RESEARCH REPORT

1. Name: Michael Musashi Adachi （ID No.: SP06401）

2. Current affiliation: School of Engineering Science, Simon Fraser University, Burnaby, BC, Canada, V2Y 1G8.

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry X **Engineering Sciences** Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Tokyo Institute of Technology, Tokyo, Japan

5. Host researcher: Professor Konagai, Shuichi Hiza

6. Description of your current research

Thin film materials offer a low-cost alternative to the market-dominant mono or multicrystalline silicon wafer based solar cells. One of these materials is amorphous silicon which can be grown on low cost substrates such as glass, stainless steels and polymers. More recently there has been considerable interest in microcrystalline silicon which is grown in the same way as amorphous silicon but by diluting the process gases with H_2. The advantage of microcrystalline silicon is that it is abundant, non-toxic, is stable against light-induced degradation and has improved sensitivity in the near-infrared wavelengths as compared to amorphous silicon. One of the challenges of this material is increasing its deposition rate to be amiable to mass-production while taking into consideration film thickness uniformity over large areas. HWCVD has the advantage of being a very simple technology allowing for easy upscaling to large areas, has potential for high deposition rates and is void of ion-bombardments present in plasma-enhanced chemical vapour deposition (PECVD), the most common method of thin film silicon deposition. My research involves the deposition of intrinsic microcrystalline silicon by HWCVD using a graphite filament. The main advantage of using a graphite filament over the more commonly used Tungsten and Tantalum is that it has been reported to have better repeatability due to greater mechanical and electrical stability during depositions.

7. Research implementation and results under the program

Title of your research plan:

P-type Microcrystalline Silicon Prepared by Hot-wire Chemical Vapor Deposition for Solar Cell Applications

Description of the research activities:

Research at the Konagai-Yamada Laboratory is focused mainly on thin film silicon and CIGS solar cells. I worked very closely with Shuichi Hiza a doctoral student doing research on HWCVD deposited solar cells. This research topic is very similar to my research in Canada, the main difference being that in the Konagai-Yamada Laboratory a Tungsten (W) filament is used for depositions whereas in Canada we use graphite (C). During my stay, Hiza-san focused mainly on the intrinsic layer optimization and I was given the opportunity to work on the optimization of the doped p^+ layer also deposited by HWCVD. Using a mixture of SiH_4, H_2 and the dopant gas B_2H_6, thin microcrystalline silicon p^+ layers with high conductivities (> 5 S/cm) were deposited. Since p^+ layers when incorporated into thin film p-i-n solar cells are normally very thin, in the range of 20-30 nm, my depositions were focused on films near this range. In addition since films which are so thin are deposited in very short times (~5 min.) preheat conditions play a significant role in the quality of the thin p^+ type films. Therefore, one of the experiments was to compare films grown under different preheat conditions. From previous temperature measuring experiments the heat transfer from heater to substrate was found to be inefficient in vacuum. Therefore, H_2 gas was used to help improve the transfer of heat to the substrate. The results of this experiment are shown in Figure 1. For each film the substrate was preheated using a heater temperature of 300 °C for 30 min. and afterwards preheated in H_2 gas for varying times. From the results in Figure 1, we found that using hydrogen for preheating helps raise the substrate temperature at which a both the conductivity and activation energy improved considerably. One explanation for this change is that the crystalline fraction also increased with preheat time which in turn leads to the higher conductivity.

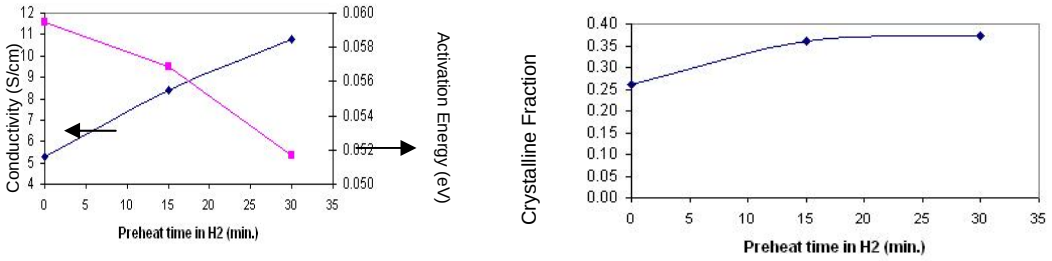


Figure 1: Electrical characteristics and Raman Crystalline Fraction of films grown using different preheat times in 14 mTorr of H_2 gas. Besides varying preheat times, all films were deposited using the same deposition conditions.

Figure 2 shows the transmission spectra of p-type microcrystalline silicon film grown on SnO_2 coated glass, which is commonly used as the top contact in thin film amorphous silicon solar cells. From this figure we notice that even for thicknesses down to 25 nm there is a considerable decrease in transmission especially between wavelengths 300 and 1000 nm which is the region of interest for silicon solar cells. This decrease in transmission can be attributed to the well known reduction of SnO_2 into Sn due to the atomic atmosphere. Therefore if these conditions are to be used to deposit p-type microcrystalline silicon for solar cells a protective layer of ZnO ontop of the SnO_2 would be necessary to improve the transmission spectra.

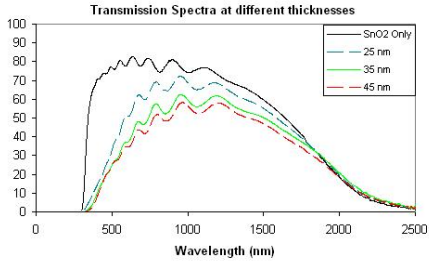


Figure 2: Transmission Spectra of films grown at different thicknesses on SnO_2 coated glass.

In addition to a number of deposition systems, the Konagai-Yamada Laboratory also consists of numerous characterization equipment such as FTIR, XRD, AFM, electrical conductivity, solar simulation, QE, Hall, ellipsometry, spectrophotometry, Constant Photocurrent Method (CPM), and Photothermal Deflection Spectroscopy (PDS). I was fortunate enough to be showed how each system worked and used most of these techniques to characterize the films I deposited. I also had some samples sent to me from Canada and was able to do both CPMS and PDS measurements on these films. PDS and CPM is used to measure the subgap absorption where higher absorption indicates an increase in defect density. The results for these measurements are shown in Figure 1. Unfortunately for the CPM measurement the electrode to film contact may not have poor as the aluminum electrodes were applied after some time after the deposition and for the PDS measurement Corning 1737 glass was used as a substrate instead of quartz or borosilicate glass so both measurements consist of quite a bit of error. Nonetheless learning the measurement setup and procedure was valuable and I will look into doing PDS measurements after returning to Canada.

