



A DECADE OF DISCOVERY

TRANSLATIONAL RESEARCH INSTITUTE



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A DECADE OF DISCOVERY

AdventHealth
Translational Research Institute
2012-2022

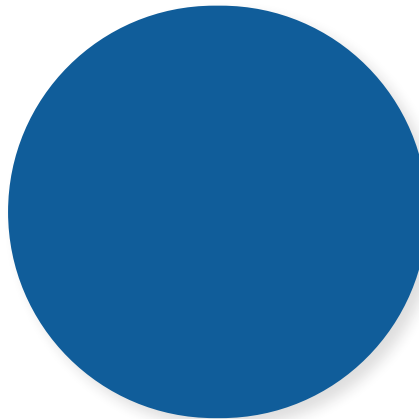
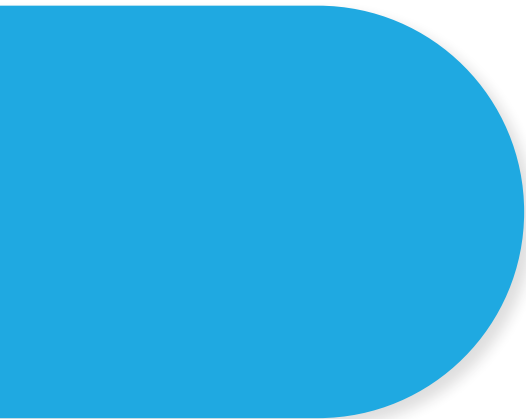
“TRI is definitely different; it has distinct advantages. Everything we need to do our science is in the building, and everybody in the building has their own unique expertise on metabolism. It makes us highly synergistic and collaborative.”

*Karen Corbin, PhD, RD
Investigator*

“The backbone of the TRI is truly the unique team that we have here and their unrelenting drive to perform the best research in the world.”

*Josh Smith
Research Laboratory Senior Manager*







A Letter From Our Chief Scientific Officer

It is difficult to believe that a decade has elapsed since the Translational Research Institute opened.

Laying the foundation was a bold move; one that is now paying off.

A Decade of Discovery and more.

First, let me provide you with some context and most importantly introduce you to the laying of the foundations of the TRI. I do this so you can put the future of translational research at AdventHealth in context.

As we look back, the TRI was the result of several converging forces. The Burnham Institute, Orange County, the City of Orlando, and the Tavistock group, along with the state of Florida under the leadership Governor Jeb Bush, joined forces in an attempt to diversify the Orlando economy. Each party made significant financial commitments to grow biomedical research in Orlando.

Florida Hospital's contribution, under the visionary leadership of Lars Houmann, was an investment in the formation of the Translational Research Institute. This included, but was not limited to, a state-of-the art translational research building, the recruitment of a founding scientific director and significant operational / financial support for the recruitment of scientists and staff. In addition, as a means to ensure the protection of our patients, Florida Hospital upgraded and modernized the hospital research administrative infrastructure. The Translational Research Institute is the sole surviving founding entity that made the original 2008 investments. As you will read in these pages the TRI continues as an example of how clinical and translational research can flourish in a large quaternary hospital.

This report will highlight those accomplishments and provide a peek into research questions that the TRI faculty are trying to solve now ... and into the future.

But there is much more to be said if we ask the right questions. For example, some may ask "why would a hospital invest in translational research?"

First and foremost the TRI is all about improving the health of the communities we serve. In 2008 the leadership of Florida Hospital believed that we have an obligation to learn from our patients. If we don't learn from our patients we will not have the knowledge or the talent to tackle the new diseases of the 21st century. The Institute of Medicine

defines a "learning healthcare system" and this should be an organizational imperative. Translational research is one of many key components of that ecosystem. In this lofty goal we have only just begun.

As an offshoot of the TRI, and important to the other service lines and institutes at AdventHealth; the TRI established - for the first time - the research infrastructure needed to compete at a national level. At the inception of the TRI, National Institutes of Health funding at Florida Hospital was non-existent. Now, we routinely compete, and succeed, in securing these prestigious grants.

