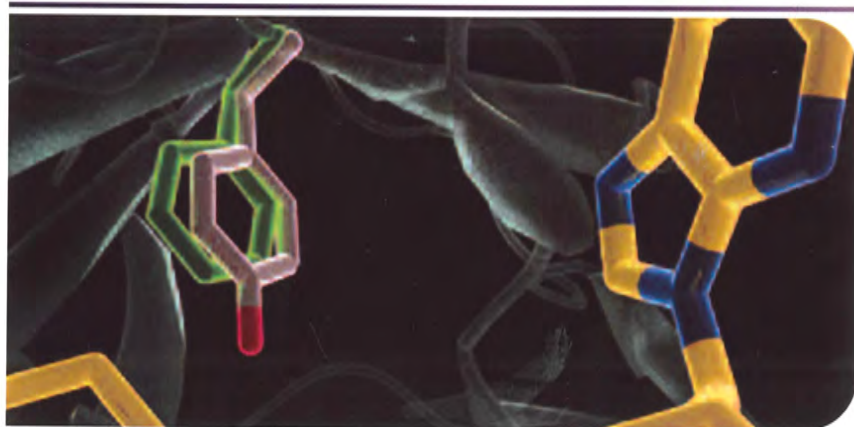
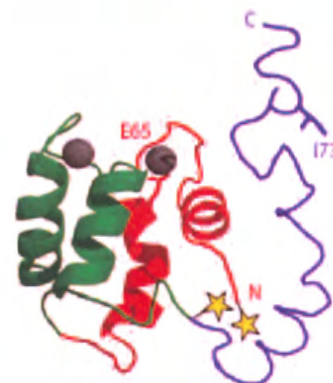
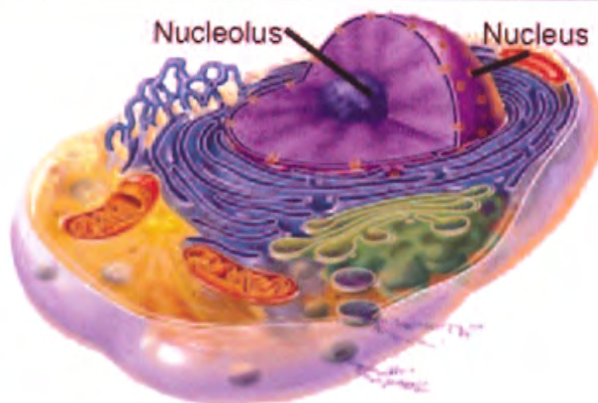
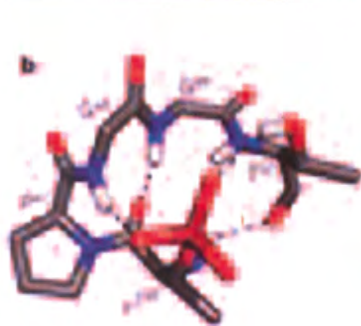




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College of Graduate Studies • **Biochemistry and Molecular Biology**



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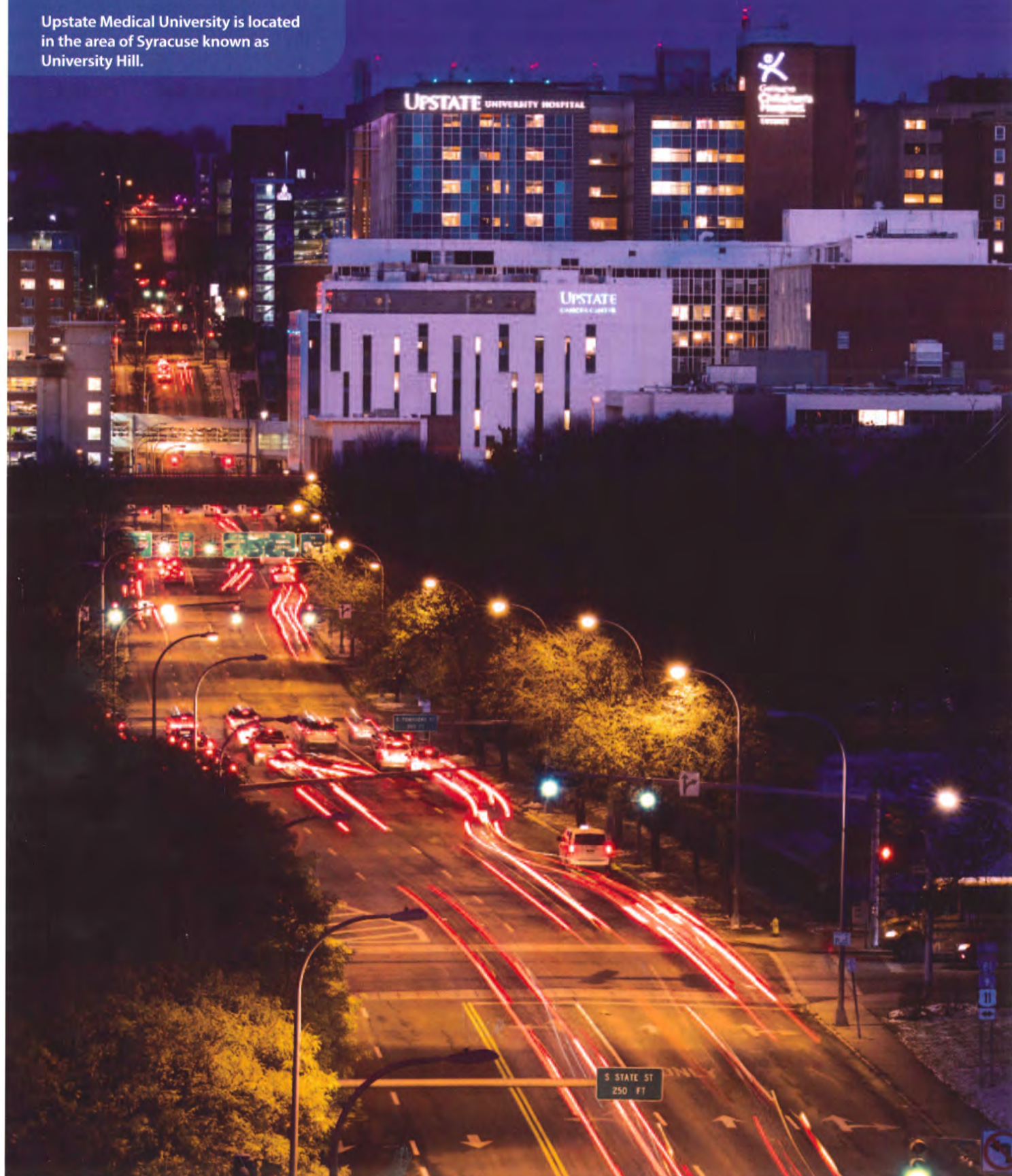
UPSTATE
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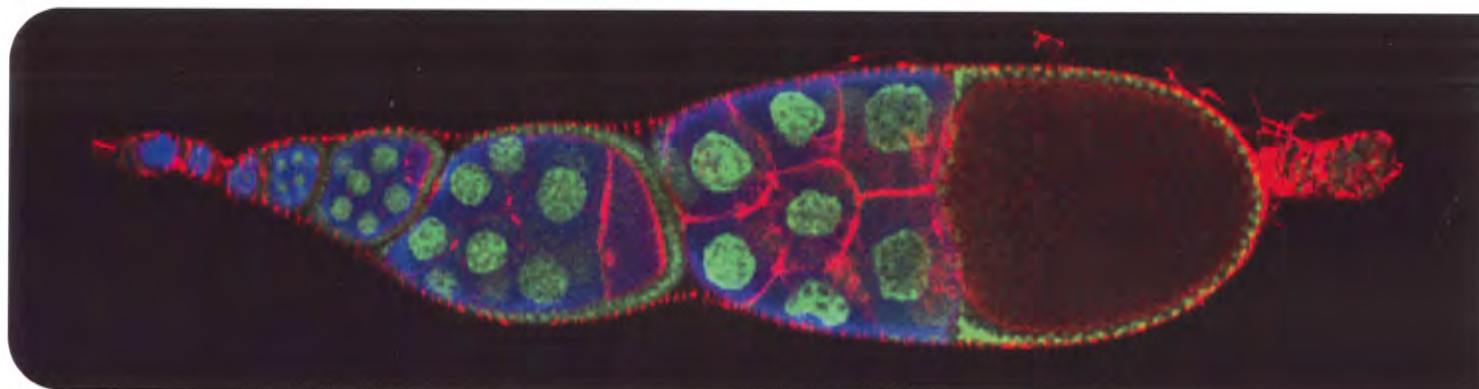
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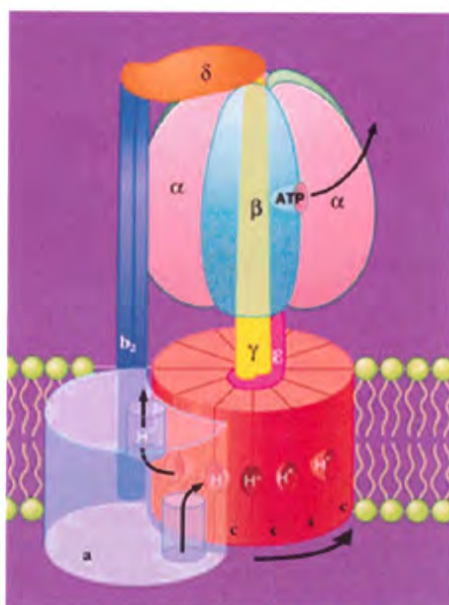
Upstate's biochemistry and Molecular Biology students reap the benefits of conducting research in a large academic medical center.

Upstate Medical University is located in the area of Syracuse known as University Hill.





CONTENTS



Overview	2	Vladimir Kuznetsov	19
Doctoral and Master's programs		Frank Middleton	20
Faculty	3	Mehdi Mollapour	20
Research areas and Facilities		Andras Perl	21
Faculty and Research Profiles	4	Francesca Pignoni	21
Patricia Kane	4	Andrea Viczian	22
David Amberg	5	Michael Zuber	22
Alaji Bah	6	Academic Programs	23
Xin Jie Chen	7	PhD Biochemistry	
Michael Cosgrove	8	& Molecular Biology	
Thomas Duncan	9	MS Biochemistry	
Wenyi Feng	10	& Molecular Biology	
Steven Hanes	11	Biomedical Sciences Program (PhD)	
Bruce Knutson	12	MD/PhD Program	
Stewart Loh	13	Admissions	24
Mark Schmitt	14	How to apply	
Stephan Wilkens	15	Summer Undergraduate	
Audrey Bernstein	16	Research Fellowships (SURF)	
Dimitra Bourboulia	16	Application Deadline	
Gennady Bratslavsky	17	Stipends and Tuition	
Peter Calvert	17	Student Life	inside back cover
Sam Herberg	18	Student Clubs and Organizations	
Barry Knox	18	Awards	
Leszek Kotula	19	College Town Atmosphere	



Alaji Bah, PhD, with a graduate student and research assistant in his lab in Weiskotten Hall.

BIOCHEMISTRY AND MOLECULAR BIOLOGY AT UPSTATE MEDICAL UNIVERSITY

The Department of Biochemistry and Molecular Biology is part of the College of Graduate Studies at SUNY Upstate Medical University in Syracuse, NY, one of only 127 academic medical centers in the United States.

RESEARCH AT A MAJOR MEDICAL CENTER

Academic medical centers — which are built around medical schools and teaching hospitals — lead the nation in conducting biomedical research, educating health professionals and providing the most advanced care to patients. Being part of an academic medical center gives our graduate students and research scientists access to the instrumentation, faculty and other resources associated with a major medical center.

