

Participating Mentors

Sanford Program for Undergraduate Research

Applicants: List 3 mentors in the indicated spaces on your application. Please note that if there is a high demand for one specific mentor, you may be placed with one of your alternate choices or another mentor who fits your research interests.

Dr. Subhash C. Chauhan, Ph.D.

Cancer Biology Research Center

Research Interest: Developing Molecular Markers for Early Cancer Diagnosis and Targeted Therapy for Cancer Treatment

Biomarkers for Early Cancer Diagnosis: Primary research interest of Dr. Chauhan's lab is to identify and characterize the diagnostic and therapeutic targets for gynecological malignancies. Main focus of our research group is to elucidate the regulatory mechanisms of cell-cell adhesion and anti-adhesion molecules that cause cancers. This research is aimed for the identification and characterization of biomarkers that aberrantly express or localize in cancer cells of reproductive tract in order to develop newer tools for early disease diagnosis. We are utilizing genomics and proteomics approach for identification of novel early diagnostic markers. Recently we have identified a novel trans-membrane mucin MUC13 which is highly over-expressed ovarian and pancreatic cancer cells. This may be potential biomarker for early cancer diagnosis as well as a good target for antibody guided targeted cancer therapy.

Optimization of Radioimmunotherapy for Cancer Treatment: The other research interest of Dr. Chauhan's lab is to develop novel radioimmunotherapy (RIT) and radioimmunodiagnostic (RID) modalities for the treatment and diagnosis of gynecological malignancies. Monoclonal antibodies/engineered single-chain Fvs offer a powerful approach to cancer therapy in view of their exquisite specificity and targeting capability *via* the delivery of cytotoxic agents (i.e. radionuclides, enzymes, genes, drugs and cytotoxins). This research project is aimed to develop novel genetically engineered antibody molecules with reduced immunogenicity, desirable size and altered pharmacokinetics for the RID/RIT applications.

Development of a Novel Nanotechnology Based Therapy: Nonspecific distribution and suboptimal delivery of the anti-cancer drug(s) to the tumor cells are the major hindrances in the successful use of traditional chemotherapy. The ovarian cancer tissues overexpress TAG-72, MUC1 and MUC16 antigens, and a combination of the antibodies against these three antigens will potentially recognize 100% of the ovarian cancer cells. These antibodies can be used to deliver the *radionuclides and nanoparticles-encapsulated drugs* specifically to the cancer cells. In addition, antibodies that have been labeled with alpha and beta emitting radionuclides (^{211}At , ^{177}Lu and ^{131}I) of different linear energy transfer (LET) and have been designed against these tumor antigens will effectively target various sizes of metastatic lesions. Additionally, we are also developing a novel nanotechnology based gene therapy for ovarian cancer.

Dr. Jetty L. Duffy-Matzner, Ph.D.

Chair, Chemistry Department, Augustana College

<http://faculty.augie.edu/~duffy/>

We are interested in several different projects that use organic synthesis and methodologies to produce novel biologically interesting compounds in the area of anti-microbial and anti-fungal agents. We are also interested in

producing chemosensors using conjugated polymers and greener methods for organic synthesis by producing solid supports for reactions that negate the use of solvents.

Novel anti-microbial: Our group would like to pursue the production of novel macromolecules based upon the Intramolecular Silyl Nitronate Cycloaddition (ISNC) reaction. The precursor molecules that result from the former reaction have been studied extensively in my group during the last six years. I would like to then convert these molecules into monomers for novel macrolides that may have ionophoric properties. With the increasing number of bacteria that have developed a resistance to known antibiotics it would be very interesting to try and produce novel biologically active molecules. It is expected that it will be very easy to change a number of variables in these potential polyester macromolecules. For example the 2,5-substituents could be derived from many commercially available products (simple alcohols and aldehydes) and thus a wide range of substituents could be explored. The symmetry of the macrocycle could be examined by altering the symmetry of the 3,4-substituents of the tetrahydrofuran ring. The size of the linker arms between the furan rings can be varied with commercially available diols. The functionality of the macrocyclization could be changed from polyester to polyether to polyamide. Thus there are many variables that could be exploited to produce a series of macrocycles that should exhibit excellent bindings of metal cations. The biological importance and ion selectivity of the new series of polyester macrocycles would then be examined.

