oculus

Volume 1 | Spring 2010 | JUROSonline.com

Selected manuscripts from The Journal of Undergraduate Research at Ohio State

OCULUS PRODUCTION STAFF

JOURNAL OF UNDERGRADUATE RESEARCH AT OSU STAFF

WHAT ARE *JUROS* AND *OCULUS?*

JUROS is an online, undergraduate research publication that accepts manuscripts from Ohio State undergraduates in any area of study. Submission to *JUROS* is electronic, and requires a faculty approval form and an author license agreement form. There is no submission fee, authors retain rights to their work, and each manuscript is reviewed in a double-blind peer review process before being accepted and published on a rolling basis on *JUROSonline.com*. Publication in *JUROSonline* automatically enters submissions to be considered for publication in *Oculus*, *JUROS*'s annual, hard-copy highlights publication. Furthermore, accepted manuscripts qualify to be used as part of a video podcast series to be published on *JUROSonline.com*. *JUROS* and *Oculus* are edited, reviewed and published by Ohio State undergraduate students. In conjunction with research manuscripts, both *JUROS* and *Oculus* publish Undergraduate Research Feature articles, Professor Spotlights and Student Research Experience commentaries. *JUROS* and Oculus can be viewed at *JUROSonline.com* or by requesting more information at JUROS@osu.edu.

Printed by: Zip Publishing, A Division of The Educational Publisher, Inc.

cover image by Shane Peterson

FEATURES

Glut-3 and Glutamate/GABA Imbalance
Sara Rapaport discusses her research aimed at discovering the causes of seizure activity in patients with Glut1D disorder.
(p. 14)

CONTENTS

ARTICLES

COVER ARTICLE:

Effect of Increased Activity on Metabolic Markers in Captive Black Rhinos: A Pilot Study

Josephine Bryk

Bryk investigates the relationship between exercise and insulin sensitivity and inflammation in both female and male rhino subjects. She explores the changes in metabolic markers in a captive black rhinoceros population in Cleveland, Ohio.
(p. 19)

ARTICLES

LETTERS

Dear *Oculus* Reader,

We are honored to present to you the premiere issue of *Oculus*, the hard-copy review of the Journal of Undergraduate Research at Ohio State (*JUROS*). The creation of the Journal of Undergraduate Research at Ohio State has taken over three years and its dream, *JUROSonline* and *Oculu*s, has finally come to fruition. *JUROS* started from humble roots—an idea and a student organization created by enthusiastic undergraduates involved in research on campus.

According to the OSU Office of Research, Ohio State faculty received approximately $703 million towards research in 2008. The *JUROS* team knew that behind each dollar spent by faculty members on their research were diligent undergraduates, toiling away countless hours in an OSU laboratory or office.

The path to the creation of *JUROSonline* and *Oculus* was not simple. Staff members were constantly being recruited along with solicitations for undergraduate manuscripts and faculty editorial board members. Furthermore, the double blind peer review process required of each submission compounded with schoolwork made the completion of review and final publication appear near impossible.

Fortunately, *JUROS* found the perfect partner—the Undergraduate Research Office at Ohio State (URO). Dr. Allison Snow and Helene Cweren, the two masterminds of URO, invested generous amounts of time and finances towards the future of *JUROS*, an all-inclusive, online, student-run journal. Three years later, following ten superior manuscript submissions and a dozen features articles and through countless hours of labor of a small print staff of only nine people, we have arrived at a completed print issue.

We must thank everyone, including undergraduates, faculty and URO staff, who supported *JUROS* and *Oculus* until its debut. We list many of them in our "Special Thanks" section, and want to express our heartfelt gratitude for their relentless work ethic and unparalleled support of a stubborn, yet not impossible, idea.

Lastly, we must thank you, our readers. We hope that through this publication, we are able to accomplish our mission: to publish undergraduate research, from various disciplines, for a wide audience and to create a forum for intellectual discussion. We hope that the publication of *Oculus* and *JUROSonline* will make undergraduate research at OSU more visible and will spur an interest for undergraduate research and in publishing undergraduate research in a professional publication. We hope you will enjoy the variety of features articles, commentaries and manuscripts that we have collected within *Oculus*.

Sincerely,

Olga Borodulin
Editor-in-Chief
JUROS

Sean M. Craig
Chief Editor
Oculus

Jinwei Hu
Chief Editor
Oculus

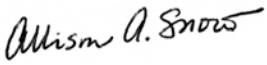
LETTERS

From the OSU Undergraduate Research Office:

On behalf of the entire OSU community, I thank editors Olga Borodulin, Jinwei Hu, Sean Michael Craig, and their many collaborators and friends for creating this unique and outstanding publication.

We are exceptionally proud of our students' research and creative activities, and it is exciting to have a new venue for showcasing these accomplishments. Congratulations to the entire *JUROS*/*Oculus* team for a job well done!

With best wishes,



Professor Allison A. Snow
Director of the Undergraduate Research Office

SPECIAL THANKS

Dr. Allison Snow
Director of the Undergraduate Research Office (URO)

Helene Cweren
Program Manager of URO

Henry Griffy & Ruth Gallegos Samuels
OSU Libraries

Erica Haugtvedt
The Ohio State University College of the Humanities

Julie Starzynski
The Ohio State University College of the Humanities

As well as our authors and their advisers.

ORIGINAL *JUROS* TEAM

Jennifer Duann
The Ohio State University Graduate School of Teaching and Learning

Joshua Everhart
The Ohio State University College of Medicine

Yoonhee Ha
London School of Hygiene and Tropical Medicine

Michael Jaung
Harvard Medical School

Jacob Deppen
University of Washington Graduate School of Archaeology

SUBMISSION TO THE JOURNAL

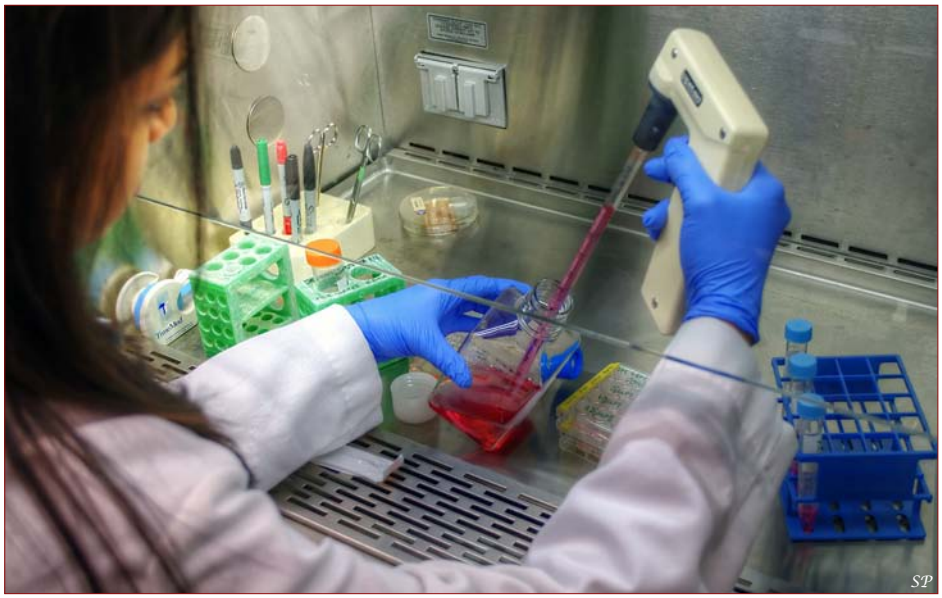
Publication in *Oculus* is simple:

1. Go to *JUROSonline.com* and click on the Submit tab.
2. Fill out the License Agreement Form and have a Faculty adviser sign the Faculty Agreement Form.
3. Fax, send or e-mail all submission forms along with the manuscript and all Figures, Tables and Images to *JUROS*.
4. Receive notification of receipt of submission and subsequent double-blind peer review.
5. Make changes to manuscripts based upon manuscript reviewer commentary.
6. Be published online after *JUROS*'s receipt of revised manuscript.
7. Await selection for publication in Oculus and volunteer to partake in the creation of a *JUROS* video podcast.