INTERDISCIPLINARY COLLABORATION

Members of the Department of Biochemistry and Molecular Biology routinely collaborate with scientists from the College of Graduate Studies' other basic science departments — Cell and Developmental Biology, Microbiology and Immunology, Neuroscience and Physiology and Pharmacology — as well as with physician-scientists from the University's 18 clinical departments.

TO APPLY

Prospective PhD students are encouraged to apply to the Biomedical Sciences Program offered by the College of Graduate Studies.

Prospective Master's students apply directly to the Biochemistry and Molecular Biology Program.

MORE INFORMATION

Visit www.upstate.edu/grad for more information



Many labs are located in the Institute for Human Performance.



Weiskotten Hall is home to many laboratories and classrooms.

FACULTY

Upstate Medical University has a long history of providing an excellent education. Our outstanding faculty includes international experts in many areas including **neuroscience, cardiovascular physiology, cellular bioenergetics** and **human viruses**.

Research in biochemistry and molecular biology explores the molecular and biochemical mechanisms of cellular function and development.

Faculty expertise covers a wide range of topics including **developmental biology, cell biology, genomics and proteomics, structural biology** and **biophysics**.

Recent papers by faculty members and students have appeared in *Science*, *Nature Cell Biology*, *Journal of Biological Chemistry*, *Journal of Molecular Biology* and others.

This dynamic group offers its students an unusually high level of interaction with faculty, modern laboratory space and a regular seminar series featuring prominent national and international speakers. Because of our commitment to the mentoring process, devotion to basic science research, and belief that future scientists need a solid grounding in grant writing, oral presentations and evaluating papers, our graduates are among the best trained scientists in the world.

MORE INFORMATION

Visit www.upstate.edu/biochem/faculty for more information on faculty members.

RESEARCH AREAS

Bioenergetics
Cytoskeleton and Cell Polarity
Developmental Neurobiology
Enzyme Structure/Function

RESEARCH FACILITIES

Confocal, Light Electron, Fluorescence and Deconvolution Microscopes
Robotic Colony Arrayer
Infrared and Circular Dichroism

Patricia M. Kane

Professor and Chair

PhD, Cornell University, 1987
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RESEARCH INTERESTS

Vacuolar H⁺-ATPases (structure, function, assembly and regulation), cellular pH homeostasis, cellular stress responses, protein sorting, genomics, yeast as a model system

SELECTED REFERENCES

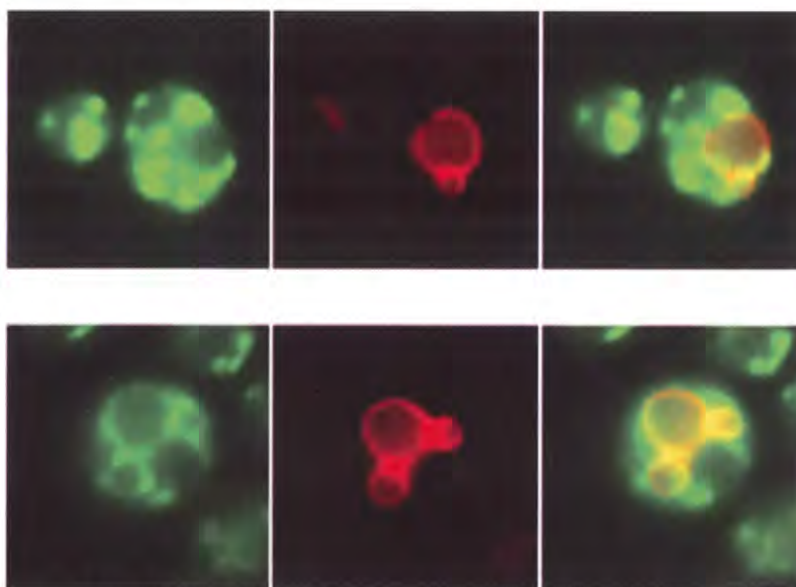
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Localization of the V-ATPase a-subunit isoform Stv1 depends on the Golgi lipid P14P.

V-ATPases and Cellular pH homeostasis

RESEARCH ABSTRACT

All eukaryotic cells tightly control cellular pH. Proper control of cytoplasmic pH is essential for normal metabolism and cell growth, and acidification of organelles such as the lysosome, endosome, and Golgi apparatus is essential for protein sorting and degradation, ion homeostasis, and signal transduction. The vacuolar ATPase (V-ATPase) is one of the central players in pH control. All eukaryotic cells have V-ATPases of remarkably similar structure, and loss of V-ATPase function is lethal at early stages of development in higher eukaryotes and conditionally lethal in fungi.

The yeast V-ATPase has proven to be an excellent model for studies of V-ATPase structure, function, and regulation. Work in my laboratory addresses three major questions using yeast as a model system: 1) definition of functional and structural relationships among the fourteen subunits of the V-ATPase 2) regulation of the V-ATPase in vivo, 3) physiological implications of organelle acidification. We approach these

questions using a combination of biochemical, genetic, molecular, and cell biological methods. Our studies of subunit structure and function combine traditional biochemistry and yeast genetics with insights from the growing number of complete eukaryotic genomes now available. Regulation of V-ATPases is proving to be rich and complex. Assembled V-ATPases can rapidly and reversibly dissociate in vivo in response to changes in growth conditions, and this appears to be a major regulatory mechanism. Current work is directed toward defining this signal transduction pathway and probing the possibility of crosstalk between V-ATPase regulation and other pathways and processes. Finally, V-ATPases are implicated in a number of unexpected roles, including resistance to oxidative stress. We seek to better understand these roles and their links to overall cellular pH control.



Kane

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PhD, 1992, Dartmouth Medical School
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RESEARCH INTERESTS

Regulation of actin dynamics and analysis of genomic influences on actin function.

SELECTED REFERENCES

Scarcelli JJ, Viggiano S, Hodge CA, Heath CV, Amberg DC, Cole CN. Synthetic genetic array analysis in *Saccharomyces cerevisiae* provides evidence for an interaction between RAT8/DBP5 and genes encoding P-body components. *Genetics*. 2008 Aug;179(4):1945-55. Epub 2008 Aug 9.

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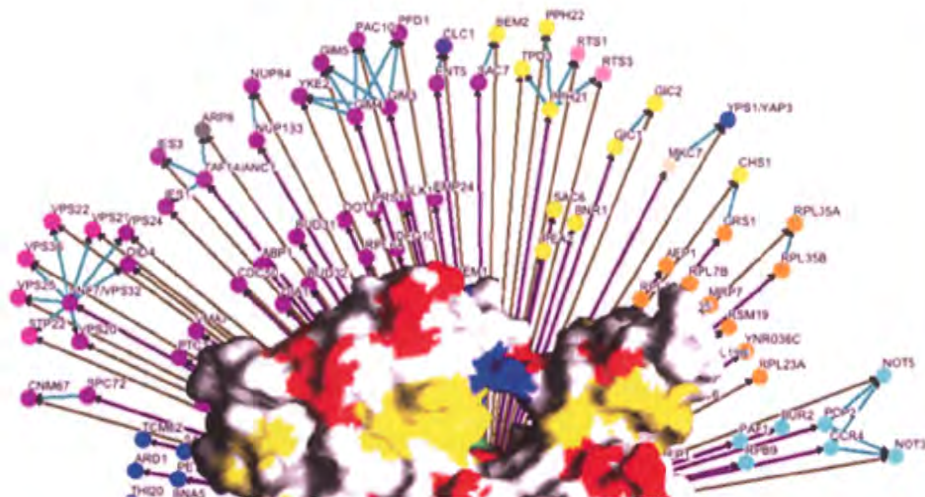
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The Actinome Project.

Actin Interaction

RESEARCH ABSTRACT

My laboratory is interested in how actin associated proteins regulate the assembly and organization of the actin cytoskeleton in eukaryotic cells. The actin protein polymerizes to form dynamic filaments that are central to the organization and remodeling of all eukaryotic cells. Our investigations into actin regulation employ a powerful model organism, the common bread/beer budding yeast called *Saccharomyces cerevisiae*. The proteins we study are conserved in structure and function thereby allowing us to use powerful tools to unravel their functions with biochemistry, cell biology, genetic, structural biology and molecular biology techniques. Our current studies are focused on understanding four actin regulators:

Aip1p catalyzes the fragmentation of existing actin filaments in cooperation with another actin regulator called cofilin.

1. Aip3p is a cell cycle controlled spatial regulator of actin polymerization as well as an important facilitator of nuclear segregation during cell division.

2. Oye2p (Old Yellow Enzyme) is an NADPH oxidoreductase that repairs oxidative damage to actin. This same damage is a major contributor to sickle cell crisis and therefore our investigation has direct relevance to the treatment of sickle cell disease.

3. Ssk2p is a MEK kinase that promotes actin cytoskeleton recovery following osmotic stress. Our goal is to understand the mechanisms by which these proteins regulate actin at an extremely sophisticated level.

Our goals are to: 1) Understand the detailed mechanisms by which these proteins regulate these processes, and 2) To use these projects to train young scientists in the application of modern technologies to important fundamental problems in biology.



Amberg

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Ph.D., Washington University, St. Louis, 2009
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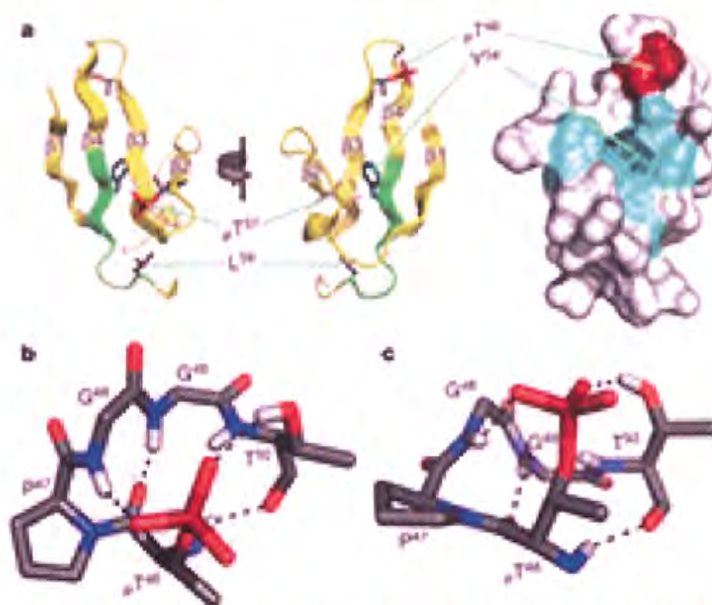
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RESEARCH INTERESTS

Elucidate the structure, dynamics and functions of intrinsically disordered proteins and protein regions (IDPs/IDRs) and their biological regulation by Post-translational modifications.

SELECTED REFERENCES

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Phosphorylation-induced structure of the major state of residues R18-R62 of 4E-BP2.

