

Dear Readers,

Welcome back to Amalgam!

Of course, some of you may not have realized there was an Amalgam to come back to. Here's a brief history:

Amalgam became part of the University of Virginia graduate community in 2004, and the first issue was published in the fall of 2005. An unfortunate hiatus followed this promising beginning, brought on when several key administrative members completed their degrees. Thanks to Tom O'Halloran (recent Ph.D. graduate from Environmental Science), Amalgam stirred back to life in the fall of 2007.

Now with your support, we hope once again to be a thriving part of academic life at U.Va. Our goal is to share with you, our readers, some of the best academic work the university has to offer—but also to serve as a forum for debating important current events.

As our name suggests, you can expect to find a wide variety of content in Amalgam. In this issue, we offer a selection of scholarly work, book reviews, and research reports. We also have a brief recap of this past year's Huskey Research Exhibition. And of course, our "Frequently Asked Questions" section offers preemptive answers to those of you interested in contributing to our next issue.

Finally, please send us your thoughts, comments, and suggestions. Or better yet, join our team!

Happy reading,

Amalgam Staff

The annual Robert J. Huskey Graduate Research Exhibition provides an environment where UVA's graduate students from various disciplines showcase their work to diverse audiences. Academic judges select the best from students' paper presentations and posters. Amalgam is happy to present summaries of some of the papers that were awarded first place in this year's exhibition.

Herpes Simplex Virus Replication: Roles of Viral Proteins and Nucleoporins in Capsid-Nucleus Attachment

Anna Maria Copeland, Microbiology

1st Place, Biological & Biomedical Sciences

Paper Presentations

Our lab studies *herpesviridae*, a large family of enveloped dsDNA viruses. These viruses are responsible for many human diseases, which range widely in severity and affect many different tissue types. Specifically, our work is done with herpes simplex virus type 1 (HSV-1). HSV-1 is the archetypal herpesvirus and has long been studied as a model for the entire herpes family. Its study has expanded knowledge of herpesvirus replication strategies and led the way for specific therapies for many of the human diseases caused by these viruses.

In order to initiate a productive infection, a herpesvirus must deliver its DNA into a host cell nucleus, a process termed "uncoating." The first step in the uncoating process occurs when the DNA-containing viral capsid docks onto the host nuclear pore complex (NPC). The viral DNA then translocates through the nuclear pore into the nucleoplasm, and virus replication begins. We have investigated the roles of both viral and cellular proteins in the process of capsid-nucleus attachment with the goal of determining which cell protein serves as the nuclear receptor for HSV-1 capsids and which herpes proteins bind to that nuclear receptor to anchor capsids to the NPC. A better understanding

of this process could someday result in therapeutic interventions. Antibody blocking studies revealed that the viral protein 1/2 (VP1/2) plays an important role early in infection at a step after entry and prior to uncoating. It is our hypothesis that VP1/2's early role is in attaching the capsid to the NPC. Studies are underway to test this hypothesis. Immunofluorescence assays showed that capsids colocalized with the nuclear pore protein Nup358 at the nuclear surface but not with other nuclear proteins.

Antibody blocking studies and experiments using protein depletion by siRNA revealed an essential role for Nup358 in capsid-nucleus attachment. Our results support the hypothesis that HSV-1 capsid docking is mediated by Nup358, an interaction that may involve VP1/2.

Developmental Regulation of microRNA Biogenesis in *Xenopus laevis*

Alexandra Garcia, Biology

1st Place, Biological & Biomedical Sciences
Paper Presentation

microRNAs (miRNAs) constitute a large family of 21-25-nucleotide non-coding RNAs which facilitate post-transcriptional gene silencing through the RNA interference (RNAi) pathway by base pairing with target messenger RNAs (mRNAs). Since their initial discovery in *C. elegans* miRNAs have been identified as key regulatory molecules in plants, animals, and fungi, and are now predicted to account for >3% of the human genome. While the miRNA biogenesis pathway has been well-defined, the regulation of the processing activities, at the pri- or pre-miRNA steps, remains poorly understood, especially during early development. As miRNAs have been shown to control key developmental events, an understanding of how they are regulated is fundamental to understanding normal development, as well as developmental disorders which arise as a consequence of their aberrant expression.

