Siemens Competition
Math : Science : Technology
National Finalist

Names: Daniel Chae, Alan Tan & Sidharth Bommakanti
High Schools: Thomas Jefferson High School of Science and Technology, Irvington High School & Amador Valley High School
Mentor: Adriana Pinkas-Sarafova, Stony Brook University
Project Title: *A Novel Study on the Effect of Surface Topography of 3D Printed Polylactic Acid Scaffolds on Dental Pulp Stem Cell Proliferation and Differentiation in vitro*

In the field of medicine, 3D printers offer a promising approach to the creation of customized dental implants. This study evaluated the extent to which 3D printed devices are equivalent to traditional molded scaffolds, which are already FDA approved products. Polylactic acid (PLA), an effective material for cell scaffolds and one of the most popular filaments used in commercial 3D printers, was used to create the scaffolds. Scanning Electron Microscope (SEM) showed significant differences in surface topography between 3D printed and spuncast (ideal molded) scaffolds. Surprisingly, differences were also observed between scaffolds produced by different 3D printers. When dental pulp stem cells (DPSCs) were plated onto 3D printed and spuncast surfaces, it was found that there were significant differences in attachment, morphology, proliferation, and expression of extracellular matrix proteins, indicating that the cells underwent differentiation. The 3D printers created scaffolds that induced higher levels of differentiation, but maintained similar level of proliferation compared to those of spuncast scaffolds. These findings are of great importance in respect to the applications of 3D printed devices for tissue regeneration.

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National Finalist

Names: Emily Cheng, Kelly Jiang & Gerald Liu
High Schools: Methacton High School & Conestoga High School
Mentor: Ying-Hsiu Su, Baruch S. Blumberg Institute
Project Title: *Simultaneous Detection of Genetic and Epigenetic DNA Modifications by Targeted Next Generation Sequencing for Cancer Screening --Assay and Data Analysis Software Development for the Detection of Hepatocellular Carcinoma*

Hepatocellular Carcinoma (HCC) is the third leading cause of cancer mortality in the United States with over 24,000 deaths annually. Due to heterogeneity of HCC, a single marker is unlikely to have sufficient sensitivity for screening. In this study we developed an assay for simultaneous detection of a panel of five genetic and epigenetic DNA modifications for HCC screening in urine by utilizing Next Generation Sequencing's (NGS) high through-put and multiplex capability. The two major limitations of NGS are the inherent error rate of 2-3% and the bottleneck of data analysis. To enhance the sensitivity of NGS in detecting mutations or methylations to 0.1 % sensitivity, we used locked or bridged nucleic acid (LNA or BNA) to suppress the wild-type templates and enrich the mutated sequence, also designed unique bisulfite specific primers in the regions that contain CpG sites for methylation detection. In order to facilitate the data analysis of millions of DNA sequencing reads, a novel software tool was developed to efficiently detect and extract mutation and methylation information of interest of the tested genes. In this study, the sensitivity improvement was validated by Sanger sequencing analysis of reconstituted standards. By using a pilot NGS data, we showed that the software was efficient and accurate in analyzing the data, thus reducing the analysis time required from 8 hours to 5 min (~100-fold reduction). The assay was then applied to 46 archived HCC patient urine DNA samples and submitted to NGS. This is the first study to successfully simultaneously detect cell-free circulating genetic and epigenetic DNA modifications using targeted NGS technology and our newly developed customizable software (fastNGSDetect) for data analysis. This method can be applied to the detection of other mutated and methylated DNA biomarkers, for other cancer detection and liquid biopsy for precision medicine to improve cancer patient care.

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Names: Robert Luo & Helen Zhang
High School: Highland Park High School
Mentor: Mi Deng, University of Texas Southwestern Medical Center
Project Title: *A Novel Therapy for the Treatment of Acute Myeloid Leukemia*