Novel anti-fungal: A quick perusal through the literature has shown that there has been little to no attempts to make lactone-isoxazole ring systems even though these compounds could be potent fungicides as well as provide an interesting synthetic challenge. This work would like to examine novel 2-propargyl nitroacetates under both Intramolecular Silyl Nitronate Cycloaddition (ISNC) and Intramolecular Nitrile Oxide Cycloaddition (ISOC) reaction conditions. It is believed that the nitroacetate will undergo different reactions under these conditions based upon previous research on propargylic nitroethers by the principal investigator. The ISNC may form the α,β -unsaturated lactone while the INOC may form the fused lactone-isoxazole ring system. The lactones could then be hydrolyzed to form compounds of considerable interest due to their probable biological reactivity (isoxazoles are known fungicides).

Bio-chemosensors: A continuing challenge in environmental monitoring is the rapid, at source detection of a variety of contaminants ranging from transition metal ions to nucleotides, organic solvents and small molecules. Conjugated fluorescent polymers represent an exciting new class of materials for chemical sensor applications. By covalently binding multiple receptors to a single conjugated polymer, fluorescent excitons along the length of the entire backbone can be quenched by a single binding event. This can lead to significant enhancements in sensitivity over traditional single receptor chemosensor designs. We have now characterized the non-linear quenching response in these polymers and with the synthetic work of the Duffy group are poised to expand the scope and utility of this new class of disposable sensory materials. In this project we will take advantage of these previous results to develop more reversible and selective classes of these chemosensors, expand the range of detectable analytes, and transition the technology to a solid state environment. New receptors targeting transition metals and organic small molecule contaminants will be synthesized and evaluated including hemi-labile ligand complexes and resorcinol derivatives.

Heterogeneous Silica Gel Based Catalysts: The formation of nitroalcohols via condensation of nitroalkanes and aldehydes yields compounds with both product and synthetic applicability, due to the new carbon-carbon bond formation. Specifically, our group is interested in silyl nitronates in regards to cycloaddition reactions to include synthesizes requiring nitroalkenes. The utilization of silica gel treated with an amino-silane compound as the basic catalyst in the nitroaldol reaction has been previously shown to be successful for a very limited range of aldehydes, allowing for the possibility of shorter reaction times, higher percent yield, and an overall greener process. We have further explored the utilization of the basic catalyst to include product selectivity via change in the amino-silane compound and catalyst regeneration.

Three recent papers written by Dr. Duffy-Matzner and her students:

1. Grandbois, Matthew L.; Betsch, Kelsie J.; Buchanan, William D.; Duffy-Matzner, Jetty L. Synthesis of Novel 2H, 5H-Dihydrofuran-3-yl Ketones via ISNC Reactions. *Tetrahedron Letters* (2009) 50, 6446–6449.
2. Grandbois, Matthew L. ; Viste, Arlen E.; Englund, Ethan A.; and Duffy-Matzner, Jetty L. Computational Comparison of Nonactin and Proposed 3,4-Tetrahydrofuro-tetraester. *Journal of Undergraduate Chemistry Research*. (2006) 4, 159-163.
3. Buchanan, William D.; Duffy-Matzner, Jetty L. Nitroaldol Reactions Via A Heterogeneous Silica Based Catalyst. *Journal of Undergraduate Chemistry Research* (2005) 4, 153-156.

Dr. Kristi Eglund, Ph.D.

Cancer Biology Research Center

Early and personalized diagnosis for breast cancer patients is crucial for optimizing treatments leading to long-term survival. It has been previously shown that cancer proteins can elicit an immune response in patients. These autoantibodies recognize tumor-associated antigens (TAA), autologous cellular proteins that are mutated, modified or aberrantly expressed in tumor cells. Because anti-TAA antibodies reflect and amplify the cellular changes associated with tumorigenesis, detection of anti-TAA antibodies in the sera of breast cancer patients may provide a non-invasive mechanism for the early detection of breast cancer. We took a molecular approach to identify potential tumor antigens that elicit an antibody response in breast cancer patients by generating a cDNA library (MAPcL), enriched with genes encoding membrane and secreted proteins, which are more likely to induce an antibody response in patients compared to intracellular proteins. Our laboratory has established an expression strategy to generate MAPcL Fc-fusion proteins that retain their native conformation and are efficiently recognized by patients' antibodies. The long-term goal of my laboratory is to develop a blood test for breast cancer based on detecting a patient's antibodies generated against cancer proteins. In addition, we have selected previously uncharacterized MAPcL genes that encode proteins overexpressed in breast cancers but have restricted expression in the normal essential organs, and we are characterizing the role of these MAPcL proteins in breast tumorigenesis.

