"Understanding innate immunity to inspire new therapies for infectious disease, autoimmunity, and human cancers"

The Ascano lab integrates Biochemical and Chemical Biological approaches with High-throughput Transcriptomic and Proteomic technologies to investigate the impact of RNA and DNA binding proteins in innate immunity, viral infection, and human disease. Current research activities include:

cGAS is a critical protein required for sensing foreign or damaged cellular DNA. Can we understand the mechanism of cGAS enzyme activity by designing small molecule activators and inhibitors, and can these compounds develop into novel drugs for treatment of autoimmune disorders or cancers?

RNA binding proteins play essential roles in regulating gene expression; without them, no protein can be made. How do RNA binding proteins like ELAVL1 and IFIT1 regulate cellular and viral RNAs to promote cell survival during infection?

What human proteins make the first contacts with viral RNA during an infection? And what role do these proteins play? Anti- or pro-viral? Over 160 viruses that infect humans contain an RNA genome, and they include: Influenza, HIV, SARS, and Ebola.

Key Publications


"Understanding mitochondrial protein assembly in human health and disease"

The focus of the Brown Lab is to investigate 3-dimensional protein structure in order to understand how certain genetic mutations can have profound impact on human health.

In several instances, proper protein complex assembly is critical for maintaining human health by modulating various cellular processes such as activity of signaling pathways, providing feedback regulation, and mediating transport and transfer of molecules among partners. Unfortunately, there are numerous painful, debilitating, and life-threatening diseases that occur due to genetic mutations that prevent proper protein assembly. Our approach is to use X-ray crystallography and other complementary biochemical techniques to understand how these various mutations lead to changes in protein structure, which is tightly correlated to protein function, thus preventing proper macromolecular assembly.

We focus on areas of human health related to mitochondrial biology and metabolism. Specifically, we seek to understand assembly mechanisms responsible for regulation of heme biosynthesis, which is altered in several blood diseases, and maintenance of mitochondrial DNA copy number, which has direct implication in proper neuronal development. In the future, our work will lay the foundation for developing therapeutics that may take advantage of previously unknown cellular avenues.
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"Assembling contractile systems to drive cell motility and muscle contraction"

Our cells produce contractile force. This type of cellular force is usually a good thing. Currently, our heart muscle cells are producing contractile force to pump blood throughout our bodies. Our immune cells can use contractile forces to hunt down and kill external threats (e.g., bacteria) and internal threats (e.g., cancer cells). However, when gone awry, contractile forces can result in catastrophic health changes.

Abnormalities in contractile forces lead to heart disease, and cancer cells also utilize contractile forces to move away from a primary tumor (i.e., metastasize). Research in the Burnette lab revolves around the molecular motor that generates contractile force: myosin II. Different versions of myosin II drive cell crawling, cell division, and muscle contraction. As such, we study the function of myosin II in these three cellular contexts.

Currently, we are fascinated with how myosin II-based contractile systems assemble within cells. By combining high resolution microscopy, high content microscopy, and genomic/proteomic analysis, we are working out the details of assembly. Our long-term goal is to determine how we can re-assemble diseased contractile systems.

Key Publications

"Focal adhesions control cleavage furrow shape and spindle tilt during mitosis," Scientific Reports, Jul 19;6:29846, 2016

"Expansion and concatenation of non-muscle myosin II A filaments drive cellular contractile system formation during interphase and mitosis," Molecular Biology of the Cell, mbc.E15-10-0725; First Published on March 9, 2016


Sarcomere Assembly in Human Cardiomyocytes
Biography

Dr. Calipari received her PhD in Neuroscience from Wake Forest University School of Medicine where she studied how self-administered drugs altered dopaminergic function to drive addictive behaviors. She then completed her postdoctoral training at Icahn School of Medicine at Mount Sinai, where she used circuit probing techniques to understand the temporally specific neural signals that underlie motivation and reward learning in behaving animals. Work in her lab integrates microscopy with molecular tools to record neural activity in the brain during behavior and determine the molecular targets that underlie changes in neural activity in response to environmental stimuli.

