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Harlem Children Society Workshop & Lecture Series #5
August 4th 2009

On Tuesday, August 4th 2009, the fifth seminar in the Harlem Children Society Summer Internship Weekly Series was held in Caspary Auditorium of Rockefeller University.

The day's program began with guest speaker, Dr. Taha Merghoub, senior research scientist at Memorial Sloan-Kettering Cancer Center, who presented his talk entitled "Testing New Therapies in Melanoma Mouse Models." He began by defining melanoma as a highly metastatic skin cancer that produces adverse skin pigments. There are four stages of the disease, each with a progressive decrease in survival rate. Dr. Merghoub research is focused on melanoma because of several factors, including the dramatic increase in the occurrence of the disease, miniscule rates of early detection, high rates of recurrence, and high resistance to treatment. He discussed the disease's chances of occurrence, but highlighted those individuals particularly at risk, e.g., fair skinned, with freckles or moles, prior sunburn, and family history of melanoma. Dr. Merghoub underscored the importance of sun protection by seeking shade, wearing protective clothing and headwear, and using sunscreen.

Following his introduction, Dr. Merghoub went into melanoma diagnosis. He presented the "ABC's" of Melanoma Diagnosis accompanied by photos depicting each of the signs of cancerous tumour. ***Asymmetry*** of dermal nests marks the first stage, in which one half of the lesion does not match the other half in shape. The lesion's ***border*** is irregular, blurred, or ragged. ***Color variation*** is an indicator with non-uniform pigmentation throughout the lesion, often in varying shades of black and brown. The lesion ***diameter*** is greater than 6 mm or there is a progressive change in diameter.

The development of melanoma originates from an association of familial/genetic aberrations, environmental factors, lack of homeostasis, and normal skin factors allowing free radicals to form tumors. He illustrated the progression of disease of a melanocyte, a skin cell with pigment ability. Melanocytes that proliferate and metastasize become cancerous by growing horizontally or vertically. Melanoma progresses from normal melanocytes, to mutations from genes, adhesion of cancerous cells and growth factors. Merghoub demonstrated the genes and pathways involved in melanoma development that cause cell mutations.

Dr. Merghoub then went into how he wanted to employ melanoma mice models to track the genetic pathways of melanoma development. He explained why he chose mice: they are physiologically similar to humans and recent technological advances have dramatically increased our ability to create mouse models of human disease. The goals of his experiment were to use genetic engineering to clone the melanoma gene and use the animal model systems for research. He planned to accomplish this by adding the melanoma gene into a transgenic animal and delete the alteration made using a process called "knock out" or "knock in." If the chromosomes of the transgenic mice were engineered, then mutagenesis could occur.

The process of inserting the gene into the animal model involved insertion of a vector into a fertilized egg before proper meiotic divisions could occur. This principal generation was then bred to produce the first filial generation with the gene. They were next bred to produce the second filial generation, in which all offspring contained the gene. Dr. Merghoub then displayed several mouse models for melanoma and the spontaneous melanoma development in the transgenic mice. He found that there was a burden created by the tumors from the disease, so Dr. Merghoub felt he needed to cure this with the usage of immunotherapy (use of the immune system and vaccination).

Next, he discussed why most cancers cannot be removed by the body's own responses. First, cancers cells of the body are usually "like," i.e., they are the body's own cells, so they cannot be destroyed. However, in this case, the cancerous melanocytes were transgenic, similar to foreign pathogens. Hence, xenogenic DNA immunization produced a cure for melanoma in most of the mice.

Dr. Merghoub furnished information on the immunization mechanism, and effectively demonstrated that most of the transgenic mice had fully recovered from melanoma. However, some of the mice did not respond to the immunization, which he displayed in his data of survival. Dr. Merghoub concluded by saying that he is tracking the mouse immune system, and thereby assessing the reasons why the mice did not fully recover.

Following Dr. Merghoub talk, HCS staffer Rishesh KC introduced the first student presenter of the day. Mena Hanna, HCS Class of 2008, and a student at Albany College of Pharmacy, spoke about his research entitled "Synthesis of Cyclophosphamide with Deuterium Substituent, " which he had done under the mentorship of Dr. Susan M Ludeman (Albany) and Dr. Wayne Schnatter at Long Island University.

Mena first introduced alkylating agents (cycle phosphates) and their effect in disrupting DNA function. The student's study has focused on the pharmacology and metabolism of cycle phosphates in the body.

