

OSU Center for Health Sciences - FY 2012 Research Abstracts

BIOMEDICAL SCIENCES

Allosteric Modulation of AMPA Receptors

The ionotropic glutamate receptors that mediate fast excitatory synaptic transmission are critical for the normal development and function of the nervous system and for the processes underlying learning and memory. These receptors have also been implicated in the etiology of neurological disorders, including Alzheimer's, Huntington's and Parkinson's diseases, ALS, epilepsy, and brain damage following stroke. Effective new therapies for treatment of the disorders may result from development of drugs that bind to allosteric sites on the AMPA subtype of glutamate receptor.

Sponsor: Intramural

PI/PD: Doris K. Patneau

AMPA Receptor Expression and Selective Neuronal Death

This project examines why certain types of neurons, including motor neurons and cerebellar Purkinje cells, are particularly vulnerable to excitotoxicity mediated by AMPA receptors. Experiments will determine whether these cells possess AMPA receptors with unique functional properties and/or molecular compositions that make them selectively vulnerable.

Sponsor: National Institutes of Health

PI/PDs: Doris K. Patneau

University of Chicago: James Brorson

Effects of Stargazin on AMPA Receptor Channel Function

Stargazin is a transmembrane protein that is known to act as a molecular chaperone in trafficking of the AMPA subtype of glutamate receptor to the cell surface. We recently discovered that stargazin and other members of this class of proteins, known as TARPs, also affect AMPA receptor channel function and is as an auxiliary subunit of the receptor. Studies focus on identification of the specific effects of TARPs on gating and desensitization of the AMPA channel, regions of interaction between stargazin and the AMPA receptor, and the underlying mechanism for TARP modulation.

Sponsor: National Institutes of Health

PI/PDs: Doris K. Patneau, Dorothy Turetsky

Alterations in Glutamate Metabolism in Sensory Neurons during Chronic Inflammation

In chronic inflammation, elevated release of glutamate from sensory nerves augments pain signals sent to the brain. This is due to an increase in glutaminase, the enzyme for glutamate synthesis in sensory neurons. Two mechanisms are being explored for increased production of glutaminase: nerve growth factor from the inflamed field, and stabilization of glutaminase mRNA.

Sponsor: National Institutes of Health

PI/PD: Kenneth E. Miller

Propriospinal Pathways Involved in Sensory-Motor Integration

The purpose of this study is to examine how neurons of propriospinal pathway(s) originating in the upper cervical spinal cord process information to modulate sensory motor integration in the

spinal cord. Stimulation of upper cervical neurons modulates the activity of neurons at lower segments and visceral, motor, pulmonary, and cardiac function. Our current attention is toward determining how cervical propriospinal neurons process information from brainstem nuclei.

Sponsor: Intramural Funding

PI/PD: Kenneth E. Miller

Spinal Cord Injury--Astrocytosis and Neural Plasticity

After spinal injury, astrocytes undergo reactive astrocytosis, producing a glial scar that inhibits neural regeneration. Little is known concerning alterations of metabolism or altered phenotype in reactive astrocytes. We are evaluating reactive astrocytosis following chronic injury with and without methylprednisolone, the major treatment for spinal injury. Our long-term goal is to reduce or eliminate the harmful parts of glial scarring in order to promote nerve regrowth or recovery of function in injured patients.

Sponsor: Intramural Funding

PI/PD: Kenneth E. Miller

Intermediate Filaments in Mitosis

The role of intermediate filaments in mitosis is currently being investigated. Immunoelectron-microscopy, immunohistochemistry, immunofluorescence, mammalian cell culture, and high voltage electron microscopy are used to study cells as they progress through mitosis. The interaction of the intermediate filament system with other cytoskeletal components (microtubules and microfilaments) is also being explored. The status of the cytoskeleton in transformed or cancerous cells is a topic of interest with emphasis on the transfer of information between the cell membrane and the nuclear membrane. The function of cyclic AMP in this mechanism is being studied.

Sponsor: Intramural Funding

PI/PD: William D. Meek

Investigating the Ultrastructure of the Radial Spoke in *Chlamydomonas reinhardtii*

The radial spoke is a component of the motile or 9+2 cilia and flagella, and plays an essential role in the control of dynein arm activity. A current project is investigating the ultrastructure of the radial spoke in *Chlamydomonas reinhardtii*, involving transmission electron microscopy of several mutants with swimming and ciliary beat abnormalities. This research is collaboration with the Department of Biology, Marquette University.