The impact of the TRI extends beyond Florida Hospital / AdventHealth. TRI now receives more NIH translational research dollars than any other academic institution in Orlando.

NIH funding, along with our publications in top tier journals, provides unimpeachable evidence of research excellence. The NIH system typically funds only one in ten applications from the largest academic medical centers and universities across the U.S.

More importantly, NIH awards are key performance indicators of how our research impacts how we think about a clinical problem. Without this evolution in knowledge, healthcare would become static and advancements would be slow. The TRI now plays an important instrument in the symphony of clinical and translational research across the US. The US is acknowledged as the epicenter of biomedical research across the globe. With collaborations across the US and Europe, the TRI is known as a center of excellence in our three focus areas.

One could argue that this kind of research is the responsibility of universities and traditional academic medical centers. If one thinks back to the original 'why' I spoke about, then the answer to this question becomes obvious. TRI research touches the lives of the communities we serve. The TRI was the first drop in an ocean of disease. A drop that sends ripples across AdventHealth, our city and beyond. We inspire others to believe that high quality translational research is not only possible at AdventHealth but necessary to solve some of the most pressing needs in healthcare today.

Under the leadership of Dr. Goodpaster, the TRI is moving beyond the original focus on obesity and diabetes. Our scientists now study a key future healthcare problem - aging and

aging associated diseases. We collaborate with clinicians and scientists in disciplines as diverse as cancer, cardiovascular disease and even study in space how the microgravity of spaceflight alters muscle function. The TRI was the first step in the development of a new translational research institute that now is addressing the upcoming healthcare crisis of Alzheimer's disease. Our scientists work to understand how our diet remodels the human gut microbiome to increase or decrease a multiplicity of diseases. These are only a few of the examples you will read about in these pages.

I am continually inspired by the creativity and rigor of TRI research and hope you are too.

Where will we go next? I strongly believe that translational and clinical research are critical to recruit the best and brightest physicians to AdventHealth. An overarching goal is to create a healthcare system that continuously asks hard questions and answers them with state-of-the-art technologies, creative and bold hypotheses and then disseminates the knowledge and wisdom across the globe.

The TRI has given AdventHealth permission to believe that we can conduct world-class research with integrity, efficiency, and impact. The next chapter in this book will require foresight and vision equal to or greater than what existed at our inception.

We hope you will join us celebrating a Decade of Discovery and more importantly will see the future need and our key role in crafting that future. Our quest to solve the hardest medical problems is just beginning and we are off to a great start!

So what comes next? That is really up to you. Our future is not assured. These are challenging times and challenging times call for bold and creative thinking. Thinking that stretches the imagination and tests our commitments. Where will we go? Let's craft that vision together.

Thank you so much and enjoy this glimpse into the past... and the future of healthcare.

Steven R. Smith, MD
Senior Vice President and CSO, AdventHealth



Origins of Translational Research Institute

In 2008, then CEO of Florida Hospital, Don Jernigan, alongside Lars Houmann, CEO of the Central Florida Division, began meeting to discuss the future of the health care organization (later rebranded AdventHealth). Their goal was to redefine the current community hospital mindset in order to become a global pace setter, improve the patient care model, advance academic standing and bolster economic development in Central Florida.

At the same time, the Sanford Burnham Institute, based in La Jolla, California, pledged to build a second research facility in Lake Nona, near Orlando. Their president, John Reid, had plans to change the existing medical structure by bringing research to the region. With Florida Hospital looking to construct their first research-focused facility, Reid and Houmann saw the perfect opportunity to align

their organizations through a partnership that would allow each to realize their goals.