Key Publications

“Granulocyte colony stimulating factor enhances reward learning through potentiation of mesolimbic dopamine system function,” J. Neuroscience, In Press, 2018


How does the brain encode information on a cellular level, and how does dysregulation in this process underlie psychiatric disease?

Our research is guided by two overarching questions:

1. How do neural circuits integrate experiences with positive and negative stimuli to guide behavior?

2. How does dysfunction in this process precipitate psychiatric disease?

One of the most fundamental forms of learning is the ability to associate positive and negative stimuli with cues that predict their occurrence. The ability to seek out rewarding, and avoid negative, stimuli is critical to survival and is evolutionarily conserved across species. However, dysregulation of these processes can precipitate a number of psychiatric disease states.

Addiction, depression, and anxiety are all examples of syndromes characterized in part by dysregulation of associative learning. These are among the most prevalent neuropsychiatric disorders and are highly comorbid. Therefore, understanding the neural mechanisms governing associative learning has widespread implications for developing treatments for psychiatric disease.

Our work aims to combine cutting-edge technology with comprehensive models of psychiatric disease to understand the circuit and molecular dysregulation that underlies these disorders.

Together, our work uses and develops cutting-edge techniques to outline the precise cells in the brain that encode information and push the boundaries of how we understand learning, memory, and disease.
"How tumors manipulate the immune system to increase cancer spreading throughout the body"

The research goals of the Cook laboratory are to understand molecular pathways regulating breast development, how these are commandeered by cancers, and to apply this information towards developing stronger, safer treatments for breast cancer patients.

Recent efforts are aimed at understanding how immune responses in the tumor microenvironment become suppressed, creating a permissive and fertile soil for tumor progression. Importantly, we are finding ways to alter immune responses in breast tumors to fight tumor cells at all stages of cancer progression.

**Key Publications**


3. "Treatment-induced tumor cell apoptosis and secondary necrosis drive tumor progression in the residual tumor microenvironment through MerTK and IDO-1." *Cancer Res*, epub ahead of print. PMID: 30413412, 2018

**How does tumor cell death suppress immune responses in tumors?**

**How can we re-direct communication between the dying tumor cell and the immune system?**
"DNA Endgame: Using frog egg extracts to unravel how copying of the DNA blueprint is terminated"

DNA inside a human cell is faithfully replicated with an error rate of ~1 in a billion. The fidelity of this process is critical to prevent a diverse set of diseases, from cancer, to dwarfism and neurodegeneration. DNA replication in humans involves loading and activation of ~60,000 DNA replication machines which copy the DNA.

Completion of DNA replication is called termination and occurs when pairs of copy machines meet head-on upon the same stretch of DNA. Termination is highly perilous in bacteria and viruses and was assumed to be equally-problematic in humans. This assumption persisted for decades, because technical limitations prevented termination from being studied in cells. However, using a 'cell in a tube' approach derived from frog egg extracts, Dr. Dewar showed that termination in humans is rapid, suggesting humans possess specific proteins to promote termination.

The Dewar lab is working to identify proteins that promote rapid termination. It is particularly important to study termination because this process is targeted during chemotherapy. The Dewar lab is also working to understand a specialized form of termination that occurs at telomeres, which cap chromosome ends and impair cellular aging.

Key Publications


"CRL2Lr1 promotes unloading of a vertebrate replisome from chromatin during replication termination," Genes Dev, 31, 275-290, 2017

"Tipping the balance in the powerhouse of the cell to kill brain tumors"

We conduct our research using an innovative interdisciplinary approach that combines cellular, biological, and biochemical assays with state-of-the-art imaging, single cell analysis and quantitative data analysis. Our specific lines of research are aimed to reveal:

- Novel modulators of stem cell self-renewal and pluripotency
- Mechanisms by which mitochondrial network dynamics and function regulate early differentiation (i.e. neuronal, cardiac) and human brain development
- Ubiquitin-mediated regulation of early differentiation and human brain development

