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Posters

John Horsley et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Controlling the conformation of a modified gramicidin S cyclic peptidomimetic with an azobenzene photo-switch

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Secondary structures in proteins contain motifs which are important in determining protein folding and arrangement. The unique folding pattern creates a well-defined structure of protein which governs the function, as emphasized by the quote structure dictates function. Thus, the ability to control the secondary structure of a protein will enable the regulation of protein activity and function. The main objective of this research is to reversibly control the secondary structure of a cyclic peptide photochemically, using UV and visible light. This is demonstrated by incorporating a cis-trans photoisomerizable azobenzene photo-switch into the naturally occurring antibiotic, gramicidin S, to produce a cyclic peptidomimetic, azobenzene-gramicidin S (Azo-GS). Gramicidin S exists as a cyclic peptide with two antiparallel β-strands, linked by two β-turns. The cis isomer of Azo-GS was found to adopt a β-sheet with a β-turn structure, while the trans isomer exists as a random structure. While gramicidin S is active against both Gram-positive and Gram negative bacteria, our experimental results showed that Azo-GS is only active against Gram positive bacteria. Both isomers of Azo-GS were tested against the Gram positive bacteria, *Staphylococcus aureus* and the Gram negative bacteria, *Escherichia coli,* respectively. The cis isomer, containing the more well-defined secondary structure, was found to be active in suppressing the growth of *S. aureus*, while the trans isomer was found to be inactive. The findings of this research form the basis for photo-switches to function as potential molecular switches to control the secondary structures and ultimately, the activity of peptides.

Biography

John Horsley has completed his PhD from the University of Adelaide and currently undertaking Post-doctoral studies from the University of Adelaide, Australia. He is working with the Abell Group focusing on peptide synthesis and has published number of papers in the reputed scientific journals.

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Notes:

Wirginia Krzysciak et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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The role of pyruvate kinase (PK) and glucokinase (GCK) in *Streptococcus mutans* mixed biofilm development

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Background: Carbohydrate metabolism is one of the key metabolic pathways subject to changes during *Streptococcus mutans*-mixed biofilm development.

Aim: The objective of this study was determination of the role of GCK and PK in *S. mutans* pathogenicity.

Material & Methods: Pyruvate kinase and glucokinase from *S. mutans*-mixed biofilm species were purified, precipitated and estimated fluorimetrically. The study was performed on type and clinical strains. In total, 21 children with caries were enrolled, (4±1.7 years). As many as 22 individuals without caries (4.12±1.22 years) served as the control group. Phenotyping of isolated bacterial strains was performed, and evaluated by 16S rDNA gene sequencing. Biofilm assay was carried out according to current protocols in microbiology.

Results: Out of 100 isolated strains, 74 were classified as *S. mutans* species. PK and GCK activities were highest after 6 and 12 hours incubation in the mixed biofilm species. PK activity was higher (1.45 mU/mg of protein) in the experimental group compared to the control (1.10 mU/mg of protein).

Conclusions: The glycolytic activity increases in the newly formed biofilm after 6 and 12 hours of incubation; however, this activity decreases with dental plaque biofilm aging. It was demonstrated that the amount of synthesized PK in *S. mutans*-mixed biofilm species grows in the caries group. Inhibition of glycolysis metabolic pathway proteins during mixed-species biofilm of *S. mutans* development may have an effect on reduction of the development of dental caries in children.

Biography

Wirginia Krzysciak has completed her PhD from Jagiellonian University, Poland. She is an Assistant Professor in the Department of Medical Diagnostics, Faculty of Pharmacy, Medical College, Jagiellonian University in Krakow, Poland. She has published more than 20 papers in peer-review journals on Caries Pathogenesis and Redox Signaling. She is a Lecturer and one of the Instructors of Laboratory Medicine where she teaches Hematology, Laboratory Medicine and Medical Diagnostics. She is also a Founder and the Instructor of Students Association of Laboratory Diagnosticians. She is a Member of Polish Society of Microbiologists and Polish Society of Biochemistry.

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Yui Umekawa et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Homeothermic control based on pre-equilibrium reaction in thermogenic skunk cabbage, *Symplocarpus renifolius*

Yui Umekawa and **Kikukatsu Ito**
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Temperature is one of the most important requirements for all living organisms. To survive in severe environments in which temperature changes continuously, some animals have gained the ability to maintain their temperature during the evolutionary process, called homeothermy, which is performed by a complex mechanism involving thermal receptors throughout the body and integration in the hypothalamus that controls shivering and non-shivering thermogenesis. Interestingly, flowers of some plants show a similar homeothermic behavior by inversely controlled respiration to temperature. To clarify the thermoregulatory mechanism in thermogenic plants, we investigated the temperature response of respiration in vivo using modified Arrhenius model using homeothermic spadices of skunk cabbage (*Symplocarpus renifolius*). Our results clearly showed that overall thermodynamic activation energy exhibits a negative value in the temperature range in which respiration control occurs. Our results suggest that respiratory control in this plant is achieved by a pre-equilibrium chemical reaction in response to temperature. Moreover, citrate-driven respiration analysis using isolated mitochondria from thermogenic spadices further suggests that chemically endothermic reactions, such as NADPH production catalyzed by mitochondrial isocitrate dehydrogenase are involved in our proposed pre-equilibrium reaction. A law of chemical equilibrium known as Le Chatelier's principle may govern the homeothermic control in skunk cabbage.

