Jan 8th, 12:00 AM

11. Genetics

Northeastern State University

Abstracts from the 2016 Oklahoma Research Day

Held at Northeastern State University

05. Mathematics and Science

11. Genetics

05.11.01 The MAPK pathway gene expression level changes in response to quick increase of glucocorticoids in external cellular environment

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Major depressive disorder (MDD) is a highly prevalent psychiatric disorder which is becoming a leading cause of disease burden worldwide. Past studies confirmed that hypothalamic-pituitary-adrenal (HPA)-axis hormones involved in MDD development. This study used corticosterone treated PC12 cells, a widely used in vitro neuronal model, to explore the potential target genes of MAPK signal transduction pathways in response to corticosterone stimulation and, therefore, to study the potential mechanisms of HPA-axis involved MDD development. The results showed that both live cell numbers and cellular neurite outgrowth were remarkably reduced in response to corticosterone treatments. qPCR results demonstrated that the expression levels of four target genes (MKP-1, ERK, P38, and PKC) in MAPK pathways were significantly increased after corticosterone stimulation. In conclusion, glucocorticoids stimulation can affect neuronal cell viability and neurite outgrowth due to the over expression of a group of genes involved in MAPK pathways. Among them, the over expression of MKP-1 was response to corticosterone induced neuronal cell toxicity while P38 was involved in cell death. MKP-1 can inhibit the function of ERK for neurite outgrowth. However, as the response to MKP-1 inhibition function, PKC expression was increased to maintain the level and function of ERK. The results indicate that HPA-axis abnormality may induce the gene expression level change and impact the normal neuronal function.

05.11.02 Sequencing of Plasmids Carrying Genes for Ofloxacin Resistance

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Antibiotic resistance in bacteria presents great challenges in the healthcare field. Understanding environmental sources of resistance genes and the mechanisms behind their spread is therefore important. We are interested in resistance to the antibiotic ofloxacin, which interferes with DNA gyrase function during DNA replication. Several ofloxacin resistance mechanisms are known, including efflux pumps that expel the antibiotic and mutations in a DNA gyrase subunit gene that render it insensitive to ofloxacin. We are interested in resistance due to a plasmid-carried gene, qnrS. This gene encodes a protein that causes destabilization of the gyrase–DNA–quinolone cleavage complex and prevents DNA damage. Ofloxacin-resistant aeromonads were collected from sediments downstream of a wastewater treatment plant between 2007 and 2010. Strains containing plasmids bearing qnrS genes were identified. We have sequenced plasmids from two of these strains using primer walking. Plasmid pT2Sofl-9 is 7973 np long and plasmid pT2Sofl-122 is 7621 np long. The two plasmids differ at only two positions: a short region upstream of qnrS and a one nucleotide indel. In addition to qnrS, both contain genes for plasmid replication and mobilization. We compare our plasmids to other qnrS-bearing plasmids obtained at different locations and dates. These data show global dissemination of qnrS-bearing plasmids over many years.

05.11.03 Cancer genes in Drosophila melanogaster can be expressed in colon tissue and produce different levels of malignancy.

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Bioluminescence is light produced by chemical reactions inside of organisms. Using the expression of the luciferase gene as a bioluminescent reporter, tumor growth in colon tissue of Drosophila melanogaster can be quantified. The amount of light produced directly correlates with the mass of tissue present, and therefore the growth or overgrowth of tissue. Our purpose is to develop models of colon cancer in Drosophila that can be manipulated for study. A screen of cancer genes was used to identify candidates that show excessive proliferation when expressed in colon tissue. A select number of cancer genes affecting the PI3 Kinase, Receptor Tyrosine Kinase, Notch, and a few other signaling pathways produced a high level of malignancy. Genes that affect PI3 Kinase and Receptor Tyrosine Kinase pathways produced the highest malignancy levels while genes affecting cell cycle pathways had little to no measured effect. The oncogenes in this experiment are important for continued study because the signaling pathways they affect are conserved in humans. By developing these models, we can develop a better understanding of how outside stimuli, such as change in diet or treatment with therapeutic drugs, affect oncogenesis in these pathways in colon tissue. This knowledge of these conserved pathways can be applied to human cancer.

