15th International Congress on

**American Pathology and Oncology Research**

&

International Conference on

**Microbial Genetics and Molecular Microbiology**

December 03-04, 2018 | Chicago, USA

# Scientific Tracks & Abstracts

# DAY 1

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# Elucidating the role of Hexokinase-2 in hepatocellular carcinoma and implications for cancer therapy

**Dannielle DeWaal**
University of Illinois-Chicago, USA

Hepatocarcinogenesis (HCC) induces profound glucose metabolism reprogramming by repressing endogenous glucokinase (GCK) and expressing the high-affinity hexokinase-2 (HK2). This quality differentiates HCC from normal hepatocytes that can be exploited to selectively target HCC. Hepatic deletion of HK2 inhibits DEN-induced hepatocarcinogenesis. Silencing of HK2 in human HCC cell lines increases cell death and inhibits tumorigenicity *in vitro* and *in vivo*, that could not be restored by GCK nor a mitochondrial binding deficient mutant. Metabolically, HK2 loss reduces glycolytic flux to pyruvate and lactate, but TCA flux is maintained. Cells were vulnerable to serine depletion, consistent with their increase in serine uptake/glycine secretion, suggesting an increase in one-carbon metabolism. Decreased glycolysis was, however, coupled to increased respiration, that could be diminished by treatment with metformin, which increased cell death and inhibited tumor growth. Interestingly, neither HK2 silencing nor metformin treatment alone inhibits mTORC1, whereas the combination inhibits mTORC1 signaling that is dependent on REDD1 and not AMPK. Lastly, HK2 silencing synergizes with the FDA-approved therapeutic, sorafenib, to inhibit tumor growth.

## Biography

Dannielle DeWaal completed her graduate studies at the University of Illinois-Chicago in the Department of Biochemistry and Molecular Genetics in the laboratory of Dr Nissim Hay. As a cancer biologist, she examined and elucidated the role of Hexokinase-2 in hepatocellular carcinoma and its relevance as a novel therapeutic target. She continues her studies at UIC and is currently a Postdoctoral Research Associate. She enjoys working on various projects, including metabolic analyses using a GC-MS, which she has been learning and teaching the lab about. She currently serves on the Editorial Board of International Journal of analytical and bioanalytical methods.

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# Characterization of PHA synthases of *Acinetobacter baumannii* isolate P39, *Bacillus cereus* isolate P83 and *Azomonas macrocytogenes* isolate P173 in a comparative approach

**Noha S Elsayed, Khaled M Aboshanab, Mahmoud A Yassien** and **Nadia H Hassouna**
Ain Shams University, Egypt

PHA synthase enzyme is the key limiting enzyme catalyzing polymerization of hydroxyacyl co-enzyme, a precursor derived from various metabolic pathways to produce polyhydroxyalkanoates (PHA) polymers. In the present study, characterization of this enzyme of three bacterial isolates namely *Acinetobacter baumannii* isolate P39, *Bacillus cereus* isolate P83 and *Azomonas macrocytogenes* isolate P173 was carried out using a 5,5-dithio-bis-2-nitrobenzoic acid assay for activity measurement. Various heterologous primers were designed for PCR amplification of the genes coded for PHA synthases of each isolate followed by analysis of the tertiary structure of the respective gene products using the Modular Approach to Structural class prediction (MODAS) software, Tied Mixture Hidden Markov Model (TMHMM) server and Swiss model software. The obtained results showed that the highest activity was for PHA synthase of *A. baumnnii* isolate P39 (600 U) and the highest specific activity was for PHA synthase of *B. cereus* isolate P83 (1500U/mg). Moreover, the results of the gel electrophoresis, their nucleotide sequencing, and conserved domain analysis showed that PHA synthase class III was found in *A. baumannii* isolate P39 and *A. macrocytogenes* isolate P173 while class IV was found in B. cereus isolate P83. The MODAS software deduced that the structural class of the tested PHA synthases was multi-domain protein (α/β) while the TMHMM server predicted the absence of transmembrane helix in the PHA synthase sequences. Swiss model software showed conserved cysteine residue and lipase box which both characterize α/β hydrolase superfamily. Taken together, the results of the enzymological and molecular characterization of PHA synthase enzymes of the tested isolates supported that the PHA formation was attained by the micelle model.

## Biography

Noha Elgendy, PhD, is a lecturer of Microbiology in the faculty of pharmacy at Ain Shams University where she has been a member since 2009. Her research interests are in the area of biopolymers particularly the biodegradable Poly (3-hydroxybutyrate) (PHB). Her journey with PHB polymer started with her master's thesis in 2010 which focused on screening for PHB producers in agricultural fields. The journey continued in her PhD at 2014 by studying the biochemical and genetic pathways of PHB production in the bacterial isolates *Acinetobacter baumannii* isolate P39, *Bacillus cereus* isolate P83, and *Azomonas macrocytogenes* isolate P173 and their large-scale production of PHB on 14L fermenter. From her research, she published five international publications and six nucleotide/amino acids sequences in the NCBI GenBank database where one of them is the first of its type entitled "PHA synthase of *Azomonas macrocytogenes* isolate P173". She has participated at different international conferences in the past four years including ASM Boston, 2016. Besides her research skills, she has been teaching the practical sessions of Microbiology to undergraduates in the faculty of pharmacy in Egypt and supervising the students' projects there. She is currently living in Chicago with her husband and daughter.

