GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following thesis (or dissertation) presentation is open to those in the University community.

Jian Fang

Advisor: Dr. Matthias Brewer

Doctor of chemistry

University of Vermont Chemistry Department

May 27th 2020

1:30 PM

Microsoft Teams

AN EXPLORATION OF β -HYDROXY- α -DIAZO CARBONYLS IN SYNTHESIS: FRAGMENTATION, VINLY CATION FORMATION AND CONJUGATE ADDITION REACTIONS

Abstract

β-hydroxy-α-diazo carbonyl compounds have been shown to display diverse reactivity profiles that can lead to a variety of useful products. This specific combination of functional groups can react in several mechanistically distinct ways depending on the presence or absences of other groups within the molecule. For example, γ-silyloxy-β-hydroxy-α-diazo carbonyls react with Lewis acids via fragmentation reactions to generate tethered aldehyde ynoate or ynone products. A portion of this thesis describes how this methodology was applied toward the synthesis of an important bioactive natural product: aspidospermidine. β-Hydroxy-α-diazo carbonyls are also convenient precursors to vinyl cations. The vinyl cation is generated by loss of N_2 gas from a vinyl diazonium intermediate, which is formed by the dehydroxylation of a β-hydroxy-α-diazo carbonyl compound. A portion of this thesis investigated the intramolecular reaction between vinyl cations and aromatic rings to form tricyclic indenones and naphthanols. Importantly, this research has also shown that the vinyl diazonium intermediates are themselves a strong electrophilic intermediate that can react with nucleophiles in conjugate addition reactions. These reactions occur faster than loss of N_2. More specifically, this thesis describes our finding that vinyl diazonium ions can be trapped by indole derivatives to provide all-carbon quaternary centers in high yield. This reaction provides a novel method to prepare structurally complex products that contain a diazo functional group that can be taken advantage of in subsequent synthetic transformations.

GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following thesis (or dissertation) presentation is open to those in the University community.

Kristian Brevik

Advisor: Dr. Yolanda H. Chen

Doctor of Philosophy

Plant and Soil Science

May 28th

2:00pm

email kbrevik@uvm.edu for link to attend remotely

RAPID EVOLUTION IN AGROECOSYSTEMS: TRANSPOSABLE ELEMENTS AND EPIGENETICS OF THE COLORADO POTATO BEETLE, LEPTINOTARSA DECEMLINEATA

Abstract

Within agricultural ecosystems, humans and insects enter into complex relationships. Humans consider many of these insects to be pests, and exert significant pressures upon them, such as efforts to kill them using insecticides. One of the ways insects respond to these efforts is by rapidly evolving resistance to insecticides - but how they do this is not fully understood. DNA methylation, an epigenetic mechanism, and transposable elements, which are mobile genetic elements within genomes, may each play a role in shaping the way insects rapidly evolve in response to exposure to insecticides. Understanding the role of transposable elements and DNA methylation in the evolution of insects who live within agroecosystems can cast light on fundamental mechanisms of evolution while informing how we might live in better relation with these species.

These four chapters together provide support for complex interactions between insecticide exposure, transposable element activity, epigenetic inheritance, and adaptation to human-dominated agricultural landscapes in insects. First, I provide an overview of how insecticide-induced epigenetic effects can be inherited and may drive the evolution of resistance via epigenetic processes, contributing to ecological success in agroecosystems. Next, I utilize a large dataset of reports of insecticide resistance to determine if insect species evolve at different rates using survival analysis methodology. I then explore the diversity of transposable elements found within different populations of the Colorado Potato Beetle, *Leptinotarsa decemlineata,* to determine if these genetic elements play a role in the evolution of traits associated with living in agroecosystems. Finally, I analyze how DNA methylation in the Colorado Potato Beetle may be affected by exposure to insecticide, and if these changes to DNA methylation patterns are heritable and associated with genes known to be involved in insecticide resistance.

GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following thesis presentation is open to
those in the University community.

