CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Rupsa B. Acharya

Project Number

S0501

Project Title

The Effect of Carica papaya Leaf on the Lifespan of C. elegans with Fatal Germline Tumors

Abstract

Objectives/Goals

The purpose of the project is to determine if C. papaya leaf extract (CPLE) extends the lifespan of C. elegans. The germline tumors of C. elegans is used to model ovarian cancer tumors. Thus the project tries to evaluate if a component of CPLE can be effective in treating human ovarian cancer.

Methods/Materials

Control [no CPLE] and 4 different concentrations [50, 100, 150, 200 ug/mL] of CPLE are mixed in the Nematode Growth Medium. Plates are seeded with E. coli OP50 for food, tumorous worms transferred, and their lifespans are observed.

Results

One CPLE concentration, 100 ug/mL, extends the lifespan by 34%, which is statistically significant with a confidence level of more than 95%.

Conclusions/Discussion

The results show CPLE is effective in extending the lifespan of C. elegans with fatal germline tumors. This indicates that C. papaya leaf may contain a chemical that could be effective in ovarian cancer treatment.

Summary Statement

The effect of papaya leaf on ovarian cancer, which is modeled by C. elegans with fatal germline tumors.

Help Received

Lab equipment at Lynbrook High School under supervision of advisor Mr. Jason Lee

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Rohan Arora

Project Number

S0502

Project Title

Using Virtual Screening Methods to Identify a Novel and Noninvasive Method of Heart Disease Treatment and Prevention

Abstract

Objectives/Goals

Heart Disease is the top killer in the United States, causing 600,000 deaths annually. Current methods of prevention for this disease cause discomfort to 30% of the population and may be invasive. This project sought a novel method to reduce the risk of heart disease by inhibiting a key interaction between LDLR (Low Density Lipoprotein Receptor) and PCKS9 (Proprotein convertase subtilisin/kexin type 9), the molecule that causes this receptor to malfunction.

Methods/Materials

In order to be a potential drug candidate, the inhibitor had to be a small molecule that could be easily administered without the use of invasive techniques (i.e injections). Inhibition criteria was established based on control interactions at key residues and a simulation program (Autodock Vina) was used to complete a series of virtual screenings which simulated various molecules bonding to the PCSK9 molecule as potential allosteric or competitive inhibitors. Then a practical verification of the simulation results was conducted by performing a competitive ELISA assay in laboratory environment.

Results

The identified molecule which met all requirements and had the lowest affinity of binding (-8.0 kcal/mol) held the ZINC ID of ZINC00990239. Its interaction with key competitive residues CSY378, ILE369, and PHE379 was observed using AutoDock Tools (binding analysis software). However, this molecule was not available for the verification step so another top molecule, ZINC04214344 (affinity: -7.6 kcal/mol, competitive inhibitor at residues ILE 369 and PHE379), was used. This molecule was shown to have practical, de facto applications through the assay and exhibited an 80% success rate as an inhibitor of the given interaction.

Conclusions/Discussion

The results show that it is very possible for the identified molecule to inhibit the interaction between LDLR and PCSK9 effectively. If shown to be successful in human trials the identified small molecule has the potential to provide a better prevention mechanism for the most deadly disease in the nation, saving thousands of lives annually.

Summary Statement

My project involved the use of virtual simulations and laboratory assays to identify and demonstrate a novel way to treat heart disease that is more cost-effective, comforting, and inclusive than current methods.

Help Received

Qualified Scientist made sure safety requirements were met

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Kyung Eun Baek

Project Number

S0503

Project Title

Cancer Targeting Activity of Salmonella Invasion Protein A

Abstract

Objectives/Goals

Due to the fact that current conventional cancer treatments, such as chemotherapy and radiation therapy, lack specificity, the development of new forms of therapy is essential to decreasing negative impacts of the treatment on patients. Past research shows that Salmonella typhimurium is able to affect metastases and also preferentially colonize 2,000-fold more in tumors, than in liver, spleen, lung, heart, and skin. However, the precise mechanisms of the attractive interaction between bacteria and cancer cells are still unknown. In this research, Salmonella Invasion Protein A (SipA), known to change actin filament activity in the host cell, was tested for its potential role in cancer specific drug delivery.

Methods/Materials

In combination with SipA, a DNA restriction endonuclease (RE) fused with nuclear localization sequences (RE-NLS) was used as the toxic therapeutic agent. The NLS was hypothesized to deliver the RE-NLS fusion protein to the nucleus of the cancer cells, where the restriction enzyme would cut the cancer cell's genomic DNA and kill the cell. SipA and RE-NLS proteins were mixed with a protein transfection agent to initiate intracellular delivery of the proteins into normal and lung cancer cells from humans and mice.

Results

Toxicity assays of the proteins showed a decrease in the number of cancer cells in a dose-dependent manner, while the number of normal cells stayed relatively consistent. Tests using different combinations of SipA and RE-NLS proteins were able to show specifically SipA's cancer targeting activity.

Conclusions/Discussion

Thus, this study gives positive evidence that the SipA protein could potentially be a useful mediator for cancer specific drug delivery in the future.

Summary Statement

In this research, Salmonella Invasion Protein A (SipA), known to change actin filament activity in the host cell, was tested for its potential role in cancer specific drug delivery.

Help Received

Used lab equipment at Thermo Fisher Scientific and AntiCancer under the supervision of Dr. Katzen and Dr. Miwa respectively

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Jessika Baral

Project Number

S0504

Project Title

Novel Usage of Natural Phytochemical 3,3-diindolylmethane as Anti-Cancer Therapeutic and Preventative Drug for Melanoma

Abstract

Objectives/Goals

Skin cancer accounts for more than 75% of all cancer diagnoses and melanoma accounts for more than 75% of skin cancer deaths. Every 57 minutes, someone with melanoma dies in US; only 10-15% of stage IV melanoma patients survive past 10 years. Brassica vegetables, such as broccoli and cabbages, represent a promising source of phytochemicals. This is the first study on the effects of 3,3-diindolylmethane (DIM), a metabolite found in Brassica vegetables, on human melanoma cancer cells.

Methods/Materials

Cells of three human melanoma cell lines (SK-MEL-28, G361, and SK-MEL-2) were cultured. Other materials used include DMSO (Dimethyl sulfoxide) [as a drug dissolving agent], DPBS (Dulbecco's Phosphate-Buffered Saline), DMEM (Dulbecco#s Modified Eagle Medium) [for the media base], Nonfat dry milk powder, Bovine serum albumen, Chemiluminescent agents, Protein Antibodies, CCK-8 Reagent, and DIM powder.

CCK-8 assays were carried out to gauge the effects of different concentrations of DIM on these cell lines by quantifying the amount of viable dehydrogenase enzymes. Flow cytometry assays and Western blots were then carried out to establish the path DIM is acting on to inhibit melanoma tumor proliferation.

Results

Results proved that DIM significantly reduced tumor size; cell proliferation rates decreased by 97.44% to 99.45% after just 24 to 48 hours of treatment respectively. Western blots show a PTEN upregulation, indicating that DIM works to significantly induce apoptosis. DIM induced a G1 cell cycle arrest in the G361 cells, which proved to be the most responsive to DIM treatment. Western blots also indicate a Cyclin D downregulation in the G361 cells, which correlates with this cell cycle arrest.