What is a cycle phosphate? To define, Mena first drew a comparison of how alkylating agents work. Similar to mustard gas in their effects, alkylating agents cause DNA damage through the formation of cross-bridges between two molecules of DNA. The cross-linking prevents DNA from being separated for synthesis or transcription and results in cell death, which Mena illustrated in a diagram. The student then discussed how cancer research involving these substances is proving successful since cancer cells generally multiply faster and with less error correcting than healthy cells.

The student next furnished a brief history of nitrogen mustard. The oldest and most widely used alkylators, they are based on the "mustard gas" used in chemical warfare during World War I. The mechanism lowers white blood cell level and rapidly attacks dividing cells. For this reason, the research suggested it might be useful in fighting leukemia.

Mena then explained that active nitrogen mustards contain two chloroethylamine chains.

CycloPhosphamide a Prodrug, that can push the active ingredient through the cell membrane, is made of lipids. Because lipids are hydrophobic (non polar), the membrane permeability calls for a hydrophobic segment that can force the drug into the cell.

Mena then discussed the metabolism of Cyclophosphamide. Experimenting has not been successful in cell cultures, but has been in living organisms. Oxidation through hepatic P450 enzyme occurs on the 4th carbon in the chain. Once oxidation occurs, the drug is separated into its active form as it enters the cell and cross-links with DNA. Oxidation triggers a cascade or series of metabolites that contribute to its toxicity and selectivity. Mena further discussed drug metabolism, in which the Prodrug is converted to an active form through P450 and mixed function oxidase enzymes. He then stated that his research involved amelioration side effects associated with administration of the drug.

The student then discussed acrolein. If oxidation occurs on the wrong carbon, side effects result. P450 cannot differentiate between similar carbons. The mechanism is unclear, but Mena stated that it is possible that the enzyme works on all three carbons. Mustard forms if the right carbon (4C) is oxidized first, and acrolein forms if the wrong carbon is oxidized. Acrolein is avoided by favoring the enzyme for the 4th carbon while disfavoring the other two similar carbons. Each carbon contains 2 hydrogen bonds, and he wanted to substitute each hydrogen in the mustard with its isotope (deuterium). Mena's hypothesis was that oxidation would continue to work on all three carbons; however, with the addition of deuterium, the C4 will be favored. Once oxidation occurs on the C4, the metabolism will follow the Phosphoramide mustard pathway.

The student then described the materials used in his experiment. He worked with the reagents Diethyl iminodiacetate, $LiALD_{4,}$ and Thionyl Chloride. To extract compounds from solvents, he used Soxhlet, a Roter Vap, and a pump. To analyze compounds, Mena used TLC and NMR.

He concluded that by modifying Cyclophosphamide in changing the mustard hydrogen to its deuterium isotope, he believes the oxidation will occur on the 4th carbon, thus preventing the acrolein side effects of the drug. The drug will affect only cancer cells because of the presence of ALDH, and a breakthrough in cancer research could potentially result if proved effective. For Mena's future work, he will continue working on synthesizing the Prodrug form then send it out for further testing in cell cultures, mice, and mammals.

Katherine Chan, HCS Class of 2008, and a student at Legacy School for Integrated Studies, next presented her research entitled "Robotics." Katherine had been working on this research with Masud Karim, HCS Class of 2009, and a student at Bronx High School of Science. (Masud was not present at the lecture on August 4th.) The two students have been working at Steven's Institute of Technology under the mentorship of Dr. Yu Dong Yao.

The student first provided an introduction to wireless technology and robotics engineering. She defined wireless fidelity (Wi-Fi) as a wireless connection linked to any computer network or that can be transmitted through radio waves. Robotics is a mechanical and functional figure formed by sensors, actuators and power source(s) that

can be functioned or programmed to be automatic or manual.

The goals of the students' research were multiple. They wanted to understand Webots and how to program them. They also wanted to simulate the robot's environment, build and activate the robot, avoid obstacles using IR sensors and camera(s) and incorporate physics principles.

Next, Katherine provided an introduction to Webots and E-Puck. Webots, a 3-D mobile robot simulation program, involves robots programmed to react on command. E-Puck is a tiny robot also in the Webots program, but is prefabricated.