Sponsor: Intramural Funding

PI/PDs: Dr. Bill Meek

Marquette University: Dr. Pinfen Yang

***Chlamydomonas reinhardtii* as a Model to Study Flagellar/Ciliary Length**

The ultrastructure of flagellar/ciliary length is being studied utilizing *Chlamydomonas reinhardtii* with special attention given to the observation of intraflagellar transport (IFT) particles that move along the length of the flagella. The location and length of these IFT particles is being viewed in various mutants.

Sponsor: Intramural Funding

PI/PDs: Dr. Bill Meek, Dr. Nedra Wilson

Analgesia Research Laboratory (ARL)

The overall mission of the ARL is to understand the detailed molecular mechanism that leads from the administration of an opioid analgesic like morphine to the end result of analgesia. Currently, studies are centered on the cloning of opioid receptors from different vertebrate species in order to investigate the molecular evolution of opioid receptor proteins. Using comparative bioinformatics, opioid receptor datasets are being investigated with respect to particular receptor domains that confer opioid-type selectivity. The overall goal is to better understand how opioid analgesics produce their pain-killing actions with the hope of designing better and safer opioid drugs.

Sponsor: NIH-NIDA

PI/PD: Craig W. Stevens

Sex Differences and the Kidney

It is well established that premenopausal women are protected from renal disease compared to age-matched men whereas postmenopausal women lose this renoprotection. Understanding sex differences related to the pathophysiology of the kidney lies in the molecular mechanisms related to estrogen- and androgen-mediated signaling. Studies are underway to examine transcriptome profiling via serial analysis of gene expression in kidneys from males and females under various physiological and pathological conditions. Identifying these sex differences will lead to newer, more effective therapies for kidney disease.

Sponsor: Intramural Funding

PI/PDs: Dr. Alexander J. Rouch

University of Paris: Dr. Alain Doucet

Dietary Protein and the Kidney

Consuming high or low protein diets greatly affects the physiology of the kidney. High protein consumption enlarges the kidney and increases the renal workload. Physicians prescribe low protein diets for patients with renal disease because this tends to slow down the progression of the disease. We study the physiological and molecular mechanisms responsible for the many effects of high and low protein diets on the kidney. Results allow us to inform the public of consequences related to dietary protein.

Sponsor: Intramural Funding

PI/PD: Dr. Alexander J. Rouch

Attenuation of Astroglial Chemokine Expression by β -funaltrexamine: Implications for NeuroAIDS Therapy

Increasing evidence suggests that neuronal damage associated with neuroAIDS results in part from inflammation. Astrocyte-derived chemokines, including CCL2 and CXCL10, have been implicated as inflammatory molecules involved in neuroAIDS. We recently characterized β -funaltrexamine (β -FNA) inhibition of astroglial chemokine expression. The long-term goal is to identify the molecular mechanism responsible for the anti-inflammatory actions of β -FNA.

Sponsor: National Institutes of Health; Intramural Funding

PI/PD: Randall L. Davis

Characterization of an In Vitro Model of Parkinson's Disease-associated Neuroinflammation

Parkinson's disease (PD) is a neurological disorder characterized by the progressive loss of dopaminergic neurons. Loss of dopaminergic neurons in PD is associated with activation of neighboring astroglia (i.e., induction of chemokine and iNOS production), which may contribute

to neuropathology. While there are numerous in vitro models of neuroinflammation, few are specifically designed to assess PD-associated neuroinflammation. Therefore, we are interested in developing an in vitro model of neuroinflammation that more closely mimics the PD condition. This model can then be utilized to identify and characterize potential, therapeutic anti-inflammatory agents.

Sponsor: Intramural Funding

PI/PD: Randall L. Davis

Heavy Metals, Neuroinflammation and Social Withdrawal

In addition to the well-characterized neurotoxic effects of metals, sub-lethal exposure to metals also disrupts immunocompetence suggesting that altered neuroimmune function may provide a link between metals exposure and neuropathogenesis. Unfortunately, relatively little is known about the effects of metals exposure on neuroimmune function and how such effects may contribute to the development of behavioral dysfunction, such as occurs with mood disorders, autism, and following traumatic brain injury. Ongoing studies are expected to fill basic gaps in our knowledge base by identifying the effects of heavy metals on neuroimmune signaling and social withdrawal.