Redox Regulation of Agonist-Induced Tight Junctions Alterations and Paracellular Leak in Intestinal Epithelium: Protection by Thiol Redox Stabilizers

Aarti Vala

I never thought a college undergrad would get the opportunity to do research on a respectable level. It seemed like a job for the professionals where students functioned as dishwashers. I soon discovered that undergraduate research at The Ohio State University is highly encouraged. I have always wanted to be a part of research, something I found to be vital to the advancement of all we know. Being a microbiology major, biological research stuck out in particular for me. There is so much that is unknown to us, and research is the key to uncovering this mysterious world. I was lucky enough to find a mentor at the Davis Heart and Lung Research Institute, Dr. Narasimham Parinandi. He has trained nearly 40 undergraduate students in research at Ohio State and welcomed me to his lab, assigning me my own project. Working in a lab offers me an opportunity to gain scientific research experience and knowledge. It also utilizes what I have learned in countless hours of biology and chemistry lectures, assuring me that school is not a total waste of time.



The process of splitting and passaging cells is done under a hood to minimize contamination.

Instead, those hours of class go toward an amazing cause: research that could ultimately affect many people's lives. Intestinal epithelial disorders are caused by the alteration of tight junctions in the gastric epithelial lining. Tight junctions are crucial for the cell-to-cell adhesion between two cells, including the gut epithelial cells. They are composed of a cytoskeleton, structural proteins, signaling cascades and lipids, which together create a membrane impermeable to macromolecules, cells, and fluids. These tight junctions not only hold cells together but control the passage of molecules through the spaces between cells utilizing methods such as paracellular transport. When there is an imbalance between the production of reactive oxygen and the body's ability to readily detoxify these toxins by thiol redox, proteins, among other critical molecules, face damage. Consequentially, the cytoskeletal proteins that make up tight junctions are impaired and fail to create an impermeable or selectively permeable barrier to fluids in the intestinal tract. This causes many gastric dysfunctions, including the leaky gut syndrome commonly encountered in autistic children. The goal of my research is to elucidate the mechanism of induction that causes loss of tight junctions in the intestinal epithelial cells and utilize thiol redox stabilization drugs to protect against this alteration.

To study the mechanisms of cytoskeletal alterations, I use the well-established intestinal epithelial cells (Caco-2 model). Alterations include actin cytoskeletal reorganization, ZO-1 tight junction protein alterations, and occludin tight junction protein disruption. Causation of these seems to stem from exposure of cells to heavy metal agonists (e.g. mercury, an agonist considered to be an etiological factor in autism) and bacterial lipopolysaccharide (LPS, known to induce tight junction alterations). Oxidative stress resulting from reactive oxygen species is known to cause signaling activation through protein kinase activation. This leads to tight junction protein deregulation and altered barrier function. Therefore, I also study the role of reactive oxygen species in tight junction cytoskeletal protein reorganization and epithelial paracellular leak upon exposure of the cells to the agonists. In this context, I use cell biology, biochemistry, and molecular biology techniques to measure cytotoxicity, reactive oxygen species determination, and thiol redox determination in Caco-2 cells undergoing agonist-induced tight junction alterations and paracellular leak. I am also being trained to utilize confocal immunofluorescence microscopy to localize and determine the alterations in the tight junction proteins responsible for the agonist-induced intestinal paracellular leak. Following the establishment of the mechanism of the agonist-induced tight junction alterations and paracellular leak of macromolecules in the intestinal cell mono-layers, I will establish the efficacy of thiol redox stabilization drugs to protect against the alterations and associated paracellular leak, as encountered in autistic conditions.

This research experience has provided me with an excellent opportunity and has opened up a completely new world in my academic life. This has been a great learning experience that teaches me the tools and techniques to conduct scientific research. Above all, my research project has significance in biomedical research, both at the basic and therapeutic levels. ■

Patient Trust in Medical Professionals

Vikas Gampa

The element of trust in the doctor-patient relationship is undoubtedly important; all of us want a doctor who we can trust. We trust our doctors to treat us with proper medication and to offer us proper care. We also trust our doctors to do what is in our best interests and to act in ways that benefit us most. Though trust is often cited as an important element of a doctor-patient relationship, it has not been analyzed thoroughly with regard to the models that represent this relationship. My research project, therefore, is focused on the topic of trust. The project is three-fold: first, I will examine the different types of trust; secondly, I will analyze what it means to "trust" a person; and thirdly, I will consider the role of trust in three contemporary models of the doctor-patient relationship. The three contemporary models that I will consider include the priestly model, the technician model, and the contractual model. After considering each of the models and the role of trust in each of these models, I will argue for the model that best represents the actual doctor-patient relationship with regard to the element of trust.

The research conducted so far reveals that there are several models of trust and several ways of understanding what it means to say that we "trust" someone. According to Buchanan, trust in a medical institution can be represented primarily in two ways (190). The first type of trust is status trust. Status trust is trust that an individual enjoys because he or she belongs to a special group in society (Buchanan 191). In the United States, individual doctors enjoyed status trust because society revered medical professionals at one point. However, that type of status trust has been waning, and focus has shifted to another model of trust.

This second type of trust, according to Buchanan, is merit trust. Merit trust belongs to a doctor because of his or her credentials or skills. There are two types of merit trust: primary and derivative. Primary merit trust is that which a patient has in a doctor because of the doctor's skills and behavior, and derivative merit trust is that which a patient has in a doctor because the doctor belongs to an institution that regulates the doctor's actions. Buchanan contends that derivative merit trust is all that is necessary in the doctor-patient relationship (191).

Buchanan's assertion does not account for all the parts of trust. When we trust someone, we mean that we not only expect certain results, but also that we expect the individual to have good intentions toward us (Baier 234). Conversely, Buchanan advocates a sense of trust that does not take into account good will or good intentions. The problem with Buchanan's account is that it relies purely on external factors and that it assumes that trust simply indicates that we are seeking certain results. From the research conducted so far, I have concluded that to trust an individual means that the person trusting expects not only certain outcomes, but also that the person being trusted has good intentions towards him.