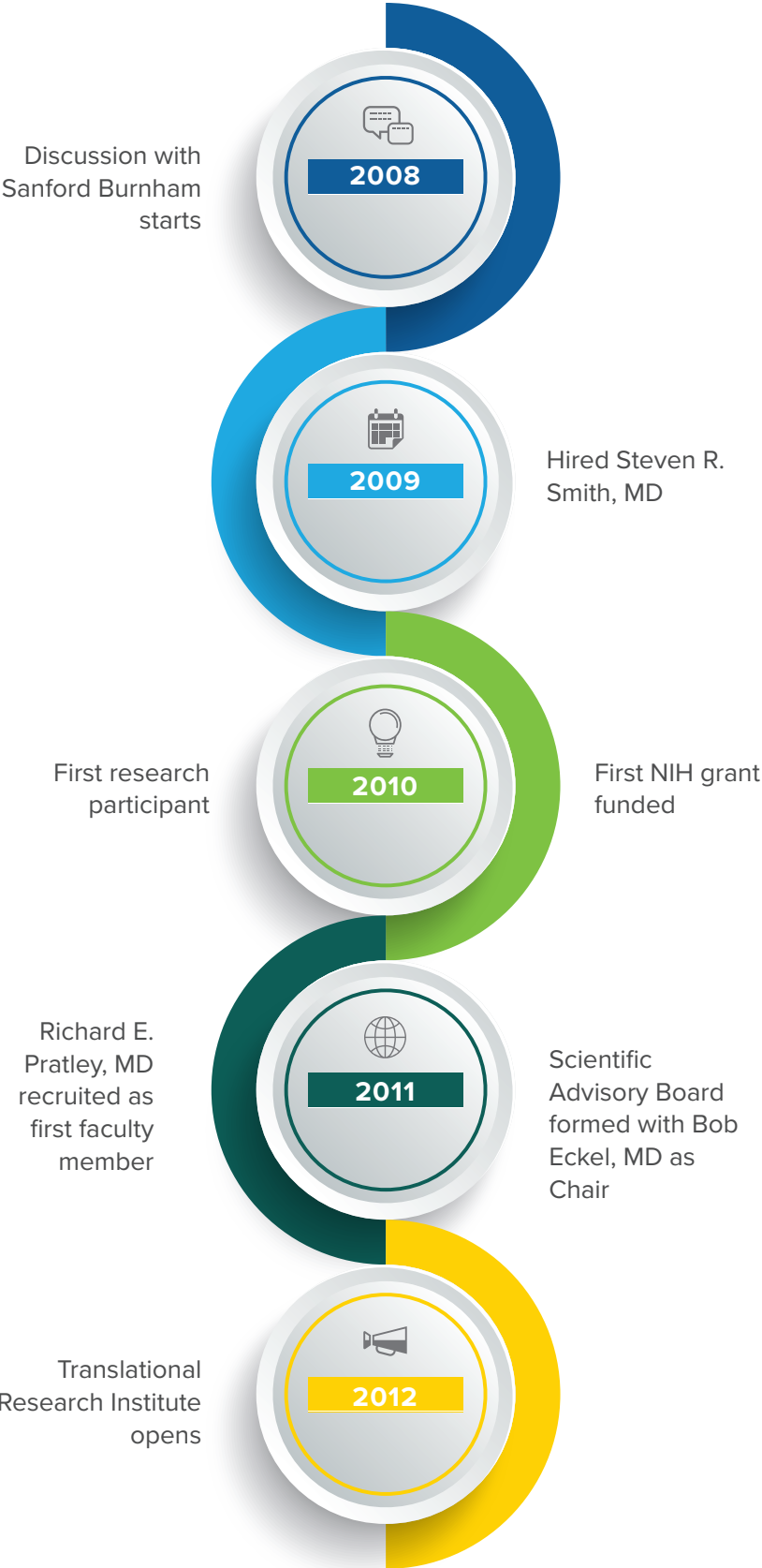
Innovation took front and center, with the question of which clinical research area Florida Hospital would pursue first. Guided by the CREATION Life principles of Whole Person Care, upon which Florida Hospital was founded, the areas of Diabetes, Obesity and Metabolism were selected. The organization appointed Steven R. Smith, MD, a world-renowned research leader in this field of science, to take charge in transforming a small research footprint into an academic medical center. Four years later, in March 2012, the Translational Research Institute (TRI) opened its doors, aiming to achieve each of Florida Hospital's organizational goals – and so much more.