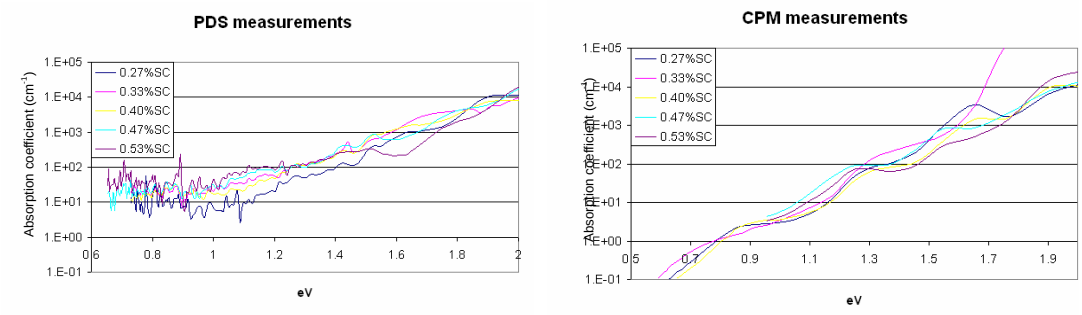


Figure 1: PDS and CPM measurements

8. Please add your comments (if any):

Although my stay at my host university was only two months, learning new characterization methods and methodology of thin film silicon fabrication in a very experienced lab was extremely useful for my current research. Research for thin-film solar cells in my school (and country) is fairly recent so these two months

have been a very good learning experience. I look forward to returning to Canada and continuing my research. Perhaps as or more important than what I learned in the lab was making new friendships with students/researchers in my laboratory and also meeting other students in the same JSPS program. I hope to be able to come back to Japan soon for research or a conference.

During my stay in Tokyo I also had the opportunity to take a day trip to the Advanced Industrial Science and Technology (AIST) laboratory in Tsukuba where they also do research on solar cells. A researcher I met at a recent conference was kind enough to answer some of my questions and show me around the laboratory. Being my first time at a national research laboratory I found it to be a valuable tour and a good learning experience.

RESEARCH REPORT

1. Name: Nikita Eriksen-Hamel （ID No.: SP06402）

2. Current affiliation: Department of Natural Resource Sciences, McGill University

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences X Biological Sciences
X Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Yokohama National University

5. Host researcher: Dr. Nobuhiro Kaneko

6. Description of your current research

My current Ph.D. research involves improving nutrient management in agriculture through understanding the role of soil biota in mediating nutrient transformations in agricultural soils. The objective of my research project is to calculate the contribution of earthworm communities to soil nitrogen pools in agricultural systems of Quebec. The majority of published research measuring nutrient fluxes through earthworm communities have largely been conducted in laboratory and greenhouse experiments. This project aims to fill a research gap by scaling up results from the laboratory to the field level, and developing a mechanistic model to explain the contribution of earthworm communities to plant yield and nutrition.

My research involves both laboratory based studies of earthworms as well as field level manipulations of earthworm communities, with the aim of obtaining some important parameters that will help in quantifying the nutrient contributions of earthworms at the field level. In the laboratory, my research has investigated how earthworm growth rates are influenced by environmental factors (soil temperature and moisture), and by increasing population density in cultures with similar and different earthworm species. My field experiments involve manipulating the functional group and population of earthworm communities and manipulating the duration of earthworm activity. My field experiments were conducted in hayfield, soybean and maize agro-ecosystems. Combining the data from my laboratory and field experiments I developed a mechanistic nutrient model that estimates the contribution of earthworm communities to nitrogen pools in agricultural systems of Quebec.

7. Research implementation and results under the program

Title of your research plan:

The Role of Earthworms in Soil Nutrient Cycles

Description of the research activities:

My research activities primarily included presenting my Ph.D. research, aiding in the design of earthworm experiments, and helping with field work as outlined below:

1. I lectured in a graduate-level course at Yokohama National University about how to present scientific results at international conferences while discussing some ecological approaches to studying the role of earthworms in nutrient cycles.
2. I presented seminars to the Soil Ecology Group of Yokohama National University and at the Tomakomai Forest Research Station of Hokkaido University. At these seminars I discussed different aspects of my Ph.D. research, showed my experiment designs and the results of my modeling efforts.
3. We initiated the “Workshop on Soil Biological Communities and Soil Management” that was hosted by the School of Agriculture at Ibaraki University. At this workshop I presented my Ph.D. research and gave advice on improving and adapting my experiments. We conducted earthworm surveys of the Ibaraki University Research Farm and nearby commercial farms. Subsequently, I have written two draft proposals for long-term experiments based on my Ph.D. research and our discussions at this workshop. These experiments will include scientists from Yokohama National University, Ibaraki University, Tokyo University and the National Institute for Agro-Environmental Sciences. We have formed an online newsgroup “Earthworm Farming” to further discuss these experiments.
4. I assisted lab members in the construction and maintenance of long-term field enclosure experiments in Yatsugatake Research Forest in Yamanashi-ken and in Tomakomai Research Forest in Hokkaido.
5. I worked alongside a student whose Ph.D. project is very similar to my Ph.D. project. He is studying the role of Japanese earthworms in soil nutrient cycles while my project involved studying the role of Canadian earthworms in soil nutrient cycles. As such I have helped him with two major experiments:

   5.1 I helped to design of an earthworm growth rate experiment that also measures the rate of litter decomposition of different earthworm species.

This experiment is currently being conducted but final results will not be available for another 2 months.

5.2 I also helped to conduct investigations on the C:N:P stoichiometry of different earthworm species from Okinawa, Hokkaido, Kanagawa, Ibaraki and Canada. Preliminary results show some differences between C:N:P stoichiometry between species but nutrient data on soil and litter composition has not been completed so conclusions cannot yet be made from this data. Final results will not be available for another 2 months.

RESEARCH REPORT

1. Name: David L. Greenshields （ID No.: SP06403）

2. Current affiliation: Department of Biology, University of Saskatchewan, Canada

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences XBiological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: RIKEN Plant Science Center, Yokohama

5. Host researcher: Dr. Ken Shirasu

6. Description of your current research

My current research focuses on iron and reactive oxygen species in plant defence and fungal pathogenicity. On the plant side, I have found that iron accumulates at pathogen attack sites on the leaf epidermis. This iron accumulation produces a localized burst of hydrogen peroxide, which works to inhibit fungal growth by strengthening the plant cell wall and directly injuring the fungus. The rapid, transient accumulation of iron and the resulting hydrogen peroxide burst also act as signalling components in plant defence by promoting the production of protective proteins.

On the fungal side, I have created a series of *Fusarium graminearum* iron uptake mutants, which are missing key proteins required for efficient iron uptake. The mutants show a range of phenotypic abnormalities, including a reduction of virulence when infecting a wheat host.

Together, these results show that iron is a key component of both plant defence and fungal virulence.