The student then discussed components. Webots employ a computer program used to simulate robots through applied nodes. The nodes dictate the simulation piece by piece, and can be dismembered and altered to ameliorate the characteristics (i.e., geometry, physics, appearance, etc.) and overall efficiency of the object. Major nodes include sensors (e.g., infrared), differential wheels, elevation grids, point light nodes, and shape nodes (e.g., boxes, cylinders, spheres, etc). Automatons, another component, chart the movement of robots such as the E-Puck. Lastly, the simulation is played by engaging the "play" button.

To date, the students have completed the preliminary simulation of a "MyBot" robot (a simple differential wheels robot) and have analyzed its function through sensors, geometry, physics, environments, etc. They have dissected certain files to observe and mimic functions, nodes, automatons, and any other crucial adjustments. Additionally, they have analyzed the impact of making adjustments to the motor speed, automatons, physics, geometry, appearance, sensors, and the environment itself.

In the future, Katherine said they would experiment with the E-Puck both physically and on the Webots program. They would like to emulate the proposed E-Puck in its proposed environment on Webots. Depending on how many E-Pucks the students are provided, they would ultimately like to create a robotic vacuum cleaner, a smart office desk, a movable feast and a mousetrap.

Bintou Fisiru, HCS Class of 2009, and a student at High School for Medical Science next presented her research entitled "Fingerprinting." She is doing her research under the mentorship of Dr. John Molina and Dr. Thomas Brennan at Bronx Community College.

Bintou first defined fingerprints as impressions of a fingertip on any surface. She explained that all fingerprints are unique, and in the 90 years since the technique was generally introduced, no two individuals have been found to have the same prints. A fingerprint will remain unchanged during an individual's lifetime. The ridges on the grasping surfaces of hands and on the soles of feet are present at birth and remain unchanged for life except for size as growth occurs. Fingerprints have general ridge patterns that permit them to be systematically classified three principle patterns, the arch, the loop, and the whorl. Bintou illustrated these patterns with slides depicting each.

At a crime scene, there are 3 different types of prints found and classified as

visible, plastic, and latent fingerprints. Bintou's goal was to develop latent fingerprints using two different techniques and match them to someone in the class using the fingerprint sheets they had each created.

Latent fingerprints are made up of chemicals that come from the pores in our fingers and are left on virtually everything we touch. The primary component is ordinary perspiration, which is mostly water and dries fairly quickly. Other components such as amino acids are solid and can remain on a surface for a much longer period of time.

Ninhydrin ($C_9H_6O_4$) is used to test for latent prints as it reacts with amino acids commonly found in latent print residue to form a purple compound, yielding latent prints visible in shades of purple. Under a fume hood, she applied a ninhydrin solution to a latent fingerprint on a piece of paper by way of "painting" and allowed it to dry. This process yielded a purple fingerprint, which could be photographed for future use.

Another substance, Cyanoacrylate (**$C_5H_5NO_2$**), aka super glue, is also used to test for latent prints. It reacts with the traces of amino acids, fatty acids, and proteins in the latent fingerprint and the moisture in the air to produce a visible, sticky white material that forms along the ridges of the fingerprint.

Bintou then delved into how fingerprint specialists determine whether a set of prints is a match. The process involves first identifying the pattern of the fingerprint. Next, the different characteristics are identified. Characteristics include two types: typica and minutiae. Typica are unique lines including ridge ends and bifurcations. Minutiae are the details in a fingerprint, such as eyes/islands and creases. To make an identification, one must find similar characteristic details between fingerprints. The number of different details needed to make a match varies by political jurisdiction.

In Bintou's experiment, she had been successful in finding out whose fingerprints from her class were on the spoon used in the experiment, and in developing the latent print with ninhydrin.

The student then went on to discuss an actual and historic case. The person in question, Will West, was received at Leavenworth prison, and denied previous imprisonment there, but the record clerk nevertheless performed measurements using the Bertillon instruments. When the clerk referred to the formula derived from West's Bertillon measurements, he located the file of one William West, whose measurements were practically identical and whose photograph appeared to be that of the new prisoner. When the clerk turned over William West's record card, he found it was that of a man already in the penitentiary serving a life sentence for murder. Subsequently the fingerprints of Will West and William West were impressed and compared. The patterns bore no resemblance, and thus ushered in the new standard method of identification via fingerprinting versus Bertillon measurements.