Dr. Paul Eglund, Ph.D.

Biology Department, Augustana College

www.augie.edu/dept/biology/Web/faculty/Eglund/Eglund.htm

Human dental plaque is a well-recognized example of a multi-species bacterial community. Dr Eglund's research interest lies in the interaction between different bacterial species found in dental plaque and the study of communication between different species of bacteria in the plaque community. This communication includes cell-cell contact and metabolic interactions between organisms in the biofilm. Eglund's current research focus include studies of communication that occurs between two members of the plaque community, *Veillonella atypica* and *Streptococcus gordonii*. When these organisms are growing together, *S. gordonii* induces expression of an alpha-amylase gene that is not expressed when *S. gordonii* is grown without *V. atypica*. Goals of the lab are to identify the mechanism of signaling that occurs between these species, identify the genes involved and determine the importance of amylase expression to development of the mixed-species community.

Dr. Amy Elliot, Ph.D.

Director, Health Disparities Research Center

Dr. Jennifer A. A. Gubbels, Ph.D.

Biology Department, Augustana College

<http://www.augie.edu/dept/biology/Web/faculty/Gubbels/Gubbels.html>

The long-term goal of this research is to determine mechanisms of metastasis and immune escape in epithelial ovarian cancer. The cells of this cancer type express a very large protein called MUC16. MUC16 is a large, heavily glycosylated protein whose molecular weight is estimated at over 3 million Da. We have shown previously that MUC16 aids ovarian cancer cells in spreading throughout the peritoneal cavity by attaching specifically to another protein called mesothelin. Mesothelin is expressed by mesothelial cells that line the peritoneal cavity as well as the organs within the peritoneal cavity—both of which are common sites of ovarian cancer metastasis. MUC16 also contributes to ovarian cancer immune evasion. Natural killer (NK) cells require close contact (called immune synapses) with a target cell to be able to lyse it. This close contact allows the NK cells to polarize molecules that are destructive to the target cell at the NK/target cell interface. When the large and anti-adhesive protein MUC16 is expressed on the tumor cell surface, NK cells are prevented from forming immune synapses and destroying the tumor cell. This research on the both the metastatic and immune evasive roles of MUC16 may lead us to new therapies for epithelial ovarian cancer.

Two recent papers written by Dr. Gubbels:

1. Gubbels J.A., Felder M, Horibata S, Belisle JA, Kapur A, Holden H, Petrie S, Migneault M, Rancourt C, Connor JP, Patankar MS. "MUC16 provides immune protection by inhibiting synapse formation between NK and ovarian tumor cells." *Mol Cancer*, 9(2):11, 2010
2. Gubbels, J. A., Belisle, J., Onda, M., Rancourt, C., Migneault, M., Ho, M., Bera, T. K., Connor, J., Sathyanarayana, B. K., Lee, B., Pastan, I., and Patankar, M. S. Mesothelin-MUC16 binding is a high affinity, N-glycan dependent interaction that facilitates peritoneal metastasis of ovarian tumors. *Mol Cancer*, 5: 50, 2006.

Dr. William Harris, Ph.D.

Director, Cardiovascular Health Research Center

The Omega-3 Research Lab at the Cardiovascular Health Research Center focuses on the analysis of blood (RBCs and plasma) omega-3 fatty acid levels. This test is currently being used in major national epidemiological research studies to learn more about the health benefits of the omega-3 fatty acids contained in fish oils. We are interested in more fully characterizing this test through the use of thin layer chromatography, gas chromatography and GC-mass spectroscopy. We are looking for a student with a strong interest and background in chemistry to work on this project.

Dr. Meena Jaggi, Ph.D.