7. Research implementation and results under the program

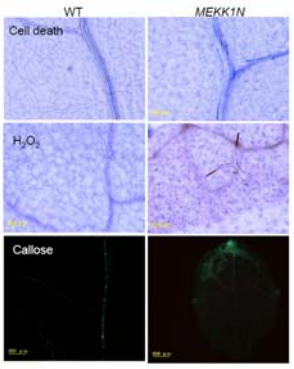
Title of your research plan:

The role of MEKK1 in *Arabidopsis* defence signalling

Description of the research activities:

MEKK1 is a protein in the *Arabidopsis* plant that relays an alarm signal from the cell surface to the rest of the cell following microbial attack. This signal triggers a range of defences, including microbiocidal hydrogen peroxide production, cell wall strengthening callose deposition, and localized cell death. *Arabidopsis* plants engineered to produce either too much or too little of the MEKK1 N-terminal regulatory domain (MEKK1N) grow abnormally and die prematurely. Dr. Kazuya Ichimura had previously produced *Arabidopsis* plants that overexpress MEKK1N and show the resulting phenotype only when exposed to the hormone estradiol. Seeds from these estradiol-inducible MEKK1N plants were chemically mutagenized, grown and the plants were allowed to self-fertilize and produce more seeds.

To characterize the estradiol-inducible MEKK1N plants, I grew seedlings in the absence of estradiol for a week and then treated them with estradiol for 4 days. Following this treatment, I stained the seedlings to reveal cell death or hydrogen peroxide or callose deposition. Compared with wild type plants, the MEKK1N overexpressing plants showed an increase in all three of these defence markers (Figure 1).



To find gene(s) required for the MEKK1 overexpression phenotype, I screened approximately 300000 chemically mutagenized estradiol-inducible MEKK1N seedlings for suppression of the MEKK1 overexpression phenotype. To date, 148 seedlings with a MEKK1N-supressing phenotype have been identified. These seedlings have been photographed and described, and labelled *smn-1* through *smn-148* (for *Suppressor of MEKK1N*).

Figure 1. Wild type and *MEKK1N* leaves stained for the indicated defence markers.

Although the limited time frame for conducting this research precluded any major advances in the project, the work sets the stage for suppressor screening of the MEKK1 overexpression phenotype. In the able hands of Dr. Ichimura, I am sure that the continuation of this project will lead to further insights into the function of MEKK1 in disease resistance signalling.

8. Please add your comments (if any):

Thank you to JSPS for providing me with this opportunity and to the Shirasu Lab, especially Kazuya, for the excellent experience.

9. Advisor’s remarks (if any):

Mr David L. Greenshields joined to the Shirasu Lab as a visiting student for two months. He conducted the MEKK1 project, one of my important research themes, to characterize the MEKK1N overexpression phenotype and isolate its suppressor mutant from the chemically mutagenized population. Although it was a short stay, he isolated 148 candidates of suppressor mutant and nearly finished the phenotype characterization. From my view, he is a talented person and obtains mature experimental techniques with high productivity. I was quite happy to work with him and I hope that he enjoyed this JSPS program.

Kazuya Ichimura

RESEARCH REPORT

1. Name: Amanda Kentner （ID No.: SP06404）

2. Current affiliation: University of Ottawa

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences X Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Kobe University Graduate School of Medicine

5. Host researcher: Dr. Susumu Seino

6. Description of your current research

My current work is an investigation of the relationship between estrogen and reward in immune activation, specifically related to cytokine-induced (flu-like) sickness behaviours in the rat. Peripheral immunity is modulated by the brain through the discharge of cytokines which are substances released by cells that have pro- and anti-inflammatory effects upon other cells; these modes of interaction provide means by which estrogen and the immune system may interact, thus inducing behavioural and physiological changes. Additionally, brain stimulation reward has been employed as a tool for tracking hedonic status in animals and has been connected to the prevention of disease in the rat. Since both the rat estrous cycle and brain stimulation reward have been associated with fluctuations in immune activation, discerning the mechanisms underlying these relationships may be important in understanding sickness responses as well as illness onset and recovery.

7. Research implementation and results under the program

Title of your research plan:

EXPLORING THE INFLUENCE OF REWARD MECHANISMS ON THE INTERACTION BETWEEN SICKNESS AND IMMUNITY IN THE FEMALE RAT.

Description of the research activities:

In the present project, we examined whether the severity of lipopolysaccharide-induced sickness behaviours was tied to reward condition (brain stimulation reward versus environmental enrichment). In addition, we wanted to determine the peripheral mRNA expression of several cytokines and their receptors (collected from tail blood) in order to distinguish how these levels change within animals over time, as a consequence of reward, as well as contribute to overall sickness severity. This work was carried out in female animals to assess the involvement of reproductive hormones in reward stimulated immune activation.

In Dr. Seino's laboratory, I was very privileged to learn numerous molecular techniques including TaqMan Real Time Polymerase Chain Reaction (RT-PCR) which was required to assess the peripheral mRNA expression of several cytokines of interest including interferon-alpha 1, interleukin (IL)-6, IL-6 receptor alpha, natural killer cell receptor, IL-2 and its alpha receptor, IL-1 beta, and IL-1 receptor antagonist. In addition to the above procedure, I became well practiced in other techniques including RNA isolation, cDNA synthesis, and electrophoresis (the latter being my favourite). During my stay in Japan I was able to complete data collection, and the final analyses will be concluded upon returning to Canada.

While in Japan, I was also very fortunate to be able to attend a Centre of Excellence seminar on Awajii Island where I learned about various on-going diabetes research projects here at Kobe University.

8. Please add your comments (if any):

I have greatly benefited from my working (and travel) experiences over the past two months. I have enormous gratitude for the students and professors in Dr. Seino's laboratory who were always very kind and available with helpful advice for both my research, and for ensuring that my stay was enjoyable. I think together we had many funny misunderstandings (who knew apartments are called mansions here?) and even more fun adventures, and I thank them all! I very much appreciate the willingness of the students to welcome me into their lives allowing me to become part of their laboratory and their culture. From wearing traditional Yukata at the Gion Festival in Kyoto, to exploring the Peace Memorials at Hiroshima, I feel as though I have been given an understanding of a deep rooted culture that I could not have appreciated otherwise.

With respect to research, I am very much impressed with the amount of interdisciplinary collaboration that occurs between departments and universities in Kobe, allowing investigators to develop interesting projects that progress scientific knowledge in various

areas. I am also pleasantly surprised by the interest of students and principal investigators in projects outside of their field of specialization. This willingness to explore different areas may hopefully lead to some collaboration in the future as we have discovered several related factors between our research fields.

Importantly, I would like to thank JSPS and NSERC for this amazing opportunity, and express my gratitude to both Professors Seino and Miki for allowing me to pursue my interest in learning molecular techniques in their laboratory! Arigotoo gozaimashita!