Following Bintou's presentation, Jaweria (Jia) Afreen, HCS Class of 2009 and a rising senior at Queens High School for the Sciences at York College approached the podium to speak about "RNA Analyses to Study Dry Eye Disease." Jia is working with Dr. Yi Wei in the Ophthalmology Department at Mount Sinai School of Medicine.

The student first provided some key terms associated with her project. Cytokines are a category of signaling molecules that are used extensively in cellular communication. PCR (Polymerase chain reaction) is a laboratory technique that allows us to produce millions of copies of a specific DNA sequence. RT (Reverse Transcription) is similar to PCR and is used for the same purpose. However, in RT the RNA strand is first reversed into a DNA sequence and then amplified.

The student then furnished some background on dry eye disease. Also known as keratoconjunctivitis sicca ("dryness of cornea" in Latin), and caused by decreased tear production, the condition dries up the tears very quickly and prevents the eye from staying moisturized. Dry eye syndrome is typically more common in seniors and especially women, because they are more likely to use hormone replacement therapy (HRT). As humans age, they naturally produce fewer tears.

Symptoms of the disease include dryness, burning, itching, pain, sensitivity to bright light, tired eyes, and pressure behind the eye. Eyes may redden and become easily irritated by wind or smoke and/or produce stringy mucous.

The purpose of Jia's experiment was to analyze the expression of inflammation related to cytokine from human eye sample. For her experiment, Jia used a Trizone Kit for RNA isolation, pipettes, RNAminelute kit for purification, DNAse Kit for DNA digestion, RNase killer, gloves, ice, a refrigerator, chloroform and a centrifuge.

Jia's methodology was to first employ impression cytology to obtain eye samples. She isolated RNA using the Trizone kit, performed DNA digestion via the DNase Kit, and then quantified and qualified the sample using the nanodrop machine. She performed PCR only with those samples, which were of good quality and quantity to see if there was further contamination of DNA. Finally, reverse transcription and a micro array were to be the final steps of the experiment.

In a data table, Jia displayed her quantity and quality results. She discussed the meaning of the data, and delved into the next steps of her work. Jia's further work will involve a microarray. She will convert Total RNA to cDNA, and then add cDNA to RT2qPCR Master Mix and Aliquot Mixture across the PCR array. Next, she will run it in a real-time PCR instrument, and finally analyze the data. The benefits of her study, Jia hopes, will be to help further the understanding and prevention of dry eye disease and blindness.

Rishesh KC approached the podium to make several announcements, and introduced the next joint student presentation by Binta Wague and Naa-akomaah Yeboah, both HCS Class of 2008, and students at High School for Medical Science. Their presentation, "Tay-Sachs Disease," represents their summer 2008 research under the mentorship of Dr. Brennan and Professor McMahon at Bronx Community College in bioinformatics.

The students first provided some definitions to provide context. Bioinformatics is the field of science in which biology, computer science, and information technology

merge to form a single approach. Computers are used to store biological information. Gene banks, on the other hand, are for preserving genetic material and sequences. They are responsible for collection, preservation and evaluation of organisms. BLAST® (Basic Local Alignment Search Tool), is a search program used to compare sequence databases.

They then provided a background on Tay-Sachs disease, which is a rare, recessive disorder that causes destruction of the central nervous system (nerve cells in the brain and spinal cord). Since Tay-Sachs is a recessive disorder. Two alleles are required for one to contract the disease, which is mostly associated with Ashkenazi Jews, and people of the Middle East.

The symptoms for Tay-Sachs vary depending on whether the patient acquires it during infancy or adulthood. The much more rare form of Tay-Sachs appears in adults, and is referred to as adult-onset Tay-Sachs disease. Symptoms in infants include slowing down of development, weakening of muscles, and loss of ability to turn over, sit or crawl. Other symptoms that may occur as the disease progresses include seizures, inability to swallow, and mental retardation.

The students then discussed the cause of Tay-Sachs disease as a genetic mutation that is passed on from parent to offspring. This defect is located on the HEXA gene on the 15th chromosome. The HEXA gene gives instructions for making part of an enzyme called beta-hexominidase A. This enzyme plays a critical role in the central nervous system, and breaks down the fatty substance known as GM2 ganglioside. Mutations in the HEXA gene disrupt the activity of the enzyme, preventing the breakdown of the GM2 ganglioside. As a result this can cause an accumulation to a toxic level in the brain and spinal cord. The students then displayed slides illustrating the location of the HEXA gene in both humans and mice.