**Model systems**

- Human Fibroblasts
- iPSCs
- Neurons
- Neural Rosettes
- Cardiomyocytes
- Brain Organoids

**Key Publications**

"A non-apoptotic function of MCL-1 in promoting pluripotency and modulating mitochondrial dynamics in stem cells," *Stem Cell Reports*, 10, Issue 3, p684–692, 2018


"Human Embryonic Stem Cells have Constitutively Active Bax at the Golgi and are Primed to Undergo Rapid Apoptosis," *Mol. Cell.*, 46: 573-583, 2012
The Traitor Within: How our immune system can betray us to promote diabetes

We study how obesity impacts health. The growing worldwide obesity epidemic is frequently linked to hyperlipidemia, inflammation, and insulin resistance leading to increased risk of diabetes and cardiovascular disease.

The long-term goal of our laboratory is to determine mechanisms by which obesity increases risk for and pathophysiological consequences of these devastating diseases.

Macrophages are part of the innate immune system that infiltrate white adipose tissue (fat) in obese rodents and humans, and produce most of the inflammatory cytokines and chemokines secreted from adipose tissue. In addition, their presence has been shown to be temporally associated with the development of insulin resistance.

Our current research focus is threefold: to determine mechanisms by which macrophages accumulate in adipose tissue, to determine the role of resident macrophages in normal adipose tissue function, and to determine how other immune cells like eosinophils and T cells also contribute to adipose tissue function.

Key Publications

"High CD8 T cell receptor clonality and altered CDR3 properties in adipose tissue of obese mice," 2018, Diabetes

"Links between Immunologic Memory and Metabolic Cycling," 2018, Journal of Immunology

"Obesity impairs adipose tissue macrophage and systemic iron handling," 2014, Diabetes
"How epigenetic traits are passed from generation unto generation"

Research in the Hodges Lab strives to understand how epigenetic features shape human genomes. We study this relationship on two levels; first, we are interested in how chemical modifications of DNA, DNA methylation, are established during the specialization of developing cell types. Second, we are interested in the relationship between genetics, DNA methylation state (epitype), and how this relationship affects cellular function (phenotype).

I. DNA methylation of genomic sequence elements in differentiating cells

Gene regulatory elements called “enhancers” are docking sites for protein-DNA interactions that control gene expression. They are the nodes of complex gene interaction networks that direct cell fate specification and maintain tissue homeostasis. Furthermore, they are believed to be a driving force behind the diversification of organisms. DNA methylation is an important component of this process but little is understood about how patterns of DNA methylation are established during development. Projects in our lab address these questions utilizing innovative biochemical, functional genomic and bioinformatic approaches.

II. Human methylation variation and disease susceptibility

Enhancers display higher DNA methylation variability between species and human individuals than other genomic elements. These differential patterns of enhancer methylation may reflect individual differences in gene regulation and disease susceptibility. We integrate our understanding of cell-type specific DNA methylation patterns with genetic and phenotype information from the electronic health record to triangulate specific functional relationships between genetic variation and disease risk.
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"Understanding normal brain stem cells to target brain tumors"

The Ihrie laboratory is focused on understanding the connections between stem cells in the brain and brain tumors. We work with basic scientists, computational biologists, and clinicians to study pediatric and adult brain tumors, with the end goal of finding more successful and targeted treatments. Current research projects are focused on tumor development in Tuberous Sclerosis Complex, pediatric gliomas, and adult gliomas including glioblastoma.

In particular, the lab uses multiple cutting-edge approaches to map the features of each of millions of individual cells within brain tumors, allowing us to reveal and target rare subpopulations of cells that are associated with clinically meaningful events like tumor regrowth and resistance to current treatment. We strive to couple clinical imaging, such as identification of tumor location on MRI, to molecular data on cancer and immune cells, with the goal of enabling precision medicine approaches in the brain.