9. Advisor's remarks (if any):

Ms Amanda Kentner is a very knowledgeable and extremely hard working student. I was very much impressed with the ease with which she has quickly learned new techniques despite such a short stay, including isolation of RNA, cDNA synthesis, and real time PCR. Because of her friendly and pleasant nature**,** Amanda can get easily along with other people in our lab. Everyone in the lab enjoyed working with her very much. Besides her scientific study, she tried to spend as much time as she could to see Japan, visiting many historical places such as Kyoto, Nara, and Hiroshima to learn Japanese culture. I trust these experiences will certainly give broader outlook both to her life as a scientist as well as a person. We are completely satisfied with the JSPS program.

RESEARCH REPORT

1. Name: Aarlenne Zein Khan （ID No.: SP06405）

2. Current affiliation: Centre for Vision Research, York University, Toronto, ON, Canada, M3J 1P3

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences X Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Division of Applied System Neuroscience
Advanced Medical Research Center
Nihon University Graduate School of Medical Science
Tokyo, Japan

5. Host researcher: Dr. Taira Masato

6. Description of your current research

We make visually-guided arm movements such as reaching or grasping or pointing to objects we see all the time. Yet these movements require very complex processes in the brain which transform visual information about an object's location in space into a correct arm movement. Indeed, visually-guided movement deficits make up a large part of many brain disorders such as Parkinson's disease.

My project this summer involved using a brain imaging technique called functional Magnetic Resonance Imaging (fMRI) to examine which parts of the brain are involved in pointing to objects in three-dimensional (3D) space. The project also aimed to explore if and how different parts of the brain are involved in processing different components of 3D space e.g. horizontal, vertical and depth.

Together with Dr. Taira and Dr. Katsuyama of the Division of Applied System Neuroscience at the Nihon University Graduate School of Medical Science, I designed an experimental setup where we asked subjects to point toward different targets they saw through stereo goggles in the fMRI scanner and measured brain activity while subjects pointed to targets in different directions. We intend to compare brain activity specific to pointing in each direction to discover how the brain processes different directions for pointing. These results will bring us a significant step closer in understanding how visually-guided movements are processed in the brain. This in turn will aid in finding solutions to aid patients who have visually-guided movement deficits.

7. Research implementation and results under the program

Title of your research plan:

Imaging of brain areas involved in pointing movements to objects in 3D space

Description of the research activities:

Previous research investigating how the brain is involved in visually-guided research has suggested that an area of the brain known as the posterior parietal cortex (PPC) is extensively involved in the early planning of pointing movements. However, this research has largely focused on how the brain represents only two dimensions of space - horizontal and vertical. For example, studies often measured reaching to a touch screen, which ignores the third dimension – depth. However, a few recent neurophysiological studies suggest that the PPC may also involved in encoding depth (how far away a target is) for pointing movements. The current project therefore investigates in humans if and how the PPC represents the complete 3-dimensional position of a target. To this aim, we used a brain imaging technique known as functional Magnetic Resonance Imaging to measure human brain activity while subjects pointed to targets in each of the 3 dimensions. We designed an experiment to be implemented in the fMRI scanner – we used two stereo goggles which projected slightly different 2-D images (shifted horizontally from each other) to the left and right eyes. Subjects are able to fuse these two images which then produces a 3D image where targets can be seen in each of the 3 dimensions. Subjects fixated on a central fixation target that appeared to be floating about 20 cm straight ahead of the subject. Pointing targets then appeared either nearer or further away, to the left or to the right or above or below the fixation target. A total of 16 subjects were trained in the task and then completed the experiment. Analysis of the resulting data will follow. We will compare activation in the PPC specific to each direction and compare whether different parts of the PPC encode different dimensions of a pointing target. To date, no one has tested for activation related to movement in depth in the PPC in humans through fMRI. This project will benefit the field of eye-hand coordination because it will expand the current two-dimensional model of the PPC to a full three-dimensional model (horizontal and vertical direction and depth) for the internal representation of space.

8. Please add your comments (if any):

I would like to sincerely thank the JSPS Summer program for allowing me to take part in this unique opportunity. I am grateful to Dr. Taira and his lab for a very successful experience. I feel I have learnt a great deal about fMRI, which I did not know anything

about. I am also very happy that we were able to implement the experiment in such a short time – an fMRI experiment is very complex and usually requires at least 4-5 months to design and carry out. It is no doubt that it was the effort that Dr. Taira's lab put in, particularly Dr. Katsuyama, that allowed its completion. I am also happy to have experienced Japanese culture and life – my visits around the country were fascinating and I will always remember them.

RESEARCH REPORT

1. Name: Anne M. Landau （ID No.: SP06406 ）

2. Current affiliation: McGill University, Montreal, Canada

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences X Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Juntendo University, Tokyo, Japan

5. Host researcher: Dr. Hideki Mochizuki

6. Description of your current research

Parkinson's disease (PD) is the second most common neurodegenerative disorder. It is a relentlessly progressive disease of the nigrostriatal system and results from the selective degeneration of dopamine neurons in the substantia nigra of the brain. The consequent deficiency in striatal dopamine gives rise to the characteristic symptoms of the disease, including tremor, bradykinesia, rigidity and postural instability.

The Fas receptor, a member of the tumor necrosis factor receptor (TNF-R) superfamily, has been extensively studied as a death-inducing receptor in the immune system. However, Fas is also widely expressed in a number of other tissues, including in neurons. Recent evidence has demonstrated that Fas has several non-apoptotic roles and we hypothesize that Fas may be playing a neuroprotective role in PD.

We have recently demonstrated that Fas can be highly protective against neuronal cell death caused by the administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in both cellular and mouse models of the disease. MPTP-treated Fas-deficient *lpr* mice develop a dramatic phenotype resembling clinical PD, characterized by severe nigrostriatal degeneration accompanied by tremor, hypokinesia, and loss of motor coordination, at a dose which causes no impairment or neuropathology in wild-type mice. This work demonstrates a neuroprotective role for Fas *in vivo*.

7. Research implementation and results under the program

Title of your research plan:

Evaluation of Fas as a neuroprotective agent in the α-synuclein-induced mouse model of Parkinson's Disease

Description of the research activities:

As we have recently shown that Fas can provide protection in the MPTP-induced model of PD, we were interested in investigating whether Fas can also be neuroprotective in the α-synuclein model of PD. α-synuclein is present in the protein aggregates found in some PD patients and models of the disease. In certain cases, α-synuclein overexpression can initiate the disease process and has provided a model in which to study the pathogenesis and progression of PD.