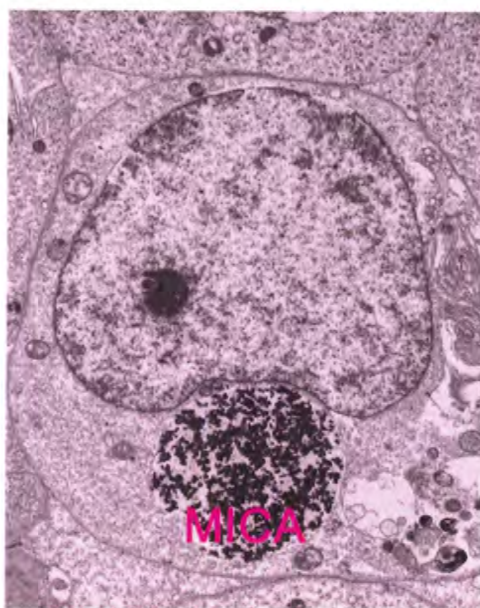
Investigating the role of IDP-Mediated Phase Separation in Epigenetic Regulation

RESEARCH ABSTRACT

Elucidate the structure, dynamics and functions of intrinsically disordered proteins and protein regions (IDPs/IDRs) and their biological regulation by Post-translational modifications. I am particularly interested in characterizing such regulation at atomic resolution using Nuclear Magnetic Resonance (NMR) spectroscopy and other biophysical tools such as microcalorimetry and fluorescence spectroscopic techniques. A recent and exciting emerging field in the IDP world is the realization that this class of proteins, either alone or in concert with Nucleic acids, can drive phase separation of biomolecules, resulting in the formation of membraneless organelles with extremely high protein concentrations. Such organelles form both within the cytoplasm (e.g. RNA granules) and the nucleus (e.g. nucleolus) as well as in the extracellular matrix (elastin coacervation). The goal of my lab is not only to understand the PTM-mediated conformational transitions (e.g. folded vs. disorder transitions) and/or monomer: phase-separation transitions in specific examples, but to also develop tools/protocols to enable characterization of such properties in other biological systems.



Bah



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RESEARCH INTERESTS

Mitochondrial biogenesis and inheritance, aging and aging-related degenerative diseases.

SELECTED REFERENCES

Liu Y, Wang X, Coyne LP, Yang Y, Qi Y, Middleton FA, Chen XJ. Mitochondrial carrier protein overloading and misfolding induce aggresomes and proteostatic adaptations in the cytosol. *Mol Biol Cell*. 2019 May 15;30(11):1272-1284.

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Chen

Mitochondrial Stress Signaling in Neuromuscular Disease

RESEARCH ABSTRACT

Mitochondria are the powerhouses that generate energy by oxidative phosphorylation (OXPHOS) to support cellular activities, and are the integrators of cellular signals that promote different forms of cell death. Mitochondria are also known as the "powerhouses of diseases and aging". Mitochondrial dysfunction is associated with a rapidly growing number of aging-related neuromuscular degenerative diseases and metabolic disorders. How the mitochondrial function deteriorates during aging and how this in turn induces cellular degeneration are not well understood. We use yeast, cultured human cell lines and mouse as model systems to address the following questions.

1. We are interested in understanding how mitochondrial dysfunction contributes to aging and aging-related neuromuscular diseases.
2. We are interested in identifying evolutionarily conserved pathways that can potentially delay and possibly, reverse mitochondria-induced cellular degeneration.
3. We investigate the mechanisms of mitochondrial DNA recombination, replication and repair.

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PhD, Syracuse University, 1998, Biochemistry
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RESEARCH INTERESTS

Epigenetic regulation of chromatin, Mixed
Lineage Leukemia, structural biology,
enzymology.

SELECTED REFERENCES

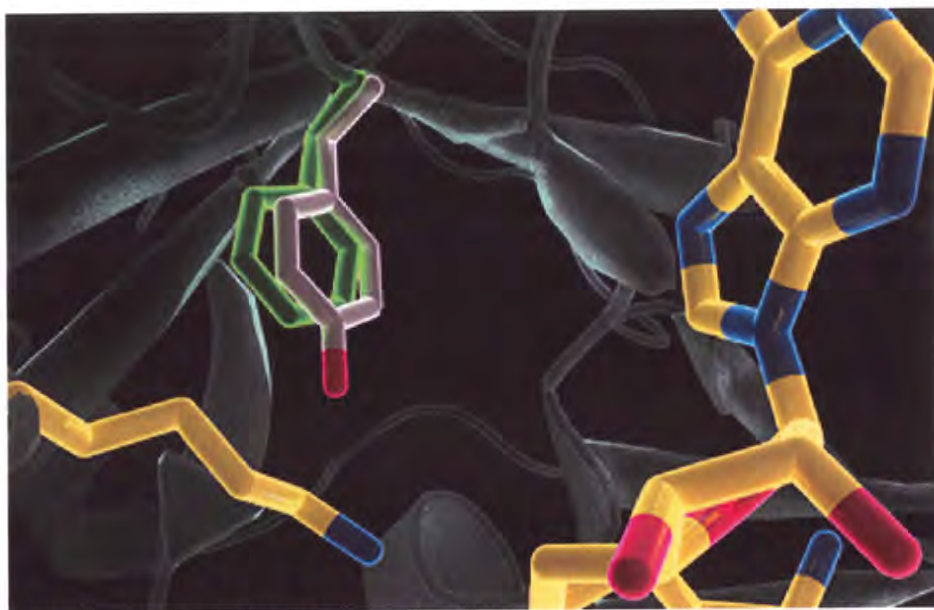
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thogonal Self-Assembly of Chimeric Peptides.
Small. 2016 Oct;12(37):5126-5131



The mixed Lineage Leukemia (MLL) histone methyltransferase is important for stem cell differentiation and is often mutated in cancer.

Structural Biology of Chromatin, Epigenetics

RESEARCH ABSTRACT

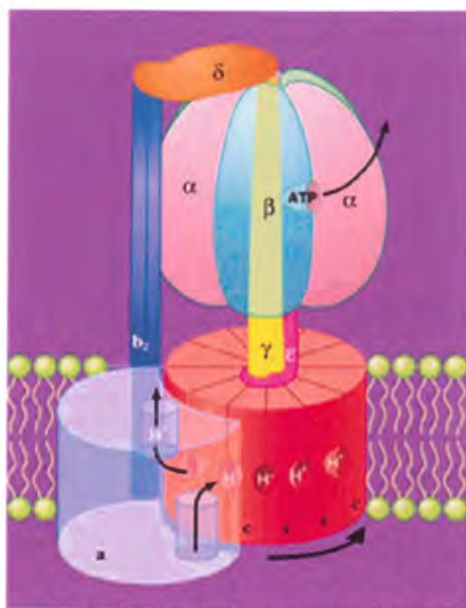
The fundamental repeating unit of chromatin, the nucleosome, is composed of a disc-shaped octamer of histone proteins around which is wrapped approximately 150-base pairs of genomic DNA. Nucleosomes regulate access to genes by forming a steric block to transcription factors and RNA polymerase. Less clear is how nucleosome positioning on DNA is regulated. Recent studies show that nucleosomes are strategically positioned throughout genomes, and that even subtle changes in nucleosome positioning can have profound effects on gene expression. These results raise the possibility that alterations in nucleosome positioning could result in heritable silencing of genes, and the generation of new forms and functions at the organismal level. Such alterations are independent of changes in DNA sequence (i.e., epigenetic alterations) and may be another source of variation acted upon by natural selection. An understanding of this process requires an understanding of how cells encode nucleosome positioning information, and how that information is inherited. The keys to this process are the evolutionarily conserved histone proteins,

the building blocks of nucleosomes; which, like DNA, are semi-conserved during DNA replication. Posttranslational modifications of histones provide a potential vehicle for the heritable transmission of epigenetic traits. Understanding how this process works is one of the central questions in biology today.

We are working to understand the molecular mechanisms that regulate methylation of histone H3 lysine 4 (H3K4), an epigenetic mark required for inheritance of transcriptionally active states of chromatin. In humans, H3K4 methylation is catalyzed by the Mixed Lineage Leukemia (MLL) group of enzymes, mutations of which are associated with leukemias, solid tumors and developmental abnormalities. We use the tools of structural biology, biochemistry and biophysics to understand the molecular mechanisms for how the family of MLL enzymes work. In addition, we are developing novel inhibitors that we hope will one day help alleviate human suffering.



Cosgrove



Idealized model for the rotary motor mechanism that couples transmembrane proton (H⁺) transport to the synthesis of ATP in F-type ATP synthases.

Bacterial ATP Synthase: Studies of the E. coli Model and of the Enzyme's Importance for Diverse Pathogenic Bacteria

RESEARCH ABSTRACT

My research focuses on the F-type ATP synthase of bacteria – a critical energy-coupling, rotary motor enzyme that is broadly conserved in the mitochondrial 'powerhouse' organelle of humans and other eukaryotes. In many bacteria, it uses energy from a proton-motive force (pmf), generated by respiration, to drive efficient synthesis ATP from ADP and phosphate (Pi). But, in many anaerobic bacteria, it primarily hydrolyzes ATP to drive proton pumping and is critical for pH homeostasis and/or maintaining the cellular membrane potential. The ATP synthase has two coupled sub-complexes: FO spans the membrane and transports protons; F1 is a peripheral complex that contains the three catalytic sites for ATP synthesis (one visible in cartoon). FO and F1 are coupled through two stalk-like connections of subunits, a central rotor shaft and a peripheral stator. In 2011, with a crystallographer colleague, we determined the first well-resolved structure of a bacterial F1 complex from *Escherichia coli*, achieving the first structural view of how the epsilon subunit (ε) can act as an autoinhibitor of the enzyme.

CURRENT EXPERIMENTAL SYSTEMS AND FOCUS

My lab continues to use *E. coli* as a simple yet powerful model system: it allows direct genetic screening and engineering of the ATP synthase, and also allows large-scale purification of FOF1 and isolated F1 for biochemical studies. The autoinhibitory feature of the ε subunit does not occur in FOF1 of mitochondria, so it may offer great potential as a means to selectively target bacterial FOF1 in developing new anti-bacterial agents, but studies are lacking on the impact of regulating FOF1 function in pathogenic bacteria. We are now pursuing such studies with 2 diverse pathogens for which FOF1 is essential: (i) *Pseudomonas aeruginosa*, which is primarily aerobic (FOF1 used as an ATP synthase), and (ii) *Streptococcus pneumoniae*, an obligate anaerobe (FOF1 used as an ATPase-driven proton pump), for which there is initial evidence that the inhibitory domain of ε is important for virulence in a mouse model of septicemic infections.



Duncan

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PhD, University of Rochester School of Medicine and Dentistry, 1986
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RESEARCH INTERESTS

Bioenergetics, enzymology, structural biology, membrane protein function.

SELECTED REFERENCES

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Wenyi Feng

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Postdoctoral Fellow, University of Washington,
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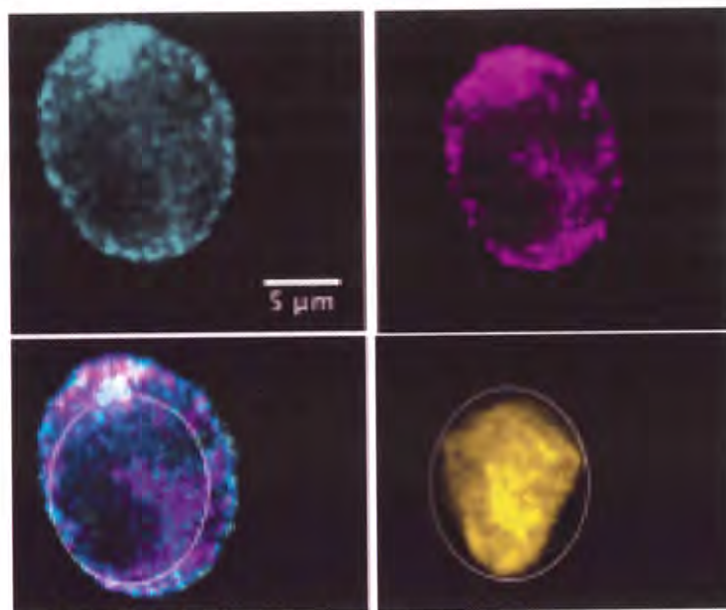
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RESEARCH INTERESTS

Chromosomal DNA replication origins (location, timing and regulation), replication fork integrity and checkpoint regulation, genomic instability and chromosome fragility in both the yeast and human genome.

SELECT REFERENCES

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Mechanisms of replication stress-induced chromosome breakage.

