

Siemens Competition

Math : Science : Technology

Regional Finalist

Names: Emily Sun & Jessica Mo

High Schools: Park Tudor & Carmel Senior High School

Mentor: Dr. Tao Lu

Project Title: *Using a novel VBIM technique to discover carboplatin resistance genes in ovarian cancer cells*

Ovarian cancer (OC) is the most lethal gynecologic cancers in the world. Carboplatin is widely used as a major standard drug to treat OC. Although most women initially respond well to treatment, the vast majority experience disease recurrence resulting in fatal relapse due to chemoresistance. Therefore, carboplatin resistance remains a major barrier to successful treatment. In this study, we used the highly innovative validation-based insertional mutagenesis (VBIM) technique to screen for novel carboplatin resistance genes in OC. We discovered the novel carboplatin resistance gene 1 (NCR1) as a responsible gene. Overexpression of NCR1 increased carboplatin resistance in OC cells, while knocking it down with shRNA had the opposite effect. Furthermore, we found that NCR1 is an activator of nuclear factor κ B (NF- κ B). Patient tissue microarray and Oncomine data revealed that NCR1 is highly expressed in OC. Cbioportal data further indicated the prevalence of genetic alterations of NCR1 in OC. We conclude that VBIM is a powerful approach for drug resistance gene discovery. With this innovative technique, we discovered NCR1 as a novel carboplatin resistance gene in OC. Future development of small chemical inhibitors targeting NCR1 could lead to completely new therapeutic approaches in combination with carboplatin for ovarian cancer treatment.

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Regional Finalist

Name: Sarvasva Raghuvanshi

High School: Neuqua Valley High School

Mentor: James Hirst

Project Title: *New Results on Ramsey Multiplicity and Graph Commonality*

If a graph G has v vertices, a copy of G inside a larger graph K is a subgraph $H \subset K$ on v vertices such that $G \subseteq H$. Similarly, we define an anticopy of G to be a subgraph $H \subset K$ on v vertices such that $G \subseteq H^c$. A graph F is common if and only if the minimum density of copies and anticopies of F in any graph G is $2^{-|E(F)|}$, where $|E(F)|$ denotes the number of edges in the graph F . Note that this minimum is attained when G is a random graph with edge density one-half. In this paper, we propose a modern proof that the graph formed from any number of disjoint copies of a common graph is itself common. This novel proof leads to innovative partial results and opens other questions about the commonality of disjoint graphs. We then prove that the graph obtained from a pentagon by adding a chord is common, resolving a central open problem in the field of graph commonality.

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Regional Finalist

Name: Vikas Maturi

High School: Carmel Senior High School

Mentor: Dr. Kimberly Vogt, Marian University

Project Title: *Engineered Intraocular Injection Guide: Pain Reduction in Ophthalmic Disease Treatment*

Purpose: I developed a novel device, the Intraocular Injection Guide (IIG), to improve patient comfort during intraocular injections (30 million/year) by eliminating the need for a painful eyelid speculum.

Methods: Using Autodesk Inventor software, I designed over 30 successive prototypes of the IIG1, tested on a model eye with a variety of needle/syringe complexes. The IIG1 vs. speculum was tested on 50 subjects needing bilateral injections with a standardized Visual Analog Scale (VAS) to determine pain levels. I subsequently modified the device based on surgeon feedback, and repeated the study.

Results: IIG1 had a mean pain score of 14.76mm (range 0-100mm) vs. 32.22mm for the lid speculum. In Part 2, IIG2 had a mean pain score of 9.94mm vs. 27.65mm for the speculum. 95% confidence intervals for pain score in Part 1 [IIG1:(9.37,20.15); Speculum:(24.65,39.79)] and in Part 2 [IIG2:(6.52,16.02); Speculum:(24.65,39.79)] do not overlap for each Part, suggesting significant reduction in pain with the IIG1 and IIG2.

Conclusions: Patients find the IIG to be less painful than the traditional speculum, and decreased discomfort generally leads to better compliance with treatment. There is interest in large scale production via injection molding.