Cancer Biology Research Center

The primary focus of my research is to identify and evaluate the functional significance of cell-cell adhesion molecules known as cadherins and catenins in cancer progression and to understand the regulation of cadherin/catenin complex activity by Protein Kinase D signaling. In-depth knowledge of molecular mechanisms involved in signal transduction of human cancers is critical for the development of biomarker for early detection of cancer and rationalized structure-based drug designing.

We have identified a novel interaction between E-cadherin/beta-catenin complex and Protein Kinase D1 (PKD1), an important modulator of several kinase signal-transduction pathways in benign and malignant human diseases.

Downstream signaling of the E-cadherin/beta-catenin and PKD1 interaction alters malignant phenotype of cancer cells. Another project investigates the alteration of signal transduction pathways in prostate, colon, breast and gynecological cancers using genomic and proteomic techniques.

Dr. DenYelle Baete Kenyon, Ph.D.

Health Disparities Research Center

Dr. Kenyon engages in social/behavioral research using quantitative and qualitative research methods to examine various adolescent health and development issues. Students would have the opportunity to be involved in several ongoing projects, which include adolescent reproductive health, American Indian ethnic identity and mental health, obesity prevention, and parent-adolescent relationships during the transition to adulthood. Students interested in adolescent health/development and health disparities are encouraged to apply.

Two recent papers written by Dr. Kenyon:

1. Kenyon, D. B., & Koerner, S. S. (2009). Examining emerging adults' and parents' expectations about autonomy during the transition to college. *Journal of Adolescent Research, 24*, 293-320.
 2. Kenyon, D. B., Fulkerson, J. A., & Kaur, H. (2009). Food hiding and weight control behaviors among ethnically-diverse, overweight adolescents: Associations with parental restriction, monitoring, and dissatisfaction with adolescent body shape. *Appetite, 52*, 266-272.
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Dr. Mark Larson, Ph.D.

Biology Department, Augustana College

<http://faculty.augie.edu/~mklarson/>

Platelets are a critical cellular component for maintaining normal blood flow and distribution by forming clots in response to blood vessel damage. We aim to elucidate some of the extracellular and intracellular signals that influence the activity of existing blood platelets and the formation of new platelets. Specifically, my lab has two main projects. The first is to determine what signals promote the formation of new platelets from platelet precursor cells called megakaryocytes. The second is to understand how dietary omega-3 fatty acids affect platelet function, a project that is run in collaboration with Dr. Bill Harris at Sanford Research. Please visit Dr. Larson's Web site (above) for more information.

Dr. John Lee, M.D.

Cancer Biology Research Center

Dr. Lee's lab goal is to improve cure rates for the treatment of Head and Neck cancer. His lab uses a variety of basic science approaches to better understand mechanisms of invasion and mechanisms of immune related clearance of head and neck cancer. He works to translate these findings into the clinic by using a mouse model of head and neck cancer that they have developed. He also works to develop new therapies by the initiation of clinical trials for the patients that he treats with cancer.

Dr. Qiangrong Liang, M.D., Ph.D.

Cardiovascular Health Research Center

Research in my laboratory is devoted to understanding the molecular events and intracellular signaling mechanisms that underlie heart failure, a clinical syndrome that occurs in virtually all cardiovascular diseases and is one of the major causes of mortality in human population. Using an approach that combines cell culture system and genetic altered animal models, we are currently conducting research in three major areas: 1. Explore mechanisms of myocardial protection by caloric restriction and develop drugs that mimic the beneficial effects of caloric restriction. 2. Investigate why diabetic patients and animals are predisposed to heart failure and suggest mechanism-based approach to reduce the susceptibility. 3. Investigate why the anti-cancer drug doxorubicin can cause heart failure and how myocardial homeostasis can be restored by coordinately promoting survival mechanisms and blocking cell death pathways.

Dr. Jared R. Mays, Ph.D.

Chemistry Department, Augustana College

<http://faculty.augie.edu/~jmays>

Consumption of fruits and vegetables has been associated with reduced incidence of cancer, especially in the gastrointestinal tract. The *Brassica* vegetables are rich sources of glucosinolates; evidence suggests that these phytochemicals are indirectly responsible for the observed cancer chemopreventive properties of cruciferous vegetables. Although glucosinolates themselves have no known bioactivity, they are converted to isothiocyanates through by the enzyme myrosinase; many of their corresponding organic isothiocyanates are well-documented chemopreventive agents. In particular, the isothiocyanate L-sulforaphane is the primary chemopreventive agent found in broccoli. The Mays research group is interested in exploiting the myrosinase/glucosinolate enzymatic processes as a means of achieving selective drug or drug candidate activation. This multi-disciplinary research program bridges the boundaries between chemistry and biology and offers students the opportunity for training in several fields of research. Multiple student projects are available with differential and cross-emphases including multi-step organic synthesis, cell culture, molecular biology, enzymology, and computational modeling.

