The enzyme AP-endonuclease 1 (APE1) repairs DNA damage but also has additional unique regulatory functions. I studied possible functions of modified (acetylated) APE1 which is associated with chromatin during cell division. My findings support a novel role for APE1 & acetylated APE1 in maintenance of chromatin structural stability throughout the cell cycle.
I examined the effectiveness of two different interventions, as compared to regular care, on helping women 16-24 years of age maintain regular birth control pill and condoms usage. Neither clinic visits nor regular phone contact increased the amount of time young women remained on birth control pills or used condoms, even though they requested the contraception.
Understanding how and why we lose muscle as we grow old is important, not only for our quality of life, but also for recovery from illness and injuries. My studies showed that eating a high-quality protein-rich diet (leucine supplemented) and walking (frequent exercise) effectively minimize muscle wasting.
My research investigated how retroviruses –viruses related to HIV enter cells. A growth factor receptor-bound protein 2 (Grb2), was shown to be needed for cell infection. I showed that Grb2 is important for host cell signaling and controls virus entry through the virus receptor.
TDP-43 is a protein found in abnormal clumps in brains of people with Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig disease) or with a type of frontotemporal lobar dementia. By expressing this protein in the fruit fly, I have shown that genetic mutations and modifications of certain amino acids can increase the toxicity of TDP-43.
Both environmental and genetic factors can increase an individual's risk of disease. Differences in genetics from one individual to another can affect how their body reacts to chemical exposures. I studied those genetic differences and how these differences impact risk of disease.
Prions are infectious particles that cause neurodegenerative illnesses. Our current understanding is that prions are composed of an aberrant form of a normal brain protein. For my research, I studied the molecular aspects of how this normal protein is involved in the formation of infectious prions.
I showed that pathogenic arenaviruses infect cells, cause little cellular damage, and effectively replicate unchecked by the immune system. Infection with a vaccine strain leads to cell death and activates the immune system. Phosphatidylserine on the surface of the virus may be responsible for this difference.
Research for the treatment of viral hemorrhagic fevers, a dangerous group of viruses with a high mortality rate, has been advancing rapidly. This capstone offers a number of decision trees compiled from leading field data. The decision trees provide critical guidance in cases of accidental infection and outbreak.
Medications used during pregnancy may harm the developing fetus. My research involved investigating active transporters in the placenta which limit the amount of these medications that can reach the fetus from the maternal blood circulation.
Pancreatic cancer cell growth is caused by increased intracellular signaling. I demonstrated that increased signaling from one receptor protein (Met) promotes this growth mainly by causing defects in shutting off Met signaling. Therefore, this receptor may be a possible therapeutic target for treating pancreatic cancer.
Rift Valley fever virus (RVFV) is responsible for large periodic outbreaks in livestock and serious human disease. I investigated host gene expression responses with virus vaccine strains. This identified host genes responsible for virus susceptibility and resistance and will assist in the design of improved vaccine strains in the future.
My research focused on the design and development of novel transducer proteins to control HIV infection. These specifically kill HIV infected cells and prevents the spread of the virus. This approach could potentially lead to the complete eradication of HIV infected cells in infected patients.
The goal of my research was to examine the effects of growth factors on cancer stem cells and to develop novel treatment strategies to target cancer stem cells in hopes of preventing tumor recurrence.
Venezuelan equine encephalitis (VEE) is a mosquito-borne virus that causes fatal disease in humans and horses. My research focused on how this virus infects and replicates differently in enzootic and epizootic mosquito strains. I also identified multiple VEE proteins required for viral infection of mosquitoes.
Small chemicals molecules act as a signaling system that allows communication between bacterial cells in a process called quorum sensing (QS) in the bacterial pathogen, Aeromonas hydrophila. My results showed that QS molecules modulate innate immune response during infection and enhances their survivability.
Ehrlichiosis is a tick-borne disease caused by an intracellular bacterium. I compared the expression of ehrlichial genes in tick and human cells, characterized a regulator of these genes and the protection mediated by antibodies. These studies have identified novel targets for development of vaccines and therapies.