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Regional Finalist

Names: Kevin Qian & David Herman

High Schools: Wayzata High School & Davis Renov Stahler Yeshiva High School For Boys

Mentor: Miriam Rafailovich, Stony Brook University; Hongfei Li

Project Title: *Analyzing the Effects of Gold Nanoparticles Coated on Various Nafion Membranes for Improved Performance through the Catalysis of Carbon Monoxide Oxidation*

Gold nanoparticles have been found to be promising candidates as a potential solution to the carbon monoxide poisoning of platinum catalysts in PEM fuel cells. They have been shown to be able to catalyze the oxidation of CO at relatively low temperatures. Gold nanoparticles were coated onto various types of Nafion membranes via the Langmuir-Blodgett method, to further understand the interaction between the gold nanoparticles and the Nafion. The gold nanoparticles were coated onto the membranes with various surface pressures. Furthermore, each of the membranes were tested in a fuel cell stack setup at various flow-rates with hydrogen gas, oxygen gas, and CO gas. The optimal surface pressure was found to be 3mN/m, and the hydrogen flow-rate to be 80ccm. There was improvement in every gold-coated membrane, with an average of 70% improvement from an uncoated to a coated membrane. When tested in an industrial cell, the gold-coated membrane delivered a power output of 6.18W, 25% greater than the uncoated membrane in the industrial fuel cell, and 1,906% greater than the coated membrane in the educational fuel cell.

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Regional Finalist

Name: Leah Umanskiy

High School: University Of Chicago Laboratory High School

Mentor: Jacquie Handley

Project Title: *A Novel Characterized Cell Culture Material with Discretely Tagged ECM Proteins and Self-Assembling Peptide Nanofibers*

In vitro cell culture provides a platform to study basic cell behavior, intercellular communication, and drug response in a simple, affordable manner; however, current models generate inaccurate results because they do not properly recapitulate the in vivo 3D microenvironment. Current 3D cell culture systems, such as Matrigel and Puramatrix, lack systems that are chemically defined, modular, and reproducible. Our lab has developed a novel self-assembling peptide and protein linker hybrid system that addresses these problems and can act as a substitute for current models. Our self-assembling peptide that we entitle bQ13 [sequence Ac-QQKFQFQFEQEQQ-Am] forms β -sheet nanofibers that are non-cytotoxic and support protein incorporation. Our protein linker, β Tail, fuses to any monomeric protein of interest, which in turn allows discrete protein incorporation into β -sheet nanofibers such as bQ13. We use β Tail-Fibronectin (9/10) as our protein of interest to cause cell adhesion in gel nanofiber substrates. Previous research characterizes fibronectin domains 9 and 10 as the sites of cell-ECM protein adhesion, and we highlight its function with our β Tail-bQ13 system in a serum-free adhesion assay. The results provide preliminary evidence that the system could be a suitable replacement for 3D microenvironment technology.

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Regional Finalist

Names: Cole Maxwell & Isabella Jennings

High School: Breck School

Mentor: Yuk Sham, PhD

Project Title: *Biomolecular modeling, simulation, and design of a bivalent CB2-CCR5 ligand for the potential treatment of HIV/AIDS in the brain*

This study reports the design of a potential drug candidate for the effective treatment of neurological disorders associated with human immunodeficiency virus (HIV) infections of the brain. Our design aims to simultaneously target two highly expressed G-protein coupled receptors found in the brain and in the immune cells, namely the cannabinoid receptor 2 (CB2), a target associated with antinociception and inflammation, and the C-C chemokine receptor 5 (CCR5), a drug target that prevents HIV from infecting host cells. The drug candidate includes a bivalent ligand with an optimal spacer length, which other studies have suggested provide synergistic effects. By optimally tethering maraviroc, a HIV/AIDS drug, to a CB2 selective agonist, we expect the designed ligand will effectively cross the blood-brain-barrier, suppress pain, lower inflammation, and reduce HIV proliferation.

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Regional Finalist

Name: Rachel Zhang

High School: Parkway South High School

Mentor: Moira Chas

Project Title: *Statistics of Intersections of Curves on Surfaces*

Each orientable surface with nonempty boundary can be associated with a planar model, whose edges can then be labeled with letters that read out a surface word. Then, the curve word of a free homotopy class of closed curves on a surface is the minimal sequence of edges of the planar model through which a curve in the class passes. The length of a class of curves is defined to be the number of letters in its curve word.

We fix a surface and its corresponding planar model. Fix a free homotopy class of curves ω on the surface. For another class of curves c , let $i(\omega, c)$ be the minimal number of intersections of curves in ω and c . Computer evidence suggests that the distribution of the random variable $i(\omega, c)$ approaches a Gaussian distribution for a fixed curve ω and a random curve c of word length n as n approaches ∞ . In this paper, we show that the mean of this distribution grows proportionally with n and approaches $\mu(\omega) \cdot n$ for a constant $\mu(\omega)$. We also give an algorithm to compute $\mu(\omega)$ and have written a program that calculates $\mu(\omega)$ for any curve ω on any surface.