Conclusions/Discussion

The results support the hypothesis that DIM is a potent anticancer drug. Current treatments, including chemotherapy, drug therapy, and immunotherapy, target only select forms of melanoma, have severe side effects including autoimmune responses, and cost hundreds of thousands of dollars. Standard dosages of DIM exhibit no major side effects and DIM is more than 1000 times cheaper than current drugs. DIM can also be used as the first drug that is a preventative agent for melanoma. Clinical trials will be started.

Summary Statement

My research determined, for the first time, the significant tumor-suppressing effects of 3,3-diinolylmethane on human melanoma cancer cells and proved that DIM can be a therapeutic and preventative drug agent for melanoma.

Help Received

Used research facility at the Department of Molecular and Cellular Biology at UC Berkeley.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Julie Barreto; Andrea Benitez; Esmeralda E. Lara

Project Number

S0505

Project Title

The Effects of Papain and Bromelain in Denaturing Bos Primegenious

Abstract

Objectives/Goals

We were expecting Papain at 100% concentration, to tenderize the meat faster than Bromelain. Meat has muscles within them that are made of strong fibers. These fibers, which are composed of tough protein bonds sorted in a chain manner, create the meat hard to cut especially the strong connective tissues that sustain the meat together. Papain cuts the protein chains in the fibrils and in the connective tissue disrupting the structural integrity of the muscle fiber and tenderizing the meat. As a result, Papain serves as a protease cutting and tearing the proteins and fats withholding the meat together. The Papain enzyme also speeds up the chemical reaction by lowering the activation energy creating the meat tender.

Methods/Materials

Metal Ring Stand, Clamps, Cow meat, 20mL graduated cylinder, Gram scale, Pineapple(Bromelain), Papaya(Papain), Various Limes(weights), Juicer

Results

Papain was a more efficient meat tenderizer than Bromelain in all trials and concentrations(100%, 50%, and 25%). We discovered that Papain required less weight to break the meat at an average of 426 grams for 100%, 532.6 grams ofr 50%, and 640.6 grams for 25% which differs from Bromelain which required 458 grams for 100%, 615.3 grams for 50%, and 736.3 grams for 25%. The higher the concentration of the enzymes the less weight required to tear the meat.

Conclusions/Discussion

Our Hypothesis concerning the enzyme, Papain, tenderizing the meat faster than the other enzyme Bromelain. As shown from our data and results the 20g strips of meat that were submerged in the Papain enzyme broke with less wight than the 20g strips of Bromelain. The Papain meat was more tnder because of its significant degradation of muscle. Papain enzyme cuts the protein chains in the tissue which then broke the muscle fiber structure in the meat, thus causing the meat to be more tenderized than that of Bromelain enzyme. Also, Bromelain is an enzyme that is known for its low activity which means that the enzyme can be easily denatured.Proving that Papain's effiecieny as a protease protein.

Summary Statement

Our project is analyzing two enzymes by the name Papain and Bromelain and proving which enzyme at different concentrations could tenderize Bos Prigmitus at a rapid pace.

Help Received

AP Biology instructor helped with some equipment including clampers, graduated cylinder, and a stand

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Charley Bi; Austin Chang; Cooper Ge

Project Number

S0506

Project Title

How Bacterially Secreted Intrinsic Factor Affects Vitamin B12 Transfer

Abstract

Objectives/Goals

To test the effectiveness of recombinant gastric intrinsic factor secreted by genetically modified E. Coli, compared to normal human gastric intrinsic factor, in the ability to transfer vitamin B12 across a Caco-2 cell membrane in a transwell setup.

Methods/Materials

Caco-2 cells, Corning (c) transwell inserts, genetically modified E. Coli K12, E. Coli K12, Vitamin B12, gastric intrinsic factor

Caco-2 cells were seeded into 24 transwell inserts and allowed to differentiate into a monolayer over 3 weeks. Then, a solution was introduced into the apical side of the insert for each testing group. Our negative control had neither E. Coli nor human gastric intrinsic factor (hgIF). Our positive control had no E. Coli and had hgIF. Our interference test had non-modified E. Coli with no hgIF. Finally, our experimental test group had our genetically modified E. Coli with no hgIF, but rather with recombinant gastric intrinsic factor. With four trials of each testing group, 30 minute timed cell-mediated transport of vitamin B12 from the apical side to the basolateral side of the insert was measured via ELISA and spectrophotometer.

Results

Plotting the samples, which were diluted 1:5 and 1:40, against the standard curve revealed that all the samples were below the limit of quantification.

Conclusions/Discussion

Because very little vitamin B12 was measured transferring through the cell monolayer, there is evidence to support the claim that our cell monolayer was healthy and effectively blocked passive diffusion of vitamin B12. In addition, if our Caco-2 cells were indeed healthy, there is evidence to support the claim that intestinal cells can remain healthy even in environments with bacteria or genetically modified bacteria.

Summary Statement

Our experiment tested whether or not bacterially produced gastric intrinsic factor would be an effective replacement for human gastric intrinsic factor that is missing from patients with pernicious anemia.

Help Received

Dr. Huff taught us proper lab technique and oversaw the purchase of equipment as well as the thawing, passaging, and seeding of the Caco-2 cells. Valley Christian High School allowed us to use the school's lab equipment and also assisted with funding the project.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Ruoxi Michelle Chen

Project Number

S0507

Project Title

Mathematical Models of the Growth of Stem Cell Driven Cell Clusters

Abstract

Objectives/Goals

To investigate the effectiveness of controlling cell cluster growth using feedback in stochastic and spatially heterogeneous environments

Methods/Materials

I created a cell lineage model using the Cellular Potts Framework (CPM) to simulate the dynamics of cell clusters where stem cells undergo negative feedback regulation from non-stem cells. The results of this model were compared with those of Mean Field Models (MFM), which unlike the CPM do not consider spatial variation and stochastic effects and are governed by a system of coupled ordinary differential equations.

Results

In contrast to MFM predictions, I discovered that in the spatial and stochastic setting, negative feedback is not always sufficient to regulate the growth of cell clusters. Given any level of feedback regulation, MFM always predict growth of clusters to a predictable size and distribution. I do find that for a range of non-stem cell death rates, negative feedback is sufficient in growth control. However, when death rates are small or large, the effects of stochasticity and spatial heterogeneity become important, and negative feedback is unable to control cluster growth.

Conclusions/Discussion

I found that classical forms of negative feedback proposed as robust control for tissue growth may not work well in stochastic and spatially heterogeneous systems. Counterintuitively, agenesis occurs when death rates are small, while uncontrolled growth occurs for large death rates. Both these extremes are highly relevant biologically. During the early stages of the developing tissue growth, death rates are expected to be small--an expectation that is confirmed in experiments. Thus, our model predicts that development requires additional feedback to prevent agenesis. At the later stages of development where tissues reach homeostasis, cell birth should balance cell death. In highly renewing tissues, such as epithelial tissues (e.g., colon, breast, lung, etc), the birth and death rates are expected to be high, which is also confirmed in experiments. Thus, our model predicts that homeostasis requires additional feedback to prevent cancer formation. Further studies are needed to identify the mechanisms by which growth control of tissues in realistic environments can be achieved, such as positive feedback factors as well as feedback through tissue stress via mechanotransduction, both of which are known play a role in both development and homeostasis.

Summary Statement

I found that negative feedback regulation on stem cells is not sufficient to provide robust control of cell numbers, distributions and tissue sizes during tissue development and homeostasis in spatially heterogeneous and stochastic systems.