Sponsor: Intramural Funding

PI/PD: Randall L. Davis

Molecular Interactions with HIV proteins with the Dopamine Transporter

These projects have been investigating the in vitro effects of gp120 and Tat (HIV proteins associated with neurotoxicity) on the functioning and activity of the dopaminergic system in tissue and cell culture model systems. The primary goal of this program is to elucidate the interaction between gp120/Tat, estrogen, and cocaine in female rats. Ultimately, the goal of this research is to provide insight into gender-related differences in AIDS-related central nervous system disorders leading to potential gender-specific treatment strategies for HIV and cocaine addiction.

Sponsor: National Institutes of Health-NIDA and Intramural funds

PI/PD: David R. Wallace

Effects of Trace Environmental Pollutants on CNS Activity

The early work in this field focused primarily on the effects of the following heavy metals; mercury, methylmercury, manganese, lead, arsenic, cadmium, and aluminum. These studies examine the effects of low-level heavy metal exposure on the dopaminergic function in cell culture and whole animal. The indices/biomarkers used to measure the activity/function of the dopaminergic system, include dopamine transporter expression, trafficking, and function as well as dopamine release and uptake and the activity/function of the D1-like and D2-like dopamine receptors. Low-level exposure to heavy metals may not cause overt CNS effects until much later. These studies have implications in forensic analysis and determining the potential cause of CNS damage.

Sponsor: Intramural Funding

PI/PD: David R. Wallace

Isolation and Characterization of Novel CNS-Acting Compounds from Natural Sources

This program investigates the use of naturally occurring compounds as centrally acting agents. One series of studies has been examining the effects of Native American plants indigenous to Oklahoma and their potential analgesic effects. A second series is investigating the estrogenic

effects of flavonoids found in soy and flaxseed.

Sponsor: Intramural Funding

PI/PD: David R. Wallace

Development of a New Animal Model to Study Autism Spectrum Disorder: Role of the Dopaminergic System.

These studies utilize the prairie vole as a novel animal model for investigating the underlying causes of ASD. By modifying the social activity/interaction of the vole one may postulate that these changes resemble the societal dysfunction normally observed in patients suffering from ASD. Current work is also focusing on alterations in dopaminergic function following exposure to environmental toxins, such as heavy metals. We have observed significant social dysfunction in male voles following exposure to mercury. Neurochemical studies in rats have demonstrated that the striatum is a dopamine-rich brain region which is robustly affected following exposure to mercury. Additional work is being performed to correlate the outcomes observed in rat and vole studies and to further examine the neurochemical alterations following mercury exposure.

Sponsor: Intramural Funding

PI/PDs: Tom Curtis, David R. Wallace

Mid-Brain Modulation of Social Attachment

These studies use behavioral, pharmacological, neuroanatomical, and immunocytochemical methods to examine the neural processes that underlie the formation and maintenance of monogamous pair bonds.

Sponsor: National Institutes of Health-NICHD

PI/PD: J. Thomas Curtis

Central Pathways and Sex Differences in Body Fluid Regulation

These studies use physiological, behavioral, neuroanatomical, and immunocytochemical methods to examine central pathways and neurotransmitter systems involved in the control of body fluid volume and osmolality, focusing on the role of ovarian hormones in sex differences in the central control of body fluid balance.

Sponsor: Intramural funding

PI/PD: Kathleen S. Curtis

Estrogen, Central Pathways, and Body Fluid Regulation

In addition to their classic peripheral effects, ovarian hormones such as estrogen have actions within the central nervous system (CNS) by actions at estrogen receptors that are broadly distributed throughout the CNS, including areas involved in body fluid volume regulation. The experiments examine neural activation in response to hypovolemia in ovariectomized female rats with and without estrogen to determine whether 1) estrogen affects activation in specific neurotransmitter systems that are important in CNS responses to volume loss; 2) estrogen affects central responses to volume loss in functionally connected central areas; and 3) estrogen effects on central responses to volume loss involve regional and neurotransmitter-specific localization of estrogen receptors. Together, results from these studies will contribute to better understanding of how estrogen actions on specific neurotransmitter systems in defined central pathways affect CNS activation in response to volume loss.