Biography

Yui Umekawa is currently pursuing PhD in Biochemistry, Bioenergetics, Molecular Biology at the United Graduate School of Agricultural Sciences, Iwate University, Japan.

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Md Abu Sayed et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Isolation and expression analysis of a cDNA encoding for phosphoenolpyruvate carboxylase in thermogenic skunk cabbage, *Symplocarpus renifolius*

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Skunk cabbage, *Symplocarpus renifolius*, is known to produce enough heat to melt the snow in early spring. We have isolated a cDNA that encodes a phosphoenolpyruvate carboxylase, termed as *SrPEPC* from thermogenic florets of skunk cabbage. *SrPEPC* is a 110.5 kDa protein that contains conserved amino acid regions such as phosphorylation and catalytic domains. Expression of SrPEPC mRNA was highly abundant in the petal and pistil of thermogenic florets. Interestingly, the expression was very low in non-thermogenic tissues including spathe and leaf. Our data suggest that *SrPEPC* plays a role for tissue-specific heat production in the skunk cabbage.

Biography

Md Abu Sayed is currently pursuing his PhD from United Graduate School of Agriculture, Iwate University, Japan. He has been serving as an Assistant Professor in the Department of Biochemistry and Molecular Biology, Hajee Mohammad Danesh Science and Technology University (HSTU), Dinajpur, Bangladesh since 16 May, 2012.

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Regulation of protein related antimicrobial activity by recombinant mussel adhesive protein (fp-151) using proteome analysis

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In this study, the antimicrobial activity of recombinant mussel adhesive protein (fp-151) was evaluated against skin flora. The skin flora used for experiments were four Gram-positive bacteria such as *Staphylococcus aureus* (*S. aureus*), *Streptococcus pyogenes (S. pyogenes), Staphylococcus epidermis (S. epidermis), Propionibacterium acnes (P. acnes)* and one Gram-negative bacteria (*E. coli*). Pour plate assay was applied for determining the antimicrobial effects of recombinant MAP (fp-151). According to the result, recombinant MAP (fp-151) showed 90% of antimicrobial activity and was as good as or even better than penicillin for five skin flora. Also, we aimed to identify key proteomic changes in a HaCaT cell line grown in treated with recombinant MAP (fp-151) peptide, applying proteomic methods using nano-LC and a 4800 Plus MALDI TOF/TOF tandem mass spectrometry device. In a narrowed down and comparative data analysis of both non-treated and treated recombinant MAP (fp-151) peptide groups, differentially expressed proteins were identified as up or down-regulated. Bioinformatic analysis was used to reveal the biological functions and predict its possible mechanism. These results indicate that recombinant MAP (fp-151) has a high antibacterial effect and resistance against bacterial infection and cell damage which therefore, implies that recombinant MAP (fp-151) has its potential use in skin care products.

Biography

Kyung Bae Pi has completed his MS from Kyung Hee University. He is a Senior Researcher and Project Leader of Incheon Business Information Technopark. He has published more than 13 papers in reputed journals and has been serving as an Editorial Board Member of repute.

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G Deka et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Structure of arginine decarboxylases from *Salmonella typhimurium* and ordering of loops close to the active site upon PLP-binding

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Salmonella typhimurium colonizes in the human gastro-intestinal tract due to its ability to withstand high acidic pH (pH<2.5). Its acid tolerance response (ATR) is due to lysine decarboxylase (LDC) and arginine decarboxylase (ADC) systems, which maintains the internal pH of the bacterium close to 4. ADC consumes one proton from the cytoplasm while decarboxylating an arginine to agmatine. The arginine-agmatine antiporter (AdiC) exchanges an internal agmatine with an external arginine. Thus, together, ADC and AdiC reduces the proton concentration within the cell. Here, we present the X-ray crystal structure of the inducible StADC (AdiA) at 3.1 Å resolutions. The crystal asymmetric unit contains a decamer (MW ~800 kDa) constitute of five homodimers related by a non-crystallographic five-fold axis of symmetry. The structure represents the apo-form of the enzyme while the earlier reported structure of the *E. coli* enzyme corresponds to the holo-form. Binding of PLP converts two disordered loops close to the active site into ordered confirmations. These conformational transitions may be important for substrate entry and product release. A large number of acidic residues are found on the surface of StADC. As proposed earlier, low pH may neutralize surface charges in homodimers that are catalytically inactive and promote the formation of functionally active decamers. Comparison of StADC with other members of group III decarboxylases shows that these enzymes are likely to follow similar catalytic mechanisms.