This summer, in Dr. Mochizuki's laboratory, we overexpressed the α-synuclein gene using an adeno-associated viral (aav) vector gene overexpression system in Fas-deficient *lpr* and wild-type mice. This was done in order to determine whether the lack of Fas expression would exacerbate the protein aggregation and neurotoxicity which may be caused by α-synuclein. We monitored mice for alterations in activity, motor coordination and rotational behavior during a four week period. We then processed brains in order to determine striatal dopamine and metabolite levels and performed immunohistochemistry in search of signs of degeneration, markers of protein aggregation and mediators of cell death.

Preliminary data from this project supports a neuroprotective role for Fas in the α-synuclein mouse model of PD. Studies of Fas as a neuroprotective factor in PD may lead to treatments which promote survival of endogenous dopamine neurons. This work will be a continued collaboration between Dr. Mochizuki's lab in Japan and Dr. Desbarats' lab in Canada.

RESEARCH REPORT

1. Name: Jeffrey M. Mativetsky （ID No.: SP06408）

2. Current affiliation: McGill University

3. Research fields and specialties:

Humanities Social Sciences X Mathematical and Physical Sciences
Chemistry Engineering Sciences Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Kyoto University

5. Host researcher: Prof. Hirofumi Yamada

6. Description of your current research

My current work is focused on using high resolution noncontact atomic force microscopy (NC-AFM) techniques to understand and control the growth of nanostructures on insulating surfaces.

Despite the importance of non-conducting surfaces in catalysis, electronics, materials science, and even biology, this domain of research is largely unexplored. This is primarily due to the fact that there are few surface science tools which enable atomic scale measurements on such surfaces. NC-AFM, a technique developed over the last decade, is unique in its ability to nondestructively probe local forces and spatially resolve surface structure with atomic resolution on insulators, semiconductors, and metals. It is expected that NC-AFM will be pivotal in developing an atomistic understanding of nucleation and growth phenomena on insulators, much as scanning tunneling microscopy has done for conducting substrates.

During my PhD studies, I am using NC-AFM to investigate the growth of various metals and molecules on an insulating substrate. In addition, the creation of surface defects and the influence of defects on growth are being examined. With an improved understanding of the processes involved in the growth, we are aiming to exercise an increased level of control over nanostructure formation, and ultimately produce nanometer-scale surface structures by design.

7. Research implementation and results under the program

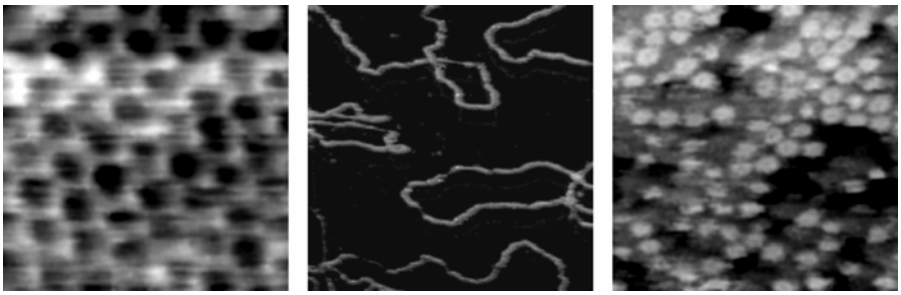
Title of your research plan:

High resolution noncontact atomic force microscopy in a liquid environment

Description of the research activities:

NC-AFM normally requires ultrahigh vacuum conditions for operation; however, last year it was demonstrated in Prof. Yamada's group at Kyoto University that NC-AFM can also be applied with sub-nanometer resolution in liquids. This has great implications for the fields of chemistry and biology where high resolution in liquids opens up new possibilities in visualizing molecules and cell structures in their native environments. During my stay in Kyoto, I had 2 main objectives: (1) to extend my current knowledge of NC-AFM to operation in liquids, and (2) to apply the technique to measuring the structure of biomolecules.

During the first few weeks, I gained familiarity with the liquid NC-AFM instrumentation by participating in ongoing experiments, and learned the required techniques for operating the microscope independently. To practice the technique, mica was imaged under water. Mica was selected as a test sample because it can be cleaved in air to expose large atomically flat surfaces which can be imaged with sub-nanometer resolution, as recently demonstrated in Prof. Yamada's lab. Moreover, mica is the substrate of choice for measuring the surface structure of biomolecules. As shown in the figure on the left side (frame size = 6 nm x 6 nm), it was possible to measure the honeycomb structure of mica. Furthermore, some small protrusions are seen at some of the vertices of the honeycomb. It is believed that spots correspond to individual aluminum ions.



In addition to mica, two biomolecules were imaged by NC-AFM under water: DNA and GroEL. A great part of the challenge in measuring these molecules was in establishing suitable sample preparation procedures for immobilizing the molecules on the mica surface. In order to measure DNA on mica (center figure, frame size =

600 nm x 600 nm), it was necessary to use nickel ions to bridge the negatively charged phosphate backbone of the DNA to the negatively charged mica. The measured thickness of the DNA is about 2.5 nm, which is in line with the true dimensions. Other AFM techniques erroneously provide heights below 1 nm, presumably due to the large forces imparted by these methods and the environments used during imaging. GroEL, a protein required for the correct folding of many other proteins, was also imaged with molecular resolution. The individual molecules (right side figure, frame size = 300 nm x 300 nm) are about 14 nm in diameter. In addition, it was possible to see the ring-like structure of the GroEL.

From July 16 to July 20 I attended NC-AFM 2006 in Kobe. This is an international conference which takes place yearly and is focused entirely on NC-AFM implementation and measurement. At the conference I presented a talk about some of my PhD thesis results related to imaging molecules on a nanostructured insulator under ultrahigh vacuum conditions.

8. Please add your comments (if any):

I very much enjoyed my stay in Japan, working in Prof. Yamada's lab. I feel that the JSPS Summer Program is a great way to learn about Japan and research in Japan. I would like to thank Prof. Yamada, JSPS, and the Canadian Embassy for this unique experience.

9. Advisor's remarks (if any):

Since Dr. Mativetsky has sufficient experimental skills on NC-AFM and a wide variety of knowledge on molecular science, he was quickly adapted to our research project on FM-AFM imaging in liquid environments, which is basically his research theme in this JSPS program. Although the period he worked here was quite short, he has made a great contribution to the project in terms of the interpretation of atomic scale contrast in FM-AFM images of mica as well as AFM imaging of DNAs in liquid. Based on his successful results and fruitful discussion, I would like to continue our project with the collaboration with him.

RESEARCH REPORT

1. Name: Dominique Robert (ID No.: SP06409)

2. Current affiliation: Université Laval

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences X Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: National Research Institute of Fisheries Sciences

5. Host researcher: Dr. Akinori Takasuka

6. Description of your current research

In marine fish, year-to-year variability in recruitment (the entry of a new age class of fish into the adult population) is tremendous and represents one of the main sources of problems in fisheries management. The ecological, political, social and economic crises that currently beleaguer the fishing industry worldwide make it vital to obtain an in-depth understanding of the processes that control recruitment. The central hypotheses in fisheries oceanography relate variability in recruitment strength to variability in larval survival. A better understanding of the mechanisms that determine larval survival could therefore become a powerful tool for managing fish stocks, including that of the Atlantic mackerel *(Scomber scombrus)* of the southern Gulf of St. Lawrence, which is the focus of my current research.