In addition, we view the generation of a random curve as a Markov Chain. We show that the Markov Chain Central Limit Theorem proves normality for a random variable that approximates $i(\omega, c)$.

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Regional Finalist

Names: Pranav Sivakumar & Paul Nebres

High School: Illinois Mathematics And Science Academy

Mentor: Sivakumar Muthuswamy

Project Title: *An Automated Search for Gravitationally Lensed Quasars in the Sloan Digital Sky Survey*

A robust automated algorithm for the detection of lensed quasars is rapidly becoming a necessity given the availability of “big data” on quasars, including the Sloan Digital Sky Survey (SDSS) Data Release 12 and the recently released Dark Energy Survey (DES) data. We report results from an automated search for lensed quasars consisting of two complementary algorithms: a morphological algorithm directed at finding wide-separation lens candidates and a PSF-difference-based algorithm aimed at identifying close-separation lens candidates. This research started with a baseline data set of over 450,000 quasars and 996,317 spatial neighbors of these quasars in the SDSS DR12. The first part of the automated method matched redshift and color characteristics of images and compared key emission lines in the spectrum of the quasar and its neighbors. The second portion applied image segmentation techniques to deblend close-separation candidates. Cross-matching with observations of the same targets across other bands and elimination of confirmed binary quasars increased the confidence level of the resulting candidate set. The automated search efficiently produced output that was consistent with results reported in the literature. In addition, the algorithms identified many new lens candidates, resulting in a 2.5-fold increase in candidates from the prior work.

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Regional Finalist

Names: Evelyn McChesney & Madeline McCue

High School: Breck School

Mentor: Dr. Yiannis Kaznessis, University of Minnesota

Project Title: *Engineering a broad-spectrum antibacterial probiotic via inclusion of antimicrobial peptide-encoding DNA, year two*

This is the second year of a two-year study to engineer probiotics to deliver antimicrobial peptides (AMPs) that show promise as an alternative to antibiotics. The work this year involved designing a digital “blueprint” in SerialCloner for a broad-spectrum Escherichia coli Nissle 1917 AMP delivery system designed to secrete two AMPs to target enteropathogenic bacterial infections. The AMPs microcin L and enterocin A were initially chosen because they show antimicrobial activity against gram-negative and gram-positive enteropathogens, respectively.

The first step included designing a plasmid (pMK-P+) with a pMK-RQ-Bb backbone and the strong promoter proTeOn+. Next, because the microcin L secretion machinery was costly, the highly homologous microcin V operon was isolated from an available plasmid (pHK22) and then mutated so it would not produce microcin V. The microcin V operon was digitally inserted into pMK-P+ to create the pMK-P+-V plasmid. Finally, gene blocks that encode for production of the AMPs microcin L and enterocin A were designed and digitally inserted into the pMK-P+-V plasmid.

Laboratory work using digestion, ligation, and PCR was successful in engineering the pMK-P+-V plasmid. Furthermore; a commercial pHK22 plasmid was successfully mutated to produce the microcin V operon (pHK22Δ).

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Regional Finalist

Name: Tushar Dwivedi

High School: Neuqua Valley High School

Mentor: Dr. Hui Zhang, University of Illinois at Chicago

Project Title: *Epigenetic and microRNA-mediated Regulation of BDNF and Apoptotic Regulatory Genes in Lithium-induced Neuroprotection*

Bipolar disorder (BD), one of the most debilitating mental disorders, is associated with increased morbidity and mortality. Lithium is the first line of treatment for BD. Given that BD is associated with structural and functional abnormalities of the brain, the neuroprotective action of lithium has recently gained enormous attention. The present study was designed to uncover the novel mechanisms by which lithium protects neurons. Using rat hippocampal neurons, we found that lithium not only increased dendritic length and number, but also increased neuronal viability against glutamate-induced cytotoxicity. In addition, lithium increased the expression of neural plasticity gene BDNF and genes associated with neuroprotection such as Bcl2 and Bcl-XL, whereas it decreased the expression of pro-apoptotic genes Bax, Bad, and caspases-3. Of various BDNF transcripts, lithium exclusively increased the expression of exon IV, which was found to be epigenetically regulated via hypomethylation. For in-vivo studies, we used Na/K-ATPase inhibitor ouabain, which induces manic symptoms in rodents. In hippocampus of these rats, we found that lithium restored decreased expression of BDNF and Bcl2, which appeared to be mediated through miR-134-5p and miR-15b-5p, respectively. Overall, this study delineates novel mechanisms by which lithium protects neurons and provides innovative targets for future drug development.