Mechanisms of replication stress-induced chromosome breakage

RESEARCH ABSTRACT

Eukaryotic chromosomal DNA replication is a process that is at once robust and vulnerable. It is accurate and able to withstand environmental stress, such as DNA damage and replication impediments, through a highly evolved checkpoint mechanism. Yet the very act of replication, if executed in an untimely or uncoordinated fashion, can give rise to genomic instability.

My laboratory (<http://fenglab-genomestabilityresearch.org>) is interested in understanding the mechanisms of genomic instability induced by DNA replication stress. Previous work including ours had established that replication stress induces extensive single-stranded DNA formation at replication forks, which ultimately results in double stranded DNA breaks (DSBs). We further demonstrated that DSBs occur more frequently at the genes that are induced by the drug used to cause replication stress—for instance—hydroxyurea, an inhibitor of the ribonucleotide reductase. This suggests that replication-transcription collision underlies DSB formation. We are currently testing the hypothesis by using a variety of replication inhibitors to induce, and systematically map, DSBs using a cutting-edge technique called Break-seq, with simultaneous gene expression mapping by RNA-seq. To this date we have generated a compendium of chromosome breakage profiles

of *Saccharomyces cerevisiae* and we are currently investigating the mechanisms that underly the formation of breakage hotspots.

We have also adapted Break-seq to map spontaneous and replication stress-induced DSBs in the human genome, known as chromosome fragile sites (CFSs), which play an important role in genomic rearrangements. We have systematically identified DSBs in cells derived from patients with the Fragile X Syndrome (FXS), the most common inherited mental retardation. We have observed that in the FXS model, replication stress-induced CFSs are preferentially localized to the R-loop forming sequences (RLFSs), which are cis-elements with high probability of forming DNA:RNA hybrids during transcription. This led to the discovery that the protein that is deficient in the FXS, FMRP, has a novel function in genome maintenance by preventing R-loop formation during replication-transcription conflict, thus shedding light on the underlying etiological basis for FXS. Our current endeavors take us beyond this disease model to examine different cancer genomes to discover new “at-risk” genes, such as novel tumor suppressors.



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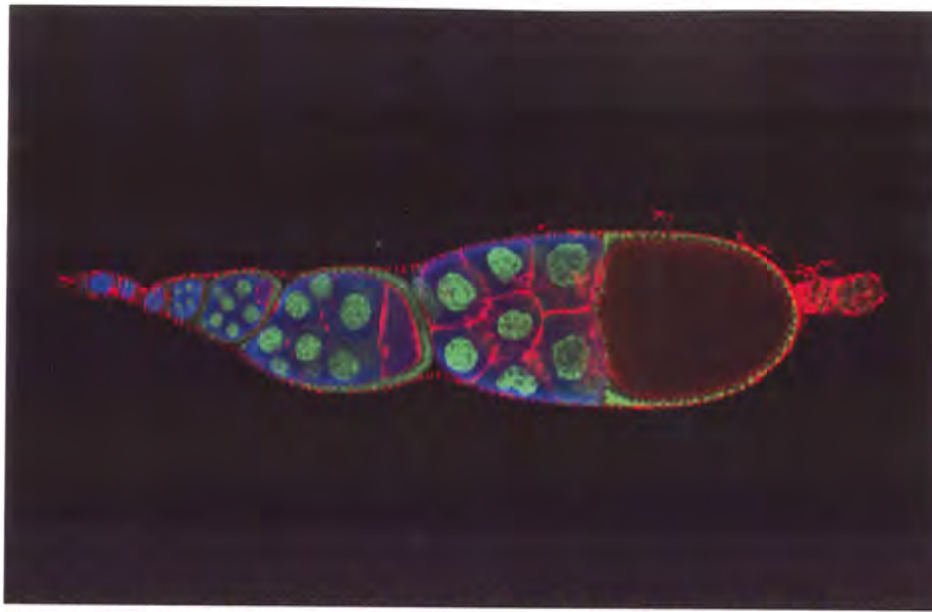
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RESEARCH INTERESTS

Gene expression in development and disease, RNA pol II regulation, homeobox genes, prolyl isomerases

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Fluorescence image of the reproductive tract (ovariole) of the fruit fly, *Drosophila melanogaster*.

Model Genes in Model Organisms**RESEARCH ABSTRACT**

Gene Regulation in Development and Disease: My laboratory is interested in how cells control the activity of genes during early development of the embryo and during the cell cycle. One key point of regulation is the synthesis of an RNA copy of individual genes. This process is carried out by RNA polymerase II (RNA pol II). We study RNA pol II in two distinct contexts (see below). Each project uses a different model organism to its best advantage, where we can apply sophisticated genetic, molecular, and biochemical tools to discover important mechanisms of gene regulation. Our findings are relevant to understanding similar mechanisms that occur in human cells, and whose disruption is often associated with disease.

Homeobox genes: In the first project we study homeobox transcription regulators in *Drosophila melanogaster* (fruit fly). For example, we study a homeobox gene called *bicoid*, which encodes a protein (Bicoid) that directs development of the head and thorax in early embryos. Bicoid works by recruiting RNA pol II to selected target genes, and how exactly it does this is the subject of our work. Our results have been important for understanding how homeobox genes function in normal cells and how their disruption causes certain human

cancers (e.g. childhood leukemias). We also discovered proteins that interact with Bicoid (Sap18 and Bin3). These proteins have human counterparts and we are trying to understand how they function.

Prolyl isomerases: In a second project, we study a gene called ESS1 in *Saccharomyces cerevisiae* (yeast), which encodes an enzyme known as a prolyl-isomerase. ESS1 is essential for growth in yeast and cells that lack ESS1 arrest in mitosis. A counterpart of ESS1 is found in humans and is called PIN1. We are learning how yeast ESS1 and human PIN1 control cell growth. We discovered that Ess1 works by controlling the conformation of RNA pol II. This understanding might lead to the development of antifungal drugs (or anti-cancer drugs for PIN1). Toward this goal, we isolated ESS1 homologs from *Candida albicans* and *Cryptococcus neoformans*, the two major human fungal pathogens. Ess1 in these organisms is important for virulence, so we are working toward an eventual goal of targeting Ess1 for inhibition as a potential antifungal treatment.



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RESEARCH INTERESTS

RNA polymerase I transcription (structure, assembly, regulation), nucleolar biology, macromolecular architecture, crosslinking, proteomics, bioinformatics, modeling, molecular genetics, biochemistry, model systems

SELECT REFERENCES

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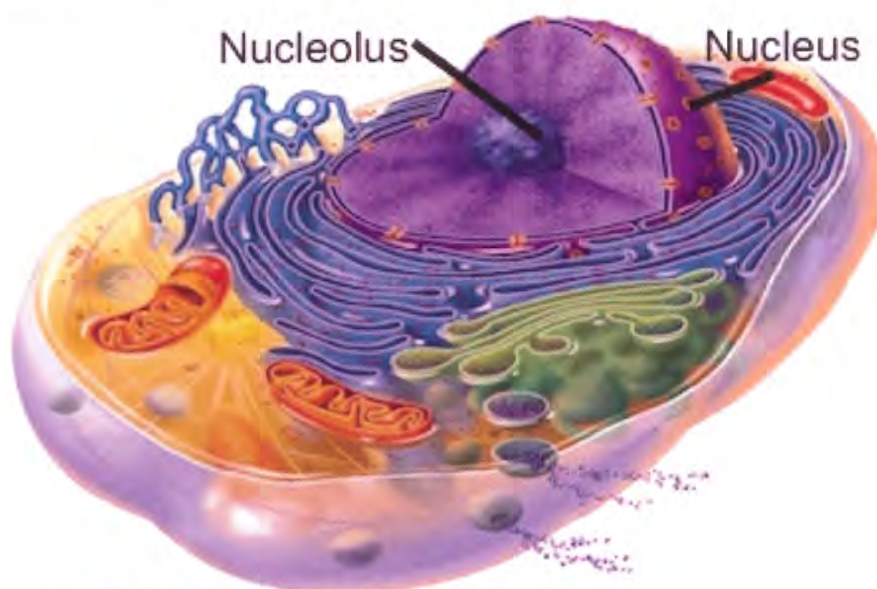
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An enlarged nucleolus is a hallmark of cancer.

Molecular basis of RNA polymerase I transcription and its dysregulation in disease

RESEARCH ABSTRACT

A century old hallmark of cancer is an enlarged nucleolus (Fig.1), a unique nuclear sub compartment where RNA polymerase I (Pol I) transcription and ribosome biogenesis take place. Pol I transcription is unregulated in cancer cells and drives cell proliferation, making it an attractive anti-cancer therapeutic target. The major focus of our research is to elucidate the molecular mechanism of Pol I transcription and how its dysregulation leads to cancer and disease. Our research uses an innovative cross-organismal and interdisciplinary approach that integrates bioinformatics, biochemistry, computational biology, genetics, proteomics and structural biology in yeast and human model system.

Molecular architecture of the Pol I preinitiation complex (PIC). Pol I transcription begins with the formation of the PIC, a macromolecular assemblage of more than 20 different proteins that function coordinately to accurately position Pol I at the promoter and to help initiate transcription. We are interested in the key structural facets of Pol I PIC formation and how its altered in cancer and diseased cells. Our lab uses an integrated combination of sophisticated protein-protein interaction mapping technologies such as combined chemical crosslinking/mass spectrometry to

determine the spatial orientation of Pol I PIC components.

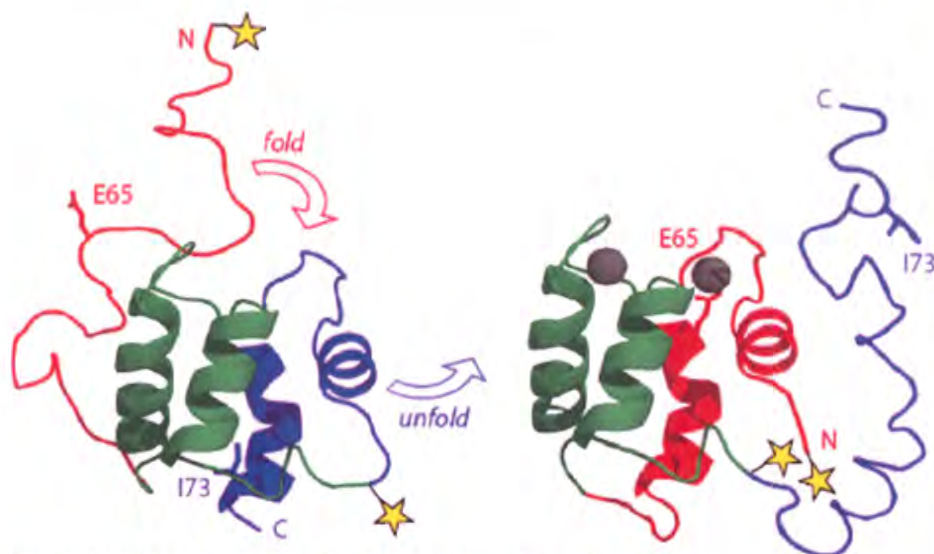
Pol I and craniofacial dysmorphology.

Mutations in Pol I cause an autosomal dominant craniofacial abnormality called Treacher Collins Syndrome (TCS). TCS is characterized by an underdeveloped lower jaw and cheekbones that is treated by an extensive multi-stage surgical reconstruction from childhood to early adulthood. We are interested in how these Pol I mutations cause TCS, how they affect Pol I activity, and how they can be suppressed to prevent the disease.

Pol I dysregulation in cancer. The upregulation of Pol I transcription in cancer cells coincides with activating mutations in many oncogenes and loss of function mutations in tumor suppressors that are believed to directly regulate Pol I activity. However, their bona fide Pol I targets and sites of interaction remain unclear. We are focused on understanding how these cancer proteins target the Pol I complex, which may illuminate new strategies to control aberrant Pol I activity.