Help Received

Professor John Lowengrub supervised the development of this project and provided useful discussions. Professor Maciej Swat provided technical support with the CompuCell3D framework for the Cellular Potts Model.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Min Jean Cho

Project Number

S0508

Project Title

Identification of Pathogen and Anti-Ebola Drug Targets Using Bayes' Theorem and Information Entropy

Abstract

Objectives/Goals

The objective is to predict anti-Ebola virus drug targets and to design RNAi-based small RNA drugs and mimotope-based peptide vaccines.

Methods/Materials

A total of 262 RNA/protein sequences of Ebola virus RNA-dependent RNA polymerase (RdRp) and glycoprotein (GP) were downloaded from the public database of viral pathogens (ViPR database). Conserved sequence region was searched using information entropy because this low information region could indicate highly conserved region across all known strains of Ebola virus. For antisense miRNA drugs, binding strength of antisense miRNA to its complementary target sequence was determined from GC% of predicted miRNA sequence. For the effective binding of anti-Ebola ligand and anti-Ebola antibody, its target region (ligand-binding site or epitope for antibody binding) should be located at the surface of Ebola viral proteins, thus the hydrophobicity of protein regions was determined according to the method of Kyte and Doolittle.

Results

Anti-Ebola drug targets were identified from the genome sequences of Ebola virus using information entropy. A total of 15 anti-Ebola miRNA targets were identified from three low entropy regions of Ebola virus RdRp RNA sequences, and three miRNA drugs were designed. Also, among highly conserved regions of RdRp protein sequences, one region was identified as a candidate target for ligand-based drugs. For preventing Ebola infection, three mimotope-based peptide vaccines were designed from the protein sequences of Ebola virus glycoprotein. The target sites of these anti-Ebola peptide vaccines were conserved in all known subtypes of Ebola virus and was predicted to be surface-exposed regions.

Conclusions/Discussion

Along with Bayesian sequence identification method, the entropy-based method for predicting drug targets and designing miRNA drugs and peptide vaccines will be a valuable tool for improving public health and for developing effective drugs against life-threatening pathogens such as Ebola virus.

Summary Statement

I used Information Entropy to design anti-Ebola miRNA drugs and mimotope-based vaccines, and to predict ligand binding sites.

Help Received

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Parsa Derakhshan

Project Number

S0509

Project Title

Examining the Role of CXCR4 on the Differential Migration of ESC-Derived Neural Stem Cells

Abstract

Objectives/Goals

The ultimate goal was to modify the ENStems for higher migratory capabilities, in turn making them more viable candidates for future methods of treatment for neurodegenerative diseases such as Alzheimer's and Parkinson's. For this purpose, much effort was devoted to investigate the impact of chemokine-receptor 4 "CXCR4" on the migratory capacities of ENStems when in contact with its ligand SDF-1a, and how CXCR4 levels differ between different generations of ENStems.

Methods/Materials

Methods: Trans-well Migration Assay: 50-100k cells were seeded to the top of trans-well plate filters and respective solutions were poured in specific areas in the wells. Cells were incubated, fixed, and stained, and visualized in a bright field microscope.

Brains: Inject ENStems into striatum of the mouse brain. After respective amount of time, take out brain place it into sucrose for dehydration. Then cut it at 40 microns. Analyze slices under fluorescence microscope. (NOTE! Student was not permitted to carry out culture or come into contact with live tissue. Student only worked with the fixed cells in the trans-well migration assay and only analyzed images obtained from confocal fluorescent microscope for in vivo assay.)

Materials: ENStems (CXCR4 overexpressed and normal), Trans-well dishes with polycarbonate filters, Microscope mounted camera, Cotton swab, Aspirator, PBS, NaN3, Basal medium.

Results

For the trans-well migration assays, P5 CXCR4 ENStems migrated successfully through the filter while P9 CXC4 and normal ENStems did not. For comprehensive measures, Western Blots were run for CXCR4 content analysis, and P5 ENStems had significantly higher levels of not only CXCR4 but also DCX, which is a microtubular transport protein for the cell. For the in vivo analysis, P5 CXCR4 ENStems were not only able to successfully survive but also to migrate and differentiate into neuronal cells.

Conclusions/Discussion

From the trans-well migration assays, I concluded that P5 CXCR4 ENStems have higher migratory capacities than their P9 and normal counterparts. Thus, from the Western Blot, due to lower levels of CXCR4 and DCX, gene silencing can thus be inferred. Finally, from the in vivo analysis, I concluded that P5 CXCR4 ENStems have the ability to migrate, survive, and differentiate, making them viable candidates for treatment of neurodegenerative diseases.

Summary Statement

The focus of the experiment was to find a way to modify ENStems so that they can migrate profusely throughout a diseased-brain environment.

Help Received

Unsafe laboratory protocols carried out by supervisor and assisting undergraduate student; used laboratory equipment at University of California, Irvine under the supervision of Dr. Mathew Blurton-Jones

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Durga Ganesh

Project Number

S0510

Project Title

Identification of NUSAP1 as a Novel Therapeutic Target for Aggressive Prostate Cancer

Abstract

Objectives/Goals

One in 7 men are diagnosed with prostate cancer, and there is currently no viable treatment for aggressive, recurrent prostate cancer. Thus, there is a need to identify novel therapeutic targets for aggressive prostate cancer post radical prostatectomy. NUSAP1 has recently been identified as a biomarker for aggressive prostate cancer. I hypothesized that NUSAP1 overexpression would promote cancerous behavior by increasing cancer cell proliferation as NUSAP1 is involved with mitosis.

Methods/Materials

I evaluated cell invasion, migration, proliferation, and morphology in androgen sensitive and insensitive cell lines. The phenotypic behavior of 22RV1 (androgen sensitive) and DU145 (androgen insensitive) human prostate cancer cells was explored in tissue culture. RNA extraction, cDNA synthesis, and RT-qPCR were performed to verify the knockdown and overexpression of NUSAP1. Cell invasion, migration, and proliferation assays were performed and optimized per cell variant. Cell morphology was characterized qualitatively. Statistical significance was determined through hypothesis testing.

Results

NUSAP1 overexpression was stably supported by androgen insensitive cells. NUSAP1 overexpression induced a two fold increase in the invasion and a four fold increase in the migration of androgen insensitive cells. Cell proliferation and morphology remained unaffected in both cell lines.

Conclusions/Discussion

NUSAP1 appears to regulate the phenotypic expression of androgen insensitive prostate cancer. As NUSAP1 knockdown resulted in rapid cell death for both cell lines, NUSAP1 is a novel therapeutic target for aggressive prostate cancer. After clinical and in vivo evaluation of the effect of NUSAP1 overexpression, the development of a drug for targeted interference of NUSAP1 expression in prostate cancer cells may be commenced. In conjunction with cancer immunotherapies, this may present a novel therapy for aggressive prostate cancer.

Summary Statement

The evaluation of cell invasion, migration, proliferation, and morphology in androgen sensitive and insensitive cell lines to identify NUSAP1 as a novel therapeutic target for aggressive prostate cancer.