I will utilize this research on trust as I consider each model. The first model is the priestly model (Veatch 5). In this model, the doctor is a mentor who both advises the patient and performs the treatment. The physician is responsible for informing the patient of medical, as well as moral matters. From the analysis of trust conducted thus far, it is evident that trust may be represented in multiple ways in this model. In Buchanan's terms, the priest has status trust because of belonging to the priestly class, as well as merit trust, both because the doctor belongs to a regulated institution and because the doctor has to have been educated in a medical school that provides him with all of the necessary knowledge and tools to practice. The last way in which trust functions in this model is that the model accounts for good intentions as well; having the role of a priest implies that the intentions of the doctor are good.

The second model, the technical model, suggests that the doctor is a technician who engages in work that is meant purely to produce beneficial results for his patients (Veatch 6). This model accounts for

Do you trust your medical professionals to discuss all of your treatment options with you?

Karen To investigates doctor patient discussions of alternative medicine. (p. 57)

merit trust as well as status trust. However, the doctor need not have good intentions, and as such, this model does not have all the necessary elements of trust.

The final model that I will survey throughout the course of my research is the contractual model (Chalmers 12). The contractual model conveys the idea that the doctor and the patient enter into an unspoken, unspecific contract. The doctor trusts that the patient will respect and pay the doctor, and the patient trusts that the doctor will provide proper treatment. The role of trust, however, seems to be limited to the results and does not account for the importance of good intentions on the part of the doctor or the patient.

The project, thus far, has been focused on compiling information and research from the works of eminent philosophers, physicians, and bioethicists. The next phase of the research project will be to analyze the role of trust thoroughly in each of the models presented above. Finally, the thorough analysis of the role of trust will enable me to advocate one of the several models as the one that best represents the concept of trust in a doctor-patient relationship. ■

References

[1] Baier, Annette. "Trust and Antitrust." Ethics 96.2 (1986): 231-60. Print.

[2] Buchanan, Allen. "Trust in Managed Care Organization." Kennedy Institute of Ethics Journal 10.3 (2000): 189-212. Print.

[3] Clark, Chalmers. "Trust in Medicine." Journal of Medicine and Philosophy 27.1 (2002): 11-29. Print.

[4] Veatch, Robert M. "Models for Ethical Medicine in a Revolutionary Age." The Hastings Center Report 2.3 (1972): 5-7. JSTOR. Web. 23 Nov. 2009. <http://www.jstor.org>.

Designing a Molten Salt Reactor for Extraterrestrial Use

Erik Lahti

Dr. Thomas Blue of the Nuclear Engineering Program recently received a grant from NASA to research and design a nuclear reactor for fission surface power systems on the moon and Mars. He hired several students during the first week back from winter break and has involved several other faculty members in the discussions and research. The grant is part of the Steckler Project and we are competing against several other teams to come up with the best design.

Currently, we are looking at an Advanced High Temperature Reactor (AHTR) that is cooled by molten salt. This reactor works similarly to those in use on Earth. The nuclear fission reaction within the reactor produces heat, which is then transferred to the coolant. The main difference is in how the heat is utilized. In typical reactors, the heat boils water that turns a turbine and generates electricity. In the molten salt reactor (MSR), the heat from the reactor is transferred to the liquid salt that, instead of tuning a turbine, transfers the heat it picked up to another coolant that boils and turns a turbine or to thermoelectric cells.

One problem that we are looking into is the reactor fuel. In current reactors, enriched uranium-235 is used as the fissionable material since it is the only naturally occurring fissionable material. The problem with U-235 is that natural uranium is only 0.711% U-235 and isotopic separation is a highly, costly process. In order to cut costs, the fuel cycle of Thorium-232 is being examined. 100% of all natural thorium is Th-232 and it decays into U-233 with some coaxing of an added neutron. This process is ideal, but might not be feasible in the long run.

Another problem area is the material to be used. The AHTR works at extremely high temperatures and radiation levels. As such, the materials that make up the reactor must be able to function and not wear out when subjected to these extreme temperatures. Several advanced alloys have been looked into including Niobium with 1% Zirconium.

Weight also plays a major role in every decision we make. Currently, it costs $50,000 per kilogram to launch something into space. As such, the weight of the materials, sensors and even the fuel must be taken into careful consideration.

So far, we have begun to look at the feasibility of the MSR and are comparing it with other reactor types such as the SP100 Space Reactor. In doing this, we not only check to see how the MSR measures up, but it allows us to see some of the key elements that are incorporated into other designs. One of the more important discoveries of this discussion was the thermoelectric-electromagnetic (TEM) pump. Since the acceleration due to gravity is different on the moon and on Mars, either we must design the reactor to adjust to these, or include the pump to adjust for the difference. In essence, this pump creates a magnetic field that will move the coolant. Other ideas are sure to come up and the prospect of creating something totally new is amazing.

Ultimately, we will select the best options from these areas of focus and incorporate them into the final design. The research of the best subsystem options will be phase one 1 of the overall project, which should last until the summer of 2010. Phase 2 will be the final design, which would take place over the summer and next fall. ■

Professor Spotlight: Experiences with Undergraduate Research

Dennis B. McKay, Ph.D.
College of Pharmacy

I was lucky. Somehow, I found Professor Mabry's laboratory, and with that discovery, I found what I enjoyed. Did I know that research as an undergraduate student was going to play such a prominent role in my life? I did not think so at the time. But my connection to research began with Professor Mabry and to him I owe much gratitude for opening his lab to me. That was more than 35 years ago. I worked with several graduate students who enjoyed their work and provided me with the guidance I needed. I worked when my social and academic schedules permitted, isolating flavanoids from plants using chromatographic techniques. During my senior year, I realized, with Dr. Mabry's support and encouragement, that I wanted to continue doing research and pursue my doctorate degree.


SP

Dr. McKay (second from right) has helped numerous undergraduates get involved with research in his 25+ years as an Ohio State faculty member.

I arrived on faculty at The Ohio State University during the summer of 1984. My first undergraduate student began working with me a few months later. Within a year, I had three all together. Throughout the years, more than 55 undergraduate students have filtered through my lab. Many of those students have completed research theses for an Honors degree. For some students, their research experiences carried over into their post-baccalaureate programs. Two students turned their undergraduate research projects into Master theses and went on to work with me while pursuing their Doctor of Pharmacy degrees. Most students who have worked in the lab were and are interested in the biological and/or chemical sciences with ambitions to be pharmacists, physicians, veterinarians, or Ph.Ds. For some students, though, one to two quarters of research was considered torture, and they would never set foot in another lab. From my perspective, or rationalization, being able to scratch 'research' off one's list of things to try is always good. Regardless of the type of student, the goals I set for each are the same: learn to think, learn to integrate, learn to problem-solve, have fun. Because of their research experiences, I am hopeful that they will look at their undergraduate studies through a more discerning lens, enhancing their learning experience and appreciating the scientific relevance of their coursework.