Biography

G Deka joined the Department of Biological Sciences at the Indian Institute of Science as an Integrated PhD student in 2010 and earned her MS degree in 2012. Currently, she is pursuing her PhD under Prof. M.R.N. Murthy. She is attempting to understand the catalytic mechanism of a subset of PLP-dependent enzymes using mutagenesis, X- ray crystallography and enzyme kinetics studies. Apart from her PhD research work, she has gained experience in computational protein design and in the development of rapid diagnostic tools for early detection of malaria. Her curiosity to understand important biological problems motivate her to explore new areas in biology.

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Subashini Mathivanan et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Crystal structure of substrate and AMPPNP bound propionate kinase from *Salmonella typhimurium*: Substrate specificity and phosphate transfer mechanism

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Propionate kinase reversibly transfers phosphoryl group from propionyl phosphate to ADP in the final step of non-oxidative catabolism of L-threonine to propionate. There are contrasting views on the phosphoryl transfer mechanism of propionate kinase. Here we report X-ray crystal structures of propionate and nucleotide analog (AMPPNP) bound *Salmonella typhimurium* propionate kinase at 1.8-2.2 Å resolutions. Although the mode of the nucleotide binding is comparable to those of other members of ASKHA superfamily, propionate is bound at a distinct site, deeper in the hydrophobic pocket defining the active site. The role of Ala88, earlier proposed to be the residue determining substrate specificity, was examined by determining the crystal structures of propionate bound Ala88 mutants A88V and A88G. Kinetic analysis and structural data are consistent with a significant role of Ala88 in substrate specificity determination. In the structure of StTdcD A88V-AMPPNP-Propionate complex, AMPPNP was cleaved to AMP and PNP either due to an unreported catalytic activity of the enzyme or due to radiation damage. The released PNP probably reacted with propionate forming propionyl-pyrophosphate, supporting direct in-line transfer mechanism. Phosphoryl transfer reaction is likely to occur via an associative SN2-like transition state. The proximity of strictly conserved His175 and Arg236 to carboxyl of propionate and γ-phosphate of ATP suggests their involvement in catalysis. Moreover, ligand binding does not induce global domain movement as reported in some other members of ASKHA superfamily. However, the active site pocket defining residues Arg86, Asp143 and Pro116-Leu117-His118 segment are also likely to contribute to substrate specificity.

Biography

Subashini Mathivanan is a PhD candidate at the Indian Institute of Science, Bangalore, India. Her research expertise is on protein crystallography, emphasized on structural and functional characterization of *Salmonella typhimurium* propionate kinase and *Photorhabdus luminescens* oxalate decarboxylase.

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Turgut Ulutin et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Glia derived neurotrophic factor: Its regulation by vitamin D and possible relation to neurodegeneration

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Whether or not glia derived neurotophic factor (GDNF) has a role in disease mechanism of bipolar disorders has been a matter of debate. Due to their role in regulation of synaptic plasticity in addition to survival and growth of neurons neurotophins are important targets. Recent studies have pointed out that vitamin D can exert protective effects on nervous system by modulating the synthesis of neurotrophins, calcium channels and calcium binding proteins. The expression of neurotrophic factors are regulated via vitamin D in several cell types. Our previous study has showed that vitamin D receptor silencing showed similar effects with beta amyloid treatment and up regulated L type voltage sensitive calcium channels alpha1 C (LVSCC A1C) and nerve growth factor (NGF). These results might indicate the potential role of vitamin D- VDR pathway in neurodegeneration. The aim of this study was to investigate the alterations in the level of GDNF release by 1,25-dihydroxyvitamin D_3 treatment in primary cortical neurons. Cerebral cortex dissected from brains of Sprague Dawley rat embryos on the embryonic day 16 and cultured. GDNF levels released to the culture medium were determined by ELISA. Our results showed that vitamin D treatment induced GDNF release to the culture media. These results indicated that the GDNF expression might be regulated by vitamin D in cortical neurons and vitamin D supplementation might be used as a tool for regulating neurotrophic factors in neurodegenerative disorders.

Biography

Turgut Ulutin has completed his PhD from Marmara University, Faculty of Medicine Department of Biochemistry and Post-doctoral studies from Istanbul University, Faculty of Medicine. He is the Head of Department of Medical Biology, Cerrahpasa Faculty of Medicine, Istanbul University. He is also the Head of National Society of Medical Biology of Turkey. He has published more than 25 papers in reputed journals.