As for diagnosis, symptoms and family history are noted and analyzed, followed by thorough screening, including a blood test. The blood test measures the activity of beta-hexasaminidase A to identify patients and carriers of the disease. It looks for changes or mutations in the gene that codes for HEXA.

Binta and Naa-akomaah then turned to treatment. While there is neither a cure for Tay-Sachs nor any way of slowing down the progression of the disease, there is treatment. Treatments, including medication, proper nutrition and hydration, are used to control the symptoms. Anticonvulsant medicine can be given to control seizures. Other measures to assist individuals with eating and staying hydrated are employed to maintain quality of life and ensure safety. In the future, the students would like to work with Tay-Sachs patients and focus on comparing gene sequences.

The students then spoke about their current work in the nutrition and healthy living group. They are looking at different neighborhoods and different factors that make up those neighborhoods such as race, population, economic status, etc. They will also try to identify relationships between obesity and other factors such as eating habits and availability of healthy foods. They concluded by saying that they are also searching different farmers markets, corner stores, and groceries and conduct surveys that pose questions about age range, medical history and food intake.

The next student on the program, Kwasi Boateng, HCS Class of 2008, and a student at High School For Medical Science, offered his presentation entitled "Bioinformatics Workshop 2008 Human Obesity Protein- Leptin (1ax8)." He had done his summer 2008 research under the mentorship of Dr. Yuying Gosser in the Computer Science Department at City College of New York.

Kwasi first defined bioinformatics as the intersection of biological, computer, and information sciences necessary to manage, process, and understand large volumes of data (for instance, from the sequencing of the human genome, or from large databases containing information about plants and animals) for use in discovery and development new drugs.

The student continued with a description of Leptin, the protein hormone that plays a key role in regulating energy intake and energy expenditure, including appetite and metabolism. Leptin acts as a weight-lowering hormone in human obesity and is an appetite suppressant, with the body's fat cells (adipocytes) being responsible for the constant production and release of it.

Next, Kwasi spoke about PyMOL, a computer software used in his experiment that enables the viewing of high quality 3D images of small molecules and biological macromolecules. According to the creator, almost a quarter of all published images of 3D protein structures in the scientific literature are made using PyMOL.

Kwasi then provided a brief history on the discovery of the effects of Leptin, which were first observed in connection with studying mutant obese mice that randomly arose within a mouse colony at the Jackson Laboratory (Maine) in 1950. The mice were called the *ob/ob* mice. Kwasi stated Jeffrey M. Friedman and colleagues at Rockefeller University had discovered Leptin in 1994 through the study of similar mice. They found the mutated *ob* gene responsible for the syndrome and purified the normal *ob* gene's product, which became known as *Leptin*.

The student then went into the function of Leptin. A very small group of humans possess a mutant form of Leptin, which leads to a constant desire for food, and thus results in severe obesity. The condition can be treated by the administration of recombinant human Leptin. Sometimes obese humans tend to overproduce the protein but cannot fully metabolize it. However, other humans are said to be resistant to the effects of the Leptin protein in the same way people with type 2 diabetes are resistant to the effects of insulin.

Kwasi then turned to discussing BLAST (Basic Local Alignment Search Tool), an Internet database for comparing biological sequence information, such as the amino-acid sequences of different proteins or the nucleotides of DNA sequences. It can also enable us to know where a certain sequence of DNA originates.

He then concluded by discussing Leptin's structure. A four-helix bundle with a very short strand segment, its molecular weight is around 16 kDa (kilodalton). The protein has 67% sequence identity among diverse species, including orangutans, gorillas,

cows and pigs.

Following Kwasi's presentation, Dr. Sat took the podium to discuss the upcoming Science Cruise that was just two days away. In addition, he spoke about student reports and posters in connection with the upcoming Sixth Annual Harlem Street Fairs and Festivals and First Annual Yatra/Parade on September 26th, 2009. The seminar then broke for lunch.

Immediately after reconvening, Dr. Sat took the podium to introduce the next guest speaker of the day, Dr. Sumanta Goswami, Assistant Professor in the Department of Anatomy and Structural Biology at Albert Einstein College of Medicine Yeshiva University.