Erin O'Neill

Advisor: Dr. Alison K. Brody

Master of Science

Biology

May 28, 2020

10 AM

TBD - virtual

The effects of ericoid mycorrhizal fungi on reproductive traits in
Vaccinium Corymbosum

Abstract

Most angiosperms rely on animal pollination to reproduce and the majority of these also interact with mycorrhizal fungi concurrently. Although these interactions have been studied separately, there are fewer studies that examine their combined effects on host plants. Linking above and belowground interactions has become an exciting new field of study.

Mycorrhizal fungi are among the world's oldest and most important mutualisms, dating back more than 400 million years and forming symbiotic relationships with 90% of extant land plants. In this symbiosis, mycorrhizal fungi receive photosynthetic carbon in exchange for providing resources such as water and nutrients to their host plants. Fungal genotypes may vary in their ability to assist their plant partners with nutrient uptake. Local inoculums may provide more for a host plant than a commercial inoculum.

Ericoid mycorrhizae (ericoids) involve a relatively specialized group of fungi that form symbioses with plants in the Ericaceae. In this work, we are asking whether, given mycorrhizal fungi can increase the health of plants, the plants can change resource allocation to benefit the development of their reproductive organs with increased input from the ericoid mycorrhizal relationship.

Vaccinium corymbosum is an Ericaceous plant that associates with ericoids. Inoculation with ericoids may change the number of *V. corymbosum* buds and flowers and/or affect floral traits, by enhancing nutrient uptake. If the floral traits that are affected are important to pollinators, mycorrhizae could indirectly affect the host plant's interaction with pollinators.

We hypothesized that inoculation with ericoid mycorrhizal fungi increases reproduction in highbush blueberry, *Vaccinium corymbosum*, through its effects on floral traits and pollinator visitation and responds more strongly to a local soil inoculum than to a commercial inoculum. To test our hypothesis, we inoculated 360, three-year old, *V. corymbosum* plants in the spring of 2018 and randomly assigned them to one of four treatments: 1) commercial inoculum 2) local soil 3) commercial inoculum and local soil and 4) a control group with no inoculum. Plants were then grown in a common garden. Plants did not differ in ericoid colonization prior to inoculation. Inoculation with ericoids increased colonization.

During the field season, data including inflorescence bud, flower, fruit and seed counts were collected. We transported plants to blueberry farms known to differ in pollinator abundance and conducted pollinator observations throughout the flowering season. In addition, we conducted hand pollination experiments to examine the degree of pollen limitation at each of these farms. Our results show that inoculation with ericoids directly enhances reproductive structures but may have more only subtle indirect effects on interactions with pollinators. Our results elucidate the importance of ericoids for the development of reproductive traits and subsequent interactions with pollinators. It also helps us further understand the ways in which belowground interactions can drive aboveground interactions.

GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following thesis presentation is open to
those in the University community.

Peter Lindquist

Advisor: Dr. Keith Klepeis

Master of Science

Geology

29 May 2020

11:00 am

via Microsoft Teams
(email peter.lindquist@uvm.edu to be added to the meeting)

The architecture of a lower-crustal shear zone and evidence for along-strike variations in strain localization and partitioning, Fiordland, New Zealand

Abstract

Rocks exposed in Fiordland, New Zealand provide a record of magmatic and tectonic processes that were active in the middle to lower crust of a magmatic arc during the Early Cretaceous. The George Sound shear zone (GSSZ) is one expression of those processes, and is a steep, lower-crustal shear zone that accommodated oblique sinistral motion within the continental margin of Gondwana. I have drawn structural and petrologic observations from five field areas that span the 50 km length of the exposed GSSZ. Synthesizing these data, I construct a model of the large-scale architecture of the GSSZ and explore the tectonic, magmatic, and metamorphic processes that may have driven its evolution.