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E Wloka et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Effect of cuticular compounds on the elastase activity of the entomopathogenic fungus *Conidiobolus coronatus*

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Entomopathogenic fungi are important natural regulatory factors of insect populations. They invade insects through the cuticle by a combination of mechanic pressure and enzymatic degradation. Insecticidal fungi produce several cuticle degrading proteases, chitinases and lipases. Among proteases of soil fungus *Conidiobolus coronatus*, elastase seems to play a key role in the hydrolysis of cuticle. Although mechanisms of enzymatic degradation of cuticle are intensively studied, the reasons of insects' differential susceptibility to fungal infection remain obscure. Susceptibility or resistance of various insect species to fungal invasion may result from the species-specific composition of the cuticle. We have examined effects of supplementation of the *C. coronatus minimal* culture medium with compounds previously detected in insect cuticle, on the activity of *C. coronatus* elastase. As additives elastin, chitin, N-acetylglucosamine, 11 fatty alcohols, 16 fatty acids, tocpoherol acetate, butyl oleate, glycerol oleate, squalene and butyl stearate were used. It was found that cuticular compounds have various effects on the elastase activity: elastin, fatty acids C13:0 and C14:1 increased the elastase activity, whereas, fatty acid C26:0 and squalene decreased elastolytic activity. Obtained data suggested that cuticular compounds repressing activity of elastase might be responsible, at least in part, for the resistance to fungal infection.

Biography

E Wloka has completed her PhD from the Institute of Parasitology-PAS. She has published 20 conference reports, 12 original papers (9 in the JCR journals) and 4 other publications in the JCR journals which are currently in the press. In 2012 and 2013 she obtained the Prize of the Director of the Institute of Parasitology for Scientific Achievements. She has participated in 28 training sessions dedicated to various laboratory techniques. Since 2014, she has been active as a Local Coordinator of the Science Festival (event organized in Poland by scientists for people not related to science).

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Do Thi Thu Hang et al., Biochem Anal Biochem 2016, 5:3(Suppl)
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Whole exome sequencing identifies a heterozygous missense variant in the GABRB3 gene in a patient with Dravet syndrome

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Background: Dravet syndrome is a rare and severe type of epilepsy in infants. Approximately 70-80% of DS cases are caused by mutations in *SCN1A*, the gene encoding the alpha-1 subunit of the sodium channel, while some proradic cases would have variants in several other genes including but not limited to *PCDH19, GABRG2, SCN1B, SCN9A* and *CHD2.*

Purpose & Methods: We performed whole-exome sequencing in 6 SCN1A-negative patients with Dravet syndrome in order to identify other related genes for this disorder. The exome sequencing libraries of 14 individuals, including 4 parent–proband trios and 2 unrelated probands were prepared using the SureSelectXT Library Prep Kit and the obtained libraries were sequenced on an Illumina HiSeq 4000. The candidate variants were interpreted and classified according to the American College of Medical Genetics and Genomics (ACMG) standards and guidelines.

Results: In one affected individual, we detected a novel de novo heterozygous missense mutation p.Arg232Gln in *GABRB3*, the gene encoding the β3-subunit of the gamma-aminobutyric acid type A (GABAA) receptor, which mediates inhibitory signaling within the central nervous system. Furthermore, a heterogeneous *SCN1A* variant p.Arg393His that had been undetected by previous Sanger sequencing was revealed in another patient, whose father was mosaic to the variant.

Conclusion: Our result extended the genetic basis of Dravet syndrome and confirmed the utility of whole-exome sequencing in genetic diagnosis.

Biography

Do Thi Thu Hang has obtained her PhD in Pharmacy in Sungkyunkwan University, South Korea in 2009 and did Postdoctoral training in Molecular and Cellular Immunology at QIA, South Korea and then at Deakin University, Australia from 2009-2012. From 2005-2009, her research focused on molecular mechanisms underlying pathogenesis of Alzheimer's disease and H1N1 influenza virus infection. She has returned to Vietnam in 2012 and started her new research on genetics of severe epilepsy syndromes, especially of Dravet syndrome. She is interested in applying next-generation sequencing for research and clinical molecular diagnostics.

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Accepted Abstracts

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Electroactive PCL nanofibers coated by polypyrrole for nerve tissue engineering

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Electrically excitable tissues like nerve and muscle have shown promising results in regeneration on conductive scaffolds. In this study, a solution of 14% PCL electrospun was used on a rotating collector forming nanofibers with the average diameter of 430 nm. The fiber mats are dip coated by the conducting polymer PPy (polypyrrole) to form a substrate capable of stimulation of nerve cells. Ninety percent porosity of the conductive scaffold with more than double the Young's modulus compared to non-coated PCL met the required properties of nerve scaffolds. PC12 cells along with nerve growth factor, cultured on the aligned nanofibers and stimulated by a constant voltage of 0.01 V/cm for 1 h/day for three days. Formation of neurites in the direction of fibers suggests that the electroactive PCL-PPy scaffold can support the differentiation of PC12 cells into nerve cells. The flexible and stable fibrous scaffold with conductivities ranging up to 1.9 S/cm showed the potential applications of these membranes in neural tissue engineering.