Xenopus laevis provides an ideal model system to study the developmental regulation of the miRNA biogenesis pathway, which includes transcription followed by coordinated nuclear and cytoplasmic processing events, as well as the subsequent miRNA-mediated mRNA silencing. In addition to miRNA biogenesis, I am also investigating the role of specific miRNAs in the cell cycle remodeling that occurs at the midblastula transition (MBT), a critical developmental transition during early embryogenesis. These studies will provide crucial insight into the

regulation of gene expression and cell cycle progression.

To determine whether oocytes are competent for miRNA-mediated gene silencing I examined the expression, subcellular localizations, and activities of the miRNA processing enzymes, Drosha, DGCR8, Dicer, and Argonaute 2. Results show all processing proteins first appear late in oogenesis and persist throughout embryogenesis. As the necessary processing enzymes are present in oocytes it follows that miRNA processing may occur before maturation. However micro-injection of ³²P-labeled pri- and pre-miRNAs into stage VI or mature oocytes revealed that miRNA processing does not occur in oocytes and is stimulated at maturation. Additionally, both pri- and pre-miRNAs are extremely unstable in the cytoplasm of stage VI oocytes raising the intriguing possibility that inhibition of miRNA processing may occur at the level of miRNA stability. I propose that this mechanism involves adenosine to inosine (A→I) editing of miRNAs by Adenosine Deaminases Acting on RNA (ADARs) triggering the subsequent degradation of the edited pri- or pre-miRNA by the staphylococcal nuclease Tudor-SN. If A→I editing is responsible for miRNA instability in oocytes this would elucidate a previously uncharacterized function of ADARs in the developmental regulation of the miRNA pathway.

To demonstrate that Drosha, DGCR8 and Dicer are responsible for pri- and pre-miRNA processing, I used antisense morpholino oligonucleotides (AMOs) to knock down the endogenous levels of these proteins in eggs. Results show that Drosha and DGCR8 are necessary for pri-miRNA processing while Dicer activity is necessary for processing of pre-miRNAs to the mature miRNAs and these activities are absent in stage VI oocytes. Taken together these results indicate that although all processing components are present in stage VI oocytes they are not active until maturation.

Results thus far demonstrate novel aspects of miRNA processing that differ from what has been characterized in somatic cells. My research has provided the first comprehensive investigation of miRNA biogenesis during vertebrate development and provides novel insight regarding the regulation of miRNA expression by specific developmental cues. It remains to be seen how miRNA expression is blocked in immature oocytes and the mechanism of activating robust miRNA-mediated gene silencing at maturation. As it is predicted that over a third of human genes may be regulated by miRNAs, these findings can be applied to many pathways outside of development including the numerous cancerous phenotypes known to arise from miRNA misregulation.

**Locating the Social Gospel Legacy:
Walter Rauschenbusch, Martin Luther King, Jr.,
Reinhold Niebuhr, and the Ethics of Christian Ethics**

Karen Guth, Religious Studies

1st Place, Arts & Humanities

Paper Presentation

My project examines the ways scholars of American religion draw lines of influence between important Christian ethicists. The paper focuses on how scholars of Rauschenbusch locate his legacy in King and the civil rights movement. This connection is so frequently, definitively, and singularly made that one would expect King to have been Rauschenbusch's ministerial apprentice and successor to the pastorate at Second German Baptist Church in Hell's Kitchen. But while both Rauschenbusch and King insisted on Christianity's relevance to social problems, Rauschenbusch's relative lack of concern with racial reform, compared with King's devotion to it, casts doubt on historians' claims that the trajectory of Rauschenbusch's work leads directly and exclusively to King.