Dr. Goswami's presentation was entitled "Interrogating Breast Cancer Caught in the Act of Invasion!" As an introduction, he began, saying that cancer is a serious problem and thus the importance of cancer research is tremendous. Cancer is not one disease to treat, but a multitude of diseases in one packet. As the population is aging there is an increased incidence of cancer. Because of the success of health care systems, fewer people are dying of infectious diseases.

With respect to breast cancer, Dr. Goswami pointed to the importance of research citing statistics from last year: 240, 000 cases were reported, out of which 80,000 people died (in the US alone). These cases occurred in both men and women. Metastasis research is important because primary tumors are removed by surgery in the majority of cases. Metastasis and drug resistance are the two main causes of mortality and morbidity in breast cancer patients.

When initially looking at cancer cases, one cannot predict if and how cancer is going to spread. He then went on to explain the process of how metastasis occurs in steps. Showing a diagram, Dr. Goswami first explained how there is initially a primary tumor, either a local invasion (micro-metastasis) or at a distant site. It enters the blood vessel, travels a long distance, survives and forms a colony. To treat this, we use anti-proliferating drugs and protease inhibitors. Also, we use new drugs that target cells as they enter the blood.

The progression and spread of cancer involves neoplasia in which cells replicate in a process called hyper-proliferation. Next, the tumor enters a phase of oxidative stress in which the tumor becomes very low in oxygen, and gives rise to angiogenesis. New blood vessels are formed in response to oxidative stress. Because they have a leaking nature, they are vulnerable and when they form, the tumor takes advantage and invades, then causing intravasation. It enters the blood vessel, and creates blood burden. Extravasation then occurs, in which leakage occurs, and then the process begins again.

Dr. Goswami then narrowed the focus of his talk to the steps of invasion and intravasation. He then went on to say that in studying cancer, we need animal models to simulate the disease. Specifically, his lab uses two types of animal models.

The first is a transgenic mouse (PyMT-oncogene mice with mammary tumors) in

which a gene has been inserted into the genome and is expressed only in the specific area of interest, and the second is a cultured cell line model. Both develop tumors in mammary glands. The second is fluorescently labeled (GFP or CFP) cultured tumor cell lines. Using the two models, Goswami's lab develops tumors in the mammary glands by injection. After waiting about 3 weeks, the tumor is palpable.

Dr. Goswami then turned to discussing how we can look deep inside tumors while animals are under anesthesia through a process known as intravital imaging. This requires making the protein fluoresce in the model. He then spoke about multiphoton microscopy and its advantages. It is a high-end instrument utilizing electronic laser. It focuses on the specimen and can go deep inside tissue without damaging it, and because it is non-bleaching and non-toxic, images can be taken for hours.

He illustrated cell behavior in vivo, and discussed how it has been discovered that cancer cells and macrophage talk to each other through ligands and receptors being expressed. The tumor needs a micro-environment to grow and spread. Dr. Goswami's lab is concerned with determining what type of micro-environment allows metastasis to occur. When they talk to each other, cancer cells produce CSFI and macrophages have the corresponding receptor. The result is cell invasion, i.e., chemotaxis ("chemically attracted"). Using chemotaxis, they talk and move from the primary tumor and off to other areas. This is the primary reason for metastasis.

In connection, Goswami then discussed "In Vivo Invasion Assay," a process in which a needle is inserted into the tumor. The tumor moves toward the needle (in chemotaxis action), and cells actively crawl in and are collected. The process takes about 4 hours and several hundred cells are collected. The technique, he added, is difficult to master.

Next, Prof. Goswami turned to correlating cell behavior with gene expression. Genes regulated in the invasive subpopulation of tumor cells give rise to 'invasion signature." Microanalysis was performed and compared to an average primary tumor, then analyzed for genetic composition in a complicated technique. Bioinformatics were also used whereby each gene was elevated to its function, was mapped, and it was discovered that three different classes of genes were connected to motility, cell cycle, and apoptosis.

In connection with the correlation of gene expression with function, he measured the cell cycle by BRdU assay. He delved into the cell cycle, and stated that he and his colleagues discovered that invasive cells have shut down the cell cycle, i.e., making DNA. Invasive cells are drug and radio resistant, and measured using fluorescence, and observed for cell death. It was determined that the pattern of gene expression and biological properties are unique to an invasive subpopulation of cells, which have been identified in his lab.