Acute myeloid leukemia (AML), as the most common adult acute leukemia, is a life-threatening disease characterized by uncontrolled proliferation and accumulation of white blood cells. The majority of patients relapse within 5 years, and no new therapies for AML have been approved for more than 30 years. Recent studies suggest that leukemia stem cells are responsible for the initiation, development, and relapse of AML, and depletion of both leukemia stem cells and mature leukemia cells is needed to eradicate this difficult disease. In our effort to identify new AML targets through bioinformatics analyses, we found that the expression of leukocyte immunoglobulin-like receptor family B4 (LILRB4), a cell surface receptor, inversely correlates with the overall survival of AML patients. To test the hypothesis that LILRB4 supports AML development, we first measured the expression of LILRB4 in AML patient leukemia cells by using the immunostaining and flow cytometry technique. We observed that LILRB4 is highly expressed on monocytic AML cells and can also be co-expressed with a leukemia stem cell marker CD34. This result suggests that LILRB4 can be expressed by both monocytic AML stem cells and mature leukemia cells. We then performed in vitro experiments to knockdown LILRB4 expression in human monocytic AML THP-1 cells using shRNA. We found that LILRB4 is essential for the growth of leukemia cells. Furthermore, from in vivo experiments we were able to show that an anti-LILRB4 blocking antibody is capable of eliminating human AML in a xenograft mouse model. Our study indicates that LILRB4 plays a key role in AML development and that anti-LILRB4 monoclonal antibodies are promising novel drug candidates for treating AML.

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Math : Science : Technology
National 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 the 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 engineered the pMK-P+-V plasmid. Furthermore; a commercial pHK22 plasmid was successfully mutated to produce the microcin V operon (pHK22Δ).

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National Finalist

Names: Kimberly Te & Christine Yoo
High School: Manhasset Senior High School
Mentor: Alison Huenger, Manhasset Secondary School
Project Title: *Natural, Cost-Effective Anodes for Optimized Sediment Microbial Fuel Cells: Engineering a Novel Approach to Harvesting Energy and Cleaning Up Oil-Polluted Regions*

To address clean energy and pollution issue, microbial fuel cells (MFCs) were hypothesized to simultaneously generate electricity and remediate oil spill pollution. The purpose of this study was to engineer efficient, cost-effective MFC anodes that optimize electrical output and oil remediation using structural and surface coating configurations. For structure, carbonized *Luffa aegyptiaca*, loofah sponges (LS), were tested as cheaper 3-dimensional (3D) alternatives to commercial materials (carbon fiber and RVC). For surface coating, hybrids were synthesized to increase electrical properties. Coatings were uncoated, TiO^2, graphene, and graphene/TiO^2 composite. Nine anode designs were made from these structure/coating combinations. MFCs were implemented in different conditions to assess oil remediation. A multimeter measured electrical outputs; UV-VIS spectroscopy measured oil degradation. Results showed anodes improved oil degradation. LS-structure groups had significantly higher power densities than standard 2D and 3D anodes. LS-graphene/TiO_2 had the highest power density (2087.1 mW/m^2) and oil remediated (93%). This suggests structure and surface coating synergistically improve surface area, biocompatibility, and electrical conductivity for optimized MFC performance. LS are over 90% cheaper than RVC and come from accessible, sustainable sources. This MFC design shows potential towards remediating oil spills and providing clean energy for industries, remote sensors, and developing nations.

Siemens Competition
Math : Science : Technology
National Finalist

Names: David Zhu & Evani Radiya-Dixit
High School: The Harker School
Mentor: Andrew Beck, Beth Israel Deaconess Medical Center
Project Title: *Automated Classification of Benign and Malignant Proliferative Breast Cancer Lesions*

Misclassification of breast lesions can result in either cancer progression or unnecessary chemotherapy. Automated classification tools are seen as promising second opinion providers in reducing such errors. We have developed predictive algorithms that automate the categorization of breast lesions as either benign usual ductal hyperplasia (UDH) or malignant ductal carcinoma in situ (DCIS). From diagnosed breast biopsy images from two hospitals, we obtained 392 biomarkers using Dong et al.'s (2014) computational tools for nuclei identification and feature extraction. We implemented six machine learning models and enhanced them by reducing prediction variance, extracting active features, and combining multiple algorithms. We used the area under the curve (AUC) of the receiver operating characteristic (ROC) curve for performance evaluation. Our top-performing model, a Combined model with Active Feature Extraction (CAFE) consisting of two logistic regression algorithms, obtained an AUC of 0.918 when trained on data from one hospital and tested on samples of the other, a statistically significant improvement over Dong et al.'s AUC of 0.858. Pathologists can substantially improve their diagnoses by using it as an unbiased validator. In the future, our work can also serve as a valuable methodology for differentiating between low-grade and high-grade DCIS.