Sponsor: OCAST

PI/PD: Kathleen Curtis

Estrogen, Exercise, and Anxiety

Inactive women are about twice as likely as men to develop depression and depression-related disorders. Moreover, reduced ovarian hormone levels at menopause are associated with increased depression, anxiety, panic disorders, and weight gain. Hormone replacement therapy (HRT) is useful in controlling these symptoms, but regular moderate-intensity exercise may have anxiolytic and/or anti-depressant effects comparable to or greater than those of HRT. The benefits of exercise in reducing anxiety and depression in rats typically have been investigated in males, using vigorous, high-intensity exercise. This project investigates the anxiolytic effects of moderate-intensity exercise in ovariectomized (OVX) rats, and the role of exercise-induced weight loss in reducing anxiety-like behaviors in OVX rats.

Sponsor: Intramural funding

PI/PD: Kathleen S. Curtis

Estrogen, Dieting, and CNS Control of Food Intake

Obesity is epidemic in the United States, and related health issues have created an enormous financial burden. Studies of rats have shown that estrogen decreases feeding and body weight in female rats, and link specific central areas, estrogen receptors (ERs), and neurotransmitters with peripheral neural and hormonal signals from the gut. The present studies use a well-established rat model of ovariectomy and estrogen replacement to 1) determine whether estrogen treatment of ovariectomized rats decreases food intake and body weight during limited access to food, and whether estrogen effects persist after termination of the 'diet'; 2) identify the peripheral mechanisms by which estrogen influences feeding by ovariectomized rats during and after limited access to food; and 3) examine central mechanisms by which estrogen influences feeding by ovariectomized rats during and after limited access to food.

Sponsor: OCAST

PI/PD: Kathleen Curtis

Reproductive Strategies and Estrogen Control of Feeding

These studies seek to determine how the estrogen-mediated enhancement of the feeding inhibitory effect of gastric distension is reversed during maintenance on a diet, and the consequences of this reversal on body weight. We also seek to determine whether estrogens influence body weight regulation and food intake in species that do not exhibit cyclic fluctuations in estrogens. To accomplish these goals, we are collaborating on studies to analyze body weight and food intake during different dietary regimens in 1) female rats that are ovariectomized and given estrogen replacement on a schedule that mimics the fluctuations which occur in their normal 4-day reproductive cycle, and 2) female prairie voles, which are acyclic unless induced into estrus by exposure to a male.

Sponsor: Intramural funding

PI/PDs: Kathleen S. Curtis, J. Thomas Curtis

Trafficking and Targeting of Muscarinic Receptors

Muscarinic acetylcholine receptors belong to the G protein-coupled receptor superfamily and five distinct subtypes (M_1 - M_5) have been identified thus far. Interestingly, subtypes of muscarinic receptor can be differentially localized in polarized cells. The primary goal of our research is to learn more about the molecular mechanisms responsible for subtype-specific differences in muscarinic receptor localization in neurons (i.e., presynaptic versus postsynaptic) of the central nervous system.

Sponsor: National Institutes of Health-NINDS and Intramural funding
PI/PD: Gregory W. Sawyer

Immune Modulation

Our knowledge of the complexity of endogenous and exogenous control agents and mechanisms that influence the immune system continues to grow. This laboratory develops new methodologies and applies them to study the action of agents on the immune system, applications of immune modulation, and immunopathology

Sponsor: Intramural Funding

PI/PD: Joseph A. Price

Interactions of Venoms and Antivenins

Snake venom and antivenin interactions are being evaluated using various methods including size-exclusion HPLC (SE-HPLC). This project is investigating correlations between formation of stable venom–antivenin complexes and antivenin protection against venom-induced toxicity and lethality. Studies are ongoing to determine which venom components are bound in venom-antivenin complexes and what effect binding has on venom reactivity as determined by standard *in vitro* assays. Methods developed in these studies may facilitate reduced use of animals in snake venom research and in antivenin production.

Sponsor: Intramural Funding

PI/PD: Charles G. Sanny

Multivariate Analysis of Antibody and Antigen Interactions

Chromatographic analyses of the interactions of antibodies and antigens using single wavelength detection (e.g. 214 nm, 280 nm) have been described in the literature. The use of a diode array detector may provide additional information such as relative concentration of reactants, component identity, and product composition. Snake venoms and antivenins are being used in this study to evaluate changes in elution profiles consistent with antibody-antigen complex formation and loss of reactive antibody and antigen. Chemometric methods described in the literature, such as multivariate curve resolution, are being used to facilitate antibody-antigen interaction analysis.