Dr. Goswami then spoke about his lab's work in connection with treating breast cancer. They are working to determine biomarkers that can predict and therefore provide early detection, since there is a better outcome with early detection. His lab is also looking at pathway analysis and stability analysis, in which they identify genes and

compare them to a known patient dataset. In another analysis, splice variant analysis, they identify splice variants, and then predict metastasis, as well as drug and radio resistance. Showing a diagram of the mobility pathway, Dr. Goswami discussed how another goal of his lab is to obtain the gene expression signature in order to compare it with a patient dataset. He also mentioned Mena protein splice variants as biometers of invasive cells.

The invasive signature derived from pathway and stability analysis correlates with metastasis-free survival of breast cancer patients, and Dr. Goswami illustrated this in a data graph. He also displayed a table that illustrates how the identification of the ratio of Mena splice variants can be used as a biomarker of invasive cells that are also drug and radio resistant. With regard to translational research, Dr. Goswami's lab employs fine needle cytology correlates Mena protein splice variants with tumor progression. He then displayed a graph illustrating pathway-directed drugs that can kill chemo and radio resistant cells.

Finally, in other research, Dr. Goswami displayed another diagram of cell cycle and DNA repair pathway, and pointed out the protein PP2A, which prevents cell from going into cycle. If LB-1 is added, it stimulates the cells, and all cancer cells die. LB-1 pushes the dormant cells into cell cycle, thereby making them radio and chemo sensitive. In vivo studies are in progress.

Dr. Goswami's conclusion:"The invasive cells constitute a population that is neither proliferating nor apoptotic, but is highly motile and resistant to chemotherapy and radiotherapy." In other words, his lab has discovered that there exists a dormant population of cells that is the root of many problems.

With this discovery in mind, Dr. Goswami drew to a close, presenting his "wish list": (1) to have biomarkers that offer earlier detection, (2) to have biomarkers that predict and differentiate between bad and worse cancer, (3) to have pathway-directed drugs which kill the dormant cells, (4) to have radio and chemo sensitizers that revert these cells back to radio and chemo sensitive state, and (5) for chemo and radiotherapy to become effective in resistant cancers.

Dr. Sat then returned to the podium and introduced a special guest in the audience, Dr. Bapanalah Penugonda, DDS. Dr. "Penny" came to the podium and spoke about his work at NYU and his private practice. Among other things, he mentioned new developments in tooth whitening, and how there is a trend in humans being born with fewer teeth as the mouth evolves to a more reduced size. Dr. Penny answered a number of student questions on dentistry and oral hygiene before returning to his seat.

Dr. Sat then approached podium and introduced HCS Class of 2005 student, Shabab Naqvi, to speak. The student, who has been studying Celiac Disease, spoke about how she personally suffers from the disease, and it has been important to her to have the opportunity to study it. Shabab also spoke about how she is preparing to apply to go to dental school.

Next on the program was a joint student presentation, "Designing Green Concrete," by Ezequiel Hernandez, HCS Class of 2009, and a student at Bronx

Engineering and Technical Academy, and Kenneth D'silva, HCS Class of 2008, and a student at the High School of Math and Engineering at City College of New York. The students are doing their research under the mentorship of Dr. Christian Meyer in the Carleton Laboratory at Columbia University.

The students went into the basics on concrete. It is a mixture of cement paste and aggregate in the right proportion, and Portland cement, a combination of particles is used in the mixture. The process of producing concrete involves hydration, and curing /healing. As time passes, concrete grows in strength and is typically tested in time intervals.

The goal of their experiment was to design a concrete mix that is both lightweight and efficient as an insulating material. The concrete was to contain recycled materials, such as EPS beads (Styrofoam) or recycled concrete, and would ultimately be used to create concrete building panels made of it.

Kenneth and Ezequiel then discussed how they had mixed their concrete. After calculating the water to cement ratio, the aggregate to concrete ratio, and the percentage of EPS beads, they gathered the materials needed and weighed the contents. Placing the aggregates and cement into an industrial mixing bowl, they started the mixer and slowly added the water. They next made 2-inch cubes to test properties. Using the newly mixed concrete, they used a trowel to place the mixture into 3 spaces of the 2-inch cube forms. They filled them higher than the brim and turned on the vibration table for consolidation. Next, they refilled them completely and evenly to the top.

For the curing process, they wrapped the forms in saran wrap, placed them into the curing chamber for 24 hours, and later removed the cubes. The students then placed the cubes into the chamber for 6 days.