Help Received

I am grateful to Dr. James Brooks and Dr. Catherine Gordon from the Department of Urology, Stanford University for mentoring and providing laboratory resources.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Paul Gauvreau

Project Number

S0511

Project Title

Artificially Formed Stable Interactions through Gene Transfection

Abstract

Objectives/Goals

Stable interactions between kidney cells allow them to adhere to each other. Kidney cell adhesions allow functional control of each other. The objective of the experiment is to cause stable interactions between two different kidney cell strains. This is significant as different kidney cell strains do not normally interact. More specifically, this experiment tested, that if plasmids containing the e-cadherin/firefly luciferase protein being transfected into hk-2 and hek-293 cells cause stable interactions or not.

Methods/Materials

The two different cell strains HK-2 and HEK-293 were cultured out separately. Then were passaged into a 24 well, 12 wells designated for each strain. In half of the wells we transfected the cell strains with the plasmid, and in other half we determined at which concentration of ampicillian stopped cell growth. After transfection the cell strains were grown out together in amp. The amp. killed all the cells with out the plasmid.

Results

The plasmid caused the two different cell strains to adhere to one another, biolumines, and continue to grow out in the ampicillin.

Conclusions/Discussion

When looking at the two experiments, the control (without e-cadherin plasmid) when mixing the two strains together the cells grew out separately and did not interact. However in our experimental (with the e-cadherin plasmid) the two different strain adhered to one another. The data supported my alternate hypothesis, that different kidney cell strains with the transfected e-cadherin plasmids will form stable interactions and adhere to each other.

Summary Statement

Developing a method in which to artificially form stable interactions to provide an alternate step towards 3D printing organs.

Help Received

My teacher/mentor Mr. Ariel Hass taught me how to work and operate in a lab and Mr. Martin Haas gave me advice towards what materials to use and corrections to make.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Priyansh Gupta

Project Number

S0512

Project Title

Investigating the Role of Antioxidants in the Prevention of Skin Cancer Using Saccharomyces cerevisiae

Abstract

Objectives/Goals

The objective of this research project was to find out how effective antioxidant protection is against skin cancer and to also find out the antioxidant that best helps prevent the harsh UV damage experienced from the sun.

Methods/Materials

To complete this research project, Saccharomyces Cerevisiae cells were incubated in rich YPD media for a four hour period and were then subject to various tests using a cellometer and a spectrophotometer. Dose response and time response experiments were completed to determine the amount of antioxidants (Ascorbic Acid, Vitamin E, and Zinc Oxide) that should be added to the Saccharomyces Cerevisiae cells' growth culture, and to find out exposure time under UV light. Antioxidants and various combinations of the antioxidants were then dissolved into the yeast culture, and were then exposed to the UV light. Cellometer slides were prepared, and using the cellometer and Trypan Blue (0.4% concentration), cell number was counted (dead and alive). Viability rates were then calculated.

Results

All the antioxidants and combinations produced significantly higher viability rates than the control group (45.53% average viability rate). Ascorbic Acid and Zinc Oxide (75.27% average viability rate) together showed the largest viability rates of all of the antioxidants, whereas Vitamin E (49.37% average viability rate) provided the least protection from the UV rays.

Conclusions/Discussion

The experiment performed proved my hypothesis right and wrong. I had correctly hypothesized that all antioxidants would help reduce UV damage, but had incorrectly hypothesized that Zinc Oxide by itself would produce the highest viability rates. Vitamin E had many adverse effects in UV protection, as it produced the lowest viability rates, while Zinc Oxide greatly helped prevent UV damage.

Summary Statement

I investigated how effective various antioxidants are in the prevention of skin cancer.

Help Received

The research was done in a school laboratory under the supervision of Dr. Malhotra; parents helped buy various supplies and drive to necessary locations.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Stephanie M. Hu

Project Number

S0513

Project Title

A Computer-Based Integrated Analysis of Genomic Signatures in Ovarian Cancer

Abstract

Objectives/Goals

Ovarian cancer is one of the deadliest gynecological cancers due to a lack of early detection methods and high rates of resistance to chemotherapy. As a result, the overall purpose of this project was to examine processes that may mediate the development of cancer. The objectives consisted of three main components: 1) to discover and analyze signatures for various types of genomic and epigenomic data, 2) to identify biological pathways that are altered in ovarian cancer based on these signatures, and 3) to utilize these signatures and other multidimensional genomic data in integrative analyses to determine possible mechanisms of aberrant gene expression in ovarian cancer.

Methods/Materials

Using data from The Cancer Genome Atlas and R programming language, the predictive potential of genomic signatures for abnormal mRNA expression, miRNA expression, and DNA methylation were determined and cross-validated. Pathway enrichment analysis was then performed on these signatures using an algorithm based on a hypergeometric function distribution. Finally, the signatures were utilized in conjunction with data collected from cBioPortal, DAVID, and published studies, as well as a number of statistical tests and algorithms implemented in R, to propose mechanisms of aberrant gene expression in ovarian cancer.

Results

Six robust genomic signatures that differentiate between tumor and normal ovarian tissue samples were generated and used in integrated analyses of ovarian cancer. Furthermore, six smaller signatures were discovered that could be used as diagnostic tools for this disease, each yielding a predictive accuracy of 90% or greater. The results also produced multiple pathways altered in this disease, in particular cell cycle-related pathways and FOXM1 signaling, and determined many processes, notably aberrant expression of miRNAs and transcription factors, that may contribute to abnormal gene expression.

Conclusions/Discussion

Various features have been proposed that could serve as diagnostic biomarkers in ovarian cancer. Moreover, the data from the integrated analyses provide important information on pathways and gene expression regulatory mechanisms in ovarian cancer that can further our understanding of the carcinogenesis process. Although the results presented here still remain to be experimentally validated, these results nevertheless hold important implications in diagnostic and therapeutic applications.

Summary Statement

Using online data and bioinformatics tools, genomic signatures were identified and used in integrated analyses to determine predictive features, altered pathways, and biological mechanisms causing aberrant gene expression in ovarian cancer.

Help Received

My mother offered advice for my project and edited my writing and my sister helped with the layout of my board.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)
Maya Jayanth

Project Number
S0514

Project Title
Development of New Primers and TaqMan(R) Probes for the Detection of Grapevine Viruses

Abstract

Objectives/Goals
To develop primers for Red Blotch Associated Virus, and to run extractions under the same conditions and same methods

Methods/Materials
i.Designing and ordering the primers
1.With this newfound region, design primers and probes using the program Primer Express 3.0.1.
2.Order the primers and probes.
ii.Collect grape shoot samples and extract DNA and RNA
1.Visit the vineyard and collect samples. a.Plant 1: Red blotch associated virus and Grapevine leafroll associated virus 1 and 3. b.Plant 2: Grapevine leafroll associated virus 1 and 3. c.Plant 3: Grapevine leafroll associated virus 1 and 3.
iii.Extract the DNA and RNA
1.DNeasy Extraction kit. 2.RNeasy Extraction kit
iv.Running qPCR
1.Apply the DNA samples to a master mix containing primers and probe. 2.Using this master mix set up for the 96-well fast PCR on the QuantStudio Dx Real-Time PCR Instrument.
v.Running Digital PCR
vi.Analyze
vii.Conclusion

Results
Each CT value for the red blotch virus (RB) and the leaf roll virus 1 (LR1) ranged between 21- 25% meaning the virus had infected said percentage to that percent. Ct is the cycle at which the fluorescence within a sample crosses a certain threshold point. Samples that cross the threshold first have a higher concentration of virus. The threshold is determined by where the amplification plot lines are most parallel to each other.
All the standard deviations were ranging between 0.4 and 0.6 allowing the conclusion that the tests worked and provided accurate data. The standard deviation is a measure that is used to quantify the amount of variation or dispersion of a set of data values.