SP

My students will likely tell you that I am not bashful about giving advice. The advice I provide to students is mostly unsolicited, typically unlimited, and sometimes unwanted; although, it is oftentimes needed. For students who are thinking about doing research as an undergraduate, my advice is always the same: start as early as you can. Finding a good research environment in an interesting area is going to be work. You should use web-based resources, read university publications and attend seminars and presentations of our faculty to learn about their research accomplishments. In addition, go to the Denman Undergraduate Research Forum and talk to students about their research and experiences. The next step is to knock on faculty doors, but go prepared. Sending emails is fine, but faculty members have an easier time saying 'no' that way. Know their research areas by reading one of their books or papers and go equipped with questions, ideas and enthusiasm. Making a good impression is important.

Over the years, many students have made lasting impressions on me, including a student named Sara. Sara took an elective course that I teach in the College of Pharmacy. One of about 30 students, Sara was quiet and blended with the rest of the class. The focus of the course was on the scientific literature. Students were asked to read and critique papers not typically found on reading lists in their other classes. As the quarter progressed, Sara opened up and contributed to class discussions. It was becoming apparent that she was a thinker - she understood how to ap-

ply and integrate information from previous courses. Sara did well in the course, but did not excel. As I have observed with other students, something was holding her back.

Sara approached me several weeks after the class ended. We talked about my area of research, nicotinic receptors, and some of the problems we were addressing in lab. She already had some background knowledge as we had discussed some of these things in class. My impression of Sara was reinforced at this meeting.

As we talked, I knew that Sara belonged in a laboratory environment - she had an exacting mind for details and thoughtful analysis of experimental design. Before I knew it, she was in the lab. Suffice it to say, it was time well spent for both of us. Sara's research experience paid off for her in many ways. She went on to complete her Doctor of Pharmacy degree, followed by a residency program. She is now a clinical pharmacy specialist and holds a position as an Assistant Professor at one of the colleges of pharmacy in the state of Ohio.

Sara's path to research was not much different from all the students who have filtered through my lab over the past 25 years. In fact, it was not much different from my own. I found a faculty member, a project and an environment that made the experience great. Just a few years ago, I went back to thank Dr. Mabry. We exchanged stories, and while it was obvious that too many years had past, I think we both felt better after our visit. ■

Recent Papers from Dr. McKay's Laboratory with Undergraduate Contibutors

El-Hajj, R.A., McKay, S.B., and McKay, D.B. Pharmacological and immunological identification of native α7 nicotinic receptors: evidence for homomeric and heteromeric α7 receptors. Life Sciences, 81:1317-1322, 2007.

González-Cestari, T.F. et al. Effect of novel negative allosteric modulators of neuronal nicotinic receptors on cells expressing native and recombinant nicotinic receptors: Implications for drug discovery. Journal of Pharmacology and Experimental Therapeutics, 328: 504-515, 2009.

Nijani: On the Way

Adrienne Strong

The United Nations' Millennium Development Goals (MDGs) established the need to concentrate on maternal health as a means for achieving a safer and healthier world for all. In 2001, 192 member states came together to pledge support for these ten goals, which were to be achieved by 2015. The fifth MDG is to reduce maternal mortality by two-thirds from the 1990 level. The only areas not making progress on MDG 5 are sub-Saharan Africa and South Asia (United Nations, 2008). The maternal mortality rate in Tanzania, East Africa is currently estimated at between 500 and 1,500 deaths per 100,000 women depending on the area, with a lifetime risk of maternal death as high as one in ten (World Health Organization, 2006). Just for comparison, the lifetime risk of maternal death in the United States is 1 in 2,500 and for Sweden it is as low as 1 in almost 30,000 (World Health Organization, 2006).

Prenatal care and giving birth, in the hospital or with a skilled attendant, are both essential for ensuring a successful outcome and protecting the mother and child. In Tanzania, as in other sub-Saharan countries, all women are not able to take advantage of these services. My project aims to examine the reasons why women in rural Tanzania do not take full advantage of the services available to them. The end goal is to identify these reasons so changes can be made to encourage increased use of these services, thereby improving maternal health. Such barriers may include culturally inappropriate care (such as not having female doctors for Muslim women), a lack of women's autonomy, and delays in recognition of danger signs and subsequent decision-making and access to care which leads to many babies being born on the way to the hospital, or njiani as it says on the health registration cards (Koblinsky et al., 2006).

The theoretical basis of my project is medical anthropology, which can incorporate novel methods of addressing the health problems of a community by critically examining ultimate causes of disease such as historical precedents, gender and class inequality, and political and economic frameworks, as well as the role of environment and evolution. An understanding of cultural differences in the perception of disease etiology and appropriate treatments can lead to increases in patient compliance and satisfaction.

I conducted my research from June 21st to September 3rd, 2009 in the Sin-

gida region of Tanzania. I spent a great deal of time interviewing women in the only government-run hospital in the region as well as in other villages in the surrounding areas. The main town is called Singida Town and is a small semi-urban center with many small businesses and very little tourism. The region has a total population of just over one million (Tanzania, 2002). The main ethnic groups with which I worked were the Minyaturu and Minyiramba with several other groups present in the region. The majority of the population is either Christian or Muslim and the average household size is five (Tanzania, 2002). The primary language is Swahili and this was the language spoken in all of the interviews.

The research question was which, if any, of the previously identified barriers to the use of healthcare services during pregnancy are present in the Singida region of Tanzania and how can they be combated to improve the health of the women in the region?

My project aims to examine the reasons why women in rural Tanzania do not take full advantage of the prenatal and birth services available to them.

All told, I conducted 76 interviews. I spoke primarily with women who were pregnant or had at least one child (n=67). I was also able to speak with several healthcare workers from a variety of healthcare settings including a traditional birth attendant (n=1), a village healthcare worker (n=1), nurses from the government hospital (n=6), and a clinical officer from the hospital (n=1).

Though this was my third trip to Tanzania I was astounded by how much more I learned and what a difference it makes to be in a place for a longer period of time. By the end of my stay, I truly felt like a part of the community both in Singida Town and in one of the villages with which I worked. I was able to form relationships with village chairmen and several secondary school teachers, all of whom were very supportive of my project. Also, my Swahili abilities definitely increased manifold during my stay. By being able to speak the language not only was I able to make friends, but also I was able to make more of a connection with the women I interviewed.

I most enjoyed the opportunity to travel to some of the remote villages. In one village of over 5,000 people they do not have any health services for pregnant mothers and they must walk at least six miles each way to the nearest dispensary. The dispensaries offer rudimentary services in most cases and this one had only one doctor. I spoke with women who had given birth to eight or nine or ten children all at home with only the help of a traditional birth attendant.

At this point, I am in the process of transcribing all the interviews and then analyzing them using text analysis and coding. Preliminary analysis of the data and observations suggest there are at least four recurring barriers in this region of Tanzania. These include:

- A general lack of infrastructure in the form of roads, either gravel or paved.
- A lack of health centers of any level in some remote villages in the study area, leading to virtually insurmountable distances to care facilities.
- A lack of transportation to care centers. Cited by many women as the reason their children were not born in the hospital.
- A lack of knowledge about the importance of prenatal care and delivering with the assistance of a trained professional, reflected by an inability to appropriately explain the complications that can arise during birth and pregnancy.