Knutson



Design of calcium-sensing molecular switch based on calbindin.

Protein engineering, folding and design

RESEARCH ABSTRACT

Our philosophy is to test central hypotheses regarding the kinetic mechanism and thermodynamics of protein folding, while at the same time improving properties of existing proteins and creating novel proteins with completely new functions.

To achieve this goal we employ a variety of structural, biophysical, biochemical, and molecular biological approaches including:

- Nuclear magnetic resonance and X-ray crystallography
- Optical spectroscopy (fluorescence, circular dichroism)
- Thermodynamic and kinetic analysis of protein folding
- Hydrogen and thiol-disulfide exchange mechanisms
- Protein functional assays

Protein-based molecular switches. We have developed two approaches (alternate frame folding (AFF) and mutually exclusive folding (MEF)) for engineering an allosteric conformational change into a protein where none may have existed previously. AFF and MEF transduce a triggering signal into an output event. In this way, an ordinary binding protein can be converted to a molecular switch. This technology is being used to create (for

example) fluorescent biosensors and artificial zymogens that selectively attack viruses and diseased cells.

Kinetic mechanism of protein folding. Why do some proteins fold in milliseconds while others require hours? Are partially structured intermediates necessary or do they represent opportunistic traps? We are addressing these questions by applying a variety of spectroscopic techniques to characterize the structure and stability of folding intermediates, and the kinetics of their formation.

p53 and cancer. The p53 tumor suppressor is the most heavily mutated protein in human cancer. Our work has shown that the folding mechanism of p53 is unusually complex. It involves multiple pathways with both productive and dead-end intermediates. We are particularly interested in how folding and misfolding mechanisms are affected by loss of the bound zinc ion and by the natural dimerization and tetramerization of p53. Our goal is to understand how tumorigenic mutations affect p53 folding and cause it to fail, and how small molecules can be designed to offset the effects of mutation.



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RESEARCH INTERESTS

Protein engineering, design and folding

SELECTED REFERENCES

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RESEARCH INTERESTS

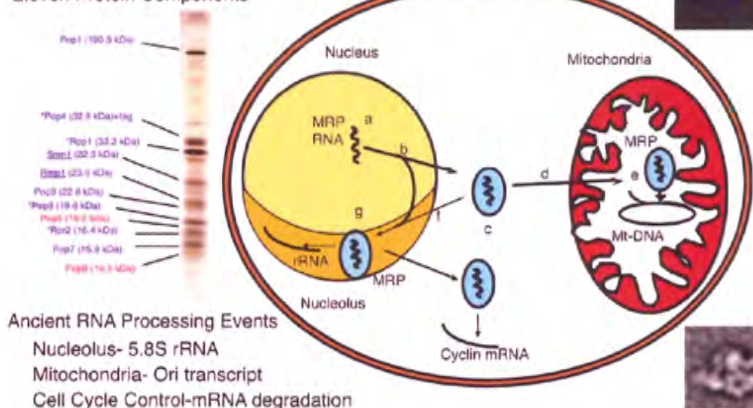
Ribonucleoprotein assembly and biogenesis; mitochondrial RNA import, mRNA degradation, cell cycle control

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Ribonucleoprotein
Endoribonuclease
RNA Component 340nt yeast (NME1)
265nt humans (RMRP)
Related to RNase P RNA
Eleven Protein Components



Structure, Function and Biogenesis of a Ribonucleoprotein Complex

RESEARCH ABSTRACT

The main goal of our research is to determine the function, regulation and structure of the ribonucleoprotein endoribonuclease, RNase MRP. RNase MRP was one of the first small non-coding RNAs implicated in a human disease. RNase MRP is conserved throughout eukaryotes and mutations in the human RNA component have implicated this enzyme as an essential growth regulator. Human mutations cause Cartilage Hair Hypoplasia (CHH) a recessively inherited disorder characterized by short stature, brittle hair, anemia, immunodeficiency, and a predisposition to the development of lymphomas and other cancers. Data from our lab in collaboration with others has shown that human RNase MRP is also playing a role in destabilizing certain mRNAs.

Previous work had found that RNase MRP is directly involved in the late stages of the cell division cycle by regulating the activity of the cyclin dependent kinase. Cells that are defective in RNase MRP have a delayed telophase. We have made extensive progress in identifying the exact molecular mechanism of this regulation. We have found that at a particular time in the cell division cycle the RNase MRP enzyme is released from the nucleus, a compartment in the cell where it is kept sequestered. The release of this endoribonuclease allows it to

break down specific mRNAs for B-type cyclins that are required for the activity of the cyclin-dependent kinase, this promotes inactivation of the cyclin-dependent kinase and the termination of the cell cycle.

These studies have also led us to discovering a new organelle, the TAM (Temporal Asymmetric MRP) body. We have found that this structure is P (processing) body "like." But in contrast to P bodies that are found throughout cells and the cell cycle, TAM bodies are temporally and spatially assembled organelles whose function is to degrade specific mRNAs at a discrete time and location in the cell cycle. RNase MRP localizes to this organelle during mitosis and it is in this location that the B-cyclin mRNAs are degraded.

More recent work has focused on the role of RNase MRP is processing rRNA and modulating the production of two different types of ribosomes, which we term the long and short forms. These two forms associate with different ribosomal protein paralogs leading to altered function and localization in a cell.



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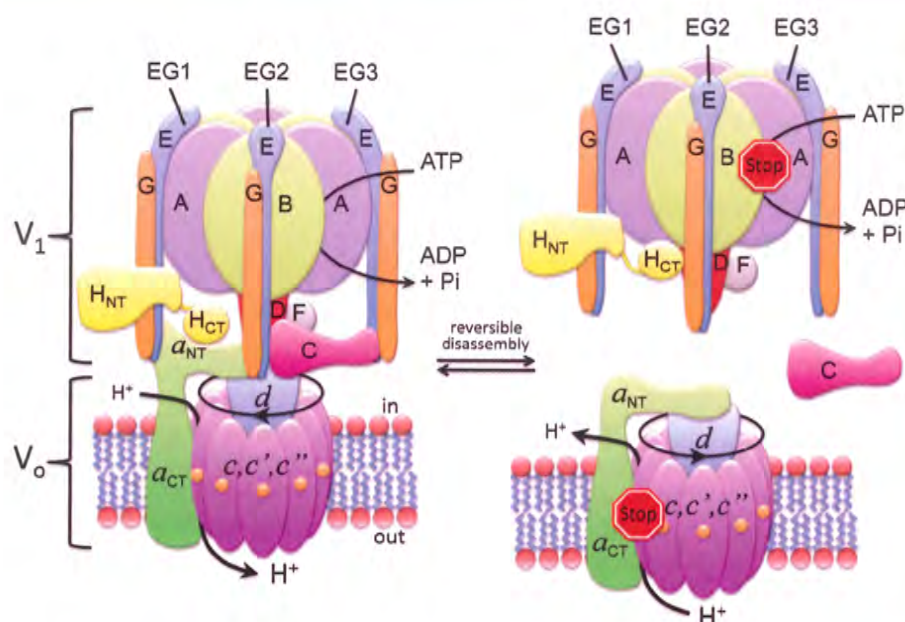
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RESEARCH INTERESTS

Structure and Mechanism of Membrane
Bound Transport Proteins

SELECTED REFERENCES

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Structure and Regulatory Mechanisms of the Eukaryotic Vacuolar H⁺-ATPase

RESEARCH ABSTRACT

Our main focus is on the structure and mechanism of the eukaryotic proton pumping vacuolar ATPase (V-ATPase; V1Vo-ATPase). V-ATPase is a large, multisubunit membrane protein complex found on the endomembrane system of all eukaryotic cells, where it functions to acidify intracellular organelles, including endosomes, lysosomes, the Golgi apparatus and synaptic vesicles. An acidic pH in the lumen of these compartments is essential for basic cellular functions including endocytosis, protein degradation, protein trafficking, and neurotransmitter loading. When found on the plasma membrane of "professional" acid secreting cells such as bone osteoclasts and renal intercalated cells, V-ATPase pumps protons to the outside of the cell, a process required for bone remodeling and urine acidification. Due to its involvement in numerous basic cellular functions, a malfunctioning V-ATPase can lead to widespread human diseases including osteoporosis, neurodegeneration, diabetes, cancer and AIDS.

V-ATPase is composed of two rotary motor subcomplexes, a membrane extrinsic ATP hydrolyzing V1-ATPase and a membrane embedded Vo proton turbine. ATP hydrolysis on V1 is coupled to proton transport across Vo by a "central stalk" that rotates up to 100 1/s to pick up protons from the

cytosol and deliver them to the organelle lumen or outside of the cell. As a major consumer of cellular energy, V-ATPase function is tightly regulated by a mechanism referred to as "reversible disassembly". When the enzyme's proton pumping is not needed, V1 dissociates from the membrane bound Vo, and the activity of both subcomplexes is "silenced" so that V1 is no longer capable of hydrolyzing MgATP, and Vo becomes impermeable to protons. Reversible disassembly is unique to eukaryotic V-ATPase and the process offers a way to modulate the activity of a disease causing V-ATPase for therapeutic purposes.

We work with the V-ATPases from the model organism *Saccharomyces cerevisiae* (baker's yeast) as well as human. We are using the tools of biochemistry, molecular and cell biology, biophysics and structural biology (including NMR spectroscopy, X-ray crystallography and cryo electron microscopy (cryoEM)) to obtain structural and mechanistic information. Our long term goal is to elucidate the mechanism of V-ATPase's unique mode of regulation and find ways for therapeutic targeting of the enzyme in the disease state.



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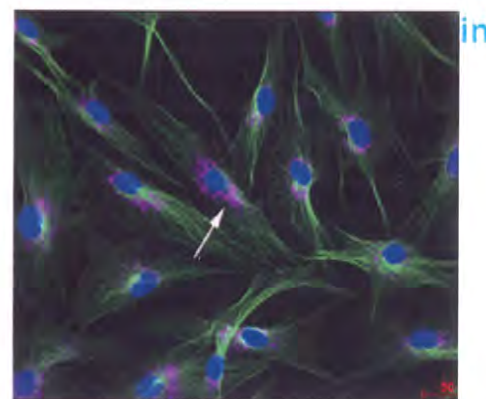
RESEARCH INTERESTS

Fibrosis; Scarring; Protein degradation;
ubiquitin; integrins; cytoskeleton; patient-
derived model systems

Regenerative Healing the Eye

RESEARCH ABSTRACT

Corneal scarring is one of the leading causes of blindness worldwide. The World Health Organization estimates that 23 million people suffer from unilateral vision loss due to corneal disease. Causes of blindness from corneal disease include infection, inflammation, ulcers and trauma. The cornea refracts light as it enters the eye so that a properly focused image reaches the retina. The normal cornea is transparent, making it an important model system in which to study fibrotic scarring. Corneal scarring results from the persistence of myofibroblasts, cells that excessively contract tissue and secrete disorganized extracellular matrix. RNA sequencing of myofibroblasts revealed significant changes in the expression of genes coding for ubiquitin pathway components including increased expression of a subset of deubiquitinating enzymes (DUBs). Our



studies are investigating the impact of DUBs in regulating scarring in the eye and testing the efficacy of targeting DUBs with self-delivery siRNAs to promote regenerative healing and prevent scarring in vivo.

SELECTED RESOURCE

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RESEARCH INTERESTS

Extracellular kinase signaling; extracellular
chaperone function; targeting extracellular
signaling networks in urological cancers

RESEARCH ABSTRACT

Tumor cell growth and migration begin with the secretion of proteolytic enzymes that degrade the extracellular matrix (ECM) followed by an invasion of the tumor vasculature leading to initiation of metastasis. Matrix Metalloproteases (MMPs) and their endogenous inhibitors (TIMPs) are key components of extracellular proteolysis and regulators of the tumor microenvironment (TME). Identification of ways to inhibit early matrix proteolysis would enhance our ability to target early tumor development and prevent metastatic

potential. Studies have suggested that MMP/TIMP balance is shifted towards MMP activation during cancer progression.