Sponsor: Intramural Funding

PI/PD: Charles G. Sanny

Microorganisms Found in Band Musical Instruments

The purpose of this study was to isolate and identify microorganisms that were found throughout band musical instruments (BMI) that had been played over various time intervals. Thirteen (13) wind instruments were sampled from the mouth-piece/reed to the bell. All BMI were found to be contaminated with a wide range of bacteria, yeasts, and molds. Length of time between playing appeared to have no effect on numbers and types of microbes. When the instruments were played, microorganisms were expelled into the environment.

Sponsor: Encore Etc. Inc.

PI/PDs: R. Thomas Glass, R. Stanley Conrad, Gerwald A. Köhler, Jay W. Bullard

Microbial Contamination of Protective Mouth Guards in Hockey Players: An *In Vivo* Study

Removable dentures harbor a wide range of pathogenic and opportunistic microorganisms that can produce disease in the wearer. Protective mouth guards are of similar construction and have been used in a variety of sports for years. Review of medical/dental literature reveals no

studies that investigate whether mouth guards can act as reservoirs of pathogenic and opportunistic microorganisms and be, therefore, potentially harmful to the wearers. A wide array of pathogenic and opportunistic gram-negative and gram-positive cocci and rods were found in the mouth guards worn by semi-professional hockey players, including one mouth guard yielding *Candida dublinensis*, a yeast commonly found in HIV positive patients. Protective athletic mouth guards do contain pathogenic and opportunistic microorganisms that might be potentially harmful to the wearer. The findings of this study would support the idea of limiting the length of wear of protective athletic mouth guards and the possibility of single-use protective athletic mouth guards.

Sponsor: Intramural Funding

PI/PDs: R. Thomas Glass, R. Stanley Conrad, Gerwald A. Köhler, Jay W. Bullard

Microbial Retention in Dentures That Have Been Stored for 1.5 Years and Exposed to Harsh Treatments

Dentures have long been associated with a concurrent stomatitis. The purpose of this study was to evaluate the effects of an extended period of drying, freezing, and boiling on the microorganisms found in dentures that have been worn from 12 days to 48+ years. Portions of polymethyl-methacrylate dentures that had been used in previous studies were frozen and thawed a minimum of two times and ultimately frozen for approximately 1.5 years. The results of these experiments revealed that subjecting dentures to such harsh treatment does substantially reduce the numbers of microorganisms, but that sufficient numbers of disease-producing microorganisms remain and a more effective means of denture sanitization needs to be found.

Sponsor: Intramural Funding

PI/PDs: R. Thomas Glass, R. Stanley Conrad, Gerwald A. Köhler, Jay W. Bullard

Synthesis of Lipid Mediators by *Candida albicans*

Candida albicans is the most important fungal pathogen in immunocompromised individuals such as AIDS, cancer or transplant patients. Recent research has shown that these fungi are able to generate prostaglandin E2, an important regulator of the human immune system. Prostaglandin production in *C. albicans* appears to follow a biosynthetic pathway that is markedly different from the mammalian cyclooxygenase pathway. The aim of our research is to identify the genes and enzymes involved in prostaglandin E2 biosynthesis in *C. albicans* using genomic and biochemical methods. New insights into the interactions of fungi with the host immune system and the identification of novel antifungal targets could be important outcomes of this study.

Sponsor: Intramural

PI/PD: Gerwald Köhler

Interactions of Beneficial Microbes with the Mammalian Host

The mammalian gut microbiome consists of thousands of microbial species that are considered commensals or even mutualistic symbionts because they can provide nutrients and protect the host from pathogens. Probiotics are microbial strains that provide additional health benefits for the host when present in sufficient quantities. We are just beginning to discover the molecular mechanisms how these microorganisms exert their beneficial effects. We are using genomic and microbiological techniques to learn more about the composition of the gut microbiota and the positive health effects of probiotics. Cell and tissue culture models are employed to characterize

how beneficial microbes interact with pathogens and host cells. These studies could open new avenues for prophylaxis and therapy of many infectious diseases.