In the long run, I intend to work with community organizations in the Singida region in order to develop and implement programs to combat these barriers and better the lives of the women and families in the area. ■

FEATURES

Inhibition of Escherichia coli in Apple Cider and Apple Juice due to Ethanol Production via Yeast Fermentation

Abigail B. Snyder[1], Stefanie Christopher[2], Malavika Tampi[1], Abdul Isu[1]
[1]Department of Food Science and Technology [2]Department of Microbiology

Escherichia coli is one of the microorganisms of which consumers are most conscious. Its association with food borne illness causes E. coli outbreaks in the food supply to be of great concern. It is because of the severity of the resulting illness that many controls are put in place to prevent such contamination, including heat treatment, increased acidity, lowered water activity and the use of inhibitors such as alcohol. E. coli O157:H7 is unusual from other spoilage and pathogenic microbes. It is able to grow in foods, such as mayonnaise and fruit juice, which are generally considered to have a pH too low for microbial survival. Juices and ciders purchased commercially are pasteurized to control for potential E. coli contamination. Nonetheless, independent farms and orchards are able to sell their ciders unpasteurized, with many of their patrons indicating a preference for this lack of processing[5].

Samples of apple cider and apple juice were inoculated with yeast, E. coli, or both and kept in cotton-stoppered flasks at room temperature over a period of 8 days.

Apple juice is the filtered product of the juice from an apple, whereas apple cider undergoes less filtration, is more opaque and lighter in color due to additives that prevent browning. Apples are grown in orchards; fruits are handpicked, put into large bins and checked/trimmed for decay, worms and dirt[1]. Fruits from the ground are not to be used in accordance with federal standards, and animals must be kept away from fruit trees, to prevent possible fecal contamination of the fruits, as harmful microbes in the ground can easily contaminate the apple[1]. Since apple cider is not filtered after pressing, there is a greater chance that microbes on the surface of the fruit can get into the final product[5]. Though many precautions can be taken to preserve the integrity of the apples used in cider and juice production, there is no guarantee that contamination is not present[2].

Independent purveyors of unpasteurized apple cider, as well as home brewers, allow fermentation to take place, yielding "hard cider." Yeast cells in the cider used in fermentation may be wild and naturally occurring, or added by the producer to accelerate the process[4]. Since the presence of ethanol inhibits the growth of many microorganisms, the hypothesis is that the production of ethanol via yeast fermentation will reduce the E. coli population.

Research was conducted in conjunction with the class Food Microbiology 636.02. Three 500 mL samples of both cider and juice were inoculated in the following combinations: (1) E. coli K12 only (~106 CFU/mL) (2) Saccharomyces cerevisiae only (~104 CFU/mL) and (3) both E. coli K12 and S. cerevisiae (combination, ~106 CFU/mL E. coli and ~104 CFU/mL Saccharomyces cerevisiae). Samples were incubated at 25° C for eight days in flasks with cotton stoppers. The samples containing E. coli were plated on MacConkey agar and the samples containing yeast were plated on DRBC four times throughout the incubation period. Most Probable Number (MPN) was used for E. coli counts on day eight. Alcohol content was measured using a hydrometer at the start and end of the incubation period.

Independent farms and orchards are able to sell their ciders unpasteurized, despite a potential risk of E. coli contamination.

The results of the hydrometer reading showed an increase from 0% to 7-10% alcohol by volume (ABV) in all samples containing yeast. No difference was noted among yeast populations in cider, and juice samples with only yeast or those containing yeast and E. coli. The E. coli population in samples inoculated with yeast had a five log reduction in E. coli population over time when compared to samples grown without yeast fermentation.

The hypothesis was supported; ethanol production via yeast fermentation reduced the population of E. coli in apple cider and apple juice. The results of this study indicated that ethanol produced from yeast fermentation in the production of unpasteurized hard cider served as a hurdle

in the prevention of E. coli contamination. This suggested an added safety benefit to small-scale production of hard cider without the use of pasteurization.

Additional research is recommended to determine E. coli inhibition at lower alcohol concentrations (i.e. 4-6% ABV); this would be more typical of commercially sold hard ciders. Also, research using E. coli O157:H7 would be needed to verify these results for pathogenic strains. Special thanks to Dr. Ahmed Yousef, Jennifer Perry, Yuan Yan, Amrish Chawla and Matt Swearingen for their suggestions and support, as well as to The Ohio State University, Lisa Robinson and the media lab for providing supplies to make this project possible. ■

For further reading on food sterilization technologies, see Johnson et al. (p. 35)

References

[1] Henderson, J. 2001. Unpasteurized Apple Cider Risk Assessment. OMAF Food Inspection Branch. [Online]. http://www.omafra.gov.on.ca/english/food/inspection/fruitveg/riskassessment_pdf/applecider/30ra.pdf. Accessed 7 November 2009.

[2] Kerry, K. and Bessin R. Total Quality Assurance: Apple Production: Best Management Practices. University of Kentucky. [Online]. http://www.ca.uky.edu/agc/PUBS/id/id137/id137.htm. Accessed 10 November 2009.

[3] Semanchek, J., and D. Golden. 1996. Survival of Escherichia coli 0157:H7 during Fermentation of Apple Cider. Journal of Food Production. 59: 1256-1259.

[4] Two Rivers Cider Company; History of Hard Cider. [Online]. http://cider.iamjp.com/history. Accessed 10 November 2009.

[5] Weeden, K. Apple Cider and E. coli. November 1996, posting date. Cornell University College of Agriculture and Life Sciences. [Online]. http://www.nysaes.cornell.edu/pubs/press/cider_safety.html. Accessed 10 November 2009.

Glut-3 and Glutamate/GABA Imbalance

Sara Rapaport

I was involved in conducting research on Glut-1 deficiency disorder (Glut1D) in the lab of Dr. Juan Pascual at UT Southwestern Medical Center in Dallas, Texas, this past summer. Glut-1 is a metabolic encephalopathy characterized by seizures, developmental delays, microcephaly, ataxia (or other movement disorders) and an abnormally low concentration of glucose in the cerebral spinal fluid (CSF). It is caused by a haploinsufficiency of Glut-1 in the blood brain barrier. Glut-1 is a protein involved in transporting glucose from the blood to the brain via facilitated diffusion. Once inside the brain, glucose is converted into pyruvate through glycolysis. Pyruvate then enters the TCA cycle, also known as the Krebs cycle, which produces a variety of metabolic byproducts and energy necessary for normal brain function (Figure 1). In Glut1D, insufficient presence of the Glut-1 transporter results in a limited amount of glucose entering the brain. Therefore, glycolysis and the TCA cycle fail to metabolize a sufficient amount of glucose, resulting in deficiencies in metabolic byproducts and energy.

Epilepsy is one of the most debilitating aspects of Glut1D disorder.

Since epilepsy is one of the most debilitating aspects of Glut1D disorder, this study set out to discover the mechanism behind seizure activity in Glut1D patients. Glutamate and GABA, the respective primary excitatory and inhibitory neurotransmitters, are byproducts of glucose metabolism. Electrophysiological data recorded from Glut1D mice suggests that decreased glucose metabolism may result in a glutamate/GABA imbalance, giving rise to the epilepsy seen in Glut1D patients. This discovery is significant in explaining seizure activity in Glut1D patients; however, questions arose about the role of another glucose transporter, Glut-3, and its possible involvement in the same mechanism. Glut-3 is involved in transporting glucose from the CSF into the neuron. Both glutamate and GABA are manufactured within the neuronal cell, thus it was hypothesized that deficiencies in glucose transport by Glut-3 would also present imbalances in excitation and contribute to a better understanding of Glut1D.