This current research has three main objectives. The first is to describe the diet and the feeding strategy of mackerel larvae and to target the potentially limiting environmental factors. The second part of this thesis deals with the relationships between the environment, larval growth and recruitment strength. The third and final objective is to quantify the initial and post-larval growth of one-year-old juveniles (survivors) from the four years of the study (1997-2000) in order to identify the precise timing of a recruitment bottleneck. These objectives will serve as the basis for testing the hypothesis that years of strong recruitment are the result of the combination of an environment favourable to rapid growth and relaxed selection pressures (such as predation) for rapid growth in the larval stage. The importance of this study is that it will be the first to completely test the linkages among feeding performance, larval growth and recruitment strength for the Atlantic mackerel. With the collapse of numerous groundfish stocks on Canada's Atlantic coast in recent years, greater fishing pressure could be exerted on the Canadian mackerel stock, currently the most abundant. In this context, an understanding of the connections between the environment and recruitment could provide extremely useful information for managing the stock and thus help to ensure that it will be healthy in the future.

The preliminary results are of great interest, because they show that the fish that have survived to age 1 are the individuals that grew the fastest during the larval stage. This study thus provides major support for the central hypotheses which predict that in the natural environment, survival is directly related to rate of growth in the larval stage. The larvae that grow faster would be vulnerable to planktonic predators for a shorter

time, thus explaining their relatively high success compared with the slower-growing larvae.

7. Research implementation and results under the program

Title of your research plan:

Study of the effects of predation on larval growth and survival of Japanese anchovy (Engraulis japonicus) through the analysis of otoliths found in the stomach of mackerel predators.

Description of the research activities:

The goal of the research in Japan was to obtain a more in-depth understanding of the connections between the selective survival of fast-growing individuals and the intensity of predation pressures in marine fish larvae. Particularly, the project was aiming at testing the hypothesis that the growth rate of the surviving larvae is on average higher than that of the larvae found in the stomach of mackerel predators. The Japanese anchovy (*Engraulis japonicus*) was used as a model for this study, because the dynamics of the larval stage of this species are comparable to those of the Atlantic mackerel.

During my research experience in Japan, I could learn the techniques related to fish stomach dissection as well as refine those of otolith preparation, mounting and reading. Unexpectedly, we found out that an important part of the predatory mackerel diet relied on the juvenile stage of anchovy. The research project was thus extended to include juvenile growth, rather than the sole larval growth as initially planned. To date, all otoliths have been picked and mounted on microscope slides. The lack of time will prevent me from analysing all otoliths prior to my departure, but the project will be continued as a collaboration between my laboratory in Université Laval (directed by Prof. Louis Fortier) and my laboratory in Japan (Dr. Akinori Takasuka).

This study will be the first one to assess if the growth-selective behaviour of predators (mackerel) evolves as a function of the ontogeny of their main prey (anchovy). The results of this study may lead to a better understanding of the juvenile stage dynamics of marine fish and will provide a powerful test of the current recruitment hypotheses in fisheries oceanography.

8. Please add your comments (if any):

I would like to thank the JSPS and the Canadian Embassy for offering me the opportunity of participating into such a formative and interesting program. I also want to express my gratitude towards my supervisor, Dr. Akinori Takasuka, as well as to everybody in the laboratory of Dr. Yoshioki Oozeki, who made my stay being a wonderful experience.

RESEARCH REPORT

1. Name: Ching Yin (Karen) Lee （ID No.: SP06411）

2. Current affiliation: McGill University

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences XBiological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Fukushima Medical University

5. Host researcher: Dr. Ikuo Wada

6. Description of your current research

During our investigation of families with low high-density lipoproteins-cholesterol (HDL-C), one patient was found to have mutations for a gene called the sphingomyelin phosphodiesterase-I (SMPD-I). This gene codes for lysosomal and secretory sphingomyelinase (ASM) proteins and its mutations cause the recessive disorder of Niemann-Pick disease type A/B (NPD-A/B). In order to understand the pathophysiology of low HDL-C in NPD-B, we investigated the structure/function of the ASM. The structure of ASM has never been well characterized. Although no known functional domain is predicted in the protein's carboxyl(C)-terminus (amino acids 462-629), this region is particularly interesting because it harbors the second most SMPD-1 mutations discovered so far. We hypothesized therefore that the C-terminus of ASM is important for the formation of a correct protein conformation crucial to its function.

In order to study the structure and function of the ASM, we have created a series of C-terminal mutants. By examining the protein expression, half-life, secretion and post-translational modifications, we have demonstrated that the C-terminus of the ASM protein, precisely its terminal disulfide bond (C591-C607), is critical for it structural and functional integrity. Two important mutants having a mutation within this region (ΔR608 and N590) have been selected for further investigation of the protein localization.

7. Research implementation and results under the program

Title of your research plan:

The Role of the C-Terminus on the Intracellular Trafficking of the Acid Sphingmyelinase.

Description of the research activities:

We have first examined by confocal microscopy the localization of C-terminally V5-tagged wildtype and mutant recombinant ASM's subsequent to a 16-hour transcient transfection in COS cells. While we found that the ΔR608 and N590 were trapped in the Endoplasmic Reticulum (ER), as predicted by their aberrant structural conformation, we also observed a strong and clear ER fluorescent pattern for the wildtype ASM. ASM is known to be located in the lysosomal compartments within a cell and this surprising observation could be explained by 2 possibilities: (1) The C-terminus of the ASM containing a free cysteine residue may be cleaved after reaching the lysosomes, as seen in some other lysosomal proteins. Thus, the V5 tag was cleaved in mature ASM and the anti-V5 antibodies could only detect the unprocessed wildtype ASM that remains in the ER compartments. (2) Or, the overexpression system has simply overloaded the protein biosynthesis machinery such that many of the overexpressed ASM proteins remained unprocessed and entrapped in the ER after the protein translation.

To eliminate the first possibility, we have subcloned the wildtype and mutant ASM into N-terminally YFP- and HA-tagged vectors and we have re-examined their localization in the presence or absence of protease inhibitors. We have consistently found that the ΔR608 and N590 mutants were localized in the ER. When the YFP-tagged wild type ASM was examined directly under the microscope, we did not observe the strong ER pattern any more but the general fluorescence was too weak to determine its localization. When the YFP- or HA-tagged wild type ASM was immunostained, we found a few lysosome-like punctates while the ER signals remained dominant. We therefore suppressed the protein overexpression by treating the cells with cyclohexamide, a drug that stops the protein synthesis. Interestingly, under this experimental condition, we could clearly observe the lysosomal fluorescence signals that were colocalized with lysosomal but not ER markers.