The paper argues that the desire to connect Rauschenbusch and King has less to do with the unique extent or strength of Rauschenbusch's influence on King than with the desire to reaffirm Rauschenbusch's legacy in the wake of Christian realist critiques, notably that of Reinhold Niebuhr. It also notes the blindness to issues of race that such an unqualified link between Rauschenbusch and King requires. More fundamentally, the paper addresses the ethics of American religious scholarship and calls for a more nuanced account of the history of Christian ethical thought. It questions the validity of teleological approaches that draw direct lines of influence from one Christian figure to another with little to no attention to the particular demands, context, and calling of each thinker. Rather than affirming the powerful witness and significant contributions of thinkers like Rauschenbusch (whose importance is not dependent on influencing King), such moves fail to do justice to the sophistication of these figures' thought and obscure their distinctive and enduring contributions to Christian ethics.

**Targeting Fel d 1 to FcγRI: Single Cell Analysis
Reveals a Novel Variation of the Th2 Response in
Cat-Allergic Subjects**

K. E. Hulse, Microbiology

1st Place, Biological & Biomedical Sciences

Paper Presentation

Cats are an important source of indoor allergens with allergy to the major cat allergen, Fel d 1, affecting ~10% of the U.S. population. Type 2 effector T cells (Th2 cells) which produce the cytokines IL-4, IL-5 and IL-13, are an important component of the allergic response to cats.

A unique feature of Fel d 1 is its ability to also induce a protective response characterized by the presence of Fel d 1-specific serum IgG in the absence of IgE and a lack of allergic symptoms. This modified Th2 response develops in subjects exposed to high Fel d 1 levels in the environment and is thought to represent a form of high dose respiratory tolerance. Several studies suggest an important role for IL-10 and IFN-γ in mediating protective responses to Fel d 1 induced either by natural exposure to allergen (modified Th2 response) or by injection of cat extract during conventional immunotherapy.

We investigated the immunomodulatory capacity of a novel fusion protein (H22-Fel d 1) which targets Fel d 1 to the high affinity IgG receptor, FcγRI, on antigen presenting cells (APC). This molecule induced a semi-mature phenotype in APCs characterized by enhanced secretion of pro-inflammatory cytokines and IL-10, with no change in surface markers of maturation (HLA-DR, CD40, CD80, CD86). Analysis of the T cell repertoire induced by Fel d 1 revealed selective increases in IL-5⁺ and IL-10⁺ T cells. IL-10-expressing T cells included diverse subtypes characteristic of Th0 (IL-5⁺IFN-γ⁺), regulatory Th1 (IL-10⁺IFN-γ⁺) and regulatory Th2 (IL-10⁺IL-5⁺) cells. Notably, these qualitative changes in T cells were restricted to cat-allergic subjects. Blocking IL-10 preferentially increased IL-5⁺ T cells suggesting that Th2 responses were controlled. Thus, targeting Fel d 1 to FcγRI induces a novel variation of the Th2 response which incorporates major elements of a protective T cell response. Our findings suggest that H22-Fel d 1 holds promise for treating patients with cat allergies.

The Effect of Arousal on the Development of False Memories

Janet Palmer, Psychology

1st Place, Social & Behavioral Sciences

Paper Presentation

There has been a recent upsurge in research focusing on the memory-enhancing effects of arousal. We know that when you arouse people, their long term memory for emotional stimuli is actually enhanced compared to neutral stimuli. We wondered, then, what effect arousal may have on the development of long term false memories. To answer this question, we first showed participants 9 word lists of 10 words each. These lists were matched in the likelihood that a word from the list would make the critical lure (a non-presented word) come to mind, and thus be falsely recalled. Three of these lists were organized around positive critical lures (love, beautiful, happy), three negative (pain, sad, kill) and three neutral (sleep, chair, needle). Then, participants were aroused by placing their left hand in ice water (which has been shown to increase cortisol levels); the control condition placed a hand in warm water. Two days later, participants came back to the lab and were asked to recall as many words as they could.