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# The new antagonistic fungus: *Aspergillus piperis*

**Samah Abd El-Kader El-Debaiky**
Tanta University, Egypt

This lecture will introduce a report about my study entitled "Antagonistic studies and hyphal interactions of the new antagonist *Aspergillus piperis* against some phytopathogenic fungi *in vitro* in comparison with *Trichoderma harzianum*". This study represents, for the first time, the new antagonistic fungus; *Aspergillus piperis*. The *in vitro* studies on the activity and antagonistic mechanisms used by *A. piperis* in attacking some isolated phytopathogenic fungi (*Alternaria alternata, Alternaria solani, Botrytis cinerea, Sclerotium cepivorum* and *Sclerotinia sclerotiorum*) was examined and the results were highly promising. Also, the antagonistic activities of *A. piperis* was compared with the common antagonist; *Trichoderma harzianum* against the same phytopathogens. The obtained results revealed that, *A. piperis* was more effective than *T. harzianum* against all the tested phytopathogens. Finally, this study was considered a base point for futured studies on this new antagonistic fungus, *A. piperis*, in the field of biological control.

## Biography

Samah Abd El-Kader El-Debaiky works as Lecturer of Microbiology (Mycology) in Botany Department, Faculty of Science, Tanta University since 24-11-2013. She has participated in 5 local conferences interested with biological science and 9 workshops in field of mycology. She also, has been serving as an editorial board member of two international journals.

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# GRP52 is a new sensitive markers for detecting metastatic prostatic carcinoma

**Shaolei Lu**
Warren Alpert Medical School of Brown University, USA

Metastatic prostate cancer is frequently presented as cancer of unknown origin. To confirm the prostatic origin, prostate-specific antigen (PSA), prostein, HoxB13, and NKX3.1 are frequently used. However, these markers are regulated by androgen receptor (AR) and their expression could be suppressed by hormonal therapy or altered by chemoradiation. Based on data mining of publicly available protein expression database and AR response gene database, we identified a new marker, GRP52, and compared it to the above markers in a series of metastatic prostate cancer. We collected 46 metastatic prostate tumors, including 16 bone metastases (10 treated by hormonal ablation or chemoradiation and 6 untreated) and 30 non-bone metastases (27 treated vs 3 untreated). Immunostains of all the markers were performed and positive expression is defined as more than 5% of tumor cells with unequivocal staining in the appropriate pattern. In 27 cases of treated non-bone metastasis, the positivity rates for GPR52, NKX3.1, HoxB13, and Prostein are 100%, 87.5%, 83%, and 67%, respectively. Out of 3 cases of untreated non-bone metastasis, GRP52 missed 1 and prostein missed 2, while NKX3.1 and HoxB13 detected all of them. For 9 cases that are negative for prostein, GPR52, NKX3.1, and HoxB13 could be detected in 4, 8,7, and 6 cases respectively. All 5 markers were detected in all 16 bone metastases, except that HoxB13 could not be detected in 2 of 10 cases of treated bone metastasis. Combination of multiple markers can increase the detection sensitivity for treated metastatic prostate cancer. Decalcification has less impact on the detection of major prostatic cancer marker.

## Biography

Shaolei Lu has completed his PhD at the University of Massachusetts Amherst and his MD from Shanghai Medical College of Fudan University. He is currently a surgical pathologist at Brown University. He has published more than 35 peer-reviewed papers in reputed journals.

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# ROS and miRNA signaling in ovarian cancer angiogenesis, tumor growth and treatment resistance

**Ling-Zhi Liu**
Uinversity of Iowa, USA

Ovarian cancer represents the fifth leading cause of cancer-related death among women. However, the mechanisms of ovarian cancer development and the treatment resistance remain to be elucidated. We found that ovarian cancer cells generate higher levels of reactive oxygen species (ROS) through NOX4 overexpression compared to immortalized normal ovarian epithelial cells, which are involved in inducing tumor growth and angiogenesis. More interestingly, ROS inhibit miR-199a and miR-125b expression through increasing the promoter methylation of the miR-199a and miR-125b genes by DNA methyltransferase 1, thus increasing their targets HER2 or/and HER3 expression in ovarian cancer cells to regulate tumor angiogenesis. Cisplatin is commonly used in ovarian cancer treatment by inducing apoptosis in cancer cells as a result of lethal DNA damage. The cytoprotective functions of autophagy in cancer cells have been suggested as a potential mechanism for chemoresistance. We also demonstrated miR-152 as a new autophagy-regulating miRNA that plays a role in cisplatin resistance. MiR-152 expression was dramatically downregulated in the cisplatin-resistant cell lines and in ovarian cancer tissues associated with cisplatin resistance. Overexpression of miR-152 sensitized cisplatin-resistant ovarian cancer cells by reducing cisplatin-induced autophagy, enhancing cisplatin-induced apoptosis and inhibition of tumor growth through its direct target ATG14. Collectively, these data provide insights into novel mechanisms for ROS and miRNAs signaling in ovarian cancer angiogenesis, tumor growth, and treatment resistance.

