Siemens Competition
Math : Science : Technology
Regional Finalist

Name: Michael Ai
High School: Canyon Crest Academy
Mentor: Professor Kang Zhang, University of California, San Diego
Project Title: *SIX6 Upregulation of P16/INK4a Linked to Retinal Ganglion Cell Death in Glaucoma*

Primary open angle glaucoma (POAG) is a blinding, widespread, irreversible neurodegenerative disease characterized by retinal ganglion cell (RGC) death and increased intra-ocular pressure (IOP). Current treatments can only slow the progression of blindness and little is known behind the genetic mechanisms of RGC death. This project demonstrates how the SIX6 risk variant (rs33912345, His141Asn) and another POAG risk gene, P16/INK4a (cyclindependent kinase inhibitor 2A, isoform INK4a) affect the etiology of POAG. We first studied lymphocyte cell lines with both the protective and risk SIX6 allele and found a strong correlation between SIX6 genotype and P16/INK4a expression. We analyzed retinas from an acute IOP mouse model and human POAG eyes and observed that increased IOP triggered the upregulation of SIX6 risk alleles and caused an increase in P16/INK4a expression, culminating in RGC senescence. In addition, our tests showed that the lack of either the SIX6 risk allele or P16/INK4A expression caused the RGC death in mice to reduce, even with the increased IOP. Our studies and results provide preliminary and important insights on POAG and link risk factors like genetics and IOP elevation to an underlying mechanism in RGC death. Furthermore, our studies suggest future targeted gene therapy strategies to combat, and possibly cure, POAG.

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Regional Finalist

Name: Andrew Chen
High School: Mission San Jose High School
Mentor: Dr. Xiaodong Tao
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.

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Regional Finalist

Names: Kenz Kallal, Felix Wang & Matthew Lipman
High Schools: Weston High School, Roxbury Latin School & Boston University Academy
Mentor: Michael Zieve, University of Michigan
Project Title: *Equal Compositions Of Rational Functions*

We study the following questions:

(1) What are all solutions to $f \circ \hat{f} = g \circ \hat{g}$ in complex rational functions $f, g \in \mathrm{C}(X)$ and meromorphic functions $\hat{f}, \hat{g}$ on the complex plane?

(2) For which rational functions $f(X)$ and $g(X)$ with coefficients in an algebraic number field K does the equation $f(a) = g(b)$ have infinitely many solutions with $a, b \in K$?

We utilize various algebraic, geometric and analytic results in order to resolve both questions in the case that the numerator of $f(X) - g(Y)$ is an irreducible polynomial in $\mathrm{C}[X, Y]$ of sufficiently large degree. Our work answers a 1973 question of Fried in all but finitely many cases, and makes significant progress towards answering a 1924 question of Ritt and a 1997 question of Lyubich and Minsky.

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Math : Science : Technology
Regional Finalist

Name: Anjini Karthik
High School: St. Francis High School
Mentor: Dr. Richard N. Zare, Stanford University
Project Title: *Rapid and Selective Detection of Viruses Using Virus Imprinted Polymer Films*

We prepared a nanopatterned polymer film of polydimethylsiloxane (PDMS) via virus imprinting. The imprinted surface exhibited cavities with the mean size of 120±4 nm. These cavities demonstrated the ability to preferentially capture a target virus from an aqueous suspension of ultralow volume (5 μL) after only 1 minute of contact. Two inactivated viruses with similar shape, Influenza A (HK68) and Newcastle Disease Virus (NDV), were employed as model strains. The polymer film, which was first imprinted with HK68 and exposed sequentially to suspensions containing fluorescently labeled NDV and HK68, was able to preferentially bind HK68 at a capture ratio of 1:8.0. When we reversed the procedure and imprinted with NDV, the capture ratio was 1:7.6. These results were obtained within 20 minutes of static exposure. The suspensions contained viruses at concentrations close to those occurring physiologically in influenza infections. The limit of detection was approximately 8 fM. Production of virus-imprinted films can be readily scaled to large quantities and yields a disposable, simple-to-use device that allows for the rapid detection of viruses.

Siemens Competition
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Regional Finalist

Names: Evan Lavery & Grant Kresge
High Schools: Oregon Episcopal School & Wilsonville High School
Mentor: Dr. Richard Watkins, Willamette University
Project Title: *Assessing the Photometry of GSC 03144-00595: a Radially Pulsating, Delta Scuti, Triple Mode Variable Star*

Many stars fluctuate in brightness at one frequency and are known as single mode variable stars. However, less common variable stars exist that fluctuate at three distinct frequencies; these stars are called triple mode variable stars. Little is known about triple mode variable stars because only four have been discovered. In 2013, GSC 03144-00595 was studied and the researchers discovered that it was a multimode pulsating star, but were unsure if a third mode was present. We collected approximately 800 data points, and using Period 04 to conduct Fourier analysis, we found that GSC 03144-00595 is a triple mode variable star. After this discovery, the light curve and modes gathered from the star were used in collaboration with data from the four other triple mode variable stars to find similarities. We determined that the period ratio of triple modes is much greater than the double mode period ratio, so a new period ratio was calculated. The new period ratio will allow for the systematic discovery of triple mode stars, with only the analysis of two modes which require less data to extrapolate. These stars have extremely accurate stellar parameters and continued discoveries will help broaden our understanding of these stars.