Sponsor: Intramural

PI/PD: Gerwald Köhler

Nonpolar Antimicrobial Agents and the Gram-Negative Bacterial Cell Surface

Bacterial pathogenesis research in our laboratory has consistently focused on the cell envelope physiology of gram-negative bacteria representing both animal and human pathogens. It has featured investigations of the involvement of membrane lipid and lipopolysaccharide composition in cell envelope permeability to lipophilic antibiotics and antiseptics, the process of acquisition of adaptive resistance to antibiotics, the molecular genetic basis of capsulation and its effect on outer surface function, cell surface lipoprotein content, and the properties of cell surface hydrophobicity and charge. Particular emphasis has been directed toward *Pseudomonas aeruginosa*, *Burkholderia multivorans*, and members of the *Pasteurellaceae* pathogenic in animals of agricultural importance.

Sponsor: Intramural

PI/PD: Franklin R. Champlin

Sequencing the Genome of Drill Cytomegalovirus

This project will sequence the genome of this virus, which resides in monkeys and is similar to human viruses, allowing comparative studies.

Sponsors: Niblack Scholar Program, Intramural Funding

PI/PD: Earl L. Blewett

Developing Diagnostic Assays to Baboon Cytomegalovirus

Baboons represent an invaluable source of xenogenetic organ donors for human patients and are needed to relieve the great lack of human donor organs. However, the risk of transmitting or allowing the establishment of a zoonotic virus in humans is a real and frightening consideration. This proposed study will focus on cytomegalovirus (CMV), since this is the most commonly transmitted virus in human transplantation procedures and is a major cause of many problems in immunosuppressed transplant recipients. This project will identify the indigenous CMV of baboons (BaCMV) and develop sensitive diagnostic assays. These tests will be capable of detecting BaCMV-infected potential organ donors and will be useful in screening baboons for the establishment of specific pathogen free (SPF) breeding colonies.

Sponsor: Intramural Funding

PI/PD: Earl L. Blewett

Hormonal Modulation of Hepatitis C Related Carcinogenesis

The hepatitis C virus (HCV) infects more than 100 million people and causes acute and chronic hepatitis and hepatocellular carcinoma (HCC). HCC is the third most common cause of cancer death associated with chronic liver disease and cirrhosis. There is no vaccine available for HCV and 40%-50% of patients are unresponsive to standard treatment. Predominance of HCC in males highlights the significance of estrogens in HCC development. We are studying the interactive role of estrogen and HCV proteins on HCV-related HCC using *in vivo* and *in vitro* models. Studies on estrogen involvement in HCC pathogenesis may open new avenues to therapeutic modalities against HCC.

Sponsor: Intramural Funding

PI/PD: Rashmi Kaul

Hormonal Linked Etiology of *E.coli* Urinary Tract Infections (UTI)

Estrogen alters the susceptibility to infections at various stages of the menstrual cycle. Hypoestrogenemia may predispose post-menopausal women to urinary tract infections. *Escherichia coli* is the leading cause of urinary tract infections. Invasive *E. coli* with dry adhesions have the capacity to invade epithelial cells and cause chronic UTIs in humans. Recent data from our laboratory directly indicates a protective role of estrogen involving estrogen receptors during *E.coli* bacterial invasion on hepatoma cells and also in our *in vivo* UTI model. Studies are on the way to study hormonal linkage to UTI pathogenesis and design novel therapies.

Sponsor: Intramural Funding

PI/PDs: Rashmi Kaul, R. Thomas Glass

Human Identity Laboratory

Project #1- New method for assessing DNA quantity/quality prior to DNA profiling: We recently devised a simpler technology that will not only quantitate the amount of human DNA in a sample, but will also determine the sex of the donor, whether there is a mixture of DNA from a male and female donor (important in sexual assault evidence), whether the sample may also contain inhibitory compounds that may block PCR amplification used in producing the DNA profile of the donor(s), and finally whether or not the DNA in the extract is degraded. Current research is attempting to add additional DNA targets present on the human mitochondrial genome to the existing targets on human genomic DNA so that the assay will also produce a quantitation estimate of mitochondrial DNA present in the sample for those labs that perform mtDNA testing in addition to the more typical DNA typing.