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Generation of avian monoclonal antibody fragments for membrane protein crystallization

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Membrane proteins are challenging targets for crystallization and structure determination by X-ray crystallography. Antibody mediated crystallization has a major impact on the advancing structural and functional characterization of difficult membrane proteins 1, 2 and 3. More than 26 unique structures of membrane protein- antibody complexes have already been determined. An update of methods for generation of recombinant antibodies from hybridomas and their production in *E. coli* was recently published. The limited availability of suitable hybridoma cell lines due to low immunogenicity of therapeutically important human membrane proteins in mice has impeded the high-throughput application of this approach. Here, we show an efficient method to obtain high affinity binders against difficult targets by phage display exploiting the avian immune system. The recombinant chicken antibodies were generated against Na+/H+ transporter and used for its structural characterization. The strategy of avian immune phage display libraries provides fast access to versatile tools for structural and functional studies and in general paves the way to generate versatile tools for research, diagnostics and therapeutics targeting membrane proteins and is of special interest for antigens highly conserved in mammals.

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Disruption of falcipains processing by blocking hotspot spot residues of domains in malaria parasite

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Falcipains are among the critical enzymes required for parasite machinery in malaria. Our previous study suggested that they have unique pro and mature domains that interact via salt bridge and hydrophobic interactions, which are essential for their activation. Designing small molecules that interfere at the hotspot residues of domains would inhibit falcipains activation. Although multiple active site inhibitors exist for falcipains, specific inhibitors that halt processing without binding to active site remains unknown. Our study suggested that azapeptide compounds based on conformationally constrained disubstituted β- and γ-amino acids inhibit the activation of falcipains. Among these, C-02 and C-07 hinders the falcipains activity by binding to intact pro-FP2 rather than mature active FP2 during hemoglobin hydrolysis and fluorogenic substrate assay. While these compounds did not affect the secondary structure of protein during circular dichroism spectroscopy, surface Plasmon resonance result demonstrated over the range of inhibitor concentration indicated specific interaction with FP3 and equilibrium constant ~80nM. Moreover, confirmation was done by MD simulations for ~5×130 ns confirms that compound-inhibitor complex provides rigidity to the pro domain to remain intact even at low pH preventing activation of the enzyme. For further authentication inhibitory concentration (IC50), of compound were examined on 3D7 strain of *Plasmodium falciparum*, parasite shows distorted trophozoite morphology with IC50 ~250 nM. Further, we reported a conserved histidine residue (His205) in pro domain of FP3, essential for pH sensing during auto-processing. Collectively, we provide a framework for targeting hotspot residues that can regulate falcipains in zymogen condition and halts its activation.

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Association between single nucleotide polymorphism +874 A/T and its susceptibility to pediatric tuberculosis in Indonesia

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Tuberculosis (TB) is one of the leading causes of morbidity and mortality worldwide especially, in developing countries. TB is a complex multifactorial disease with genetic as one of the substantial factors for TB development. Our hypothesis is that single nucleotide polymorphism (SNP) +874 A/T affects low production of IFN-γ level that increased susceptibility of pediatric TB. The aim of this study was to investigate association between SNP +874 A/T and its susceptibility to pediatric TB in Indonesia. DNA samples were obtained from 50 patients with pulmonary TB, 1 patient with extra pulmonary TB and 51 healthy controls. SNP +874 A/T was identified using the amplification refractory mutational system polymerase chain reaction (ARMS-PCR) method. The result of this study showed the presence of AA, AT and TT genotype in TB patients were 31 (60.8%), 20 (39.2%) and 0 (0%); respectively (p=0.023). Significant decreased in production of IFN-γ level (p=0.042) was found in TB patients (10.49±6.26 pg/ml) which contrast to healthy controls (10.80±14.48 pg/ml). Low production of IFN-γ level was identified among AA genotype patients (10.44±8.24 pg/ml) compared to AT genotype patients (11.17±13.71 pg/ml), but not significantly proven. An allele was found to be a risk factor for development of TB disease (OR, 1.51; 95% CI=1.04-2.21, p=0.018). In conclusion, this study has provided evidence of the association between SNP +874 A/T and its susceptibility to pediatric TB. AA genotype and an allele were found significant among pediatric TB patients in Indonesia.