05.11.04 Investigation of Possible PilR-Regulated Promoters in Myxococcus xanthus

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Myxococcus xanthus is a predatory bacterium that goes through multicellular development and spore formation. Significantly, M. xanthus utilizes Type IV pili motility to control important developmental processes. Many of these processes are regulated by two-component signaling systems (TCS). In M. xanthus, Type IV pili motility is regulated by the PilSR TCS. In the PilSR TCS, PilR is a response regulator that binds within the promotor region of pilA and upregulates the production of PilA. Reports have shown that PilR from other organisms may regulate additional genes. Therefore, we hypothesize that PilR may also recognizes other promoter regions with a similar sequence upstream of their respective genes to aid in motility. Previous research in the Kirby Lab identified a putative PilR consensus sequence in the promoter region of pilA. From this sequence upstream of pilA, it was compared to other sequences within the M. xanthus genome via Patter Locator. The promoters of interest were isolated and ligated upstream of lacZ for β-galactosidase activity assays. The lacZ plasmid was transformed into both WT (DZ2) strains and PilR lacking (ΔpilR) strains. The β-galactosidase activity assay showed a significant level of activity in promoters of mxan_4844 and mxan_7415. Mxan_4844 appears to be negatively transcribed in the presence of PilR while mxan_7415 appears to be positively regulated by PilR. Our results suggest that PilR may regulate other genes to aid in motility

05.11.05 Novel Functional Mutations in GCKR Affect Triglyceride Concentrations in Diabetes

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Dyslipidemia is a well-known risk factor for cardiovascular disease and type 2 diabetes (T2D). Despite high heritability (50-80%) of lipid traits, genome-wide association studies have only been able to account for a fraction of this heritability (<10%) in genes for lipid metabolism. Here, we performed targeted sequencing of 14 candidate genes (~215 kb) for 940 individuals with diabetic dyslipidemia [572 high serum triglycerides (TG) cases (>150mg/dl), and 368 low TG (<100mg/dl) controls] from the Asian Indians Diabetic Heart Study. Of the 2361 high-quality variants analyzed, 953 variants (40%) were unique to high TG cases, and 321 variants (13.6%) were unique to controls. Thirteen functionally damaging and deleterious rare mutations were identified within the glucokinase regulatory protein (GCKR) gene. The GCKR inhibits glucokinase (encoded by GCK) by forming a complex, which plays a role in the control of blood glucose homeostasis. The lead variant with a missense mutation of Serine/Asparagine was restricted to few cases and more than 60% of the carriers were diabetic and 90% of carriers had high TG (ranging 182-560 mg/dl). However, this variant was absent in large (n=48,689) multiethnic exome consortium data. We are currently testing phenotypic effects of this variant to evaluate in vivo metabolic consequences in a transgenic zebrafish (Danio rerio). Taken together, our findings have the potential to find novel pathway for diabetes linked with hypertriglyceridemia

05.11.06 Assessing the Utility of Microsatellite Markers in Identifying Geomys Species in Central Oklahoma and the Oklahoma Panhandle

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The goal of this project is to utilize genetic markers to address the distribution of members of the genus Geomys (pocket gophers) in Oklahoma. Specifically, what are the distribution boundaries of G. bursarius (plains pocket gopher) and G. breviceps (Baird's pocket gopher) in Central Oklahoma and does G. jugossicularis occur in the Oklahoma panhandle? A boundary between G. bursarius and G. breviceps in central Oklahoma was proposed based on cranial measurements. Additionally, a contact zone between the 2 species was identified in Norman, Oklahoma. A third species has been suggested, G. jugossicularis, to occur in the Oklahoma panhandle. Genetic data will be used to reassess the proposed boundary line and the known contact zone, as well as to confirm the identity of samples collected in the panhandle. We used 9 microsatellite markers to analyze specimens from central Oklahoma and the panhandle to identify unique genetic clusters. Data obtained from specimens will be compared to samples collected from within the well-defined ranges of the 2 species (western Oklahoma– G. bursarius; southeastern Oklahoma –G. breviceps) to ensure correct identification and to account for the possibility of hybridization. Preliminary data has identified 3 distinct clusters of pocket gophers in Oklahoma, 2 in central Oklahoma and a 3rd in the panhandle. Admixture between the 2 clusters in central Oklahoma suggests the possibility of hybridization between G. bursarius and G. brevic