Project #2- Development of a DNA typing methodology suitable for attributing the source of pathogens targeting agriculturally important plants: Research underway in the Human Identity Laboratory has as its goal the development of a generic DNA typing method that will be able to trace the source of a wide range of bacterial pathogens that target crops. The method currently under investigation has been used to create genetic fingerprints of several bacterial pathogens including *Serratia marcescens* (infects cucurbit crops), *Pseudomonas syringae* (infects tomatoes and is also an opportunistic pathogen of humans), and *Staphylococcus aureus* (and opportunistic pathogen of humans). Thus far, we have found the method to be highly discriminatory both for distinguishing members of different bacterial species and even distinguishing among different strains of the same bacterial species.

Sponsor:

PI/PD: Robert W. Allen

CLINICAL SCIENCES

Screening for Risk of Mental Disorder in Primary Care

The incidence of mental disorders in primary medical care is high, but the rate of detection is relatively low. This pilot project examines the utility of using two screening tests—the Patient Health Questionnaire (PHQ) and Drug Abuse Screening Test (DAST)—and a brief standardized interview to identify risk and confirm the presence of one or more of the most commonly occurring mental disorders.

Sponsor: Oklahoma Department of Mental Health and Substance Abuse

PI/PDs: Richard A. Wansley, Richard H. Bost

Assessing Empathic Communication in Medical Students

Some research links empathic communication by physicians to better medical outcomes and to higher ratings of clinical competence. This research attempts to rate medical students on their performance of empathic behaviors during standardized patient interviews and examines the association of these behaviors with ratings of clinical competence in clinical clerkship rotations and with scores on scales assessing empathic attitudes.

Sponsor: Intramural Funding

PI/PDs: Michael H. Pollak, Susan K. Redwood

Cognitive Rehabilitation Following Brain Injury

Injury of brain tissue occurs in many diseases and traumatic incidents. Impaired perceptual abilities, cognitive functions, and emotional distress secondary to these injuries often prevent patients from returning to productive work and family life. Rehabilitation therapies have been widely available for only the past twenty years; research into their effectiveness is in its infancy. Current investigation involves examining the efficacy, clinical utility, and cost effectiveness of on-line computerized cognitive/perceptual rehabilitation and Cognitive Behavior Therapy systems. In addition, web-based tools for evaluating the statistical significance of clinical changes in individual patients are being developed. This research involves collaboration among OSU-CHS faculty and staff, as well as faculty from other institutions.

Sponsor: Intramural Funding

PI/PD: Richard H. Bost

The Effect of Cephalo Pelvic Disproportion on Otitis Media

Otitis Media is a frequently occurring, yet rather perplexing condition causing inflammation of the middle ear. It is perplexing because numerous conditions fall under the umbrella of Otitis Media, including viral infections, bacterial infections, and the presence of various fluids, which can be categorized as either acute or chronic depending on the duration of fluid build-up. There is no distinct determination of the cause(s) of Otitis Media. Some postulate that allergies, whether resulting from environmental conditions or digestion of particular foods, trigger Otitis Media. Unfortunately, many experts do not believe an allergen triggers Otitis Media. The purpose of this study is to examine the effect of Cephalo Pelvic Disproportion on Otitis Media.

Sponsor: Intramural Funding

PI/PDs: Kayse Shrum, Jenny Alexopoulos

The Effect of Osteopathic Manipulative Treatment, as Newborns, on the Health of Children in the First Six Months of Life

The study was an outpatient chart review of children's first six months, matching 58 who had received OMT as newborns with 58 who had not. Comparison of the clinical variables yielded a few differences between the cohorts in the direction of less of the following symptoms in the intervention patients for at least one month: food intolerance, colic mentioned, chaliasia-associated symptoms, antibiotic usage, spitting, diarrhea, and otitis media.

Sponsors: American Osteopathic Association, American Academy of Osteopathy (Robuck Fund)

PI/PD: Miriam V. Mills

Fidgeting During Daily Life

An imbalance between energy intake and expenditure may lead to weight change which results in obesity. Energy expenditure related to physical activity is an important determinant of such an imbalance. This research focuses on one component of non-exercise daily physical activity

(i.e., fidgeting) that may contribute to this energy imbalance. This research attempts to demonstrate that individuals differ characteristically in fidgeting in ways that can be measured during daily life using unobtrusive body-worn monitors.