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In vivo anti-hyperlipidemic activity of *Tetracarpidium conophorum* (African walnut) oil

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Hyperlipidemia, a disorder of lipid metabolism characterized by elevated levels of lipids circulating in the blood, has now become a global concern. It is considered as one of the five leading cause of death in the world. Its prevalence is greatly influenced by adaptation to sedentary lifestyle and an increase in the consumption of a high fat diet. Hyperlipidemia is strongly linked to the development of cardiovascular events and metabolic syndrome diseases. Thus, regulating blood lipids levels is vital in the prevention and treatment of hyperlipidemia and its related diseases. A total of 35 rats were used in this study. The animals were randomly assigned into seven groups (five rats per group). Group I (control group) was fed with normal diet (ND) only, group II, V, VI and VII were fed with high cholesterol diet, which contain 1% cholesterol and 0.5% bile salt for five weeks (37 days) to establish hypercholesterolemia, while groups III and IV were fed with normal diet for five weeks and thereafter administered with 250 and 500 mg/kg body weight of *Tetracarpidium conophorum* oil (TCO) respectively for a period of 20 days. Group II were maintained on hyper cholesterol diet, while Group V and VI was administered 250 and 500 mg/kg body weight of TCO respectively for a period of 20 days, while group VII was given 80 mg/kg body weight of atorvastatin used as a reference drug. After six weeks of feeding with the respective diets, rats were deprived of food overnight. Blood sample was collected and biochemically analyzed for Total Cholesterol (TC), Triglyceride (TG), High Density Lipoprotein Cholesterol (HDL-C) and Low Density Lipoprotein (LDL-C), Malondialdehyde levels (MDA), Aspartate Transaminase (AST), Creatine Kinase (CK) and Lactate dehydrogenase (LDH) activities. The results showed that there was significant increase ($P<0.05$) in TC, LDL-C, CK, LDH and MDA levels with a reduction in HDL-C in rats induced with high cholesterol diet after 37 days when compared to the initial values at day 0. Oral administration of *Tetracarpidium conophorum* oil and atorvastatin drug for a period of 20 days resulted in significant lowering ($P<0.05$) of the levels of TC, LDL-C, CK, LDH and MDA levels with increase in HDL-C in rats induced with high cholesterol diet. However, there were also significant decrease ($P<0.05$) in TC, LDL-C, LDH, CK and MDA levels with increase in HDL-C in rats administered with 250 and 500 mg/kg body weight of *Tetracarpidium conophorum* oil alone for 20 days in rats fed with normal diet when compared to control. There was no statistically significant difference in AST level in both rats fed with normal and hyper cholesterol diets when compared to control throughout the period of the experiment. *Tetracarpidium conophorum* oil could effectively reduce or control the amount of serum cholesterol and LDL-C. It is apparent that the oil could contribute to new formulation with significant hypolipidemic effect and cardioprotective properties.

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Hereditary spastic paraplegias: Identification of a novel SPG57 variant affecting TFG oligomerization and description of HSP subtypes in Sudan

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Hereditary spastic paraplegias (HSP) are the second most common type of motor neuron disease recognized worldwide. HSP can be pure or complex according to the absence or presence of additional neurological and non-neurological manifestations. There are more than 67 known HSP genes with different patterns of inheritance. Autosomal dominant HSP forms are the most frequent in western populations while recessive HSP predominates in highly consanguineous communities. Our goals were to estimate the relative frequencies of known HSP genes in Sudanese families with the disease and perform genotype-phenotype correlation to extend the clinical spectrum associated with HSP genes. We have used next generation sequencing to screen 74 HSP-related genes in 23 consanguineous families from Sudan and candidate gene sequencing in two other families (total of 25 families). We established a genetic diagnosis in six families with autosomal recessive *HSP (SPG11* in three families and *TFG/SPG57*, *SACS*, and *ALS2* in one family each). An autosomal dominant HSP (ATL1/SPG3A) was also identified in one additional family. Six out of seven identified variants were novel. The *TFG/SPG57* variant (*p.(Arg22Trp)* in the PB1 domain) is the second SPG57 HSP variant to be identified worldwide, and we demonstrated its impact on TFG oligomerization *in vitro*. There were no patients with visual impairment as observed in a previously reported SPG57 family (p. (Arg106Cys) in coiled coil domain), suggesting unique contributions of the PB1 and coiled coil domains in TFG complex formation/function and a possible phenotype correlation to variant location. Some families manifested marked phenotypic variations implying the possibility of modifier factors complicated by high inbreeding. In conclusion, we identified the first Sudanese families carrying novel variants in 6 HSP genes. The difficulty to reach a genetic diagnosis in the majority of studied families suggests the possibility of new genes, unusual models of inheritance or noncoding variations underlying spinocerebellar degeneration.