Conclusions/Discussion
The project focuses around finding a faster way to examine plants and diagnose them for a given virus. With thorough research and experimentation I can conclude that a great amount of farmers will willingly

Summary Statement
My project is about finding a fast and cost-manageable method to detect DNA and RNA based viruses under the same conditions.

Help Received
Dr. Mysore Sudarshan helped provied facilities and opporutnity to learn under his expertise at the UC Davis Plant Pathology Lab. Trent Lawler mentored and guided me in learning how to run tests.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Nivedita Kanrar

Project Number

S0515

Project Title

Testing for Predicted Transposable Elements in Citrus sinensis and C. clementina

Abstract

Objectives/Goals

The goal of this project is to characterize DNA transposable elements (TEs) of the citrus species Citrus sinensis and C. clementina. TEs are noncoding segments of DNA, popularly known as #jumping genes,# capable of moving from one location in the genome to another. They have been shown to play a major role in gene regulation of various species. They may hamper the ability of critical genes or play a major role in citrus diseases, some of which are substantially overwhelming the citrus industry. The main objective of this project is to isolate and functionally characterize a TE in citrus.

Methods/Materials

Various methods were used to predict and isolate this TE. First, analysis of the genome sequence of C. sinensis was performed using bioinformatics. Primers were designed for this predicted TE and PCR was conducted on genomic DNA from citrus varieties Nules, Cutter, and Olinda. The amplified TE was cloned into the Zero Blunt TOPO cloning vector. Afterwards, primers were designed for the transposase gene of the TE. The transposase was amplified using the TE clone and was cloned. Partial sequencing of this transposase has been completed and sequencing of the entire TE is in progress. Primers were designed for the mini-hAT of this TE, the sequences surrounding the transposase. The left mini-hAT of this TE has been successfully amplified and cloned. Another mini-element related to this TE was predicted using a bioinformatics program. Primers were designed for this TE and it was amplified from citrus genomic DNA and cloned.

Results

The existence of TEs in citrus has been validated. A TE has been isolated and cloned from C. sinensis. The transposase gene, left mini-hAT, and a related element to this TE have been cloned. Partial sequencing of this transposase has been completed and sequencing of the entire TE is in process.

Conclusions/Discussion

The presence of two predicted TEs in citrus has been verified. Due to the major effects of TEs in gene regulation, their presence in citrus has broad implications for citrus genetics. Their activity and location in the citrus genome, which can be determined by later analyses, may play a role in citrus diseases and influence the functions and abilities of genes. To analyze the activity of citrus TEs, a yeast assay will be used to study the transposition of both TEs with the isolated transposase.

Summary Statement

Testing for the presence and activity of transposable elements in citrus species by a molecular and biochemical approach.

Help Received

I was allowed to conduct research at the Neil A. Campbell Science Learning Laboratory in UCRiverside with the permission of Dr. Susan Wessler, Distinguished Professor of Genetics. Dr. James M. Burnette has been my mentor for this project. Mr. Alejandro Cortex has also assisted me in data analysis.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Emily A. Kim

Project Number

S0516

Project Title

Electrophysiology-Based Screen to Discover Genes Involved in Synaptic Homeostasis

Abstract

Objectives/Goals

Homeostatic feedback systems are omnipresent forms of biological regulation which play crucial roles in the development of the nervous system, regulation of synaptic strength, and the establishment of the proper balance of excitation and inhibition. Dysfunction in these systems may contribute to the onset of neurological diseases such as schizophrenia, autism, epilepsy, and other complex neurological diseases. This experiment is intended to identify genes which are involved in the maintenance of the stability of neural function in regards to synaptic plasticity.

Methods/Materials

Seven different mutated Drosophila stocks were crossed against a T15 cross which knocked down the targeted genes and a C15 cross, the control. The resulting 3rd instar larvae were dissected to reveal the neuromuscular junction. Electrophysiology was performed to gather mEJP (miniature excitatory junction potentials) and EJP (excitatory junction potentials) values. If a gene appeared to have a role in homeostatic plasticity, imaging was also conducted to see if there were any morphological changes. The NMJ of the larvae was dissected and was fixed in fixative, PFA, and then stained with primary and secondary antibodies. A confocal microscope was used to take pictures of the synapses of the larvae.

Results

Results showed that one of the seven tested genes, unc104, may potentially be involved in homeostatic plasticity as the average size of the mEJP and EJP values when unc104 was knocked down were significantly smaller than in the larva expressing the gene. Imaging revealed that knocked-down unc104 resulted in postsynaptic densities defects.

Conclusions/Discussion

This experiment proved my hypothesis that if a gene is essential in synaptic homeostasis, then there will be no compensation for the synaptic challenge to restore proper physiological excitation as a retrograde signal will not be sent from the post synaptic neuron to the presynaptic neuron to release more vesicles. A future experiment could be to overexpress the genes and observe the effects on homeostatic plasticity.

Summary Statement

This project uses the D. melanogaster neuromuscular junction as a model to discover genes involved in synaptic plasticity by using electrophysiology.

Help Received

Received help from Dr. Dion Dickman and Koto Kikuma.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Cody L. Lim

Project Number

S0517

Project Title

Optimizing Viral Vectors for Site-Specific Gene Therapy in Hematopoietic Stem Cells

Abstract

Objectives/Goals

Gene therapy in hematopoietic stem cells (HSC) is a powerful potential treatment for hematologic diseases such as sickle-cell anemia. Changes are retained throughout differentiation. Previous treatments in HSC added genes randomly throughout the genome, possibly disrupting/activating oncogenes. This could be ameliorated through using a site-specific nuclease (i.e. zinc finger nuclease, or ZFN) to cause a break at a predetermined site. Genomic repair mechanisms can be hijacked by adding a repair template to correct/replace a gene. Adeno-associated viral vectors (AAV) are an efficient way to provide the repair template, capable of inserting/repairing genes at frequencies over 20%. Though AAV-ZFN treatments are efficient for site-specific gene therapy, there is some toxicity associated with this, which I aimed to reduce through improving AAV efficiency.

Methods/Materials

I took two approaches to modifying AAV: 1) improving the suitability of the template by converting the normally single-stranded DNA genome (ssAAV) to a compact, self-compliment, double-stranded (scAAV) form; and 2) modifying the viral capsid to avoid cellular detection and disposal. For both methods, HSC were treated in vitro with various forms of AAV, then electroporated with ZFN RNA, and allowed to incubate for 96 hours. To compare the efficiency of ssAAV and scAAV, DNA was extracted, and gene addition efficiency was measured through RFLP assays. To test the capsid mutants, GFP expression in HSC was measured by flow cytometry and compared to the efficiency of wild-type AAV capsid.

Results

Results show that scAAV is actually less efficient than ssAAV, meaning that changing the genome did not improve efficiency. The capsid mutant experiments are currently underway.

Conclusions/Discussion

There are two main possibilities as to why ssAAV is more efficient than scAAV in gene addition: 1) the ssAAV genome contatemerizes greatly during vector genome replication; or 2) the ss configuration of template DNA is more conducive to cellular DNA repair mechanisms.

Summary Statement

A single-stranded configuration of AAV is more efficient than a self-compliment configuration for gene addition in HSC.