Siemens Competition
Math : Science : Technology
National Finalist

Name: Andrew Chen
High School: Mission San Jose High School
Mentor: Dr. Xiaodong Tao, University of California, Santa Cruz
Project Title: *Enhancing Imaging Resolution and Depth With Adaptive Optics Focal Modulation Two-Photon Microscopy*

Optical microscopy is a fundamental tool for imaging biological samples and making new scientific discoveries. However, imaging resolution and imaging depth are restricted by aberrations and background noise, which result in image distortion and blur. The introduction of spatial time-variant aberrations at the focal plane (focal modulation) of a two-photon microscope with adaptive optics enabled the desired signal to be separated from the background fluorescence and scattering noise. A fast algorithm was developed to perform spectral analysis. Adaptive optics also removed system aberrations so that only photons from the very small focal region can be detected, which substantially increases image resolution and contrast.

For regular microscopy, visualization stops at about 10 microns of tissue depth. However, fluorescent microbeads up to a depth of 600 microns could be imaged in an artificial tissue sample with adaptive optics focal modulation two-photon microscopy. The measurements showed that the lateral resolution was more than doubled and the signal-to-noise ratio was improved by 7 dB at a depth of 500 microns. This novel method allows optical sectioning and near diffraction-limited spatial resolution to be achieved when imaging deep inside a highly scattering medium.

Siemens Competition
Math : Science : Technology
National Finalist

Name: Maria Elena Grimmett
High School: Oxbridge Academy of The Palm Beaches
Mentor: Hui Li, Michigan State University
Project Title: *Adsorption of Sulfamethazine from Environmentally Relevant Aqueous Matrices onto Hypercrosslinked Adsorbent MN250†*

Sulfamethazine, a prominent agricultural antibiotic, contaminates groundwater with subsequent ecological toxicity. Remediation methods are not universally effective, necessitating newer techniques. Hypercrosslinked polystyrene adsorbents show promise because of high surface areas, durability, and regenerable properties. Using batch techniques, sulfamethazine adsorption onto Purolite MN250 was evaluated with dissolved humic acid, common groundwater ions, varying pH, and increasing ionic strength. The adsorption capacity of MN250 for sulfamethazine (Q_e) was high, ranging between 80.33 at pH 9 and 181.0 mg g^{-1} in 0.005 M KCl. The capacity with humic acid was 109.3 mg g-1. Q_e decreased one-third as the aqueous solution became alkaline, with optimal performance at pH 7 (144.0 mg g^{-1}), because sulfamethazine speciation and MN250's zeta potential vary as a function of pH. Increasing ionic strength initially decreased Q_e by 34% by altering the activity coefficient of sulfamethazine and by altering the properties of the electrical double layer, while salting-out increased Q_e by 26% at seawater concentration (153.4 mg g^{-1}). Adsorption kinetics appear sufficient for field applications. MN250's high sulfamethazine capacity in environmentally relevant aqueous matrices highlights its potential for groundwater remediation.

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† All statements, data, and figures presented herein have been published in whole, or in part, at:

Competition Entrant. 2015. Adsorption of sulfamethazine from environmentally relevant aqueous matrices onto hypercrosslinked adsorbent MN250. J. Environ. Qual. 44:1183–1192. doi:10.2134/jeq2015.02.0109

Competition Entrant. 2013. Removal of sulfamethazine by hypercrosslinked adsorbents in aquatic systems. J. Environ. Qual. 42:2–9. doi:10.2134/jeq2012.0219

Siemens Competition
Math : Science : Technology
National Finalist

Name: Milind Jagota
High School: Liberty High School
Mentor: Melissa Waldron, Liberty High School
Project Title: *Computational Study of Random Nanowire Networks: Optimization of Conductivity through Orientation*

Transparent conductors are ubiquitous in modern electronic devices. The majority of devices use Indium Tin Oxide (ITO) for this purpose. ITO, however, is plagued by issues including material scarcity, high manufacturing costs, and brittleness. Random metal nanowire films show potential as transparent conductors, but their performance must be improved before large-scale displacement of ITO can occur. In this study, nanowire orientation was investigated as a method for optimizing performance of random metal nanowire films. A computational model was developed to generate random nanowire networks and calculate their electrical conductivity. The model was then used to investigate the effects of nanowire orientation on network conductivity using three different distributions: normal, uniform, and discrete bimodal. For all three, conductivity is maximized for an optimal degree of restriction, corresponding to standard deviations of 35°, 33°, and 21°, respectively. For the first two distributions, conductivity increases with respect to the isotropic control by 25% and 20%, respectively. Surprisingly, the bimodal distribution showed no such enhancement, emphasizing the crucial role of randomness in orientation effects. These results are expected to support wider adoption of metal nanowire networks as transparent conductors, which will reduce costs and accelerate development of electronic devices.