Our laboratory investigates molecular mechanisms of MMPs and TIMPs regulation in the extracellular space that impact homeostasis and cancer progression. Current areas of research includes: (1) How c-Src mediated tyrosine phosphorylation of TIMP-2 affects extracellular proteolysis, (2) The role of TIMP-2 as a regulator of extracellular protein homeostasis, (3) Targeting extracellular kinase signaling for the development of novel cancer therapies.

SELECTED RESOURCES

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Scott KA, Li G, Manwaring J, Nikolavsky DA, Fudym Y, Caza T, Badar Z, Taylor N, Bratslavsky G, Kotula L, Nikolavsky D. Liquid buccal mucosa graft endoscopic urethroplasty: a validation animal study. *World J Urol*. 2019 Jun 7

Necchi A, Bratslavsky G, Shapiro O, Elvin JA, Vergilio JA, Killian JK, Ngo N, Ramkissoon S, Severson E, Hemmerich AC, Ali SM, Chung JH, Reddy P, Miller VA, Schrock AB, Gay LM, Ross JS, Jacob JM. Genomic Features of Metastatic Testicular Sex Cord Stromal Tumors. *Eur Urol Focus*. 2019 May 27

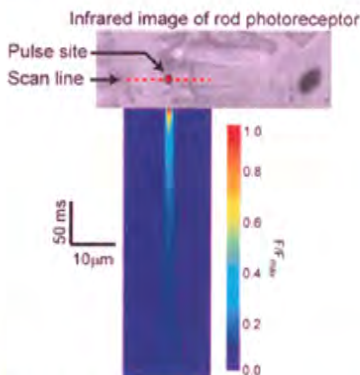
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Necchi A, Bratslavsky G, Chung J, Millis S, Gay LM, Ali SM, Ross JS. Genomic Features for Therapeutic Insights of Chemotherapy-Resistant, Primary Mediastinal Nonseminomatous Germ Cell Tumors and Comparison with Gonadal Counterpart. *Oncologist*. 2019 Apr;24(4):e142-e145.

RESEARCH ABSTRACT

Research in my laboratory is aimed at understanding the mechanisms of signal-dependent protein localization and transport in neurons. Dynamic protein localization within cells is often determined by environmental stimuli. In rod photoreceptors of the retina transitions between darkness and light result in the massive translocation of several key signal transduction proteins between two major compartments. The second and third most abundant proteins in rods, arrestin and transducin, respectively, move in opposite directions. A third phototransduction protein — the calcium binding protein, recoverin — also shifts its position toward the synaptic end of rods when they are exposed to steady light. All of these proteins are transported through a thin connecting cilium, within tens of minutes of light onset. The functions of, and mechanisms underlying these massive protein



Difusion of PAGFP in the inner segment of a dark-adapted rod.

redistributions that occur day in and day out are not known despite decades of study.

We employ multiphoton and confocal microscopy and the expression of fluorescently labeled proteins in transgenic animals to monitor protein dynamics in living cells in real time, particularly after changes in the cell's signaling state. We monitor intracellular signaling using fluorescent indicators such that the changes in protein dynamics may be correlated with the signaling state of the cell.

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MD, Albany Medical College, NY, 2000
Residency, Albany Medical
Center Hospital, 2005, Urologic Surgery
Fellowship, National Cancer Institute, NIH,
Bethesda, MD, 2007, Urologic Oncology

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RESEARCH INTERESTS

Basic, clinical, and translational prostate, bladder and kidney research.

Peter D. Calvert

Associate Professor

*Biochemistry and
Molecular Biology
Associate Professor of
Ophthalmology
Associate Professor of Cell and
Developmental Biology
Associate Professor of
Neuroscience Graduate Program
Associate Professor of
Neuroscience and Physiology*



Calvert

PhD, University of Wisconsin
at Madison, 1996
Postdoctoral Fellow, Harvard Medical School,
2003
Postdoctoral Fellow,
University of Pennsylvania, 2006

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505 Irving Ave.
Syracuse, NY 13210
calvertp@upstate.edu

RESEARCH INTERESTS

Molecular mechanisms of protein transport and localization in retinal neurons; mechanisms of retinal degenerative diseases

Sam Herberg

Assistant Professor

Assistant Professor of

Ophthalmology

Assistant Professor of

Cell and Developmental

Biology



Herberg

PhD, Augusta University,

Georgia, 2013,

Cellular Biology

Postdoctoral Fellow,

Wake Forest University

Baptist Medical Center, 2018

Postdoctoral Fellow, Case Western

Reserve University, 2017

Postdoctoral Fellow, Augusta University,

Georgia, 2014

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herbergs@upstate.edu

RESEARCH ABSTRACT

In addition to my primary research projects in ocular biology, I am interested in SLC13A5 - a transporter that mediates Na⁺-coupled entry of citrate into cells. Loss-of-function mutations in SLC13A5 in humans cause severe neonatal epilepsy and defective skeletal and tooth development. Citrate is critical for multiple metabolic pathways. As ~70% of citrate in the body is in bone and teeth, it is likely that the Ca²⁺-chelating property of citrate is obligatory for its role in these tissues. However, the source of citrate in mineralized tissues and the precise role of SLC13A5 in bone physiology are not well understood. Our primary goal is to determine what SLC13A5 does in bone and why loss of function in SLC13A5

impacts skeletal development in humans. Surprisingly, Slc13a5^{-/-} mice do not have epilepsy, but they do show decreased bone mineral density that gets corrected with age. The relatively mild phenotype in Slc13a5^{-/-} mice raises an important question: Is mouse an appropriate model to delineate the mechanisms underlying the brain or skeletal pathology arising from loss of function in SLC13A5 in humans? Major functional differences exist between mouse Slc13a5 and human SLC13A5. To that end, we have generated a humanized mouse that expresses human SLC13A5 in place of mouse Slc13a5. This unique mouse model allows us to investigate the biological role of the citrate transporter SLC13A5 in bone in a manner that is relevant to humans.

Barry E. Knox

Professor

Professor of Ophthalmology



Knox

PhD, Johns Hopkins University

School of Medicine, 1984

Postdoctoral Fellow,

Massachusetts Institute

of Technology

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Performance

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RESEARCH INTERESTS

Visual transduction, Gene Expression, Membrane proteins

SELECTED PUBLICATION

Baker SA, Haeri M, Yoo P, Gospe SM 3rd, Skiba NP, Knox BE, Arshavsky VY. The outer segment serves as a default destination for the trafficking of membrane proteins in photoreceptors. *J Cell Biol.* 2008 Nov 3;183(3):485-98.

RESEARCH ABSTRACT

Our laboratory is studying light transduction and development in the retina using molecular biological, biochemical and physiological approaches. Light transduction is carried out in specialized cells (rods and cones) that express a group of proteins designed to efficiently capture photons and transmit the information as a change in the conductance of the plasma membrane. The visual pigments (opsins) are a large family of proteins that absorb light and initiate the intracellular signal transduction pathway through a G-protein cascade. Opsins differ from each other in their wavelength of maximum absorbance (permitting color detection), their conformational changes after light activation and

in retinal expression patterns. These issues are crucial for shaping a photoreceptor's characteristic response properties. We have a long standing research effort to understand how photo-receptors develop and the molecular basis of rod/cone opsin functional differences.

The control of retinal gene transcription involves numerous cis-acting DNA elements in the proximal promoter, as well as more distant sequences. A complete understanding of the mechanism of transcriptional control that leads to cell-specific expression will require detailed experiments *in vivo*. We have developed transient transfections assays of embryos and transgenic *Xenopus* approaches that are ideally suited to answer these questions.

RESEARCH ABSTRACT

The goal of our research is to understand the molecular and cellular processes underlying human cancer. Cancer models are an important tool that we use to investigate the molecular changes, which occur as a normal cell transforms and progresses into a pre-malignant lesion, then a tumor, and finally metastatic disease. My lab developed a novel preclinical model of prostate cancer in mice by introducing a conditional knockout mutation of Abi1. The function of Abi1 is not fully understood. It appears to have a key role in growth factor receptor signaling and actin cytoskeleton remodeling. Importantly, our mouse model demonstrates that Abi1 is a tumor suppressor

gene. We will use the Abi1 knockout mice to identify the molecular changes associated with the development of prostate cancer. This model will also enable us to dissect the mechanisms underlying Abi1's role in prostate cancer. These studies include the role of actin cytoskeleton dysregulation in tumor initiation and progression (i.e. the role of Abi1 in regulation of cellular adhesion and cell motility), regulation of c-Abl and PI-3 kinases by Abi1, and regulation of macropinocytosis (a type of endocytosis) by Abi1. In addition, we plan to evaluate Abi1 as a possible target for drug development in anti-cancer therapy. These studies will ultimately help us develop personalized anti-cancer therapies.

Leszek Kotula

Associate Professor

Associate Professor of Urology

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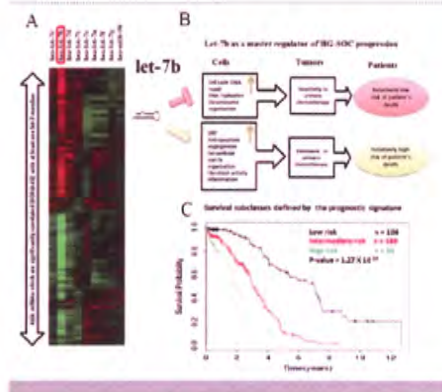
Kotula

RESEARCH INTERESTS

Cancer biology, cell signaling, the role of actin cytoskeleton in tumor progression, mouse models of cancer

RESEARCH ABSTRACT

Current research projects and focus areas: computational and systems biology of cancer, genome and transcriptome integrity and instability, statistical genomics and bioinformatics, secondary nucleic acid sequence structures, RNA-DNA hybrids and computational R-loop biology, non-coding DNA and RNA, single cell transcriptome kinetics, diversity, bifurcations in cell differentiation and proliferation, integrative sequence databases, big data and NGS data analytics strategies, quantitative oncoimmunology, methods for personalized cancer diagnostics and prognosis and non-invasive detection of malignancy, and the development of innovative methods of identification and validation of clinically relevant onco-markers.



Vladimir Kuznetsov

Professor

Professor of Urology

PhD, Moscow State University, Russia, 1984, biophysics
Additional Training, NIH, Bethesda MD, 2004, bioinformatics and cancer genomics

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Kuznetsov

RESEARCH INTERESTS

Cancer systems biology, bioinformatics, big data and survival prediction analyses, predictive and personalized medicine, computational genome and transcriptome biology, non-B DNA structures, RNA:DNA hybrids, R-loops, G-quadruplexes, ncRNAs, clinical biomarker discovery and validation

Frank A. Middleton

Associate Professor

Associate Professor of
Neuroscience and Physiology
Associate Professor of
Pediatrics
Associate Professor of
Psychiatry and Behavioral
Sciences

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Middleton

RESEARCH INTERESTS

Genetic, epigenetic, and neuroanatomical basis of neurological and psychiatric disorders; Basal ganglia and cerebellar circuitry in normal and disease states; Neural-immune and gut-brain interactions Machine learning approaches for biomarker discovery; Next generation sequencing for multiomic data analysis (genome, transcriptome, microbiome, methylome).

RESEARCH ABSTRACT

Our research focuses on defining substrates of normal and abnormal motor and cognitive function. This is accomplished by performing high-throughput genetic, epigenetic, and functional genomic studies involving human subjects or animal and cellular models of various neuropsychiatric, neurodegenerative and addictive disorders. The specific disorders of most interest include autism, schizophrenia, ADHD, Parkinson's disease, alcohol abuse, and traumatic brain injury. In addition to the use of similar analytical methods to study these conditions, another common underlying theme is the attempt to define their relationship to neural-immune responses.