The George Sound shear zone is defined by a zone of rocks that exhibit evidence of deformation at amphibolite facies conditions and dominantly sinistral kinematic indicators in N- to NE-striking fabrics. This zone varies from meters to kilometers in width, and contains segments that split into up to four separate branches. Apparent variations in the amount of strain accommodated by different fabrics within the shear zone suggest that, over time, strain localized into narrower zones. These strands of high-strain fabrics variously correlate with more extensive hydration metamorphism or lithologically heterogeneous areas containing weaker lithologies, indicating that strain localization processes in the lower crust can vary at the kilometer scale within a single shear zone. The geometry of fabrics also varies along strike within the GSSZ, expressed, from north to south, as a shallowing of mineral lineation directions. We suggest that this may be the result of strain partitioning within the lower crust, with contractional structures adjacent to the GSSZ along its southern extent enabling more strain partitioning than in the north where the GSSZ exhibits more transpressional behavior. The architecture and along-strike variations in deformation processes in the GSSZ highlight the possible complexities of lower-crustal shear zones and the numerous factors that may control the rheology of the lower crust.

GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following thesis presentation is open to
those in the University community.

Jamie Deutsch

Advisor: Jessica Heath

Master of Science

Cellular, Molecular and Biomedical Sciences

May 29th, 2020

1:00 PM

location (remote)

IMPLICATIONS OF THE CALM-AF10 ONCOGENIC FUSION PROTEIN ON WNT SIGNALING IN LEUKEMIA

Abstract

Hematopoiesis is the complex differentiation process involving the formation of all blood cells from a common progenitor; the hematopoietic stem cell. Errors in this process can lead to acute leukemia, or a rapid accumulation of immature blood cells which hinders proper immune function. While survival rates of this devastating disease have increased dramatically over the last several decades, certain cytogenetic abnormalities remain risk factors for treatment resistance and relapse. One of these abnormalities is a chromosomal translocation involving the transcription factor, AF10

Mix-Lineage Leukemia, Translocated to, 10 (MLLT10, referred to as AF10) is involved in several oncogenic translocations involved in high-risk leukemia. Functionally characterized as a cofactor of the histone methyltransferase, DOT1L, the extent of AF10 function has not been determined. Examination of AF10 structure and interaction partner, b-Catenin, has lead us to develop a hypothesis regarding the role of AF10 in canonical Wnt signaling. Wnt is a highly complex signaling pathway which plays roles in cell fate determination and self-renewal, and is thought to be vital for the onset and progression of leukemia. We hypothesize that the AF10 fusion protein, CALM-AF10, impacts the normal AF10-b-Catenin interaction, and acts to dysregulate Wnt signaling as a mechanism for promoting leukemia.

We have developed a luciferase reporter system in HEK293T cells by which to test this hypothesis, and utilize immunoprecipitation to investigate the interaction between CALM-AF10 and b-Catenin. We determine through the work of this thesis, that CALM-AF10 upregulates Wnt signaling in a manner independent of an interaction with b-Catenin.

GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following thesis (or dissertation) presentation is open to those in the University community.

Andi Kur

Advisor: Dr. Eric Bishop-von Wettberg

Master of Science

Plant and Soil Science

June 2nd, 2020

1:00 pm

Virtual, Microsoft Teams

The Potential of Refugee Seed Systems to Promote Contemporary Evolution in Traditional Crops: A Case Study of African Maize in New England

Abstract

There are many mechanisms by which landraces evolve in a contemporary agricultural setting; however, the influence of forced human migration on landrace redistribution and evolution has received little attention in comparison to the stochastic effects of drift, mutation, and gene flow in the centers of origin. Although the seed systems of forcedly-displaced people remain poorly understood, evidence suggests that refugees often continue to grow traditional crops after resettlement. From a genetics perspective, the crops that are transported to highly disparate environments provide an interesting opportunity to study adaptation.

This research addresses how forced human migration has impacted contemporary landrace evolution in a specific case study of African maize being grown by new American farmers in Vermont and New Hampshire. We utilize a Whole Genome Sequencing approach and methods in population genetics to investigate the origin, genetic diversity, and potential adaptation in these crops. Our findings suggest that maize grown by new American farmers in the study does in fact originate from Africa and that each farmer is growing a genetically distinct crop, although we are unable to link origin of the crop to immigration history of the farmer. We also found that genetic diversity is remarkably high across all samples, even compared to landrace panels assembled from the U.S. National Plant Germplasm System. Lastly, we found numerous signatures of positive selection across all farmer samples, and through a Gene Ontology analysis, we identified two significant biological processes enriched by positive selection, (1) cinnamoyl-CoA reductase biosynthesis and (2) glutathione synthase activity, that may indicate recent adaptation and be correlated to increased cold tolerance. Overall, through this case study we show a specific example of how forced human migration has affected landrace redistribution, subsequent evolution, and potential adaptation to a disparate environment. We believe these findings hold interesting implications towards agrobiodiversity conservation and suggest the potential of refugee seed systems to promote contemporary adaptation in traditional crops.

