2009 SABRE Participants

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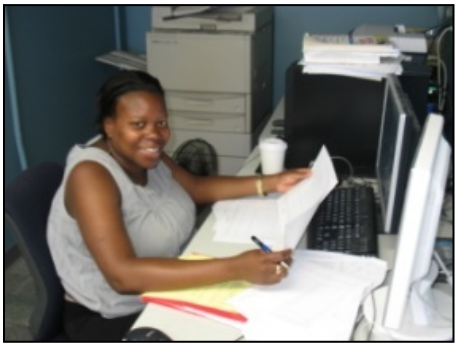
USE OF CINNAMON COMPOUNDS TO INHIBIT ADVERSE REACTIONS OF TAU ASSOCIATED WITH ALZHEIMER'S DISEASE

Although specific life-time diagnosis and treatment are lacking, polyphenolic polymers known in cinnamon are found to be effective against the agents that lead to the devastating neurodegenerative disorder, Alzheimer's disease. Extracellular β-Amyloid plaque and intracellular neurofibrillary tangles of microtubule associated protein, tau, serves as the hallmarks of this chronic dementia and is characterized by progressive cognitive impairment of intellectual abilities and memory loss. The primary objective of this research is to identify and study the effects of cinnamaldehyde (CA) a purified compound of cinnamon on the neurofibrillary tangles formed by the aggregation of tau. The hypothesis is that this compound interacts with the cysteines in tau protein and would potentially interfere with its aggregation. To elucidate the mechanisms, we modulate pH to determine the effects of neighboring groups on its availability. Reaction of 5,5'-dithiobis(2-nitrobenzoate) and N-Acetyl-L-Cysteine (substrate) in various buffer solutions at different pH values and at different time points are performed *in vitro* to obtain a baseline. These measurements were used as a control to compare the reaction of tau and a tau peptide containing cysteine (SKCGS) with cinnamaldehyde. Our results show that the cysteines in tau and its' peptide are highly reactive and suggests that the lysine residue adjacent to the cysteine affects its reactivity. Tau thiols in vitro reactivity may help us to generate effective inhibitors of tangles that will be tested in cellular culture system and subsequently deliver cinnamaldehyde intranasally to help improve the condition of patients with AD.



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UTILIZING MATLAB TO MATHEMATICALLY MODEL THE DYNAMICS OF ANTIBIOTIC RESISTANCE IN HOSPITALS

Antibiotic resistance is not a surprising dilemma for scientists, indeed it has been expected since the existence of antibiotics in 1944. In particular, nosocomial (hospital acquired) infections are the most publicized issues with antibiotic resistance. Nosocomial infections are often transmitted by direct contact, through the contamination of an institution's environment, or by the inadvertent help of human vectors, such as health care workers. In order to control nosocomial transmission, hospitals have implemented interventions to reduce antimicrobial resistance in nosocomial pathogens which includes hand washing barrier precautions, increasing the prophylactic use of drugs other than those which resistance is currently a problem, and using the cycling of formularies in hospitals. However, these interventions have been administered without any quantitative measures or time factors for their effectiveness to actually determine their success. Using Lipsitch's compartmental model, which describes the transmission dynamics of bacteria that commonly resides in or on our skin, respiratory passage or digestive track of humans i.e E. Coli, meningitides, tuberculosis, makes it possible to get quantitative measures. These measures make it accessible to evaluate the effectiveness of interventions to protect patients from transmission of antibiotic resistance bacteria in hospitals. The model predicts that as the rate of nosocomial infection transmission reduces, so does the spread of resistance infections. The spread of resistance to a drug is linked to the level of its usage. After a successful intervention, changes will occur in a matter of weeks to months, which is considerably faster than community acquired infections. A parameter study will be conducted using Lipsitch's model and the results will then be compared to those obtained by Lipsitch's.

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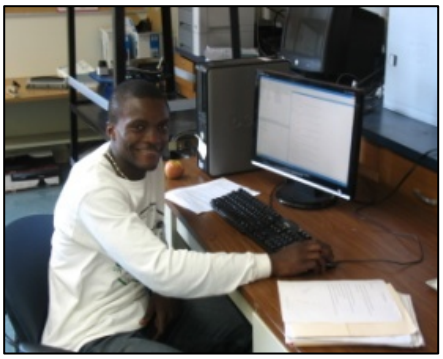
PRODUCTION AND CHARACTERIZATION OF BIOMIMETIC PATTERNED REVERSIBLE ADHESIVES

Hierarchical structures consisting of and contained within the feet of geckos all work together to give geckos the remarkable ability to climb along walls and walk on ceilings. The objective of this research project was to produce and characterize biomimetic patterned reversible adhesives (BPRA). Additionally, this project focused on creating polymer pillar structures that are tilted which would mimic two hierarchical structures of the gecko. For the fabrication of the pillars, a poly(dimethylsiloxane) (PDMS) mold was made from a patterned silicon master, partially cured, and sheared. Then, poly(mercaptopropyl)methylsiloxane (PMMS) was added to the PDMS mold. Additionally, the surface preparation of the silicon master and the curing parameters were the variables altered during the fabrication of the PDMS molding. The pillar structures were analyzed using various microscopy techniques. Lastly, the effects of varying the surface preparation and the curing paraments were evaluated for the fraction of successfully molded tilted pillars. Ultimately, the successful fabrication of reversible adhesives could have applications in wall-walking robots to serve purposes during construction, fire rescue, and military applications to name a few. Additionally, these adhesives could have medical application in which they may be utilized as temporary adhesives during surgery.