Thus, the neural-immune axis forms a major lab interest as well, and this has been pursued through several collaborative efforts in studies of central and peripheral inflammatory and immune system alterations in these and other conditions, such as lupus, multiple sclerosis, and Zika virus infection. Comparisons across disorders can help define the specificity of the changes that are seen and may lead to the identification of novel biomarkers or therapeutic agents. Recent publications from the lab describe several novel discoveries of DNA mutations causally linked to schizophrenia, or microRNA biomarkers in peripheral blood or saliva that are strongly associated with alcohol abuse or autism spectrum disorder.

Mehdi Mollapour

Professor

Professor of Urology

PhD, University of London,
UK, 2001, Biochemistry
Fellowship, University of
Sheffield, UK, 2007
Fellowship, University of
London, UK, 2003



Mollapour

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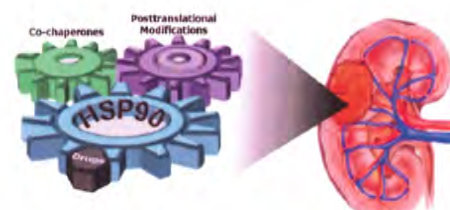
RESEARCH INTERESTS

Post-translational regulation of the Hsp90 molecular chaperone machinery in cancer

Hsp90 and the Chaperoning of Cancer

RESEARCH ABSTRACT

Heat Shock Protein-90 (Hsp90) is a molecular chaperone critical to the folding, stability and activity of many proteins known as "client proteins" including many responsible for tumor initiation, progression and metastasis. This makes the chaperone Hsp90 an attractive target for cancer therapy. Hsp90 chaperone function is coupled to its ATPase activity. Small molecule inhibitors of Hsp90 bind to the ATP-binding pocket on Hsp90, which prevents its interaction with the client proteins therefore, leading to their degradation by the proteasome. In contrast to other anti-cancer drugs, Hsp90 inhibitors simultaneously inhibit multiple drivers of oncogenesis. Examples include Raf-1, HER2/ErBb2, VEGF receptor, DNA repair proteins, HIF1α and other regulators of the tumor growth, angiogenesis, metastasis and survival. Inhibition of Hsp90 therefore leads to simultaneous inhibition of a broad range of oncogenic pathways. Our work on post-



Role of molecular chaperone Hsp90 in kidney cancer and improving the efficacy of the Hsp90 drugs in the kidney cancer therapy.

translational modifications of Hsp90 has re-defined the regulation of its chaperone activity and revealed the reciprocal regulatory mechanisms between the "kinase clients" and Hsp90. My group currently focuses on dissecting this process in kidney cancer.

For further reading please visit our website <http://www.mollapourlab.com/>

RESEARCH ABSTRACT

My research is focused on the contribution of genetic and environmental factors in shaping immune response with a focus on autoimmunity. In search of potential genetic interactions between the host and the environment, we identified HRES-1, a human T-cell leukemia virus-related endogenous retrovirus, mapped it to chromosome 1q42 and identified Rab4a as its gene product that confers susceptibility to HIV infection via increased recycling of surface receptors, such as CD4 and transferrin receptor. Polymorphic haplotypes of the HRES-1 endogenous retrovirus are associated with development and disease manifestations in patients with SLE. The overexpression of Rab4A gene product of

HRES-1, which is detectable in T cells of SLE patients and in all lupus-prone strains prior to disease onset, also contributes to oxidative stress and mTOR activation by inhibiting mitochondrial turnover via autophagy, also called mitophagy. This newly uncovered pathway to lupus pathogenesis can also be exploited for therapeutic intervention through blocking the enzymatic activity of the Rab GTPases, such as Rab4A using 3-PEHPC. Our discoveries have been published in 170 original peer-reviewed papers. Our work has been widely cited, credited and inspired a recent explosion of research on the role of metabolic pathways in the pathogenesis of lupus and other rheumatic diseases.

RESEARCH ABSTRACT

Eye (retina) development - Ongoing work focuses on three areas: 1) the identification and characterization of genes involved in eye formation through a large-scale transgenic RNAi screen. In collaboration with the Viczian lab, the potential role of selected genes during vertebrate eye development will be investigated in *Xenopus*. 2) functional dissection of the Sine oculis (SO) protein. The SO transcription factor controls multiple aspects of eye development (e.g. specification, neurogenesis and differentiation) in concert with different cofactors. We are investigating the role of specific SO-partner interactions in vivo. 3) genetic control of regional specification in the developing eye epithelium. Multiple signaling pathways and transcription factors control the emergence of regional or tissue identity within the eye-antennal disc (the progenitor epithelium that gives rise to the fly head and the eye). Genetic and molecular studies aim to characterize the genetic network active during the early stages of head/eye formation.

Fly models for the study of human diseases - We use the *Drosophila* model to characterize the activity of mutant genes linked to human diseases (e.g. RD). Pharmacological or genetic modification of an abnormal phenotype induced in the fly eye can provide insights into the disease mechanism at the molecular level and/or suggest novel therapeutic targets.

Cancer - The goal of this project is to identify, and then investigate, the cellular processes that underlie the transition from tumor-like to cancer-like behavior (induction of metastases) in cells already compromised by an initial 'oncogenic hit' (e.g. with activated Ras or Raf kinase). The extensive collection of transgenic RNAi lines each targeted to one gene available in *Drosophila* allows us to explore a large number of genetic pathways and cellular processes.

Stem Cells - We are characterizing a novel receptor-ligand pair required for the maintenance of germ-line stem cells in the *Drosophila* ovary. Further studies in other *Drosophila* stem cell systems (e.g. male germ line and/or intestinal stem cells) and testing in vertebrate species are planned.

Andras Perl*Professor**Distinguished Professor of Medicine**Professor of Microbiology and Immunology**Division Chief of Rheumatology*
Co-Director, MD/PhD Program

Perl

MD, Semmelweis Medical University, Budapest, Hungary, 1979

Residency, Semmelweis Medical School, Budapest, 1982

PhD, Semmelweis Medical University, Budapest, Hungary, 1984

Fellowship, University of Rochester Medical Center, 1988, Rheumatology/Immunology

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perla@upstate.edu**RESEARCH INTERESTS**

Genes and Viruses Predisposing to Autoimmunity, Genetics, Apoptosis, Endogenous Retroviruses, Transaldolase

Francesca Pignoni*Associate Professor**Associate Professor of Ophthalmology**Associate Professor of Cell and Developmental Biology**Associate Professor and Interim Chair of Neuroscience and Physiology*

Pignoni

4610 Institute for Human Performance
505 Irving Ave.

Syracuse, NY 13210

pignoni@upstate.edu**RESEARCH INTERESTS**Neurogenesis; Retinal Progenitor Cells Specification and Proliferation; Genetic Control of Stem Cell Identity and Maintenance; Disease Genes Analysis in *Drosophila*

Andrea S. Viczian

Assistant Professor

Assistant Professor of

Ophthalmology

Assistant Professor of Cell and

Developmental Biology

Assistant Professor of

Neuroscience and Physiology



Viczian

PhD, University of California
at Los Angeles, 1998,
Neuroscience

Postdoctoral Fellow, Marshall-
Sherfield Fellow, University
of Cambridge, 1999

Postdoctoral Fellow, University of Cambridge,
Cambridge, England, 2002

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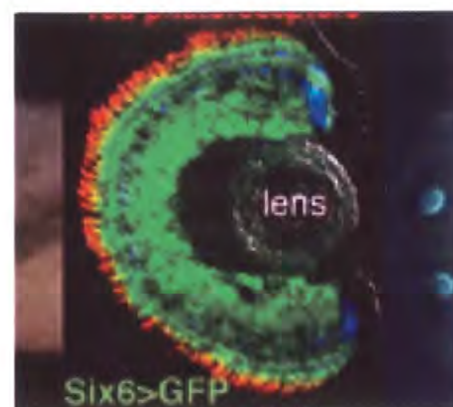
RESEARCH INTERESTS

Mammalian retinal stem cells formation;
molecular mechanism of retinal cell fate
decisions; using cell replacement therapy
to heal the blinded eye.

RESEARCH ABSTRACT

Eyes develop in the anterior region of the embryonic neural plate and are one of the first organs to form. Among other eye tissue, this region gives rise to the complex neural tissue, the retina. In blinding diseases like Age-Related Macular degeneration or Retinitis Pigmentosa, these light-sensing cells are lost and the human body cannot replace them. The Viczian team is interested in understanding the genes encoding transcription factors that drive the development of retina formation from pluripotent embryonic cells. In a 20-plus year collaboration with the Zuber lab, our groups have been discovering the transcription factors and their roles in driving both of these processes. We use the relatively simple frog to better understand early eye formation.

We generate transgenic tadpoles to determine elements driving gene expression.



We use transplantation studies to determine transcription factors necessary and sufficient for eye formation.

We believe in group effort and we champion our trainees to discover the best of their abilities in performing their research. Our current work has transitioned from using frog to knockout mouse studies and embryonic stem cell cultures to determine conservation of gene function from frog to mouse. We look forward to you joining us in this supportive, yet exciting, environment.

Michael E. Zuber

Associate Professor

Associate Professor of

Ophthalmology

Associate Professor of

Neuroscience and Physiology



Zuber

BS, Truman State University,
1988, Biology & Chemistry
PhD, University of Wisconsin at
Madison, 1995, Biochemistry
Postdoctoral Fellow, University
of California at San Diego,
1997

Postdoctoral Fellow, University of Cambridge,
Cambridge, England, 2002

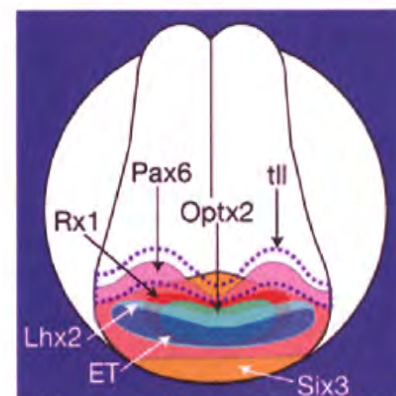
RESEARCH INTERESTS

The molecular basis of retinal stem cell formation; regulating retinal stem/progenitor cell proliferation; using retinal stem/progenitor cells to heal the injured or degenerating retina.

How are Retinal Stem Cells Specified?

RESEARCH ABSTRACT

Our laboratory studies the molecular mechanisms driving the specification, proliferation and differentiation of retinal stem and progenitor cells. The eye begins as a patch of ectodermal cells that are first patterned to form the beginnings of the anterior brain. These cells are further specified to become the retinal stem cells of the embryonic eye field. We have been investigating the genes responsible for retinal stem cell formation. We discovered that seven eye field transcription factors (EFTFs) are coordinately expressed in the anterior neural plate during retinal stem cell specification. Since each of these genes are required for normal eye formation, we reasoned that they might act together to specify retinal stem cells. To test this hypothesis, we coexpressed all seven genes at ectopic locations in the developing frog embryo. Remarkably, these genes were able to induce a third eye, demonstrating



The relative expression patterns of the eye field transcription factors during retinal stem cell specification.

that they are not only expressed during, but also sufficient for eye formation. Is every one of the eye field transcription factors required to generate the third eye? How do these genes interact to generate an eye? What are the downstream targets of these transcription factors? What upstream regulators coordinate the expression of these genes during eye formation? These are just a few of the questions we intend to answer in this project.



ACADEMIC PROGRAMS

The Department of Biochemistry and Molecular Biology offers PhD and master's degree programs.

PhD students apply through Upstate's Biomedical Sciences Program, which allows students access to all faculty at SUNY Upstate, including those of the Department of Biochemistry and Molecular Biology.