## Biography

Ling-Zhi Liu has completed her MD, PhD in 2000 from China Medical University. She is an Associate Professor in the Department of Pathology, University of Iowa. She has published more than 50 papers in high profiled journals and has been serving as an Editorial Board Member and Ad-hoc reviewers of several journals.

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# Biological control of early blight of tomato plant by *Aspergillus piperis*

**Samah Abd El-Kader El-Debaiky**
Tanta University, Egypt

In this lecture I will introduce a report about my study entitled " Effect of the new antagonist *Aspergillus piperis* on germination and growth of tomato plant and early blight incidence caused by *Alternaria solani*". The present work is considered the first record of studying the ability of the new antagonist, *Aspergillus piperis* in decreasing the disease incidence of early blight of tomato plant caused by *Alternaria solani*. The pathogen *A. solani* was isolated from naturally diseased tomato fruits and identified genetically by sequencing of rRNA gene using ITS1 and ITS4 primers. For the field experiment, the toxicity of spore suspension of *A. piperis* on germination of tomato seeds was performed using soaking and irrigation methods where the germination percentage and vigor index were calculated. The results indicated that the irrigation method recorded better results than soaking where the germination percentage was 81.81 % and vigor index was 794.37 related to that of control which recorded 90.9% and 715.83 respectively. The values of vigor index indicated that, the spore suspension of *A. piperis* had induced the plant growth. In the meantime, the spore suspension of *A. piperis* was applied on tomato leaflets by several methods to reduce the incidence of early blight disease. The application of *A. piperis* spore suspension directly on the leaflets exhibited the best result where the percentage of infection was 10.25 % to the control (25 %) after 4 days.

## Biography

Samah Abd El-Kader El-Debaiky works as an Assistant Professor of Microbiology (Mycology) in Botany Department, Faculty of Science, Tanta University since 24-11-2013. She has participated in 5 local conferences interested with biological science and 9 workshops in field of mycology. She also, has been serving as an editorial board member of two international journals.

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## Microsatellite instability pathway and molecular genetics of colorectal cancer

**Juel Chowhdury, Khatja Batool, Sidra Mubasher, Humera Batool** and **Hani Pharaon**
University of Illinois, USA

Colorectal cancer (CRC) is a very common and lethal disease that is caused by the interaction of genetic and environmental factors. It is a stepwise process in which the genetic mutations get accumulated over time. Molecular basis of colorectal cancer has helped us to understand the key steps which lead to the advancement of tumorigenesis. There are many ways which can initiate the CRC development. CRCs are diverse genetically. Genomic instability is a crucial feature in tumor development. There are at least 3 distinct pathways in colorectal cancer pathogenesis: the chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) pathways. Out of which genetical event which contributes significantly, is the microsatellite stable pathway. Microsatellite instability (MSI) is caused by the loss of DNA mismatch repair activity. Microsatellites are small repeating stretches of DNA scattered throughout the entire genome. microsatellites are prone to high mutation rate due to their repeated structures. MSI can be detected by direct or indirect ways. The most common method to detect MSI is direct PCR amplification of specific microsatellite repeats.MSI can also be detected in an indirect way by MMR protein analysis and Immunohistochemical (IHC) expression staining. MSI is detected in many colorectal cancers; Most importantly Lynch syndrome and the other sporadic form. MSI hypermethylation of the promoter of the MLH1 gene. The sporadic form of the CRCs arises over a process that involves the CpG island methylator phenotype (CIMP). Human genomes have promoter region which contains clusters of cytosine-guanosine residues called CpG islands. DNA methyltransferases can methylate the cytosine residues. Methylation is a permanently silencing of genes. Silencing of key regulatory genes makes cells more susceptible to escape the apoptotic and regulatory pathways and which eventually progresses towards the tumorigenesis. MSI early detection can play a pivotal role in the chemotherapeutic and overall outcome of the CRC. For these reasons, microsatellite instability analysis is becoming more and more important in colorectal cancer patients.

### Biography

Juel Chowdhury earned his Bachelor of Medicine and Bachelor of Surgery (MBBS) at Gulf medical university and perused his research career at the University of Illinois in Chicago with Dr. James A Radosevich. His works have led him to exchange scientific ideas with Nobel laureate Dr. Fred Murad and many well-known scientists such as Dr. Robert Winn Director of UI health. He taught at the National College of Health. He has consulted on cancer genetics and bioinformatics solutions for the Winn Lab at the University of Illinois in Chicago, Cancer Center. His innovative iGenX lab is a genetical research lab based on data-mining and data analysis of the gene-chip and RNA Seq experiments. He authored many books and part of the Editorial and Reviewer Board for many international journals like Journal of Integrative Oncology, Allied Journal of Medical Research. He is also part of many professional societies like ASCO and ISOBM. Dr. Chowdhury is also proficient in many aesthetics medicine procedures like Botulinum Toxin and Dermal Fillers and hair transplant procedures.

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