GRADUATE COLLEGE
DEFENSE NOTICE

Please Post

The following dissertation presentation is open to
those in the University community.

Emma Ste.Marie

Advisor: Dr. Robert Hondal

Doctor of Philosophy

Chemistry

June 4th, 2020

10:00 am, EDT

Virtual link TBD.

SULFUR AND SELENIUM IN PEPTIDES AND PROTEINS:
PART I – CHEMOSELECTIVE METHODS FOR DISULFIDE BOND FORMATION,
PART II – FUNCTION OF SELENIUM IN ENZYMES.

Abstract

Selenocysteine (Sec), the 21st proteogenic amino acid, was first identified in 1976 by Thressa Stadtman. In proteins, Sec replaces the far more common sulfur-containing amino acid cysteine (Cys). A key question since Stadtman's discovery is: Why does Sec replace Cys? This question is especially relevant since Cys-orthologs of Sec-enzymes catalyze the identical reaction with only slightly reduced efficiency, and incorporation of Sec into a protein is much more complicated and bioenergetically costly compared to Cys. The study of selenoproteins is very difficult because Sec is incorporated into proteins by recoding a UGA stop codon as a sense codon. Production of recombinant selenoproteins involves reconstituting the recoding machinery. Alternatively, selenoproteins can be produced using a combination of recombinant DNA technology and peptide synthesis. While the development of solid phase peptide synthesis has provided a synthetic route for studying Sec, the Sec side chain requires the use of sturdy protecting groups (PGs) during synthesis.

Work herein first addresses complications associated with Sec and Cys PGs, which until now have required harsh conditions for removal. My work has developed facile new methods for the deprotection of Sec and Cys residues. For Sec, we found that the use of DTNP to remove various PGs with subsequent ascorbolysis results in a Sec-selenol. Likewise, we developed 2,2'-dipyridyl diselenide (PySeSePy) to deprotect Cys, which can be used with subsequent ascorbolysis to provide a Cys-thiol. Notably, we found the ascorbolysis step to be chemoselective; ascorbate can reduce a selenosulfide bond, but not a formed disulfide bond. We harnessed this chemoselectivity for the synthesis of peptides that contain multiple disulfide bonds, which we demonstrate by synthesizing guanylin and tachyplesin-1 using PySeSePy as a chemical tool.

Another chemical tool that we utilize to explore selenoprotein chemistry is alpha-methyl selenocysteine (αMe)Sec. This unique amino acid has a methyl group in place of its α-H. We found that a peptide containing (αMe)Sec (compared to a Sec-peptide control), showed enhanced stability when incubated in oxygenated buffer for prolonged periods of time. We also utilized our (αMe)Sec-peptide as a glutathione peroxidase mimic to reduce peroxides, and postulate that this peptide could serve as a therapeutic in times of high oxidative stress.

Finally, it is now commonly accepted in the field that selenoproteins evolved to resist oxidative stress. Herein, we expand this hypothesis: Sec replaces Cys in proteins to resist all types of electrophilic stress. We found that when Sec residues are alkylated by reactive biological electrophiles (such as acrolein), the formed adduct can be reversed. There are many potential mechanisms of reversal, but we provide evidence supporting a selenoxide elimination mechanism using a mutant form of thioredoxin reductase that contains (αMe)Sec in place of the native Sec residue at the C-terminal active site. Taken together, the works described in this dissertation expand the chemical toolbox for the study of Se-containing biomolecules and provides new hypotheses for the chemical role of Se in proteins.