TRI Today

The Institute bridges the gap between the research bench and the patient's bedside. The researchers bring medical discoveries from the laboratory to the community for further testing through clinical trials, in an effort to tackle some of today's biggest health care concerns.



Origins Timeline



“Being able to be part of a research institute from the ground up has been very rewarding. One’s opinions and ideas are heard and respected making TRI an agile and cutting-edge research institute.”

– Rebecca Z. Essner, PhD
Senior Research Scientist,
Genomics Senior

Fast Facts

54,000 SQUARE-FOOT LEED GOLD CERTIFIED FACILITY

TWO 27,000-LITER WHOLE ROOM CALORIMETERS

TWO FLEX CALORIMETER CHAMBERS FOR SHORT-TERM OBSERVATION AND TESTING

11-ROOM OVERNIGHT CRU

IMAGING INCLUDING DEXA, 3T MRI, AND FIBROSCAN

DEDICATED RESEARCH KITCHEN

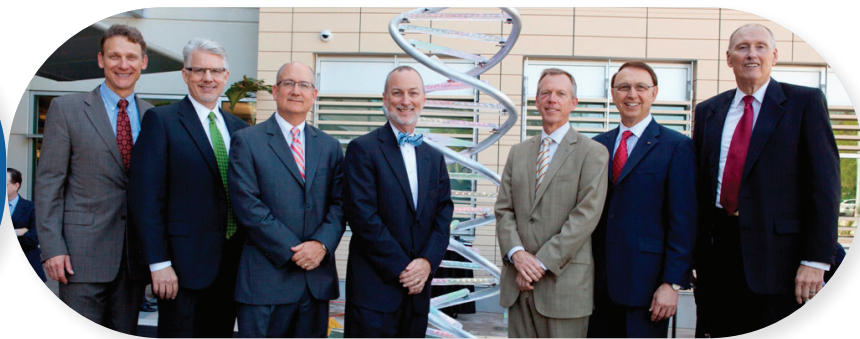
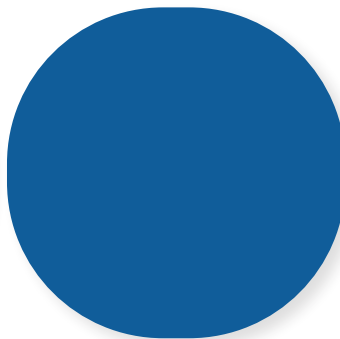
BIOREPOSITORY WITH OVER 7,000 SQUARE FOOT WET LAB