A recent paper written by Dr. Mays:

1. Mays, J.R.; Hill, S.A.; Moyers, J.T.; Blagg, B.S.J. "The synthesis and evaluation of flavone and isoflavone chimeras of novobiocin and derrubone." *Bioorg. Med. Chem.* **2010**, *18*, 249-266.
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Dr. Keith Miskimins, Ph.D.

Director, Cancer Biology Research Center

Our laboratory examines the molecular mechanisms that regulate proliferation and survival of cancer cells. One goal of our experiments is to determine the mechanisms that control expression of the tumor suppressor p27. This protein is down regulated in most types of cancer and its levels are inversely correlated with prognosis. We have found that translation of the p27 mRNA is an important step in controlling cellular levels of the protein. We are characterizing the mechanisms that influence this process and how they vary in breast cancer cells. The second major area of interest in our laboratory is directed at understanding tumor metabolism. Neoplastic cells undergo metabolic reprogramming that may make them sensitive to drugs that target specific metabolic pathways. We have found that certain metabolism-modulating compounds are able to selectively promote cell cycle arrest and cell death of cancer cells. We are examining

the molecular pathways that mediate these effects and characterizing the effects of the compounds in preclinical mouse models of cancer.

Dr. Timothy O'Connell, Ph.D.

Cardiovascular Health Research Center

Dr. O'Connell's lab goal is to understand the role of adrenergic receptors in the pathogenesis of heart failure. His lab is studying the physiologic role of alpha-1-adrenergic receptors in preventing heart failure using transgenic mouse models as well as the basic biochemical and biophysical aspects of alpha-1-adrenergic signaling in cardiac myocytes.

Dr. David A. Pearce, Ph.D.

Director, Children's Health Research Center

Neuronal Ceroid Lipofuscinoses is caused by autosomal recessive inheritance of mutations in the genes CLN1-10. Juvenile Neuronal Ceroid Lipofuscinosis (Batten Disease) is the most common neurodegenerative disease of childhood resulting from mutations in CLN3. This devastating disease results in loss of vision around age 5 years of age, followed by slow decline in cognitive and motor function and a progressively increased frequency of seizures. Batten disease is universally fatal. The Pearce lab uses multiple approaches to investigate the underlying pathological mechanisms of Batten disease. The following are ongoing projects in the Pearce lab:

- Cell Biology/Biochemistry:
 - We have identified several proteins that physically interact with CLN3.
 - Project 1-Characterization of CLN3 protein-protein interactions and how they regulate CLN3 function.
 - Project 2-Characterization of protein-protein interactions for a protein associated to another form of Batten disease, namely CLN8.
 - Molecular Genetics/Molecular Biology:
 - CLN3 has a homolog in yeast designated Btn1p. Manipulating this model system is a powerful way to determine the function of a protein.
 - Project 1- Through molecular genetic techniques we are characterizing the function of Btn1p in yeast.
 - Stop mutations in CLN1, CLN2 or CLN3 result in the corresponding mRNA being degraded.
 - Project 2-Investigation and stabilization of mRNA's that bear nonsense mutations as a therapeutic approach to Batten disease.
 - Neuroscience:
 - Project 1-Pathological and behavioral characterization of cln3-mouse models of Batten disease.
 - Project 2-Charcterization of the underlying neurochemical abnormalities in cln1, 2 and 3 mouse models of Batten disease. Targets for therapeutic intervention.
 - Proteomics:
 - Project 1-Characterization of the changes associated to Batten disease in the central nervous system of mouse models for Batten disease.
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Dr. Alexei Savanov, M.D.

Sanford Project

Generation of Tie2-TIMP-2 Transgenic NOD mouse – a valuable tool to study development of Type 1 diabetes.