Our results strongly support our previous data on the ASM structure and function: mutations in the C-terminus lead to aberrant structural conformation that prevents the protein from trafficking through the ER quality control checkpoint.

RESEARCH REPORT

1. Name: Janay Brianne MacNaughton （ID No.: SP06412）

2. Current affiliation: Department of Physics and Engineering Physics, University of Saskatchewan, Saskatoon, SK. Canada

3. Research fields and specialties:

Humanities Social Sciences X Mathematical and Physical Sciences
Chemistry Engineering Sciences Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Institute for Molecular Science (IMS), Okazaki, Japan

5. Host researcher: Professor Nobuhiro Kosugi

6. Description of your current research

The desire to build devices on the nanoscale motivates molecular electronics research. DNA is an attractive choice for this field because it is widely available and readily manipulated. However, one source of controversy is whether or not DNA is an electrical conductor. The number of atoms and the complexity of the molecule and its surrounding environment makes designing experimental setups and theoretical models difficult in the quest to understand the material's properties. Therefore, there is motivation to uncover the problems and study the electronic properties of DNA. My Ph.D. project investigated the electronic structures of DNA and several DNA-related compounds using synchrotron radiation. Using x-ray absorption spectroscopy (XAS) and x-ray emission spectroscopy (XES), the electronic structure of the molecule can be probed. These experiments were performed at beamline 8.0.1 at the Advanced Light Source synchrotron in Berkeley, California. Two different calculation programs, one based on Hartree-Fock theory (GSCF3) and another on density functional theory (StoBe) were used to model the measured spectra of several of the smaller molecules investigated in this study.

7. Research implementation and results under the program

Title of your research plan:

Radiation Damage Effects on the Electronic Structure of Glycine

Description of the research activities:

Soft X-ray absorption and emission spectroscopy are synchrotron-based experimental probes of the electronic states of a material. These techniques can be used to determine structural, electronic and magnetic properties. However, large biological molecules such as proteins and DNA are prone to radiation damage and understanding the mechanisms that lead to the damage is essential. Amino acids are the building blocks of proteins and their simplicity makes them ideal candidates to study the effects of radiation. Radiation damage can cause organic molecules to undergo both structural changes and chemical modifications. Understanding radiation damage is important in both molecular spectroscopy and biological processes.

The first step to gain insight into the radiation damage process was to optimize the geometry of several models of glycine using the Gaussian computational code. A neutral version (Gly, structure common in gas phase), a zwitterion version (ZGly, structure common in liquid/solid phase), and many damaged versions of glycine were constructed. The damaged versions of glycine were made by removing hydrogen atoms from the structure in an attempt to model the deprotonation process that is likely to occur during radiation damage. Numerous models were attempted and it was found that models that involved the removal of one hydrogen atom from the structure of glycine proved to be difficult to calculate. The best result was for a model where hydrogen atoms were removed from both the nitrogen and carbon, causing a double bond to form between the atoms (DGly model). Additionally, many different calculations were performed to compare the results of using different basis sets with the Gaussian computational code. Ultimately, the 6311G**MP2 basis set was chosen for the Gly and DGly models, while the 631G was used for the ZGly model.

The GSCF program package (written by Nobuhiro Kosugi) was used to perform ab initio calculations of inner shell excitation and ionization of the glycine molecules to gain insight into the changes in the X-ray absorption spectra that occur after amino acids are irradiated. Additional calculations were performed with additional basis functions included to better represent Rydberg states. The following key results were found by calculating the X-ray absorption spectra using the GSCF3 calculation code for the Gly, ZGly, and DGly models at the carbon, nitrogen, and oxygen edges.

1. The two carbon sites are nonequivalent since they are involved in different types of bonding. The C1 and C2 atoms have different spectral contributions.
2. The agreement with the pre-radiation damage experiment is better for ZGly than Gly, which is in agreement with solid glycine likely having a

zwitterionic structure.

3. Radiation damage results in the formation of a new feature in the carbon and nitrogen spectra at low energy. This feature is reproduced in the calculation of the damaged glycine model, DGly because the removal of hydrogen atoms which results in the formation of a nitrogen – carbon double bond.

4. Like the carbon atoms, the two oxygen atoms are also nonequivalent. The oxygen spectra for the three models (Gly, ZGly, and DGly) are quite distinct.

5. Comparing measurements at the oxygen edge to calculations will be useful in determining further information about the radiation damage of the glycine molecule.

6. The results from the calculations which were focused on good representation of the Rydberg states were found to be very similar to the calculations that did not include these extra basis functions.

Further experiments will be useful for this study and will be completed in October at the Advanced Light Source. Taking many spectra over time will be useful to see how the radiation damage evolves over time. Additionally, measurements at the oxygen edge are also very important as they may give the best indication to what kind of structures are present in the sample. Calculations of other damaged models of glycine may be useful. Overall, it is found that deprotonation (loss of hydrogen atom from the structure) is a possible change occurring during the irradiation of glycine with soft X-rays.

8. Please add your comments (if any):

The JSPS Summer Program has been an excellent experience which has allowed me to experience Japanese culture and the scientific community at a research institution. My experience at the Institute for Molecular Science (IMS) has been extremely positive; the atmosphere was very friendly and welcoming. Living in Okazaki has been truly remarkable, I have had many wonderful experiences, and I have felt very much at home here. I have learned many things this summer and look forward to future collaborations with Prof. Kosugi. This research experience has proven to be invaluable to my continued development as a scientist. Thank you for this opportunity to participate in this outstanding program. Domo arigato gozaimasu!

RESEARCH REPORT

1. Name: Ekatherina Stoyanova （ID No.: SP06413）

2. Current affiliation: University of Montreal

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences

Chemistry Engineering Sciences X Biological Sciences

Agricultural Sciences Medical, Dental and Pharmaceutical Sciences

Interdisciplinary and Frontier Sciences

4. Host institution: Institute of Development, Aging and Cancer, Tohoku University

5. Host researcher: Dr Yoshifumi Saijo

6. Description of your current research

β-Thalassemia is a hereditary disorder caused by over 200 mutations that decrease or abolish the synthesis of the β-globin chains composing the hemoglobin protein in red blood cells (RBC) . In addition to the chronic anemia, patients are suffering from diverse blood circulatory problems such as transitory ischemic attacks and arterial and venous thromboembolic events. The main purpose of my current research is to study *in vivo* and *ex vivo* cardiovascular physiology in untreated transgenic mouse models of β-thalassemia. The specific objectives of my research project are : 1) To evaluate cardiac morphology and function using high frequency ultrasound imaging and compare with pathological and histological results; 2) To investigate *in vivo* microcirculatory blood flow with intravital microscopy and non-invasive high frequency ultrasound; 3) To evaluate *in vivo* and *ex vivo* endothelial vasomotor function in thalassemic mice.