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Name: Clarence Nakano
High School: Flintridge Preparatory School
Mentor: Professor Mohamed Y. El-Naggar, University of Southern California, Los Angeles
Project Title: *Biological Electron-Transfer Dynamics in Multiheme Cytochrome Complexes*

Electron transfer (ET) governs all known energy-conversion processes in biology. A remarkable example is the recent discovery of rapid ET along electrically conducting bacterial nanowires produced by Shewanella oneidensis MR-1. The outer-membrane cytochromes, MtrF and OmcA, are hypothesized media for ET, but how these multiheme cytochromes are assembled into a conducting complex remains a mystery. I solved this mystery by constructing an entire scientific workflow that integrates mathematical modeling, biophysics, electrochemistry, computing, and entertainment technology. Specifically, I determined the structure of MtrF-OmcA complex and study ET dynamics in it by combining homology modeling, protein docking, geometrical/biological screening, and kinetic Monte Carlo simulation. For visualizing the simulated ET dynamics with enhanced depth perception, I further built an immersive visualization system using a commodity virtual-reality platform and a game engine. My immersive simulation results reveal novel nonequilibrium phase transitions with which Shewanella efficiently responds to a change in its electrochemical environment. These results shed useful light on boosting the efficiency of Shewanella-based microbial fuel cells by increasing the ET rate, in order to produce electricity and water from sewage toward solving the global energy and environmental problems.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Edward Park, Emory Kim & Gina Choi
High Schools: Larchmont Charter School & Harvard-Westlake School
Mentor: Ji Hoon Lee
Project Title: *A Cost-effective Chemiluminescent Biosensor Capable Of Early Diagnosing Cancer Using A Combination Of Magnetic Beads And Platinum Nanoparticles*

Using thyroid stimulant hormone (TSH) detection antibody-conjugated horseradish peroxidase (HRP) immobilized on platinum (Pt) nanoparticle, a highly sensitive biosensor designed based on the principle of 1,1'-oxalyldiimidazole chemiluminescent enzyme immune assay (ODI CLEIA) was developed for the early diagnosis of thyroid cancer. Trace levels of TSH, cancer biomarker widely used for the early diagnosis of thyroid cancer, in human serum was rapidly quantified with the highly sensitive biosensor. The time necessary for the quantification of TSH using the biosensor with ODI CL detection was at least 3 times more rapid than commercially available enzyme immunoassay with colorimetric detection. The linear calibration curve (0.013 ~ 12 mU/L) of biosensor obtained with 3 ~ 6 % coefficient of variation was wider than that of the commercial product. Also, the limit of detection (LOD = background + 3 × standard deviation, 0.005 mU/L) of biosensor was about 100-fold lower than that of commercial enzyme immunoassay and as much lower than that of other biosensors recently reported by several research groups. We expect that the newly developed biosensor, which has excellent accuracy, precision, and reproducibility, can be applied as a new method for the early diagnosis of thyroid cancer.

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Regional Finalist

Name: Ethan Shen
High School: Cupertino High School
Mentor: Ryan C. Ransom, Stanford University
Project Title: *Genetic Lineage Tracing of Axin2+ Cells Reveals a Stem/Progenitor Cell Population that Executes Skeletal Regeneration*

How does the skeleton maintain homeostasis and regenerate after injury? The postnatal skeleton performs a range of vital functions, necessitating molecular mechanisms to repopulate functionally specialized cell types in response to injury. We hypothesized that the Wnt pathway specifies distinct functional subsets of skeletal cell types to mediate bone regeneration. Here, we genetically trace Axin2-expressing cells during homeostasis and injury, which revealed a novel population of multipotent stem/progenitor cells in adult long bone, termed Wnt-responsive cells (WRCs). Focal induction and long-term labeling methods demonstrate a unique periosteal niche from which long-living WRCs are activated by injury to quickly regenerate bone. Furthermore, we therapeutically target this injury-responsive population to enhance the regenerative potential of the adult skeleton, suggesting promising translational applicability of WRC-derived treatments for skeletal diseases.

Siemens Competition
Math : Science : Technology
Regional Finalist

Names: Tara Thakurta & Kathryn Li
High Schools: Castilleja School & Palo Alto High School
Mentor: Dr. Edwin Chang, Stanford University
Project Title: *Imaging Human Glioblastoma Cell Migration in a Preclinical Model*

Glioblastoma Multiforme (GBM) is the most common form of primary brain tumor. It is highly invasive, a result of its exceptional motility and diffuse manner of growth. However, its migration patterns are not yet well understood. This project identifies a distinct and reproducible path of glioblastoma tumor cell migration. Nude mice were injected with GBM1 and GBM2, two patient-derived tumor cell lines. The two cell lines were genetically modified to express firefly luciferase, and tumor growth and cell movement were monitored using bioluminescent imaging (BLI) in whole-body scans. In order to identify tumor cell migration pathways within the brains themselves, brains were extracted, sliced, and then imaged again. The slice data were used to create three-dimensional renderings of the whole murine brain. The migration pathway is identified using these 3D renderings. In conclusion, GBM was repeatedly found to migrate preferentially to the subventricular zone/olfactory bulb regions of the brain, as well as to the spine. These results can potentially provide insight into the molecular mechanism for GBM migration. More importantly, knowledge of GBM migration patterns can be utilized to impede the spread of tumor cells, which would be a boon to drug therapies.

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Regional 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.