Key Publications

"Decreased survival in glioblastomas is specific to contact with the ventricular-subventricular zone, not subgranular zone or corpus callosum," J Neurooncol, Apr;132(2):341-349, 2017


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"Artificial intelligence for human biology: using computers to discover cells & tailor treatments"

Single cell biology and data science are revolutionizing our understanding of complex, multicellular diseases and therapies. This is especially the case with cancer targeted therapies and immunotherapy, where an understanding of signaling interactions among cancer cells, microenvironment cells, and immune cells is critical.

A central goal of our research is to understand how cell signaling mechanisms govern healthy development and control the outcomes of human diseases and treatments. Our lab creates cutting-edge single cell mass cytometry and phospho-specific flow cytometry tools to search through billions of cells from human tumors, lymph nodes, bone marrow, and blood samples in order to precisely target rare, abnormal cells.

We are especially focused on targeting signaling networks and immune interactions in rare cell populations from patient clinical samples obtained over time during therapy. Our lab members have diverse scientific backgrounds and work at the interface between multiple fields, including computational biology, chemical biology, neuroimmunology, and precision medicine.

We believe great potential exists to detect diseases earlier and to tailor a patient's therapy to the biological alterations detected in the cells of their disease. By better understanding biological systems which control development and cell-cell interactions in healthy and diseased contexts, we can learn to program cells to become therapeutic agents or target malignant signaling events to specifically kill cancer cells.

Biosketch
Dr. Irish received his PhD in Cancer Biology from Stanford University where he trained in cancer biology, immunology, and computational biology. He completed postdoctoral training at Stanford in tumor immunology. During this time, he created a new precision medicine approach based on single cell measurements and co-created Cytobank, a cloud computing platform used by thousands of researchers worldwide. His lab now uses artificial intelligence tools to identify and study diseased cells, improve clinical tests, and create new therapies that specifically target rare cells. His group also operates the Cancer & Immunology Core and Mass Cytometry Center of Excellence shared resources.

Key Publications
"Computational immune monitoring reveals abnormal double negative T cells present across human tumor types," Cancer Immunology Research, in press, 2018

"Discovery of human cell selective effector molecules using single cell multiplexed activity metabolomics," Nature Communications, 2;9(1):39, 2018


Human tissue & cancer research
Single cell biology
AI & machine learning
Precision medicine
"Calcium Channels: Structure, function, and pharmacology"

Research in the Karakas Lab focuses on structural and functional characterization of calcium channels to elucidate the molecular mechanism of ion channel activity and regulation in healthy and diseased states. Calcium acts as universal messengers required to regulate diverse physiological processes including fertilization, muscle contraction, apoptosis, secretion, and synaptic plasticity. Calcium channels are essential components of the calcium signaling toolkit and their aberrant activity is associated with a number of diseases including cancer, metabolic and neurodegenerative diseases. Specific targets being studied include:

- **N-methyl-D-aspartate receptors (NMDARs)**, ligand-gated calcium channels that belong to the ionotropic glutamate receptor family. NMDARs are involved in synaptic transmission in the central nervous system and essential for basic brain function including learning and memory. Aberrant NMDAR activity is implicated in various neurodegenerative diseases including Alzheimer’s and Parkinson’s diseases, and psychological disorders such as schizophrenia and depression.

- **Inter-organelle calcium signaling machinery**, which mediates sustained calcium transfer from endoplasmic reticulum (ER) to mitochondria to maintain cellular bioenergetics. Excessive or reduced calcium transfer leads to apoptotic cell death or autophagy, respectively. Consequently, calcium signaling at ER-mitochondria interface plays an essential role in cell fate decisions and could be an invaluable target when the cell fate decision machinery is compromised, as observed in cancer (evasion of apoptosis) and neurodegenerative diseases (excessive apoptosis).
"Big data modeling of cell-microbe social networks"

The Lau lab considers every one of the 30 plus trillion cells in the body to be unique, thus, utilizes state-of-the art technologies to profile tissues at the single-cell resolution. Resulting "big data" consisting of thousands of data points and dimensions are analyzed by data science-driven computational techniques to determine:

- how altering different cell types in the gut influences the cell-microbiome ecosystem of Inflammatory Bowel Disease
- how interactions between the gut microbiome and epithelial cells contribute to benign colonic polyps progressing to colon cancer
- how the origins of colon cancer stem cells affect the progression of cancer and responses to therapies
- how different mutations affecting the same pathway can lead to different outcomes depending on the cellular ecosystem
"From Molecules to Organisms: Numerical methods to explain and predict how cells make good and bad decisions"

The work in the Lopez lab is driven by two overarching goals:

1. Can we understand the physical and chemical rules that govern cellular processes?

2. Can we predict how a cell will respond to a perturbation in health or disease?

Cells must respond to external and internal perturbations such as mutations or toxins. How do cells employ complex biochemical reaction networks to process these intra- and extracellular signals to commit to a given outcome?

The Lopez lab employs computational modeling, Machine Learning, and dynamic network analysis methods to explain and predict cell behaviors in health and disease. A central goal in the lab is to understand the molecular mechanisms that drive cancer cells to respond to treatments or avoid treatment and seed drug resistance and cancer relapse.

Despite the immediate significance of this work to cancer, a fundamental understanding of cell-decision processes will be generalizable to other areas of biology, including drug development and bioengineering applications.
"Seeking a healthy balance among the many paths leading to protein destruction"

The main objective of the MacGurn Lab is to dissect cellular mechanisms of protein degradation and ultimately to leverage this knowledge towards the development of strategies to fight human disease.

Objective #1: Harness protein degradation pathways to fight cancer.

In the MacGurn Lab, we are learning how to manipulate protein degradation machinery to target destruction of cancer-driving proteins. This has led to the identification of novel chemical strategies for inhibition of important signaling pathways that promote cancer progression. For example, we have identified one protein degradation switch that we are currently exploring as a possible therapeutic target for treatment and prevention of advanced forms of prostate cancer.

Objective #2: Develop strategies for "tuning up" global protein degradation.

In the course of aging, and particularly in neurodegenerative states like Alzheimer's disease and Parkinson's disease, our cells suffer a dramatic decline in protein degradation capacity. Furthermore, there is an emerging consensus that restoring degradation capacity can reverse cellular pathologies associated with neurodegeneration and aging. We have discovered a novel mechanism for "tuning up" global protein degradation in eukaryotic cells, and we are actively investigating how this affects aging in eukaryotic cells.

Biosketch

Jason obtained his undergraduate degree at The University of Chicago and received his PhD in Biochemistry and Biophysics from UCSF. He conducted postdoctoral research at Cornell University using biochemical and imaging approaches to study how cellular proteins are targeted for degradation. In 2013, Jason started his lab in the Department of Cell and Developmental Biology at Vanderbilt to investigate mechanisms of cellular protein degradation in the context of human disease. Jason has been the recipient of the Blavatnik Award for Young Scientists, the NIH Pathway to Independence Award, and a Junior Investigator Award from the American Federation for Aging Research.

Key Publications

"Ubiquitin turnover and endocytic trafficking in yeast are regulated by Ser57 phosphorylation of ubiquitin," *eLife*, 2017, e29176

"COPI mediates recycling of an exocytic SNARE by recognition of a ubiquitin sorting signal," *eLife*, 2017, e28342

"TORC1 Regulates Endocytosis via Npr1-mediated Phosphoinhibition of a Ubiquitin Ligase Adaptor," *Cell*, 2011, 147(5): 1104-17
"Understanding how an individual cell perceives and responds to its environment in healthy and disease conditions"

The Neuert lab combines quantitative single cell and single molecule experiments with dynamic cellular perturbations, genetics and computational biology to explore the fundamental mechanism that enable cells to perceive and respond to physiologically relevant environmental changes. Specific questions of interest are:

- How do individual cells perceive physiologically relevant environments?
- How do proteins generate dynamic behavior within a single cell?
- How do cells regulate genes in physiologically relevant dynamic and stochastic environments?
- How to computationally model and predict single cell behavior to gain novel biological insight?
"Probing how the cell nucleus senses and responds to mechanical forces, one molecule at a time"

Two fundamental questions my lab aims to address are: how does the cell use mechanical forces to drive biochemical processes across lipid bilayers, and how does the nucleus sense and transform mechanical force into biochemically meaningful signals that influence cellular development and function? Much evidence suggests that the nucleus can directly sense physical forces through protein complexes spanning the nuclear envelope (NE), though the molecular mechanisms of nuclear force sensing are not well understood.

