UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 20, 2016 Mary Gates Hall

Online Proceedings

Poster Session 1

MGH 241, Easel 128

11:00 AM to 1:00 PM

Duplication of *CYCLOIDEA* Genes in Rhododendrons

Jacob Fong-Gurzinsky, Junior, Biology, History, Lewis & Clark Coll
Mentor: Valerie Soza, Biology
Mentor: Benjamin Hall, Biology

CYCLOIDEA (*CYC*) is a member of the *TCP* family of transcription factors, whose name stands for *TEOSINTE BRANCHED 1*, *CYCLOIDEA*, and *PROLIFERATING CELL FACTORS*. The members of this transcription factor family are involved in regulating plant growth and cell proliferation by binding to DNA. Previous studies show that *CYC* has duplicated at least twice in the core eudicot angiosperms and that the *CYC2* paralog is involved in controlling flower symmetry. The goal of our research was to characterize duplications of *CYC* in *Rhododendron*, with the long-term goal of seeing how these duplications affect flower symmetry. To accomplish this task, we used the *R. williamsianum* genome sequence to design primers specific to each paralog in order to PCR-amplify the *CYC* genes from four *Rhododendron* species, representing two subgenera (*Hymenanthes*, *Rhododendron*). Amplified products were cloned and sequenced to recover all alleles. We used our *Rhododendron* sequences and sequences from the conserved TCP and R domains of other species as out-groups in a Bayesian analysis to reconstruct the gene tree. From this tree, we have identified 2 main duplications in *RhododendronCYC* genes as seen in other core eudicots. We also found that the *CYC2* paralog has undergone at least 2 gene duplications and that the *CYC1* paralog underwent one. Future research will focus on finding when *CYC2* duplications occurred in rhododendrons and determining if, where, and when these *CYC2* duplicates are expressed in *Rhododendron* flowers.

Session 1O

Plant Genetics, Ecology and Evolution

Session Moderator: Veronica Di Stilio, Biology

JHN 026

12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Exploring the Genetic Basis for Diverse Floral Symmetry among Rhododendrons

Haley Alyssandra (Haley) Deal, Senior, Environmental Science & Resource Management
Mentor: Benjamin Hall, Biology
Mentor: Valerie Soza, Biology

Flowering plants exhibit diverse forms of floral symmetry that represent many independent changes throughout their evolutionary history. The selective and genetic basis to these changes has provided scientists with a complex puzzle that Darwin once referred to as an "abominable mystery." Recent genetic studies began to uncover the genetic causes for this mystery, revealing the presence of certain genes that show correlations with this evolutionary trend. One such gene, the *CYCLOIDEA* (*CYC*) gene, has been identified as a major contributor to changes of floral symmetry. We have found this gene in the sequenced genome of *Rhododendron williamsianum* where it has experienced multiple duplications. The goal of my research is to identify the main duplications in one of the *CYC* copies (*CYC2*) in the Rhododendron genus. I accomplished this by using polymerase chain reactions to isolate any *CYC2* copies present in two species from each of the subgenera of *Rhododendron*: *Hymenanthes*, *Azaleastrum*, *Therorhodion*, and *Rhododendron*. I then used cloning and sequencing to obtain the sequences of the *CYC2* copies from each of the sampled species. I will conduct a phylogenetic analysis of these sequences in order to reconstruct a gene tree that will display a summary of the main *CYC2* duplications that have occurred in the genus and when they emerged. Preliminary results from four species sampled thus far show that two independent duplications in *CYC2* have arisen in both *Hymenanthes* and *Rhododendron*. My expanded analysis, sampling species from additional subgenera, will provide a more thorough history of this gene and its duplications throughout the genus. This will allow for more robust testing

for correlation between symmetry and gene duplication in the future.

SESSION 2D

PROTEIN CHEMISTRY AND METABOLOMICS

Session Moderator: Daniel Ratner, Bioengineering
MGH 234
3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Determination of Key Locations to Disrupt Aggregation in Light Chain Amyloidosis
Michael Christopher (Michael) Liao, Senior, Bioengineering
Mary Gates Scholar
Mentor: Valerie Daggett, Bioengineering

Light Chain Amyloidosis (AL) is a disease defined by the deposition of aggregated immunoglobulin light chains in the form of fibrils in several organs. While these fibrils are insoluble, the soluble oligomers that precede them in the pathway involving unfolding and then aggregation of the protein are toxic to the cell. A novel secondary structure, alpha-sheet, was hypothesized to be the cause of toxicity. This structure is rarely seen in normal proteins, but it is populated in all peptides and proteins involved in amyloid diseases studied so far in our lab. In addition, the correlation between thermal stability and fibril formation has led to the study of the impact of amino acid mutations on the unfolding pathway. As is the case for most amyloid diseases, Light Chain Amyloidosis is incurable and fatal . The determination of specific patterns and mutations that destabilize the protein and lead to increased toxicity is important to better understand how to intervene. To this end, we are comparing two patient-derived light chains, one non-amyloidogenic and the other amyloidogenic. By analyzing their differences, we can determine regions of the protein that contribute to aggregation. We performed molecular dynamics simulations of each protein and analyzed their unfolding pathways and characterized the structure of the amyloidogenic interemediate associated with toxicity. The docking of pre-existing amyloid inhibitors developed in the lab to the resulting structures was done to determine a lead compound. Through rational and evolutionary design, several iterations were done on the lead compound and an inhibitor with an overall better binding score was developed.

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Application of Synthetic α-Sheet Peptides Rescues a Human Cell Model from Aβ42 Cytotoxicity
Nathan Lee (Nathan) Maris, Senior, Biochemistry
Mary Gates Scholar, UW Honors Program
Mentor: Valerie Daggett, Bioengineering

Amyloid diseases like Alzheimer's disease, type 2 diabetes, and Parkinson's disease represent some of the most pressing concerns facing our healthcare system today. Human consequences aside, these disorders place an enormous economic burden on society; Alzheimer's disease care in the United States alone costs upwards of $226 billion annually, and these expenses will continue to rise as the population ages. As such, substantial effort has been invested in the development of novel compounds that would halt or reverse the effects of these diseases. Our group's previous research suggests that amyloid diseases, though caused by the selective dysfunction of different and unrelated proteins, share a common mechanism of pathogenicity, wherein misfolded proteins aggregate into toxic oligomers typified by novel α-sheet secondary structure. Synthetic peptides designed to adopt a structure complementary to this motif inhibit in vitro aggregation of several different amyloid systems. In this study, we show that the inhibitory effects of these molecules also extend into the realm of simple biological models, in this case inhibition of toxicity in neuroblastoma cells. We co-incubated IMR-32 cells with Aβ42 peptide (whose aggregation is associated with Alzheimer's disease) and our synthetic α-sheet compounds for periods of twenty-four to forty-eight hours, then assessed cytotoxicity by a MTT cell viability assay. When compared with neat Aβ42, the designs were able to rescue cells from necrosis, significantly lessening detectable toxicity. While preliminary, these results suggest that our peptides may have promise as potential therapeutic agents for treating a broad spectrum of amyloid diseases.