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In vitro interaction of soluble and amyloid form of serum amyloid protein with amyloid P component to hepta 1-6 cells

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Hepta 1-6 cell binding study is important in relation to the activity of membrane proteins, because losing the activity of such systems will ultimately lead to malfunction or death of the cell. The interactions of Serum Amyloid A (SAA) and Serum Amyloid A protofibrils with Serum Amyloid P component [SAP ($CaCl_2$)] to hepta 1-6 cells of the mouse are dealt with in detail to study the binding of SAA protofibrils in various conditions. The induced fluorescence, circular dichroism, FACScan and MTT assay results have shown the SAA and SAA fibrils binding with SAP ($CaCl_2$) 0.12-1.2 nM and cell toxicity with the hepta 1-6 cells. Specifically, interaction of serum amyloid A fibrils with a cell surface binding site/receptor might alter the local environment to cause cellular dysfunction and to be more favorable for amyloid formation. Already RAGE (receptor for advanced glycation endproducts) a polyvalent receptor in the immunoglobulin super family has been implicated in binding with the isoform of SAA (SAA1.1) which has the highest fibirillogenic property. In the present study, SAA fibrils have more binding and cell cytotoxicity than SAA protein and has protective role with SAP ($CaCl_2$).

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Sialic acid profile and sialidase activity in HIV infected individuals

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Sialic Acids and sialidases have been implicated in many disease states particularly bacterial and viral infections which are common opportunist infections of HIV disease. A study was carried out to determine sialic acid profile and sialidase activity in HIV infected and apparently healthy individuals. Blood samples were collected from 200 subjects (150 HIV infected individuals and 50 apparently healthy individuals, divided into four groups: HIV ART naive, HIV stable (on ART but have been stable with no clinical episodes), HIV-OI (on ART with opportunistic infections), and apparently healthy). Complete blood count, erythrocyte surface sialic acid (ESSA), free serum sialic acid (FSSA) concentrations and sialidase activity were determined for all 200 subjects. Analysis of variance was used to compare the results of the different groups of HIV infected individuals as well as controls. Anemia and neutropenia were the most common hematological abnormalities observed in this study with highest prevalence of anemia found in the ART naive group. There was significant difference ($p \leq 0.05$) between groups in FSSA level. The highest levels of FSSA were observed in the HIV ART naive (0.65±0.5 mg/ml). The mean ESSA value for the study population was 0.54±0.35 mg/ml with no significant difference ($p \leq 0.05$) between groups. No significant difference ($p \leq 0.05$) was found between groups and also in gender and age. The findings in this study of higher mean sialidase activity and FSSA levels in the ART naive HIV group compared with other groups indicate that the virus and other opportunistic pathogens may be sialidase producers in vivo which cleave off sialic acids from erythrocytes surface, leading to high levels of FSSA, anemia and neutropenia seen in this group. The higher ESSA concentration found in the HIV stable group along with lowest FSSA concentration in the group suggests the presence of sialyltransferases.

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To study allelic variants of *PON1* gene in ischemic stroke patients with high LDL/HDL ratios

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Stroke continues to be the leading cause of morbidity and mortality worldwide. Oxidative stress is a characteristic of ischemic stroke. Elevated LDL/HDL ratio is an important factor for predicting arteriosclerosis. Paraoxonase 1(*PON1*) protects LDL from oxidative modifications and has a protective effect against arteriosclerosis. Two common polymorphisms, *Q192R* and *L55M*, in *PON1* gene can affect PON1 levels and function. The aim of this study was to evaluate *Q192R* and *L55M* polymorphisms in ischemic stroke patients with high LDL/HDL ratios and to investigate ox-LDL levels as a marker of oxidative stress. The study included 100 patients of ischemic stroke admitted in ICU of Base Hospital, Army College of Medical Sciences, Delhi and 100 controls. Patients were in the age group of 55-85 years. *PON1 Q192R* and *L55M* were determined by PCR-RFLP method, ox-LDL by ELISA kit method. *PON1 L55M* was associated with high LDL/HDL ratios in ischemic stroke patients. So, the L55M polymorphism can contribute in decreasing the antioxidant function and decreasing HDL particles. Plasma levels of ox-LDL were increased in stroke patients ($P<0.001$) compared to controls. In conclusion, it is important to explore the effects of *PON1 L55M* genetic polymorphisms and the inflammatory response associated with stroke. We hypothesized that elevated ox-LDL levels and lower *PON1* activity may contribute for the development of oxidative stress. The present study was carried out to emphasize the importance of these markers for early diagnosis and therapeutic interventions in ischemic stroke patients.