Synucleinopathies are diseases with increased clumps of a normally soluble protein, synuclein, in the brain. The clumps cause holes in neural cells, allowing toxic molecules to enter the cell and alter proteins important for normal cellular function. I found that nitration of synuclein increases its toxicity in the brain.
I studied a novel therapy for preeclampsia (pregnancy-induced hypertension). I tested VEGF-121 therapy to repair maternal endothelial damage. This therapy improved maternal endothelial function, pregnancy outcome, and prevented abnormal vascular function in the offspring.
Ebolavirus causes up to 90% mortality and there are no effective therapies for these infections. Ebolavirus recruits proteins to the cell surface which allows their entry into cells. My work has identified a novel virus entry pathway, and potential drug treatments for preventing and treating EBOV infection.
Longstanding liver disease often is complicated by accumulation of large amounts of fluid in the abdomen (ascites). Water pills are the conventional medications used in the treatment of ascites. My goal was to use metolazone as an additional medication in patients with ascites that is not controlled by conventional water pills.
Prion diseases cause fatal and infectious disorders of brain. Disease results from the accumulation of a misfolded and infectious form of the prion protein. My research focused on calcineurin in preventing neurodegeneration which may provide a novel strategy for clinical therapies.
Arboviruses are viruses transmitted by mosquitoes and ticks. Chikungunya virus is transmitted by mosquitoes and infects millions of people in the tropics. My work focused on chikungunya virus infection of mosquitoes and their cell entry pathways and the impact of co-infection with other viruses.
Burn injury induces a hypermetabolic response characterized by elevations in cardiac work, metabolic rate, and muscle catabolism. Post-burn catabolic effects cause bone mass decrease and severe growth arrest. Use of oxandrolone improves the long-term recovery of severely burned children in all of these areas.
In cells, it is important to know how macromolecules in cells interact. This is a challenge given the large number of molecules present. My research found that DNA binding proteins overcome this obstacle using various kinetic mechanisms and provides an understanding into macromolecular interactions.
Cellular proteins must fold to a native state. My work investigated mutations which did not affect the crystal structure of adenylate cyclase but did alter its conformational “excited” state. This supports the concept of local protein unfolding for function and adaptation in enzyme activity.
My project concerned specific neurotransmitters and their receptors in the brain involved in cocaine addiction. The goal was to target specific receptors with novel chemical compounds that affect their function in order to better understand how altering these receptors may lead to an eventual treatment for cocaine addiction.
The speed at which proteins are synthesized by cells can affect how well those proteins fold properly to assume a functional structure. I studied the effects of making proteins at different rates and found that, when a protein is made slowly, it folds more properly and functions better.
Causes of Alzheimer’s disease are not well understood but may involve a cellular protein called amyloid precursor protein (APP). My research focused on another protein, ubiquilin that interacts with APP and prevents its deposition. Age-related declines in ubiquilin may help explain the age-associated cognitive decline seen in Alzheimer’s.
Chronic pain management poses a challenge, particularly for patients with chronic pancreatitis who may experience severe adverse side effects with traditional opiates. Salvinorin A is a unique, plant-derived alkaloid that binds to a specific opiate receptor subtype and may serve as a model template to develop better analogs for treating pancreatic pain.
Genome replication requires the interaction of numerous proteins which complex with DNA. My work examined some of these critical protein-DNA interactions. Results shed new light on why human cancer and genetic disorders result from dysfunctional protein-DNA interactions.
Venezuelan equine encephalitis virus causes inflammation of the brain. In experimental models, we determined the role of T- and NK cells in the disease process. NK cells respond early to infection while T-cells helped prevent disease. This is a novel model to study VEE brain inflammation.
I examined the influence of spirituality and religion in the experience of American hospital birth. Both theoretical examinations of childbirth spirituality and the results of interviews with 48 providers and patients who labor in hospital settings and believe that spirituality or religion are important to hospital birth were used.
Chikungunya virus (CHIKV) causes an infectious disease in tropical regions characterized by high fever and severe joint pain. This work investigated CHIKV and the immune system. I found that the immune response plays a complex role in controlling the infection and resulting tissue damage.