Master's students apply directly to the Department of Biochemistry and Molecular Biology.

Students in PhD and master's programs participate in the College of Graduate Studies core curriculum, which is designed to give students a broad-based education in the biomedical sciences and to develop a sense of commonality and collegiality. Original research conducted under the direction of a thesis advisor plays a major role in both programs.

PhD Biochemistry & Molecular Biology

The PhD degree program in Biochemistry & Molecular Biology requires completion of 30 credit hours of didactic course work, successful performance on a cumulative qualifying exam, advance research study, and an oral defense of an original research dissertation. The program normally takes five years, though can be completed in less time. In the first year, students complete rotations in the labs of three departmental faculty members. Students choose a thesis advisor by the end of the first academic year, and begin an individual program of

advanced dissertation study in the summer between the first and second years.

Upon successful completion of the written and oral qualifying exams at the end of the second year, students are free to pursue their thesis research full-time. The qualifying exam covers areas of Biochemistry & Molecular Biology applicable to a student's training and research interests as well as general aspects of protein biochemistry, membrane biology, gene regulation, macromolecular structure, intermediary metabolism, cellular physiology, enzymology and related areas. A final oral presentation of the doctoral research is scheduled after the thesis has been submitted and evaluated.

MS Biochemistry & Molecular Biology

The master's program in Biochemistry & Molecular Biology takes two years and includes 20 hours of didactic course work, plus a thesis. A master's degree is not required for a PhD degree, and students seeking a PhD should apply to the PhD program.

In the first year, students complete rotations in the labs of three departmental faculty members. Students choose a thesis advisor at the end of the first academic year, and begin their thesis research in the summer between their first and second years. Master's students are required to write and defend a thesis dissertation, but do not take a qualifying exam.

Biomedical Sciences Program (PhD)

Upstate's College of Graduate Studies offers a Biomedical Sciences Program for PhD students who would like to study among different labs for one year before selecting a department with which to affiliate. This year of study is applied to the PhD. Students select their three lab rotations from the college's five basic science departments: Biochemistry & Molecular Biology, Cell & Developmental Biology, Microbiology & Immunology, Neuroscience & Physiology and Pharmacology.

After completion of the lab rotations and a first-year core curriculum taught by faculty from throughout the college, students select their thesis mentor and transition into the appropriate degree-granting department or program.

MORE INFORMATION

For more information on the College of Graduate Studies Research Program in Biomedical Sciences, visit the website www.upstate.edu/grad

MD/PhD Program

Students interested in pursuing careers in medical research and academic medicine may select Upstate's seven-year MD/PhD program that combines medical school and graduate school and awards both degrees.

ADMISSIONS

All applicants to the Department of Biochemistry and Molecular Biology must have a bachelor's degree or its equivalent. In general, all applicants must present evidence of knowledge of physics, inorganic and organic chemistry, mathematics (preferably including calculus) and biology.

Selected applications are invited to visit the Upstate campus. This visit includes a personal interview, meetings with faculty and students and a tour of the campus. Offers of admission are based on applicants' qualifications, records and personal interviews.

HOW TO APPLY

PhD students are encouraged to apply to the Biomedical Sciences Program. Application materials can be found at www.upstate.edu/grad

Applicants are required to provide the following:

- **One completed College of Graduate Studies application form.** There are two forms – one for PhD applicants and one for master's applicants that can both be located at the above web address.
- **Three original letters of reference** from people familiar with your academic record and potential for investigative research. These forms are in the application booklet.
- **Official transcripts** from all undergraduate and graduate school attended.
- **Official Graduate Record Examination (GRE) scores.** (The advanced subject test is helpful, but not required)
- **Official TOEFL and IELTS scores.** International students only.

Masters students apply directly to the Department of Biochemistry and Molecular Biology; visit www.upstate.edu/grad



Geneva Tower, Upstate's residence hall.

UNDECIDED ABOUT RESEARCH?

SURF Program for undergraduates

Are you interested in PhD-level biomedical research but uncertain whether it is right for you? If you are a college junior or sophomore, consider applying to the SUNY Upstate Summer Undergraduate Research Fellowships (SURF) program. SURF students participate in an intensive ten-week summer research program under the supervision of a faculty mentor. SURF students are provided with a \$3,500 stipend plus on-campus housing. For details, go to: www.upstate.edu/grad/programs/summer.php

APPLICATION DEADLINE

The Department of Biochemistry and Molecular Biology accepts applications on a rolling cycle for the PhD program. However, it is recommended that you complete your application by **January 15**. The Admissions Committee begins reviewing applications on that day and continues until all positions are filled.

STIPENDS AND TUITION

PhD students receive a competitive 12-month **stipend of \$26,572** and a full tuition scholarship.

Master's students For more information, visit the College of Graduate Studies website: <http://www.upstate.edu/grad/>

For information on Financial Aid, please contact the office of Financial Aid at 315-464-4570 or finaid@upstate.edu or visit www.upstate.edu/students



STUDENT LIFE

JOIN THE CLUB

Upstate offers 40 student clubs and organizations. Through involvement in these organizations, students in the college of Graduate Studies can participate in student and university life. Following are a few organizations that may be of particular interest to graduate students.

Graduate Student Association

This organization is devoted to increasing interaction among graduate students. Events sponsored include orientation get-togethers, class socials and the GSA-sponsored annual speaker each May.

Graduate Student Council

Consists of class officers from each of the medical classes and one per 30 students from the college of Graduate Studies and graduate-level students from the College of Nursing and College of Health Professions. Subcommittees, which deal with topics of interest to the student body include Social, Cultural and Professional, Finance, Orientation, Graduation and Yearbook.

Faculty Student Association

The Faculty Student Association administers scholarships, loan funds and student activity fees and sponsors special projects.

GRADUATE STUDENT ASSOCIATION AWARDS

Each year, the Graduate Student Association honors three students with awards at the Graduate and Medical School Awards Ceremony.

The awards are:

Written Research Proposal Award: \$500
Award for the best grant proposal based on overall merit, feasibility and significance

Volunteer and Service Award: \$250
Award for volunteer service based on length of service, duties performed, training required and benefits to others.

Research Poster Award: \$500
Award for the best scientific poster based on clarity of presentation, logic of technique, significance and relevance, and creativity.



Downtown Syracuse at Clinton Square, home to summer festivals and winter ice skating and close to restaurants and entertainment venues.

COLLEGE TOWN ATMOSPHERE

Syracuse is New York's fourth largest city. Upstate Medical University, along with its neighbors Syracuse University and the SUNY College of Environmental Science and Forestry, form a dynamic hub known as University Hill. Combine our three campuses with nearby LeMoyne and Onondaga Community College, and you have a town filled with students, academics, research centers, libraries, activities and great sports.

Many restaurants, nightclubs and shops are within walking distance of campus on "the Hill," and in nearby downtown's Armory Square.

Also nearby are Destiny USA shopping and entertainment complex, the Onondaga County Civic Center, the Everson Museum of Art (designed by the famous architect I.M. Pei), the Museum of Science and Technology (which houses an IMAX movie theater), Syracuse Stage, the Landmark Theatre, Syracuse University's Carrier Dome, and the Onondaga County War Memorial (home of the Syracuse Crunch hockey team).

A short drive will take you to the Rosamond Gifford Zoo at Burnet Park, the New York State Fair, which attracts national musical acts and nearly 1 million visitors each August, and NBT Bank Stadium, home of the Syracuse Mets baseball team.

Throughout the summer, downtown is host to many music festivals and cultural fairs.



Syracuse is surrounded by beautiful countryside. Numerous parks, mountains and lakes offer countless opportunities for boating, fishing, golfing, hiking, hunting, skating, skiing and swimming.

The Finger Lakes, Lake Ontario and the Thousand Islands are within an hour's drive of Syracuse. A bit farther you will find the Adirondack Mountains and the major winter recreation areas of New York state. Located in the very center of New York state, Syracuse is just half a day's drive from New York City, Boston, Philadelphia, Toronto and Montreal.



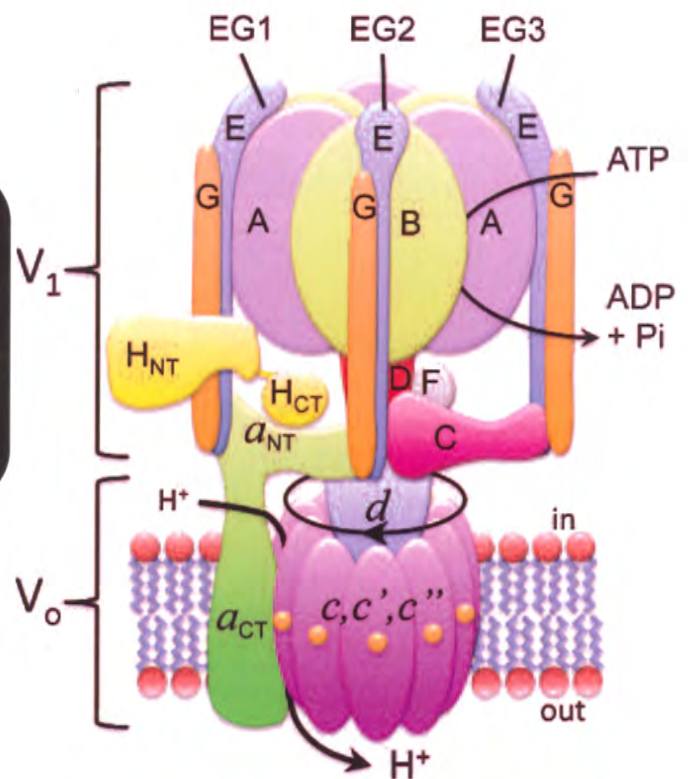
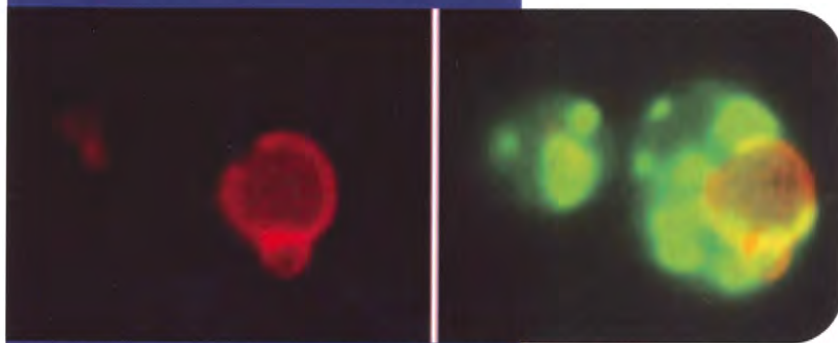
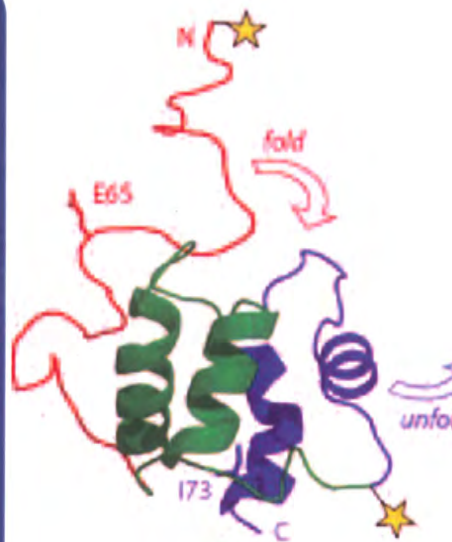
STATE UNIVERSITY OF NEW YORK

UPSTATE
MEDICAL UNIVERSITY

COLLEGE OF GRADUATE STUDIES
Department of
Biochemistry and Molecular Biology

750 East Adams Street
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www.upstate.edu/biochem/



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