Mutations or dysfunction within this network of membrane embedded and associated proteins lead to changes in NE architecture and to human disease including neurological disorders, cardiomyopathy, muscular dystrophy, and cancer. Though much work has been done to characterize how cell adhesion molecules and the underlying cytoskeleton sense and convert mechanical force into biochemically meaningful reactions, a mechanistic understanding of nuclear mechanical signaling is lacking.

Using a combination of single-molecule force spectroscopy, biochemical reconstitution of NE components responsible for mechanical signaling, and biophysical methods, we hope to unravel the molecular details governing mechanical signaling at the nucleus.
Evading the Invaders: Reverting unhealthy nuclear imprisonment of human RNA by viruses

All cellular life relies on the integrity of gene expression. Human cells carry more than 20,000 different mRNAs. Fully processed mRNAs in the nucleus are exported to the cytoplasm where protein translation occurs. This **nuclear mRNA export process** is exploited by a large number of **viruses to block host gene expression as a strategy to counteract host defenses**.

The Ren lab combines the power of biochemistry, structural biology, and cell biology to elucidate the molecular details of viral strategies targeting nuclear mRNA export.

- **Influenza A Virus (IAV)**
  Influenza virus remains a major public health threat killing ~250,000-500,000 people yearly. **Specific questions being studied include:** What is the cellular target of IAV? How does IAV **inhibit nuclear mRNA export**? Which mRNAs are retained in the host nucleus upon IAV infection? How does **blockage of nuclear mRNA export** contribute to inhibition of host immunity?

- **Vesicular Stomatitis Virus (VSV)**
  VSV blocks host mRNA export and limits expression of interferons, a family of signaling proteins that activate host defense systems. **We seek to understand the molecular underpinnings of VSV mediated host mRNA export blockage.**

Our work brings conceptual novelty to the fields of virology, immunology, and cell biology of nuclear transport. **Results** generated from these studies will provide significant implications for **developing therapeutic interventions** aiming to revert nuclear imprisonment of host mRNAs by viruses.
"How do human membrane proteins contribute to various diseases?"

The Sanders lab uses the tools of Biochemistry, Structural Biology, and Chemical Biology to explore the roles of membrane proteins in human diseases. Specific questions being addressed include:

- How does the binding of cholesterol to the amyloid precursor protein promote Alzheimer's disease?
- How does a healthy TREM2 receptor help suppress neuroinflammation that otherwise might accelerate Alzheimer's, Parkinson's, and other neurodegenerative diseases.
- Can folding defect in human peripheral myelin protein 22 be suppressed with pharmacological chaperones as a route to treating the common peripheral neuropathy, Charcot-Marie-Tooth disease?
- How do the more than 600 known mutations in the KCNQ1 potassium channel act to alter the function of this channel, resulting in the long-QT syndrome (LQTS) cardiac arrhythmia and associated sudden death? Can this information be leveraged to help predict patient predisposition to LQTS for preventive personalized/precision medicine?
- What roles do cell surface integrin receptors play in promoting fibrosis in chronic kidney disease, the most common killer of patients with type II diabetes?

Key Publications

"Mechanisms of KCNQ1 Channel Dysfunction in Long QT Syndrome Involving Voltage Sensor Domain Mutations," Science Advances, 4, eaar2631, 2018

"The Amyloid Precursor Protein has a Flexible Transmembrane Domain and Binds Cholesterol," Science, 336, 1168-1171, 2012

"Implications of the differing roles of the β1 and β3 transmembrane and cytoplasmic domains for mammalian integrin function," Elife, e18633, 2016
"Neural basis of motivation and maladaptive decision making"

A major focus of the lab is to understand the neural mechanisms of individual differences in decision making - that is, why do behavioral responses vary even when given the same experience. For example, although a large portion of the population will be exposed to alcohol, only some will go on to develop an alcohol use disorder.

