPGA is more effective compared to its synthetic monomer. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity, and supports its clinical application.

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Urinary protein changes in subcutaneous walker-256 tumor-bearing rats even before tumor mass palpable

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Early diagnosis of cancer can significantly improve survival rates for cancer patients. Cancer biomarkers are measurable changes associated with the cancer and without homeostatic control; urine reflects early changes in the body with a prospect in cancer early diagnosis. In this study, the Walker 256 tumor rat model was established by subcutaneous injection of Walker 256 tumor cells. To identify urinary proteome changes during the entire development of cancer, urine samples of Walker 256 tumor bearing rats were collected at five time points corresponding to before cancer cell implant, before tumor mass palpable, tumor mass appearance, tumor rapid growth and cachexia respectively. The urinary protein patterns on SDS-PAGE change significantly as tumors progress and urinary proteome was identified using a Fusion-Lumos mass spectrometry by label-free quantitation. Interesting, several differential urine proteins before tumor mass even palpable could be identified with a fold change >2 and p value <0.05, and these early changes in urine could be also identified at tumor mass appearance, tumor rapid growth and cachexia. Twenty-four differential proteins were annotated before as biomarkers of cancer diseases and nine proteins as biomarkers of breast cancer. Additionally, it was found that those differential proteins were involved in several pathways related to cancer, including IL-6 and IL-12 signaling, production of nitric oxide, ROS and apoptosis. Finally, 30 dynamically changed urinary proteins were selected as more reliable cancer biomarkers, and they were validated by targeted proteomics. Our study suggested that urine is a sensitive biomarker source for early detection of cancer and systemic changes reflected in urine proteome during cancer progression can improve the understanding of pathophysiological changes of cancer.

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