Sponsor: Intramural Funding

PI/PD: Michael H. Pollak

Human Identity Laboratory

Standards under which forensic DNA-typing laboratories operate mandate that the amount of human DNA recovered from forensic samples be determined. Currently, methods used for quantification of human DNA in extracts rely on technology that is completely different from that used normally in the crime laboratory to develop DNA profiles. Over the past two years, we have undertaken to develop and validate a DNA quantification method relying upon quantitative PCR amplification of the human amelogenin locus. The amelogenin gene in human DNA is six base pairs longer in males than in females and serves as a way to determine the sex of a DNA sample. In previous studies from the laboratory, the validity of the quantitative PCR method was established. Current work aims to validate its use to quantify male and female contributions of DNA to mixed samples, which are common in sexual assault cases.

Sponsor: Intramural Funding

PI/PD: Robert W. Allen

Oklahoma Area Health Education Center Program

The Oklahoma Area Health Education Center Program (OkAHEC) is a sponsored program of OSU-COM that is conducted through regional AHECs located in Enid, Poteau, Lawton, and Pryor, and a training/health care facility in the Osage Hills Complex in Tulsa. The program combines academic and community resources to improve the supply and distribution of primary care professionals and to increase the accessibility of quality health care services in rural and medically underserved areas. The OkAHEC mission is accomplished through community-based training for health professional students and medical residents with rural and underserved populations; educational interventions that promote disease prevention and improved health through access to primary health care services; continuing education for health practitioners in rural communities; health careers recruitment with a special focus on minority and underserved populations; locally-based initiatives that respond to emerging health care needs; and coordination with other state and federal primary care initiatives.

Sponsors: Oklahoma Department of Health, U.S. Department of Health and Human Services

PI/PD: Richard Perry

Roles of a Multidrug Efflux System and Lipopolysaccharide in Antimicrobial Resistance of *Pasteurella haemolytica*

Pasteurella haemolytica is a primary etiological agent of bovine respiratory disease (BRD) in cattle resulting in significant economic losses in the cattle industry. The development of antibiotic resistance among feedlot cattle fed prophylactic doses of various antibiotics to prevent BRD is a matter of particular concern. This project begins by determining the minimal inhibitory concentration (MIC) of 13 commonly-used antibiotics among 22 clinical isolates of *P. haemolytica*. Strains with unusual resistance patterns will be grown up in sufficient biomass to allow the extraction of lipopolysaccharides (LPS), which are major components of the bacterial cell wall that determines antimicrobial accessibility. Chemical characterizations of these LPS will be used to determine if antibiotic resistance can be correlated to the specific chemical composition of the outer membrane.

Sponsor: Targeted Research Initiative Program

PI/PDs: R. Thomas Glass, Leigh B. Goodson, Robert S. Conrad

Rotavirus Vaccine Study

The Department of Pediatrics is evaluating the safety of a bovine viral vaccine for infants for the prevention of acute gastroenteritis due to Rotavirus. This virus is the most common cause of dehydration, with hospitalization in children less than three years of age. Over 60,000 children will be involved in the study worldwide.

Sponsor: Merck

PI/PD: Stanley E. Grogg

Student-Led Stress Management Program for First-Year Medical Students

The medical education community has emphasized repeatedly the importance of teaching stress management and self-care skills to medical students. However, descriptions and evaluations of intervention programs are infrequent. This project collects and disseminates program evaluation data from medical students who have participated in the OSU-COM Stress Management Program.

Sponsor: Intramural Funding

PI/PDs: Susan Redwood, Michael Pollak

Suicide Among American Indians in New Mexico

Analysis of quantitative and qualitative data is continuing with Philip May of the University of New Mexico to update epidemiological information regarding completed suicides among the Apache, Navajo, and Pueblo Indians in New Mexico from 1957-1998. Age and gender differences, behavioral interactions prior to the event, and trends in suicide rates are being explored in these populations.

Sponsor: Indian Health Service

PI/PD: Nancy Van Winkle

The Use of Osteopathic Manipulative Treatment and Adjuvant Therapy in Children with Recurrent Acute Otitis Media

Patients with recurrent earaches (otitis) were followed for six months, with 32 patients receiving routine pediatric care and 25 receiving routine care plus adjuvant manipulation. Clinical status was monitored by review of medical records, audiograms, parent behavior rating, and tympanograms. The treatment group experienced a greater decrease in average monthly episodes of average monthly antibiotics prescribed, fewer surgical interventions, and more normal tympanograms.

Sponsors: American Osteopathic Association, American Academy of Osteopathy (Robuck Fund)

PI/PDs: Miriam V. Mills