Mice of non-obese diabetic (NOD) strain serve as the best model of human type 1 diabetes (T1D). The development of T1D involves autoimmune destruction of insulin-producing β -cells. This destruction is done by activated lymphocytes - cells of the immune system, called T cells. In order to kill β -cells, which are located in the pancreas in clump-like structures called pancreatic islets, T cells first should travel from the bloodstream into the these pancreatic islets. This process of activated lymphocytes migration from the bloodstream into the underlying target tissue is called homing. Homing takes place in the small blood vessels called capillaries. Homing of diabetogenic T cells into pancreatic islets consists of several steps of interaction between a migrating T cell and cells comprising the capillary wall – endothelial cells. In essence, during their homing, autoimmune T cells, freely disseminated in the bloodstream, first attach themselves to the endothelial cells of pancreatic capillaries, and then make their way through the endothelial cell layer into the underlying islets.

Our previous studies have demonstrated that homing of autoimmune T cells into the islets depends on a certain molecule - T cell proteinase, called MT1-MMP. This proteinase sheds some of the adhesion molecules providing for the firm initial attachment of T cell to the capillary wall, and thus facilitates their transmigration. We used small-molecule, synthetic inhibitor of MT1-MMP in NOD mice with acute diabetes, and observed an enhanced immobilization of autoimmune T cells on the capillary walls, a reduced rate of T cell transmigration, and a partial restoration of the β -cell mass. Unfortunately, the potentially serious side-effects of these drugs prevented small-molecule synthetic inhibitors of MT1-MMP from being used in clinical trials in T1D patients.

Our proposed study will explore a novel, alternative approach for regulating T cell MT1-MMP, and thus, impeding the homing of diabetogenic T cells. We proposed to create a transgenic NOD mouse, which will carry additional gene, encoding for a natural inhibitor of MT1-MMP, a molecule called TIMP-2. In these transgenic mice the additional TIMP-2 molecule will be strongly expressed only in the cells which form capillaries, i.e. endothelial cells. Thus, TIMP-2 will be readily available at the necessary concentrations at the precise site where homing of the diabetogenic T cells starts - at the pancreatic capillaries. We are confident that the endothelial expression of TIMP-2 will place it in the right place at the right time to efficiently suppress the autoimmune T cell MT1-MMP, and curtail homing of the diabetogenic T cells into the pancreatic islets. We believe that reduced level of homing will support the restoration of the β cell mass in the pancreas, and at least partial reversal of T1D.

Dr. William C. Spanos, M.D.

Cancer Biology Research Center

A subset of head and neck cancer is caused by human papillomavirus (HPV). We found that an immune response is required for the clearance of HPV positive cancer in mice during treatment with chemotherapy and radiation. My lab is currently focused on determining the components of the immune system important for this tumor clearance. In addition, we are investigating several ways of augmenting the immune response to HPV positive cancer.

A recent article written by Dr. Spanos:

1. Spanos, W.C. et al. Immune response during therapy with cisplatin or radiation for human papillomavirus-related head and neck cancer. *Arch. Otolaryngol. Head Neck Surg* **135**, 1137-1146(2009).
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Dr. Peter Vitiello, Ph.D.

Children's Health Research Center

Dr. Vitiello's lab researches the toxicological effects of oxidative injury on the developing lung, focusing on alterations in redox-sensitive pathways. Specifically, we study the role that thiol oxidoreductase proteins play in regulating redox-sensitive developmental pathways. To investigate lung biology, we utilize multiple approaches including tissue culture, lung explant studies, and animal models. The overall goal of our research is to apply biochemical, molecular, cellular, and system biology approaches to understand signals which regulate normal lung development and how environmental stresses which affect these signals alters the human condition.

Dr. Seasson P. Vitiello, Ph.D.

Children's Health Research Center

The focus of Dr. Vitiello's research is to use the budding yeast *Saccharomyces cerevisiae* to study the human disease cystinosis, an autosomal recessive pediatric lysosomal storage disorder characterized by the accumulation of cystine in the lysosomes of patient cells. It is caused by mutations in *CTNS*, which encodes the lysosomal cystine transporter Cystinosin. Although the causative gene and biochemical defect have been identified, it is still unclear what defective pathway(s) are contributing to the cell death that is observed in cystinosis patient cells. To identify the pathways that have gone awry when cystinosin is absent, we exploit the yeast *S. cerevisiae*, a single-celled eukaryote that is highly amenable to genetic manipulations, as well as cell biological and biochemical applications.