To test this hypothesis, a Glut-3 deficient mouse model, created from gene trap embryonic stem (ES) cell clone XG611, was obtained (Schmidt, Richter et al., 2008). Brains were removed from both Glut3D and wild-type mice, cut into 350 µm coronal slices and placed in an artificial CSF (aCSF) bathing solution to maintain normal cerebral conditions. Whole-cell patch clamping experiments were performed in sensory barrel cortical layer V-pyramidal cells. Patch clamp-

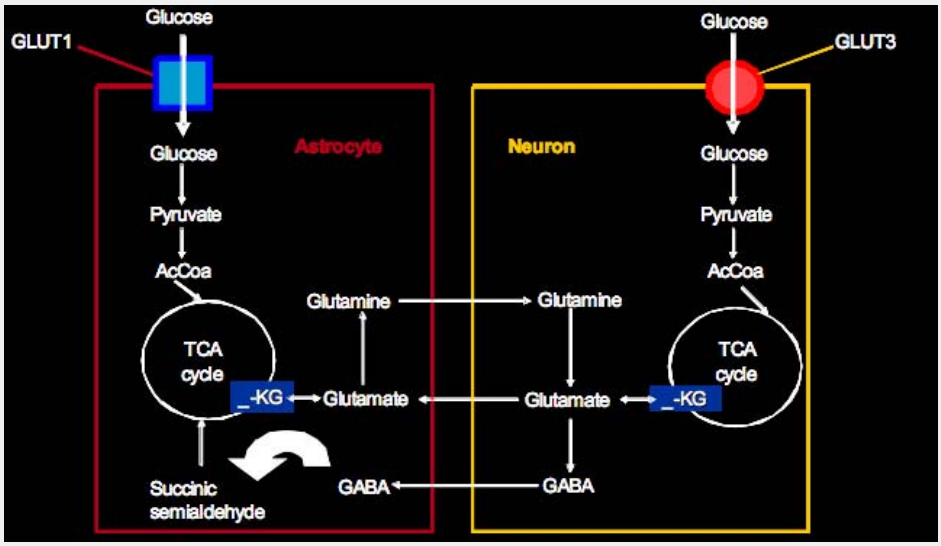


Figure 1. Production of Glutamate and GABA via the TCA cycle

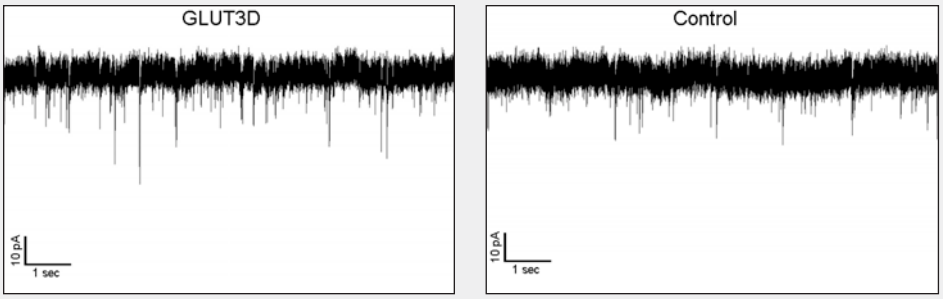


Figure 2. 20 mM glucose aCSF, 10 seconds of spontaneous mIPSC event data from a Glut3D and control neuron

ing involved an electrode creating a high resistance seal (gigaohm seal) with the membrane of a neuron. The electrode then punctured into the neuron, allowing it to record the ion current passing along the membrane. Electrodes were able to record ion currents across neuronal membranes by transferring them to electrical current, which was recorded through patch-clamping computer programs (Figure 2).

In this experiment, action potentials were blocked and only mEPSCs (mini excitatory post-synaptic currents) and mIPSCs (mini inhibitory post-synaptic currents) were recorded. Two conditions were tested for each the Glut3D and the wild-type mice: (1) brain slices placed in 2.5 mM glucose in aCSF and (2) brain slices placed in 20 mM glucose in aCSF. The 2.5 mM concentration of glucose closely mirrored the physiological concentration of glucose in the human brain; therefore, it gave realistic and accurate measures. However, in comparison with 20 mM glucose, the 2.5 mM condition demonstrated glucose deficiency.

Averages of both amplitude and frequency of mini events in Glut3D mice were recorded and plotted against the averages of the wild-type mice. Significance was measured using the Kolmogorov-Smirnov test for statistical differences. Data pertaining to mEPSC originally indicated that the amplitude of events in Glut3D mice was greater than that of the wild-type, with no significant differences between 20 mM and 2.5 mM. However, most of the data in this group was discarded due to leaky electrode seals with neurons. The mIPSC data also indicated that the amplitudes of inhibitory events in Glut3D mice were greater than that of the wild-type. Events in the 2.5 mM group were considerably smaller than that of the 20 mM group (Figure 3). In comparing frequencies between Glut-3 deficient mice and that of the wild-type, it was noted that the average excitatory events

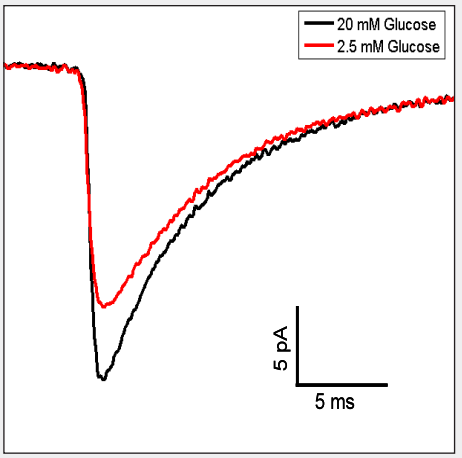


Figure 3. Average of mIPSC events in GLUT3D from 20 mM (n=2 cells) and 2.5 mM (n=2 cells)

(~26 pA) were significantly greater in amplitude than that of the inhibitory events (~22 pA). Moreover, both excitatory and inhibitory events in Glut3D mice were greater in frequency and amplitude than that of the wild-type.

This data led to the conclusion that a mutation in Glut-3, similar to Glut-1, demonstrated an imbalance between excitatory and inhibitory events. In contrast with the Glut1D trend, in which both excitatory and inhibitory events were decreased in comparison with controls, spontaneous synaptic function in the Glut3D cortex was characterized by increased excitatory and inhibitory events. Furthermore, GABAergic activity was decreased as a function of aCSF glucose concentration in Glut3D mice. This suggested impaired neurotransmitter recycling, in which GABA was derived from glutamate. The significant amplitude and frequency differences between the mutant and the wild-type suggested that Glut-3 provided glucose as an important energy source of the neuron and played an essential role in metabolic regulation. In order to confirm these assertions, it is necessary to repeat this experiment again with more cells (most of the data was for two to three cells). Furthermore, EEG experiments must be done to determine if the data is consistent with epilepsy in Glut3D mice. ■

Pulmonary Fibrosis Inducer, Bleomycin, Activates Phospholipase D and Generates Bioactive Lipid Signal Mediator, Phosphatidic Acid in Lung Microvascular Endothelial Cells

Rishi Patel, Sainath R. Kotha, Narasimham L. Parinandi

I joined my research lab, Dr. Parinandi's lab in the Davis Heart and Lung Research Institute, in June 2008 and was immediately given my own project. Our lab is different than most other labs at OSU, in that our lab is mostly composed of undergraduate researchers who have their own projects. My undergraduate colleagues and I have been lucky enough to present our research in multiple research forums not only in Ohio, but also at national and international conferences. In addition, my work has been supported by OSU research grants and by Dr. Parinandi.