GYM FOR INTERVENTIONAL EXERCISE STUDIES



Data Tells the Story

2012-2021



Mission

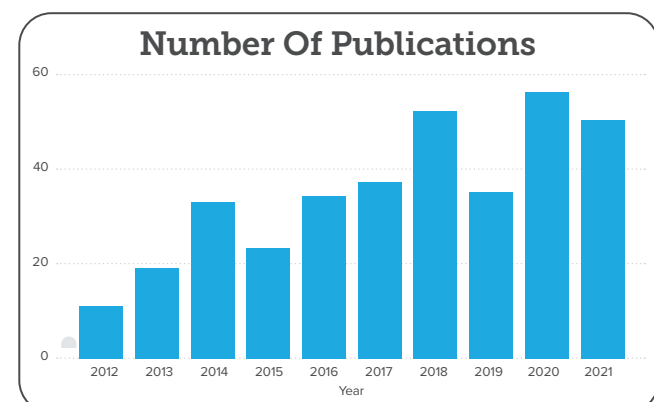
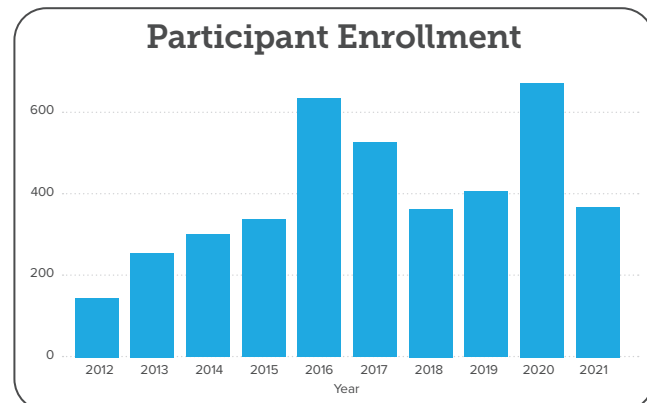
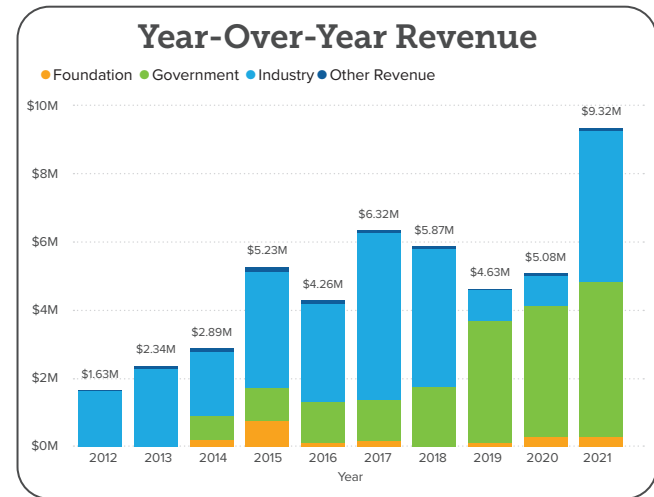
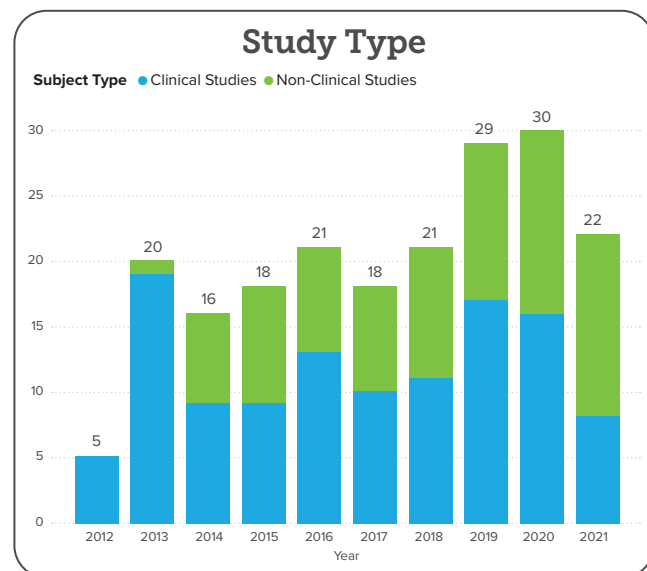
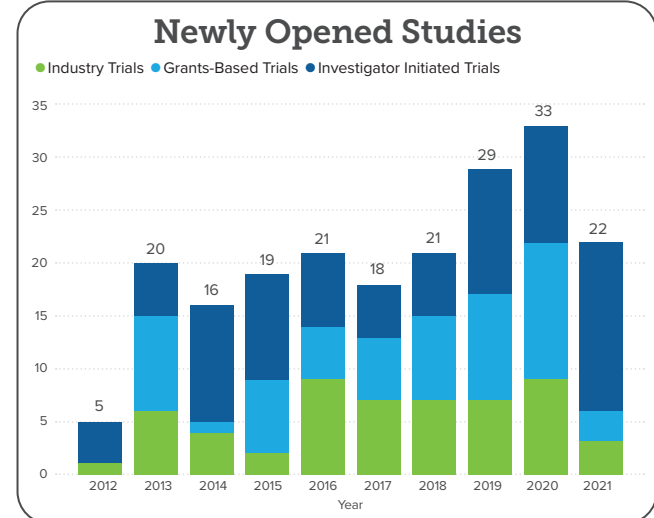
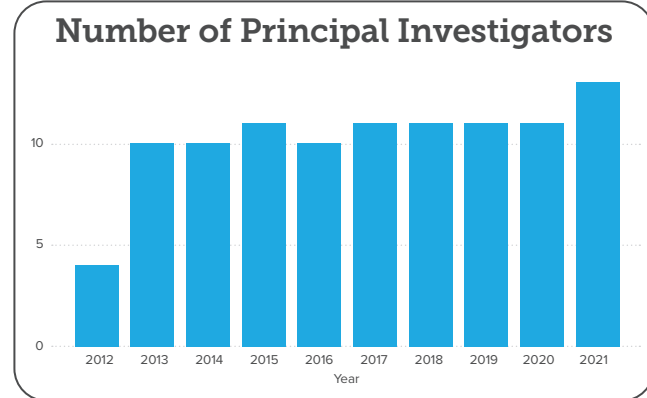
To extend and improve the quality of lives through innovative translational research that leads to discoveries, and ultimately treatments and cures, for metabolic diseases such as obesity, diabetes and cardiovascular disease.