Siemens Competition
Math : Science : Technology
National Finalist

Name: Vikas Maturi
High School: Carmel Senior High School
Mentor: Dr. Kimberly Vogt, Marian University
Project Title: *Engineered Intraocular Injection Guide (IIG): 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.

Siemens Competition
Math : Science : Technology
National Finalist

Name: Sanjana Rane
High School: duPont Manual High School
Mentor: Shunying Jin, University of Louisville
Project Title: *Effects of the Environmental Pollutant Acrolein on Renal Fibrosis*

Acrolein decreased Nuclear Factor-Erythroid derived protein 2 (NF-E2) protein expression in human-renal-tubular (HK-11) cells, induced HK-11 cell apoptosis and increased expression of pro-fibrotic Connective Tissue Growth Factor (CTGF) protein. Over-expression of NF-E2 ameliorated acrolein effects in HK-11 cells. Interestingly, NF-E2 was released in acrolein-treated HK-11 cell supernatants (Acr-sups). Danger associated molecular patterns (DAMPs) are proteins released by dying renal cells that play a role in activating and recruiting inflammatory cells and exacerbating renal injury. Renal fibrosis is associated with DAMP-mediated inflammation. Therefore, we hypothesized that secreted extracellular NF-E2 acts as a DAMP and promotes neutrophil activation, recruitment, survival and promotes renal fibrosis. Neutrophils were exposed to control and Acr-sups and cell lysates were immunoblotted with appropriate antisera.

Acr-sups stimulated pro-survival ERK phosphorylation (pERK) and promoted neutrophil survival by inhibiting cleavage and activation of pro-apoptotic protein, caspase-3. Acr-sups also stimulated neutrophil actin polymerization and chemotaxis. To determine if NF-E2 mediates these effects, Acr-sups were subjected to anti-NF-E2 immunoprecipitation. Depletion of NF-E2 from these supernatants inhibited pERK, stimulated pro-apoptotic pP38MAPK and enhanced caspase-3 cleavage. Recombinant NF-E2 stimulated neutrophil pERK, actin polymerization, chemotaxis and survival. Anti-NF-E2 antibody therapy may serve as a therapeutic option to reduce inflammation and ameliorate acrolein-induced renal toxicity.

Siemens Competition
Math : Science : Technology
National Finalist

Name: Dominick Rowan
High School: Byram Hills High School
Mentor: Dr. Stefano Meschiari, The University of Texas at Austin
Project Title: *Determining The Frequency Of Jupiter Analogs And The Announcement Of A Jupiter Analog Orbiting HD32963.*

Using 109 radial velocity measurements from Keck Observatory for the Sun-like star HD32963, we identified a Jupiter analog with a 6.5-year period and a minimum mass of 0.70 Jupiter masses. Since Jupiter was a catalyst for the developing Solar System, calculating the frequency of Jupiter analogs is a precursor to determining the occurrence of Solar System analogs. Due to the long period of Jupiter analogs, an extensive baseline of observation is needed. Stars in the Keck radial velocity survey have accumulated baselines up to 18 years, providing ample data for analysis. We first fit planets using local minimization and the Markov-Chain Monte Carlo algorithm in the Systemic application. Planets with periods between 5 – 15 years and mass between 0.3 – 3 M_{Jup}, with an eccentricity < 0.3, are considered Jupiter analogs. The raw frequency was calculated to be .71%, since there are 8 Jupiter analogs within the Keck radial velocity survey. We then calculated the detection limit to assess the ability to recover Jupiter analogs within the parameter space for each star in the sample. Using this information to correct the raw frequency for detectability, we found the frequency of Jupiter analogs to be 3%.