Dr. Michael K. Wanous, Ph.D.

Biology Department, Augustana College

<http://www.augie.edu/dept/biology/Web/faculty/Wanous/Wanous.html>

The objectives of the research project are to identify, map, and study the genes that regulate the expression of the genes in the starch biosynthesis pathway in bread wheat, *Triticum aestivum* L. The starch biosynthesis pathway in cereals is the major contributor to human nutrition worldwide. These genes also represent a valuable model system for studying the regulation of orthologous and paralogous genes in polyploid species, and the evolution of the regulatory systems controlling these genes. This project represents the first comprehensive search of the wheat genomes for genes regulating the transcription of the starch biosynthesis genes, and the first assessment of their relative strength and the interaction between these regulatory circuits.

A recent article written by Dr. Wanous:

Storlie, E.W., R.J. Ihry, L.M. Baehr, K.A. Tieszen, J.H. Engbers, J.M. Anderson-Daniels, E.M. Davis, A.G. Gilbertson, N.R. Harden, K.A. Harris, A.J. Johnson, A.M. Kerkvleit, M.M. Moldan, M.E. Bell, and M.K. Wanous. 2009. Genomic regions influencing gene expression of the HMW glutenins in wheat. *Theoretical and Applied Genetics* 118:295-303.
<http://www.springerlink.com/content/vj66507n405840h6/>

Dr. Jill M. Weimer, Ph.D.

Children's Health Research Center

The research objective of the Weimer lab is to understand novel mechanisms controlling the development of the cerebral cortex with an emphasis on events regulating neural stem cell proliferation and neuronal differentiation. Disruption in various aspects of neuronal proliferation and placement have been shown to contribute to an array of neurodevelopmental migration defects, including leptomeningial heterotopias, subcortical band heterotopias, and periventricular heterotopias – all which can lead to severe mental retardation, developmental delays and moderate to severe epileptic seizures and are thought to contribute to developmental disorders such as Lissencephalies, Autism, and Schizophrenia. Our current work focuses on understand the developmental role of two proteins: 1) Myristoylated alanine-rich C-kinase substrate protein (MARCKS), an actin-cross-linking protein and prominent cellular substrate of PKC, which is required for proper proliferation and placement of cortical neurons in the developing cerebral cortex and 2) CLN6, the protein mutated in variant late-onset neuronal ceroid lipofuscinosis (vLINCL), a childhood neurodegenerative disorder resulting from aberrant neuronal cell loss and pathological accumulation of lysosomal autofluorescent storage material in the central nervous system.

A recent article written by Dr. Weimer:

1. Weimer, JM, Yokota, Y, Stanco, A, Stumpo, DJ, Blackshear, P, and Anton, ES (2009) MARCKS modulates radial progenitor placement, proliferation, and organization in the developing cerebral cortex. *Development*. 136(17):2965-75.

Dr. Daqing Yang, Ph.D.

Sanford Project

Ataxia-telangiectasia (A-T) is an autosomal recessive childhood disorder characterized by cerebellar ataxia and oculocutaneous telangiectasias. Patients with A-T also have high incidences of type 2 diabetes mellitus. A-T patients who have type 2 diabetes exhibit symptoms of insulin resistance and glucose intolerance. The gene mutated in this disease, *ATM* (A-T, mutated), encodes a 370-kDa protein kinase. We recently demonstrated that ATM protein regulates glucose uptake in response to insulin in muscle cells. Previous studies also show that *ATM* knockout mice have defective insulin secretion, possibly caused by decreased beta cell mass. Our goal is to study the mechanisms underlying defective glucose uptake and insulin secretion observed in A-T patients and A-T mice and to search for a cure for both type 2 and type 1 diabetes. In addition, a main characteristic of A-T disease is the progressive neuronal degeneration of cerebellar Purkinje and granular cells. Despite the extensive research that has been conducted, the cause of neuronal degeneration in A-T disease is still unclear. Therefore, another project that is currently ongoing in my lab is the study of the mechanism behind progressive cerebellar ataxia of A-T patients.