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SIMULATION OF GENETIC TOGGLE SWITCH IN E COLI

There is a growing concern on improving medical practices in order to minimize deaths due to diseases especially cancer. Understanding the functioning of the disease causing agents is one process of achieving this goal. In an attempt to understand this, Gardner et al proposed a model of genetic toggle in Escherichia Coli. This work presents the simulation of his model. The genetic toggle switch in Escherichia Coli demonstrates bistability in gene regulatory network. Here the model is simulated by the process of stochastic simulation algorithm. The Monte Carlo simulation gives the characteristic properties of the system. Each iteration of the Monte Carlo simulation is done by the Gillespie stochastic simulation algorithm. The Gillespie stochastic simulation algorithm involves the determination of two random variables so as to predict the next reaction and reaction time respectively. The simulations demonstrate bistabiliy in the genetic toggle switch.

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SYNTHESIS OF MESOPOROUS ZINC OXIDE VIA NOVEL METHOD

Zinc Oxide (ZnO) is a compound that has unique optical, magnetic, piezoelectric and semiconducting properties which enables widespread applications in different fields of science. This research seeks to develop a novel way of producing highly ordered mesoporous zinc oxide. Successful production of which, it is hoped, would be beneficial in the exploration and optimization of the beneficial qualities of Zinc Oxide. It is hypothesized that using phage display a specific peptide sequence that binds to Zinc Oxide can be selected and the peptide sequence can be bound to a surfactant which can then be used for surfactant templating. In this part of the research, the effect of varying pH and Zinc Oxide particle size on the binding peptide sequences selected during phage display is evaluated. Results from this work would provide information on ideal pH levels for surfactant templating and appropriate peptide sequences suitable for synthesizing mesoporous Zinc Oxide with different powder sizes using this method at different pH levels. Information from the pH studies would also break new ground and provide valuable background for further work on phage display with Zinc Oxide.

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TRACKING MULTI-PROTEIN TRANSCRIPTIONAL COMPLEXES THROUGH TOTAL INTERNAL REFLECTANCE FLUORESCENCE PROTEIN BINDING MICROARRAYS (TIRF-PBM)

Total Internal Reflectance Florescence Protein Binding Microarrays (TIRF-PBM) have been used to study the DNA binding specificities and affinities of several general transcription factors. Total internal reflectance and fluorescence (TIRF) measurements capture both equilibrium binding intensities and kinetic rates in a single experiment. In TIRF-PBM, DNA is mixed with polymers and printed on a chip. Next, the chip is eradicated with UV light to crosslink the polymer, forming hydrogel spots. This serves as a platform for the analysis of dye-labeled protein binding to DNA. When fluorescent proteins are added, the fluorescent intensity at a spot corresponds to protein binding. Utilizing this methodology, TIRF-PBM obtains detailed binding kinetics, giving comparable kinetics data to gel shifting methods. This approach has recently been extended to analyzing transcription factors Myc and Max. Studies have shown that Myc is a TF involved in the regulation of 15% of all genes, which dimerizes with its partner Max. It is known that Myc/Max are hyper activated in many cancers. TIRF-PBM is being used as a platform to evaluate libraries of novel compounds that may inhibit Myc:Max interaction in a sequence selective fashion. The goal of this research is to target protein: protein interaction at specific promoters for increased specificity chemotherapeutics.

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IDENTIFICATION OF AcrB MUTATIONS THAT CONFER RESISTANCE TO CONTACT DEPENDENT GROWTH INHIBITION IN *ESCHERICHIA COLI*

Contact Dependent Inhibition (CDI) is a method by which bacterium can inhibit the growth of neighboring cells by direct cell-to-cell contact. *Escherichia coli* (E. coli) is the only microbe that has been identified to undergo complete CDI, although it is believed that this phenomenon is widespread throughout the bacterial world. There are several key proteins that make CDI possible. CdiB is a β-barrel outer-membrane protein on the surface of the inhibitory cell and CdiA, an outer-membrane protein exposed to the extracellular environment, passes through CdiB. CdiA is believed to be processed upon contact with its receptor BamA and the cleaved carboxy terminal (C-terminal) end of CdiA then enters the outer membrane of the target cell via BamA. Once in the periplasm of the target cell, CdiA is thought to interact with inner-membrane protein AcrB. AcrB, normally an electron efflux pump, is responsible for exporting small molecules out of the cytoplasmic matrix. In the presence of CdiA, AcrB reverses the direction of flow, therefore allowing CdiA to enter the cytoplasmic matrix of the target cell. Previous research has shown that the addition of a histidine tag to the C-terminal end of AcrB in target cells prevents CDI. The goal of this research project is to identify additional regions of AcrB that may be responsible for interacting with CdiA, therefore allowing CDI to occur.Plasmids containing AcrB were mutagenized in an *E. coli* strain that is deficient in DNA mismatch repair. Mutations in AcrB were found that increased resistance of target cells to CDI. Future work will identify whether these regions in AcrB are important for binding CdiA.