Help Received

I used lab equipment at the Keck School of Medicine at USC under the supervision of Dr. Paula Cannon and Dr. Colin Exline.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Vincent Lok

Project Number

S0518

Project Title

DNA Damage Induced by a Novel Drug Cocktail Regulates Chemokine Production in Leukemia through Cytosolic DNA Sensing

Abstract

Objectives/Goals

This project seeks to elucidate a second possible mechanism of tumor death by treatment with a novel chemotherapy cocktail (3-AP, DI-82, and VE-822). This drug combination induces DNA permanent damage in tumor cells by targeting cells' nucleotide metabolism pathway (3-AP inhibits ribonucleotide reductase, DI-82 inhibits deoxycytidine kinase) and DNA repair pathway (VE-822 inhibits ATR). In addition to tumor death by apoptosis, this DNA damage can lead to cytosolic DNA leakage and sensing, prompting the secretion of immunostimulatory proteins, causing the infiltration of immune cells into the tumor node and inducing the tumor to undergo an immune-mediated cell death. This project seeks to establish a correlation between this cocktail treatment and chemokine production, suggesting a potential heightened immune response.

Methods/Materials

A cell culture was used as an in vitro model to directly measure chemokine production after treatment. A xenograft of these tumor cells into mice with subsequent treatment accounted for a functioning immune system on the regulation of the chemokines. For the cell culture, precursor B-ALL (Acute Lymphoblastic Leukemia p 185) were grown in media with a drug concentration of 500 nM 3-AP, 100 nM VE-822 for 4 days.

For the xenograft, 200,000 pre B-ALL cells were injected into mice via tail vein. Mice in the cancer group were orally given 50 mg/kg DI-82 daily, 40 mg/kg VE-822 daily, and 7.5 mg/kg 3-AP twice a day. Chemokine levels in blood samples and cell culture supernatent were analyzed using the Multi-Analyte ELISArray (Qiagen) according to the protocol provided with the kit.

Results

12 chemokine levels were examined. In vitro the chemokine levels of RANTES, MIP-1a, MIP-1B, SDF-1, MIG, Eotaxin, and KC increased. The in vivo model showed an increase in MCP-1 and IP-10, and a reduction in MIG, MDC, KC, and 6CKine.

Conclusions/Discussion

There is a direct correlation between chemokine production (RANTES, MIP-1a, MIP-1B, SDF-1, MIG, EOTAXIN, KC) and drug treatment, suggesting a secondary mechanism to this drug cocktail: an immune-mediated tumor death mechanism.

Summary Statement

This project investigates the possible immunostimulatory effect of this novel drug combination on chemokine production in treated ALL cells and treated mice xenografted with ALL cells.

Help Received

Dr. Caius Radu and Dr. Soumya Poddar from Ahmanson Translational Imaging Division at UCLA provided samples and lab facilities. Dr. Malhotra from Thousand Oaks High School, thank you for scientific enlightenment.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)
Edward Park

Project Number
S0520

Project Title
Hybrid Biosensor Capable of Early Diagnosing and Rapidly Monitoring Breast Cancer

Abstract

Objectives/Goals
I plan to develop an enzyme free hybrid biosensor with ODI-CL detection using HRP-mimicking DNAzyme for the early diagnosis of breast cancer.

Methods/Materials
Hemin and bovine serum albumin were purchased from Sigma Aldrich.

Bis (2,4,6-trichlorophenyl) oxalate (TCPO) and 4-methylimidazole (4MImH) were purchased from TCI America. 3 and 30 %

H2O2 were purchased from VWR. Amplex Red was purchased from Cayman Chemical.

Deionized H2O, Ethyl acetate, and Iospropyl alcohol were purchased from EMD.

CEA diagnostic kit for ELISA and 0 calibrator were purchased from Monobind, Inc.

CEA antigen (25 μg) was purchasedfrom Lee Biosolutions.

8-well EIA/RIA strip-well plate was purchased from Costar.

Results
The hybrid biosensor with ODI-CL detection can beapplied as a new tool for the diagnosis of breast cancer.
It is possible to develop hybrid biosensors capable of diagnosing various human diseases such as cancer and infectious diseases, as well as monitoring toxic materials in food and drink.

Conclusions/Discussion
The hybrid biosensor with ODI-CL detection can beapplied as a new tool for the diagnosis of breast cancer.
It is possible to develop hybrid biosensors capable of diagnosing various human diseases such as cancer and infectious diseases, as well as monitoring toxic materials in food and drink.

Development of hybrid biosensor capable of early diagnosing other cancers such as prostate cancer, ovarian cancer, and lung cancer

Summary Statement
My project is about a novel and cost-effective method of diagnosing breast cancer early, so that the patient has a higher rate of survival.

Help Received
Used the equipment provided by Lumi MD under the supervision of Dr. Ji Hoon Lee.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Jayani R.T. Ratnam

Project Number

S0521

Project Title

Effective Targeted Therapy for Non-Small Cell Lung Cancer using EGFR Tyrosine Kinase Inhibitors Based on the Mutation ty

Abstract

Objectives/Goals

To enhance the treatment of patients with Non-small cell lung cancer (NSCLC) by finding out how and why individuals respond differently to varying inhibitors based on their mutation type and location in the EGFR tyrosine kinase domain, and generate a more effective way to prescribe medications to patients in order to present them with the best treatment plan possible. To study the differences between each mutation, and each tyrosine kinase inhibitor (TKI). Find the molecular formula and other information about each inhibitor. Find amino acid, nucleotide, and property changes for each mutation.

Methods/Materials

Data was collected and analyzed from many data warehouses, and studies. BioMart, and I-TASSER were used to sort the mutations by type and location, and to study the baseline EGFR domains/exons in depth. A program was written in R to compute the mean values of response for various TKIs.

Results

The two most common mutations, L858R and exon 19-deletions account for 90% of EGFR mutated NSCLC. Based on the analysis, it was concluded that for patients with an exon 19-deletion or L858R mutations the best treatment option is erlotinib with 73% average response rate. Another important mutation is T790M-mutation, which is also known as an acquired mutation because it appears in more than 50% of patients after they get treated with certain TKIs. The T790M-mutation behaves differently from most mutations, the amino acid threonine is replaced by methionine, which affects the binding capability of many TKIs. However, AZD9291 and CO-1686 have irreversible binding capabilities, and hence prove to be the best treatment options for T790M-mutations, with average response rates of 64% and 58% respectively.

Conclusions/Discussion

It was concluded that if cancer patients with EGFR tyrosine kinase mutations were treated with EGFR TKIs based on the mutation pattern then EGFR TKIs will be more effective. This is because each mutation is caused by an amino acid change, changing one or more properties of the protein being made. Each property change results in a different chemical structure change of some part of the protein. Each drug has a specific chemical structure, and because of this, they will bind differently to the EGFR protein, either successfully inhibiting the EGFR or not. This means that patients with a NSCLC EGFR tyrosine kinase mutation will have a clear plan on how to continue their treatment.

Summary Statement

Finding optimal treatment for non-small cell lung cancer patients based on their mutation type and location.

Help Received

Professor Gazdar and Wakelee answered a few questions I had on this topic.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Swetha Revanur

Project Number

S0522

Project Title

Enabling Precision Medicine with Big Data: A Cross-Platform Framework to Characterize Gene Presence and Function

Abstract

Objectives/Goals

The current design of gene expression studies makes data sets susceptible to bias and hinders cross-platform comparison. To address these issues, an unprecedented global-scale meta-analysis of gene expression distributions was conducted.