The long term memory results revealed a very interesting pattern: those who were aroused did not remember a different amount of words than those who were not aroused, but they remembered different kinds of words. An arousal by word type interaction showed that those who were aroused had higher rates of false memories for the positive critical lures. This memory benefit for positive information for those who were aroused can be explained by the arousal task itself—placing the left hand in water may activate the left amygdala, which is sensitive to positive information. Future experiments will activate the right amygdala, which should result in a memory benefit for negative information in those who were aroused.

Live Stock Nation: Improving Domestic Animals and the Political Economy of Nineteenth-Century America, 1815-1876

Eric Stoykovich, History

1st Place, Arts & Humanities

Paper Presentation

Historians have labeled the early nineteenth century as the era of internal improvements, but they have largely ignored the subject of agriculture and its impact on national economic development. During this era, many American politicians, statesmen, and political economists came to believe that the new republic could only be held together if physical infrastructure, such as canals, steam-boat monopolies, turnpikes, and railroads, were built. The Erie Canal in upstate New York, the National Road that ran from Baltimore to St. Louis, and the Baltimore and Ohio Railroad, symbolized the early days of nineteenth-century America.

However, historians have forgotten that agriculture was significant. In 1800, some 75% to 80% of Americans were farmers, and more citizens were connected to farming through their residences in rural, farming communities. Agricultural improvements and the improvement of domestic animals, specifically, were important components of the project to improve the infrastructure of the early American nation through a mixture of public government expenditures and private capital investments. Gentleman farmers, natural scientists, and civil servants believed that domestic animals, as much as canals, turnpikes, and railroads, were useful to the creation of the national economy. Improvements to livestock were considered achievable goals of a modernizing nation. Politicians and country gentlemen imagined with Stephen Goodale of Maine in 1860 that “the improvement of the domestic animals of a country so as greatly to enhance their individual and aggregate value, and to render the rearing of them more profitable to all concerned, is surely one of the achievements of advanced civilization and enlightenment, and is as much a triumph of science and skill as is the construction of a railroad, a steamship, an electric telegraph, or any work of architecture.”¹

Improvements in agriculture were political markers of American economic development. Improvements offered a forward-looking vision of what the nation ought to become under the guiding hand of a diversified economy of agriculture, commerce, and manufacturing. Though

¹ Stephen L. Goodale, *Fifth Annual Report of the Secretary of the Maine Board of Agriculture* (Augusta: Stevens and Sayward, 1860), 59.

not always paid for by the government, improvements in domestic animals were infrastructural. Thus, improvements in agriculture were similar to and often fed into internal improvements.

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AN INTRODUCTION TO TRAUMA AND POLITICS: VICTIMHOOD, REGRET, AND HEALING

Justin Snyder, Sociology

Traumatic memories have become central to politics in the West and other Westernized societies. Some intellectuals believe that the attentiveness to victimhood has dire consequences. Most commonly, scholars worry that the focus on victimhood undermines moral accountability, political community, and future-oriented politics. While there is plenty support for those concerns, evidence also suggests the opposite. When we take into account expressions of regret, for example, the attentiveness to victimhood, it appears, leads to increased moral accountability and political solidarity and a revised vision for the future. However, people must be careful how they attend to victims, or the politics of victimhood will obstruct individual therapy, persisting suffering rather than mediating it.

Traumas do not fade easily in our age. Over the past century, Westerners and people living in Westernized societies have become more and more willing to show their wounds and recognize the suffering of others (Barkan 2000; Bartov 2000; Buruma 1999; Confino 2005; Hughes 1993; Maier 1993; Marrus 2006; Novick 1998; Sommers and Satel 2005; Sykes 1992; Torpey 2003, 2006; Winter 2006). As a result, victimhood is a defining feature of politics in the West. But how should we regard this? What is the value of a politics centered on trauma? Is it good that people are so willing to bare their wounds? Is being responsive to everyone else's trauma always commendable? Not surprisingly, scholars are divided on these questions. As Martha Minow suggests, there are fundamentally two sides:

Too much memory or not enough; too much enshrinement of victimhood or insufficient memorializing of victims and survivors; too much past or too little acknowledgement of the past's staging of the present (1998: 2).