We develop behavioral procedures in rodents to model these phenomena, allowing us to determine the pre-existing differences that may contribute to individual differences as well as how they change with experience.

By combining these models with various techniques for observing and manipulating neuronal activity, we dissect the circuitry of maladaptive decision making.

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**Key Publications**


"Dopamine enhances signal-to-noise ratio in cortical-brainstem encoding of aversive stimuli," *Nature*, 563(7731):397-401, 2018

"Amphetamine reverses escalated cocaine intake via restoration of dopamine transporter conformation," *Journal of Neuroscience*, 38(2):484-497, 2018
"How hormones impact red blood cells in health and disease"

The Venters lab leverages their expertise in Molecular Biology, Functional Genomics, and Bioinformatics to study the molecular mechanisms underlying hematological diseases. Our research is guided by two overarching questions:

1. How does EPO signaling control RNA polymerase II kinetics during red cell development?

2. How are early EPO-responsive genes regulated by transcription factors and enhancers?

Erythropoietin (EPO) is the primary hormone regulator that controls erythroid cell maturation, a process that is required for the daily replenishment of nearly 1% (200 billion) of the circulating red blood cells. Recombinant human EPO (trade name Epogen) is a $5 billion/year drug that is used to treat chronic anemia. However, the therapeutic use of EPO has been controversial since reports have emerged of its link to increased risk of heart attacks, tumor growth, and death in some cases. An understanding of EPO function has advanced substantially, but certain aspects of the EPO signaling pathway remain unknown. In particular, how EPO signaling controls erythroid expression patterns through epigenetic and transcriptional mechanisms remains poorly understood.

Thus, the overarching goal of our research is to understand the gene regulatory mechanisms governing EPO-induced erythroid differentiation, and translating these discoveries into potential therapeutic interventions.
Biosketch

Dr. Zanic received her PhD in Physics from the University of Texas at Austin, followed by postdoctoral training at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, Germany. She spent a year as an Associate Research Scientist at Yale University prior to starting her independent laboratory at Vanderbilt in 2014. The Zanic laboratory combines the tools of biology and physics to elucidate the fundamental mechanisms underlying dynamic intracellular architecture. Zanic is a recipient of the Career Development Award from the Human Frontier Science Program, the Maximizing Investigators’ Research Award from the NIH, and the Searle Scholars Award.

Key Publications

"Microtubule minus-end aster organization is driven by processive HSET-tubulin clusters," Nature Communications, 9:2659, 2018

"Human CLASP2 specifically regulates microtubule catastrophe and rescue," Molecular Biology of the Cell, 29(10):1168-1177, 2018


"Building the cell's skeleton to understand how cells change shape, move, and divide"

A look inside of every living cell reveals a world of dynamic intracellular structures. One of the core cellular building blocks are microtubule polymers, vital for processes such as cell division, intracellular transport and neuronal development. Not surprisingly, misregulation of the microtubule network causes human disease, including many types of cancers, as well as neurological disorders.

Our research aims to discover the molecular mechanisms that drive dynamic remodeling of the microtubule network architecture, essential for its proper cellular function. What are the molecular rules that govern whether a microtubule grows or shrinks at any given moment in time? What are the mechanisms used by the microtubule-associated proteins that regulate microtubule behavior? How does this complex network of regulators collectively orchestrate dynamic remodeling of the microtubule cytoskeleton in vastly diverse cellular contexts? To address these questions we take an interdisciplinary approach, combining molecular and cell biology, biochemistry, engineering and physics.

Uniting the tools of many disciplines, our work aims to provide a fundamental understanding of how cells engineer large-scale, dynamic structures essential for life. Understanding of the underlying mechanisms will allow us to manipulate dynamic intracellular architectures, ultimately facilitating new, better strategies to fight human disease.