Methods/Materials

All microarray data (1,350,000 samples from 14,000 platforms) were downloaded from Gene Expression Omnibus onto a high-performance computing cluster and normalized. My project has two phases: (1) development of a robust gene detection call algorithm and (2) extrapolating gene function from statistical features. Detection calls (indicating gene presence) are necessary to gain a concrete understanding of a gene's behavior. However, existing software has limited platform support. In Phase 1, I proposed and developed a detection call algorithm that is extensible across all platforms and species. Unsupervised machine learning with Gaussian Mixture Models (GMMs) was leveraged to dynamically determine gene-specific thresholds for on-expression. In Phase 2, essential and immune genes were predicted based on GMM characteristics. Gene functions were verified using Gene Ontology enrichment analysis (enrichment score > 1.0), pathway over-representation analysis ($p = 0.01$), and existing databases such as Database of Essential Genes and NIH ImmPort.

Results

Of the 70686 probes (from 15 tumor samples) marked Present in published calls, the proposed detection call algorithm successfully identified 68449, achieving a remarkable 97% accuracy. In Phase 2, GMM feature extraction proved to be a successful predictive model for essential and immune genes. This workflow identified 83 potential essential genes and 6449 immunology-related genes across 5 platforms.

Conclusions/Discussion

My work represents the first comprehensive framework for characterizing gene presence and function from several gene expression platforms. Detection calls can now be used to filter RNAi assays, assign clinical phenotypes to unknown samples, and define patient subgroups for personalized treatment. Furthermore, essential and immune gene prediction enables systematic drug target and biomarker identification. Ultimately, this project revolutionizes the framework for analyzing gene expression big data, and has implications in both research and clinical medicine.

Summary Statement

As part of an unprecedented gene expression analysis, I developed a machine learning algorithm to determine gene presence, and constructed novel computational workflows to predict essential and immunology-related genes.

Help Received

Drs. Bhaskar Dutta and Iain Fraser (National Institutes of Health) for guidance and summer internship

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)
Alap A. Sahoo

Project Number
S0524

Project Title
Adaptations to Restriction Enzymes in Various Bacteriophage Genomes

Abstract

Objectives/Goals
My project aimed to determine if various bacteriophages had adapted their genomes to avoid restriction enzymes commonly produced by their hosts. Restriction enzymes are used by bacteria as an immune system to combat viruses. They operate by splicing phage genomes based on the location of predetermined sequences of DNA, called restriction sites. My project studied the frequency of restriction sites on various phage genomes to determine if phages had evolved to avoid restriction.

Methods/Materials
I assembled a large set of restriction enzymes and bacteriophage genomes using data gathered from the NCBI database. I wrote a program in R to determine the number of restriction sites on each phage that would be generated by an enzyme derived from the phage#s host. I also calculated the expected number of restriction sites given a random distribution of DNA bases, and compared the actual and expected values using standard statistical methods.

Results
I found that the vast majority of the phages genomes had significantly lower actual restriction site counts than expected restriction site counts for many of the restriction enzymes derived from their hosts, and that several hosts tended to have phages that exhibited this correlation for all most all of the native restriction enzymes.

Conclusions/Discussion
My results indicated that many bacteriophages had evolved to avoid splicing by host-produced restriction enzymes, and that in particular, phages that attacked specific genii had evolved these properties to a larger degree. Further research would focus on studying the exact relationship between these adapted phages and their hosts.

Summary Statement
My project aimed to determine if bacteriophages had evolved genomes resistant to restriction enzymes.

Help Received
My father helped me construct my board.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Japmeet Sandhu; Ashima Thusu

Project Number

S0525

Project Title

Role of Taste Receptor Gene TAS2R38 and Fat Sensor Protein CD36 in Supertasting Ability and Childhood Obesity

Abstract

Objectives/Goals

Our primary goal is determine if tasting ability is correlated to obesity in terms of our genetic makeup. Last year we found that nontasters had higher amounts of leptin and higher BMI#s. This year we are investigating deeper into how genetics play a role in the predisposition of tasting and obesity.

Methods/Materials

A group of 50 children, aged 6-18 years, signed an ethics committee approved informed consent with assent from their parents to participate in the study.
Study included completion of questionnaire, medical examination, anthropometric measurements. Anthropometric measurements included weight, height. All instruments were validated and standard procedures were followed for collecting data. Analysis of both parametric and non-parametric data will be adopted to address the objectives of the study using statistical software Sigma plot where appropriate. The intensity of taste perception was measured directly by Phenylthiourea (PTC strips-Precision Laboratories FL). Cognitive eating behaviors were evaluated using study designed questionnaires.

Results

Associations of various SNP loci with obesity and tasting ability in children:
Associations were determined by measuring the significant odd ratios (OR) which were observed between three out of the four tasting ability related genes with obesity related genes.
Four out of five BMI associated genes showed significant relationship with obesity.
The strongest association with obesity was found with FTO and CD36 SNPs (at 3.45 OR).
The associations, although showing a trend, are not statistically significant due to the smaller data set.

Conclusions/Discussion

This is the first time reporting allele frequency for rs713598, rs17817964, rs1558902 in the subjects of the Mexican ancestry (MEX; source SNPedia). We have identified five out of the eleven SNPs that would need further investigation to link the BMI associated SNPs to obesity. Significant associations were observed between tasting ability and tasting ability related genes: rs10246939, rs1726866, and BMI associated SNPs and obesity: rs713598, rs3211908, rs17817964, rs9939609, rs1558902.

Summary Statement

We set out to establish a genetic link of tasting ability and obesity.

Help Received

Used lab equipment at Universal Biopharma Research Institute Inc. under the supervision of Dr. Amardeep Khushoo

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Anin Sayana

Project Number

S0526

Project Title

Novel Design and Optimization of an EGFRvIII-based Cancer Peptide Vaccine

Abstract

Objectives/Goals

Cancer vaccines are a revolutionary field of cancer therapeutics that aim to utilize the body's natural defenses to treat cancer. Traditional chemotherapy strategies focus on targeting malignant cells directly, either by damaging DNA or otherwise inducing apoptosis. However, an alternative approach to this methodology is a peptide vaccine that stimulates an immune response. Through my research, I was able to design and optimize an effective anti-cancer vaccine based on the existing EGFRvIII vaccine by computationally and experimentally evaluating optimal proteasome processing, MHC reception, and ultimately malignant cell death.

Methods/Materials

Mass Spectrometry (MS) was conducted on five separate variations of the LEEKKGNYVVTDHC (LEEK) peptide that were fed to the human proteasome. Normalization offset was calculated, and I used a (Screen Pixel)/Dalton ratio to normalize the data. Effective and ineffective peptides were compared with other effective and ineffective variations, respectively. Finally, I designed a Java-based algorithm to evaluate the MS data in order to validate graphical analysis.

Results

Based on mouse survival data obtained from previous research, variations A and B consistently performed poorly, with survival rates averaging less than 40%. Several trials of MS analysis I conducted with A and B revealed that beyond the parental peptide, the proteasome did not process the parental peptide significantly further. As demonstrated, around 2600 Daltons, the presence of a synthesis peptide greater than the original molecular weight for both variation A and variation B is almost non-existent. Variations C, D, and E performed significantly better than A and B, with survival rates in mice generally averaging above 50%. Several repetitions of MS demonstrated large amounts of the breakdown of the effective peptides above their original molecular weight, around 2600 Daltons.