In density testing, they first placed the cubes of concrete in water-filled beakers and weighed them. Then, they placed the cubes into an oven and heated them to over 100^{o}C for 24 hours, and again weighed them. From these values, the density and water absorption values could be acquired.

In compressive testing, the students had to place the 2-inch cubes one at a time onto the lower layer of a Universal Testing Machine. There they measured how many pounds per square inch of force the cubes could withstand until failure.

Though they don't yet have the density results yet, Kenneth and Ezequiel concluded that higher percentages of EPS create weaker mixtures, and that there is a negative correlation between EPS and compressive strength. In the future, they would like to work on recycled concrete, physical characteristics of recycled concrete and fly ash, and production for building panels.

Dr. Sat returned to the podium and made his suggestions about the presentation. He then introduced the final student presenter of the day, Fatih Aytekin, HCS Class of 2009, and a student at Brooklyn Amity School. His presentation, "Near Field Thermal Radiative Transfer Between Spherical Objects" is on the research Fatih is doing under the

mentorship of Prof. Arvind Naranayaswamy at Columbia University in the Department of Mechanical Engineering,

Fatih's aim was to investigate near-field thermal radiative heat transfer between closely spaced spherical objects. He wanted to propose scaling laws for near-field thermal radiation heat transfer between two microspheres using an experimental apparatus.

He provided an introduction, saying that German physicist Max Planck was the first to discover blackbody radiation due the tunneling of electromagnetic waves from one object to another. In his project, Fatih would be able to exceed the predictions of Planck's theory. Basically, he was interested in understanding energy transport at nano-scale and how radiation transfer changes as the gap between the objects becomes very small.

Next, the student defined thermal radiation as the light emitted by hot objects. As the temperature of the object increases, it emits most of its light at higher and higher energies. Higher energy light means shorter wavelength light. He then displayed a wavelength spectrum.

Fatih then defined a cantilever as a very sensitive force measurement device. He displayed a slide depicting some example pictures of a cantilever. A spring is used to measure force - for instance, if one applies 1 kg to a spring, it will stretch by a certain distance. If the mass is doubled, the spring will stretch almost twice the distance (mass meaning force - the gravitational force due to the mass). The spring can be calibrated by recording it's stretching for various weights or masses and can be used to record any unknown mass by measuring the stretching of the spring. The cantilever is such a spring, except it is very sensitive. The cantilever Fatih used can measure forces 1 billionth of the force used in everyday life. In the case of his work, he also used it as a temperature sensor because cantilevers are most often bi-material. The bi-material cantilever is composed of two materials: gold (70 nanometer (nm) thickness and Silicon Nitride (500 nm)). The elements have different thermal expansion coefficients, hence the cantilever responds to temperature by bending.

Fatih then went into the reasons to use spherical objects in his experiment. A parallel plate configuration, while reasonable to analyze was experimentally very challenging. Conversely, a sphere-plate configuration is harder to analyze, but experimentally easier.

The main components of the apparatus used in his experiment were the laser diode module (LTG, LaserMate Inc., Pomona, CA), a lens system to focus the laser beam, the AFM cantilever and its holder, a substrate mounted on a motion control device (Oriel motor mike), and a position sensing detector (PSD) (duolateral PSD, On-trak Photonics Inc.). The AFM cantilever was used because it is very sensitive, and in his experiment Fatih would use it in order to understand the radiative heat transfer at nano-scale.

In the experiment, a drop of glue was first deposited at the edge of a glass substrate. The cantilever position was adjusted using a micro-manipulator so that the tip just touched the glue. This was done under a microscope (100X magnification). Next, a microsphere was adjusted so that it was just at the edge of a clean glass substrate. The sphere adhered to the glue near the tip. The beam from a laser diode module was focused at the tip of an AFM cantilever and the reflected portion is directed onto a PSD. A position-sensing amplifier (OT-301, On-Trak Photonics Inc.) was used to convert the output of the PSD into a X and Y output corresponding to the position of the spot on the PSD and a sum output proportional to the laser power incident on the PSD. All these components were mounted on a standard aluminum optical breadboard (10”× 12”).

As for results, Fatih has completed the number of the cantilevers that are attached to sphere. In the future, he will measure the near-field radiative transfer between the substrate and sphere, which he has attached to cantilevers.

Dr. Sat again approached the podium with a few last words, and concluded the fifth seminar of the HCS 2009 summer program. The meeting was then adjourned.

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