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Evaluation of nephrotoxicity induced by chemotherapy with salts platinum between Cockcroft-Gault method and MDRD method

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The platinum salts are one of the most chemotherapy drugs used in cancer (particularly in the lung, bladder, testis, ovary, cervix, endometrial, colon and rectum), however they have a potential renal toxicity requiring an evaluation of tolerance kidney patients before and after treatment cures. This study compares the different methods of assessing renal function used for patients receiving chemotherapy with cisplatin or carboplatin (between the measurement of plasma urea, and the calculation of creatinine clearance as well as changes in the methods of estimating creatinine clearance with the Cockcroft-Gault method and the MDRD method Modification of Diet in Renal Disease). The study was performed on 25 male patients aged 42-74 years admitted to the Oncology Department of the University Hospital Oran for treatment of various cancers, mainly lung cancer. After the spectrophotometric determination of plasma creatinine and urea, the creatinine clearance was calculated by the methods of Cockcroft-Gault and MDRD, the distribution of the urea after the platinum salt of cure is essentially inside the reference interval with an average of (0.38 and 0.36 g/l) after the first treatment and cure 2nd respectively, while the clearance of creatinine is below the range with an average of (69.28 and 72.25 ml/min) after the 1st and 2nd cure respectively, we see that for older patients over age 65 underestimation clearance calculated by Cockcroft-Gault, however it is overestimated by the same method in patients weighing more than 70 kg. Indeed, the evaluation of nephrotoxicity cannot be done on a simple determination of urea or plasma creatinine, but it requires the calculation of creatinine clearance by Cockcroft-Gault or MDRD methods depending on the age and patient weight.

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Effect of anti-diabetic drugs and adipokine levels

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T2DM is a consequence of complex interactions among multiple genetic variants and environmental risk factors. This complex disorder is also characterized by changes in various adipokine. In this study, our objective was to estimate the levels of adiponectin, leptin and resistin (ALR) in Type 2 Diabetes Mellitus (T2DM) patients, besides studying the effect of various drugs on their levels. Study participants included 400 diabetic and 300 normal patients from the Department of Endocrinology and Department of Biochemistry, Government Medical College Srinagar. Subjects were categorized under various groups i.e., (group one: metformin treated), (group two: Glimepiride treated) and cases were also categorized as obese with T2DM (group A), obese without T2DM (group B) and T2DM only (group C). The serum ALR levels were estimated by ELISA (Alere), and also biochemical parameters were evaluated before and after treatment. Adiponectin levels were found to be significantly lower in T2DM cases as compared to controls (12±5.5 vs. 22.5±7.9 μg/ml), while as leptin and resistin levels were found to be significantly higher than controls (14.3±7.4 vs. 7.36±3.73ng/ml) (13.4±1.56 vs. 7.236±2.129 pg/ml). Taking the effect of drugs into consideration, the effect on adiponectin and resistin levels were found to be highly significant in group two before and after treatment (11±5 vs. 19.2±4.5 μg/ml) (13.6±2.5 vs. 7.3±2.9 pg/ml), while as more effect was observed in leptin among group one (metformin) treated cases (27±15 ng/ml vs. 15±15 ng/ml). Further the adiponectin levels were found to be significantly lower in group B, while as leptin and resistin levels were found to be significantly higher among obese cases when compared to T2DM cases only. Glimepiride also shows more effect on FBG, HbA1c% levels while as metformin shows more effect on lipid profile levels. From the study, it can be concluded that ALR levels are affected by use of anti-diabetic drugs among which glimepiride shows more effect on adiponectin and resistin levels while leptin gets affected more by metformin. It can also be proposed that ALR levels are not affected by diabetes only, suggesting that their alterations in T2DM may be due to obesity as we observed more ALR changes in obese cases when compared to T2DM cases and so there might be an important link between adiposity and Insulin resistance.

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Targeting of increased copper level in diethylnitrosamine (DEN) induced hepatocellular carcinoma cells in rats by epigallocatechin-3-gallate (EGCG)

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To account for the observed anticancer properties of plant polyphenols, we have proposed a mechanism which involves the mobilization of endogenous copper ions by polyphenols leading to the generation of reactive oxygen species (ROS) that serve as proximal DNA cleaving agents. Over the last decade, we have proceeded to validate our hypothesis with considerable success. For example, polyphenol induced growth inhibition in breast cancer cell lines is inhibited by copper chelators and copper overload in lymphocytes leads to increased cellular DNA degradation by polyphenols. As a further confirmation of our hypothesis, we have induced hepatocellular carcinoma in rats by diethylnitrosamine (DEN). The induction of carcinoma was confirmed by visual examination of liver and various liver cancer markers. We show that in such carcinoma cells there is a progressive elevation in copper levels at various intervals after DEN administration. Concurrently with increasing copper levels epigallocatechin-3-gallate [(EGCG), a potent anticancer plant polyphenol found in green tea], mediated DNA breakage in malignant cells is also increased. This is further confirmation of the increased copper levels in such cells. The cell membrane permeable copper chelator neocuproine inhibited the EGCG mediated cellular DNA degradation whereas the membrane impermeable chelator bathocuproine was ineffective. Iron and zinc specific chelators desferrioxamine mesylate and histidine respectively were also ineffective in inhibiting EGCG mediated DNA breakage.

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