Conclusions/Discussion

This vaccine complex, as validated computationally, biologically, and graphically, was prevalent in effective peptides, but not present in ineffective peptides. The cancer vaccine variations show improved survival data, which correlate with the production of the larger processed peptide. In summary, my research discovered the optimal EGFRvIII-based cancer vaccine for glioblastoma through characterizing its processing in the proteasome using the experiments and analysis methods I developed.

Summary Statement

Overall, I was able to successfully design and optimize an EGFRvIII-based cancer peptide vaccine using the methods I developed, which can potentially be used to improve the efficiency of any peptide vaccine.

Help Received

Worked under Dr. Albert Wong at Stanford University.

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Rebecca M. Sine

Project Number

S0527

Project Title

Allopregnanolone Site of Action for Promoting Regeneration of Human Neural Stem Cells: Uncovering the Paths

Abstract

Objectives/Goals

This project's overall objective is twofold: (1) to optimize the treatment of allopregnanolone/Allo (a neurosteroid proven to reduce Alzheimer's symptoms in mice) with human neural stem cells for the accurate detection of proliferation (as a transition from treatments with rat neural stem cells), and (2) to elucidate the GABAergic site of action required for Allo to have an optimal effect in the promotion of regeneration of human neural stem cells in the model of Alzheimer's disease (using structural analogues of Allo to target specific GABA subunit conformations). The main experimental parameters that have required optimization for human neural stem cells are growth factor concentration, incubation and treatment time, Allo concentration, and cell-seeding density.

Methods/Materials

MTS colormetric assays were used to quantify cell proliferation for experimental optimization, and western blot (which quantifies protein expression) and immunocytochemistry (which provides qualitative analysis of protein expression) were used for preliminary testing with Allo analogues.

Results

Optimization data shows that seeding human neural stem cells in a 96-well plate at a density of 10,000 cells per well, growing them for five days, starving them for 48 hours (which resets the cells' mitotic cycles), treating them with an Allo concentration of 50nM and a growth factor concentration of 100%, and allowing them to incubate with their given treatments results in an optimal and accurate detection of neurogenesis prompted and upregulated by Allo. Data regarding analogue efficacy is currently preliminary.

Conclusions/Discussion

My current goal now is to use the newly found experimental parameters to find the Allo analogue required to induce optimal neurogenesis, and perform genetic analysis to determine the GABA site of action conformation required for this effect. Knowing this will allow me know exactly which types of neurons that a particular analogue is targeting. It is also important to point out that Alzheimer's disease is not the only disease that can benefit from the optimization of Allo experimentation like this one; Allo plays a role in the treatment of epilepsy, depression, stress, and much more. Although optimization may not be the final solution endpoint, it definitely paves the way to get there.

Summary Statement

In my project, I have optimized the experimental parameters required for the treatment of human neural stem cells with allopregnanolone, a neurosteroid proven so far to reverse Alzheimer's symptoms in mice only, but not yet in humans.

Help Received

Used lab equipment at the University of Southern California under the supervision of Christine Solinsky

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Varun J. Venkatesh

Project Number

S0528

Project Title

HDX Mass Spectrometry Study to Identify a Key, New Thrombin-TM Complex Mechanism Used to Prevent Blood Clotting

Abstract

Objectives/Goals

Blood clotting plays a vital role in the functioning of the human body. One of the most important proteins involved in this pathway is thrombin. When activated, thrombin is able to initiate coagulation and promote clot formation. However, when it forms a complex with thrombomodulin (TM), its function changes drastically to an anticoagulant, halting the coagulation cascade and preventing further clotting. Researchers don't fully understand how exactly TM alters thrombin. My goal is to gain an understanding about this complex that can help to develop better anti-clotting drugs as well as solutions to many different thrombin-induced diseases.

Methods/Materials

HDX works through the concept that the isotope of hydrogen protium (one neutron) switches with deuterium (two neutrons) when in deuterium solution. This exchange gives us valuable information regarding the structure of the protein as well as on how it folds and interacts. We can gain this information by breaking up the protein into small peptides after it exchanges in the deuterium solution and running it through a mass spectrometer.

Results

When we compare our data to another dataset, we can see differences that we never would have been able to see with just looking at the crystal structure. I can observe that TM is changing the active site of thrombin because the amount of deuterium it takes up is changing once TM binds. When we look at the active site on thrombin (also the n-terminus) on a crystal structure, we see that it is already buried in thrombin. The HDX data I collected tells us something different from what scientists previously had understood in that there is a decrease in the amount of deuterium on the n-terminus that is taken up by thrombin when thrombomodulin binds.

Conclusions/Discussion

We know TM binds on the opposite side of thrombin from the active site. The data tells us that TM is altering thrombin through allosteric changes, or changes away from the binding site. When it changes the active site, TM is changing which molecules can bind to thrombin and therefore changing its function. The data specific to the n terminus tells us that the n-terminus is going from outward to inward and that the crystal structure fails to see this movement. This new information is extremely important because the burial of the n-terminus cause serine proteases to turn into their most catalytically active state.

Summary Statement

My project used hydrogen deuterium exchange mass spectrometry to identify the key mechanism that allows thrombomodulin to alter thrombin's function when they bind and prevent it from facilitating blood clotting.

Help Received

Worked at UCSD under the supervision of Dr. Elizabeth Komives

CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

Clare Zhu

Project Number

S0529

Project Title

Development of Feature-Based Receptor-Ligand Docking Using POVME

Abstract

Objectives/Goals

The objective of this work was to develop an efficient receptor-ligand docking method integrated into a binding pocket analysis tool (POVME) that can potentially be used to increase the rate of drug discovery. Two major goals include the generation of uniform rotations in 3-D space and the evaluation of the accuracy of the docking and scoring functions in determining the correct position of a ligand within a receptor.

Methods/Materials

A computer with access to the Binding Database (a public, web-accessible database of measured binding affinities, focusing chiefly on the interactions of proteins considered to be drug-targets with small, drug-like molecules) was used to write and test coloring, docking, and scoring functions. Functions were written in Python and C++. Visualizations were produced using VMD.

Results

When testing methods for generating uniform rotations, point-repulsion-generated points on a sphere had the lowest standard deviation between point distances. Testing of the docking and scoring functions showed that there existed a strong negative linear association between feature scores and distance from correct ligand binding position.

Conclusions/Discussion

The low standard deviation of distances between points generated by the point repulsion method helped to fulfill design goal #1, producing more uniform and regular rotations in 3-D space. In addition, due to the strong negative linear association between feature interaction score and distance from the correct ligand orientation position, there is moderate evidence supporting that design goal #2 has been met. Overall, results show that the docking function, in a naïve case, produces scores that increase as the distance from the true ligand conformation decreases. This data suggests that the docking and scoring functions have the potential to reliably select the true ligand conformations of any given receptor and ligand maps. These advances allow accurate docking and scoring to be implemented within POVME.

Summary Statement

This work introduced binding-pocket analysis-based receptor-ligand docking and optimized scoring functions in order to expedite future drug discovery.

Help Received

Participant in BioChemCoRe program at University of San Diego, California; continued research using lab equipment from the Amaro Lab under the supervision of Mr. Jeffrey R. Wagner.