This research project will provide important insights on cardiac and vascular pathophysiology of β-thalassemia. This achievement will be accomplished through *in vivo* and *ex vivo* studies of cardiac function, microcirculatory blood flow and endothelial vasoactive function. Expected findings will not only elucidate pathological mechanisms but also contribute to future development of novel therapeutic strategies.

7. Research implementation and results under the program

Title of your research plan:

Evaluation of the acoustic properties of the arterial vascular wall in β-thalassemic mice

Description of the research activities:

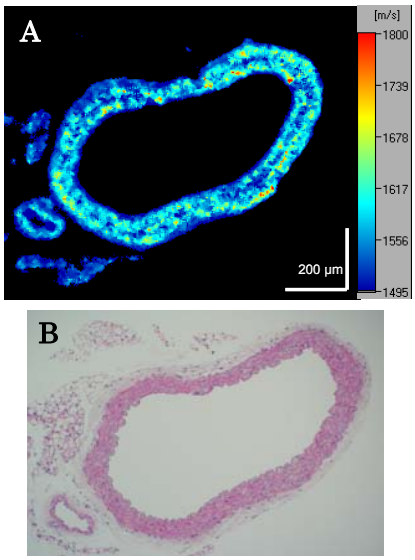


Figure 1 : Abdominal aorta of control mouse: A) Acoustic image of the speed of sound and B) Optical microscopic image of hematoxylin and eosin staining.

Vascular endothelium is indispensable for the regulation of vascular tone and vascular homeostasis. The primary characteristic of endothelial dysfunction is the impairment of endothelium-dependent vasodilation. However, endothelial dysfunction also generally comprises a proinflammatory and procoagulant state, which favours the development of arterial wall lesions. Studies in β-thalassemic patients report impaired endothelial vasoactive function. One research group even reported increased atherogenic risk in β-thalassemia patients. These findings lead us to hypothesize that the endothelial dysfunction in β-thalassemia causes a structural alteration of the arterial wall that may even contribute to the development of atherosclerosis-like lesions.

The objective of this study was to analyze the mechanical properties and composition of the arterial walls of pathological mice and to compare them with normal and atherosclerotic arterial walls. The laboratory of Dr Yoshifumi Saijo (proposed host researcher) is an internationally renowned research group in high-frequency ultrasound imaging. Acoustic microscopy is a unique powerful high-frequency ultrasound imaging technique allowing the characterization of the mechanical and structural properties of tissues at a microscopic level.

Two groups of 7 and 13 month old mice were studied: homozygous β-thalassemic mice and C57Bl6 mice. Mice were euthanized and the abdominal aorta, left carotid artery, right femoral artery and one second order mesenteric arteriole were excised. Samples were fixed by formalin, embedded in paraffin and cut in 5-µm thick sections with a microtome. In order to evaluate the structure of the vascular wall, acoustic microscopy measurements were performed on the blood vessel tissue samples using a HUM-1000 Ultrasonic Microscope (Honda Electronics Co., Toyohashi, Japan). Sound speed images were obtained from these measurements (Fig.1). Afterwards, the identical samples were stained for normal and polarized microscopy. Quantitative evaluations of the speed of sound in vascular walls will be performed on all the data obtained.

This study provides unique valuable mechanical and structural information of the arterial vessel wall in β-thalassemic mice. By investigating vascular physiology in β-thalassemic mice, this project contributes to the potential elaboration of new treatment strategies and possible genetic therapies improving the quality of life and increasing life expectancy of affected patients.

RESEARCH REPORT

1. Name: Alison Burgess （ID No.: SP06414）

2. Current affiliation: University of Toronto, Toronto, Canada

3. Research fields and specialties:

Humanities Social Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences X Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Juntendo University, School of Medicine

5. Host researcher: Dr. Tatsunori Seki

6. Description of your current research

Polysialic acid (PSA) is a large carbohydrate molecule which is abundant during neuronal development. Interestingly, the expression of PSA is very restricted in the adult brain. My PhD thesis is focused on understanding the function PSA in the developing and adult brain. In the embryo, we examined the role of PSA on the development of the septal cholinergic neurons. We discovered that removal of PSA potentiates the ability of neurotrophins to increase cholinergic activity. The specific binding of neurotrophic factors to their receptors on the neuronal membrane was low in the presence of PSA. However, when PSA was removed enzymatically, neurotrophin binding was increased and the neurons expressed a more mature cholinergic phenotype. These results indicated that PSA limits the availability of neurotrophins to developing neurons and may be important for preventing maturation of embryonic neurons before they reach their target site.

In the adult brain, there are 2 brain regions which exhibit continuous generation of new neurons from a source of neural progenitor cells. Interestingly, newly generated neurons express PSA and develop in a supportive microenvironment containing PSA-expressing cells. My future work will focus on investigating the role of PSA in these newly formed cells in the adult.

7. Research implementation and results under the program

Title of your research plan:

The role of polysialic acid in adult neurogenesis.

Description of the research activities:

PSA is expressed by newly formed neurons in the dentate gyrus of the adult rat however the role of PSA on these cells is unknown. We used a bacteriophage derived enzyme, endoN, known to specifically cleave PSA from the cell membrane to investigate the effect of PSA removal on these cells. We delivered endoN to 8 week old Wistar rats using stereotaxic injections into the dentate gyrus. 2 days after the surgery, animals were treated with BrdU, a chemical reagent which is used to label proliferating cells. Animals were left for 3 or 7 days and then perfused and processed for immunocytochemistry.

To study the early differentiation events of newly formed neurons, we used immunocytochemical markers to identify cycling cells and cells expressing an immature neuronal phenotype, 3 days after BrdU injection. These data will demonstrate if PSA has an effect on the early differentiation of progenitor cells into immature neuronal cells. We also performed immunocytochemistry 7 days after BrdU injection, using markers for immature and mature neurons. These data will describe the role of PSA in maturation of newly generated cells in the adult dentate gyrus. Overall, preliminary analysis suggests removal of PSA improves the differentiation and maturation of newborn neurons in the adult.

This research will be continued through a collaboration between Dr. Seki and Juntendo University and Dr. Aubert at the University of Toronto.

9. Advisor's remarks (if any):

She has been so far working in the *in vitro* analysis of embryonic neural development, and in our lab she challenged to do the *in vivo* analysis of adult neurogenesis. Finally, she has obtained some results that suggest an important role of the PSA in adult neurogenesis. During her stay in our lab, I realized that she is a very excellent PhD candidate and enjoyed our collaboration very much.