My research focuses on an enzyme, Phospholipase D, activation and production of secondary signaling molecules in bleomycin-induced pulmonary fibrosis in endothelial cells (ECs). Bleomycin is an anti-cancer drug whose familiar side effect is pulmonary fibrosis (PF), and is thus a widely accepted model for inducing PF in research models. PF is a disorder of the interstitial tissue between the alveoli, characterized by extensive scarring and vascular leak.

Phospholipase D (PLD), an intermembrane enzyme that catalysis the site-specific hydrolysis of the phospholipids at the sn3 position, is ubiquitously found in all mammal cells and plays an important role in daily housekeeping as well as cellular signaling. Phosphatidylcholine (PC), a very abundant phospholipid in the cellular membrane, is hydrolyzed by PLD to form phosphatidic acid (PA) and choline. PA can then be further metabolized to create lipid secondary messengers such as lysophosphatidic acid (LPA) and diacylglycerol. These messengers are involved, amongst other factors, in regulating the cellular cytoskeleton; this is seen with the actin cytoskeleton, which regulates cell morphology and movement. This is important because ECs form a tight monolayer that is crucial to their function. Thus, the proper morphology of these cells plays a vital role in the proper function of the blood vessels and the diseases associated with it, such as the vascular leak associated with PF.

Our lab is different in that it is mostly composed of undergraduate researchers who have their own projects.

The uniqueness of the PLD enzyme is its preferential use of a primary alcohol instead of water to hydrolyze the phospholipids (Figure 1). This process, known as transphoshpatidylation, allows us to calculate the activity of the enzyme and the amount of its final product, PA. When PLD hydrolyzes a phospholipid like PC, the phosphate group stays with the product PA. Thus, when a primary alcohol such as ethanol is present during the action of PLD, the PA formed will also have an ethyl group. Since PA can be formed from multiple pathways, the contribution from the PLD pathway during signaling events can be calculated using radioactive phosphorus labeled phospholipids. The amount of radioactive phosphatidylalcohol, a unique product formed only through PLD, can be calculated and its production can be used as an index of the PLD activity.

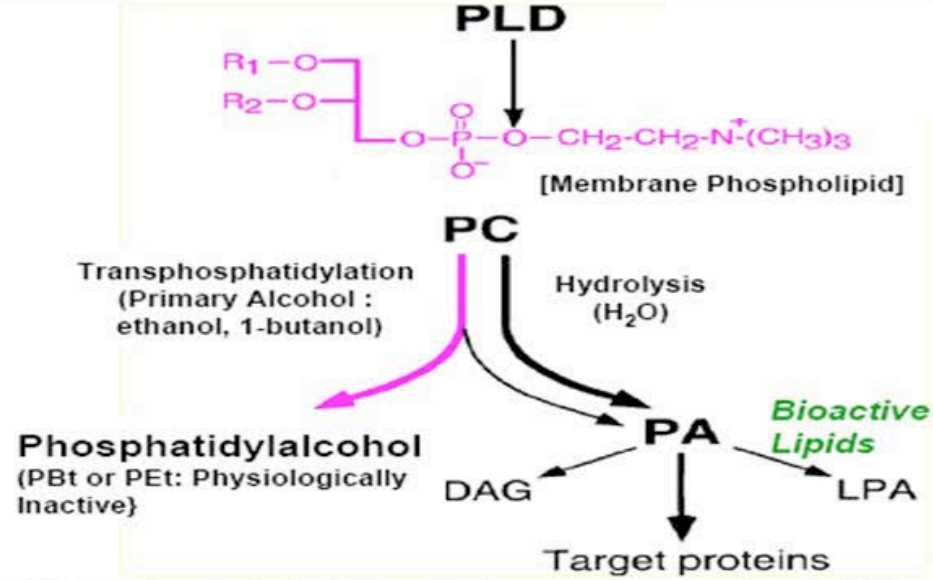


Figure 1. Transphosphatidylation activity in PLD indicating preferential use of a primary alcohol over water to hydrolyze the membrane phospholipid

Using this method of measuring PLD activity, we showed that when ECs were exposed to lower-than-pharmacological doses of bleomycin, PLD was activated in a time and dose dependent fashion. We found that using 5 μUnits for an exposure time of 12 hours caused significant enough activation of PLD for further studies, although PLD activation was evident as early as 8 hours. Previous studies have shown that PLD is redox and oxidative stress sensitive. In order to understand the mechanism of bleomycin-induced PLD activation, we pre-treated the cells with thiol-protectants such as N-acyl cysteine, dithiothreitol and antioxidants such as vitamin C, vitamin E and propyl gallate. These treatments were effective in attenuating the PLD activation, thus concurring with previous studies and establishing that bleomycin causes redox-alterations and oxidative stress in cells.

We measured and confirmed that cells exposed to bleomycin had lowered glutathione (GSH) and higher reactive oxygen

species (ROS) levels at a much earlier time period. ROS was evident as early as 1 hour after exposure, while GSH levels were reduced by 8 hours of exposure to bleomycin.

To understand the physiological changes, cellular morphological alterations and electrical cell impedance sensing (ECIS) were measured. As the ECs are perturbed, gaps in the monolayer are evident by the morphological alterations and this gap formation can be measured using ECIS. When gaps in the monolayer are formed, the electrical resistance across the cell layer is decreased. Thus, using these methods to measure the bleomycin-induced physiological alterations in ECs, we showed that there was a dose- and time-dependant formation of gaps in the EC monolayer along with decreased electrical resistance.

Vitamin C, which was successful in attenuating bleomycin-induced PLD activation, was also able to protect against the bleomycin-induced physiological alterations. Since there were no PLD inhibitors available in the market till recently, we used 1-butanol as a means to replace the physiologically active PLD-derived PA to form the transphoshpatidylation product, phosphaditylbutanol, which is physiologically inactive. This was also, to a certain degree, successful in attenuating the bleomycin-induced physiological alterations.

Thus, we were able to propose a mechanism about the role of PLD in the bleomycin-induced morphological alterations and the vascular leak associated with PF. Bleomycin causes ROS formation and GSH depletion, which activates the redox and oxidative stress sensitive PLD. PLD will catalyze the formation of PA, which then causes the gap formation and vascular leak in the ECs. Further studies into the specific pathways of PLD activation, such as kinase signaling, are underway. We are also trying to understand how the PLD-generated PA, or its metabolites, are implicated in the morphological alterations. A newly available PLD inhibitor is also being used to better understand the roles of PLD and PA in vascular leak. ■

The Cultural Logic of the Mind in Anglo-Saxon Literature

Gregory M. Webb

Where is your "mind"? Is it behind your eyes, or part of an eternal, incorporeal soul? Now, once you have pinned down the location of this beast, you are forced to wonder about its function. Does it think for you, hold treasured memories, or give birth to passionate emotions? Within the frozen idioms of modern English, assumptions exist about the different functions of the mind. When people speak of knowledge or memory, for instance, they refer to their head. A tap on the forehead sometimes accompanies statements such as a thought "escaping" memory or "slipping" from the mind.

One way to gain prospective on these idioms is through the examination of an antecedent society with strong cultural and linguistic ties to our own: early-medieval, or Anglo-Saxon, England. The lexicon of the language spoken in Anglo-Saxon England, Old English, is remarkably rich in terms denoting the "mind."[1] The density of this specific lexical field demonstrates the centrality of the mind's functions in Anglo-Saxon literature and, in places, creates great confusion[2]. By looking at the literature produced in Anglo-Saxon England, one can begin to develop an idea about the cultural constructs that informed their beliefs in the mind and the proper use of thought. In order to increase one's own wisdom, one asks what being wise meant to them.

In essence, the clergy is attempting to co-opt the ethics of mental exchange, supplanting the vernacular tradition's wise men.

The mind was imagined as a closed container to the Anglo-Saxons. The corpus of Old English literature is filled with kennings, two-word compounds designed to create miniature metaphors. Examples include ferðlocan (stronghold of the mind) or hordcofan (chamber of treasure), which illustrate the mind's insular characterization. When these strongholds are opened, the movement of knowledge between them is a risky proposition overseen by a set of skilled men. Just who these men are, however, remains in contention. There are two main traditions that struggle with the right to determine the cultural logic governing the opening and filling of the mind in Anglo-Saxon culture. One tradition is the native, or vernacular, tradition, which represents thought that has arisen primarily before contact with the larger corpus of Latin learning[3] . In popular thought, this is depicted as hoary-bearded men surrounded by the smoke of a mead hall fire. The second tradition is ecclesiastical. This group links itself to the Roman Catholic Church and the larger world of Latin philosophy, drawing authority from God and the Church Fathers.

Research on these two strains primarily involves translations and close readings of the primary texts. Sets of Old English texts that are not explicitly Christianized represent the cornerstone of the vernacular tradition. Among these are works such as Maxims I, a poem composed mainly of different proverbs that contains explicit instructions for governing the mind. "Frige mec frodum wordum," commands the poet, "Ne læt þinne ferð onhælne // degol þæt þu deopost cunne" (Ask of me with wise words. Do not let your mind be concealed, that which you most deeply know stay hidden)[4]. The writings of the vernacular tradition appear to inform a culture that gives the control of wisdom and the ethics of mental exchange to an elite group of supra-wise men. These men are identified both by their age and by their ability to explicate the wisdom dormant in proverbs and apply it to novel situations.

The ecclesiastical tradition, in contrast, is built upon numerous homilies, biblical translations and prefaces. Proponents of this tradition, such as the late 10th century cleric Ælfric, define a set of unlearned men below them in learning and spiritual understanding whom they, as proctors of divinely revealed wisdom, must instruct to

prevent them from sinning. As Ælfric declares, "man sceal læwedum mannum seccgan be heora anjust dgites mæð" (one must speak to laymen according to the measure of their understanding)[5]. In essence, the clergy is attempting to co-opt the ethics of mental exchange, supplanting the vernacular tradition's wise men. In examining these works, it is often as important to look at what is not said, as it is to look at what is said. In the act of establishing a set of laymen possessing limited understanding, Ælfric implicitly sets himself above others, as a person knowledgeable enough to discern the varying levels of others' intelligence.

Though it is tempting to see the vernacular tradition as a pagan tradition coming before the ecclesiastical influenced by Latinate literature, one must avoid the temptation to construct such a diachronic argument. It is far more likely that these two traditions existed simultaneously in competition with each other. The very fact that clerics like Ælfric felt the need to assert their control is an indication that their authority was being challenged. The constant power struggle between the two traditions for control of the mind, a concept indicated by the Old English lexicon, is central to Anglo-Saxon culture and suggests that the Anglo-Saxons believed that the mind was in need of governance. In neither tradition is there a question of whether the mind should be enclosed; the only question is who should be the gatekeeper. It is this implicit control that sheds light on modern English idioms. In the case of a fact "escaping" memory or "slipping" the mind, the implied container metaphor is made clear. You can only escape from something designed to hold, only slip away from something attempting control. Thus, an examination of early-medieval English texts provides a lens through which modern Western assumptions about the mind and thought can be exposed and observed. By using Anglo-Saxon literature, one transforms yesterday's culture into today's cultural microscope. ■

Further Reading

Cavill, Paul. *Maxims in Old English Poetry*. Suffolk: D. S. Brewer, 1997.

Hanson, Elaine Tuttle. *The Solomon Complex: Reading Wisdom in Old English Poetry*. Univ. of Toronto Press, 1988.

Honeck, Richard P. *A Proverb in Mind: The Cognitive Science of Proverbial Wit and Wisdom*. Mahwah: Lawrence Erlbaum Associates, 1997.

Larrington, Carolyne. *A Store of Common Sense: Gnomic Theme and Style in Old Icelandic and Old English Wisdom Poetry*. New York: Oxford Univ. Press, 1993.

Wierzbicka, Anna. *Semantics, Culture, and Cognition: Human Concepts in Culture-specific Configurations*. New York: Oxford Univ. Press, 1992.

References

[1] Soon-Ai Low, "Approaches to the Old English Vocabulary for 'mind,'" Studia Neophilologica 73, no.1 (2001): 11. See also Antonina Harbus, The Life of the Mind in Old English Poetry (Amsterdam: Rodopi B. V., 2002), 21.

[2] Dieter Kastovsky, "Semantics and Vocabulary," in Cambridge History of the English Language, vol. 1, The Beginnings to 1066, ed. Richard M. Hogg (Cambridge: Cambridge Univ. Press, 1992), 299. Anna Wierzbicka, Semantics, Culture, and Cognition: Human Concepts in Culture-specific Configurations (New York: Oxford Univ. Press, 1992), 20. Wierzbicka discusses the categorization and interpretation of the world implied by each culture's varying lexicon.

[3] Malcolm R. Godden, "Anglo-Saxons on the Mind," in Learning and Literature in Anglo-Saxon England:Studies Presented to Peter Clemoes on the Occasion of His Sixty-Fifth Birthday, ed. Michael Lapidge and Helmut Gneuss (Cambridge and New York: Cambridge University Press, 1985), 271. I follow the division of vernacular and Latinate literature established by Godden in his now classic article.

[4] Elliot Van Kirk Dobbie and George Philip Krapp, ed., "Maxims I," in The Exeter Book (New York: Columbia Univ. Press, 1936), 156, lines 1-2a.

[5] Malcolm Godden, ed., Ælfric's Catholic Homilies: The Second Series (London: Oxford Univ. Press, 1979), 160, lines 4-5.