Vision

With diligent respect to the mission and values, the AdventHealth Translational Research Institute develops and conducts world-class translational research addressing diabetes, obesity, the metabolic origins of cardiovascular disease and aging.

Values

- **Scientific Achievement:** Development of predictive biomarkers, mechanisms and phenotypes to translate into clinical medicine and revolutionize health care delivery.
- **Collaboration:** Across disciplines of science, health care, academics and business to create a translational research platform that positively impacts medicine and society.
- **Integrity:** In all aspects of our work and business.
- **Ethical Treatment:** For persons and society, which guide our applications of all research.
- **National and International Recognition:** To broaden reach and identity of AdventHealth.
- **Education:** Of physicians, scientists, health care providers, industry and society is an imperative to our mission.





A Letter From Our Scientific Director

As I reflect upon the past 10 years of the TRI, I am struck by how Dr. Smith's clear vision has allowed us to accomplish so much in such a short period of time and has paved the way for us to do so much more. We have been steadfast in working to achieve our goal to translate scientific discoveries into clinical care and prevention of some of our most common complex diseases and conditions.

When I assumed the role of Scientific Director of the TRI in January of 2020, we strategically removed 'Metabolism and Diabetes' from our name to become, perhaps more simply in name, the Translational Research Institute. While we will continue to develop as a world-class clinical-translational research institute focused on Diabetes, Obesity, Aging and Exercise, 'Metabolism' is so much more. We are also excited to make significant contributions in Neuroscience, Orthopedics and Cancer. As we continue to develop and grow, the TRI has helped to provide AdventHealth the vision and conviction to be a leader in innovative research of metabolism in these other important areas of human health and disease.

The TRI is now comprised of 11 faculty, 7 Research Scientists, and 10 post-doctoral fellows. We are on track to earn \$7 million in revenue this year. Our NIH grants now represent most of our research revenue.

The TRI continues to build upon its reputation for conducting cutting-edge proof-of-concept and proof-of-mechanism research studies aimed at understanding the molecular underpinnings of Metabolic Disease. As we enter our second decade, the future of the TRI looks bright. We will explore Precision Medicine treatments for obesity and diabetes, provide a deeper understanding of why and how exercise improves health, and discover why aging is more than just a number.

Sincerely,

Bret Goodpaster

Bret Goodpaster, PhD
Scientific Director/ Senior Investigator

Scientific Advisory Board

Current SAB Members

David D'Alessio, MD
Allison B. Goldfine, MD
Juleen R. Zierath, PhD
Stephen B. Kritchevsky, PhD
Martin Walsh, PhD
Michael R. Rickels, MD, MS

Duke Medical Center
Novartis Institutes for BioMedical Research
Karolinska Institute
Wake Forest University
Mount Sinai School of Medicine
University of Pennsylvania

Past SAB Members

David E. Kelley, MD
Andrea Dunaif, MD
Robert Eckel, MD
Robert Henry, MD
Thomas Hughes, PhD
Samuel Klein, MD
Ronald Krauss, MD
Robert Sherwin, MD

Merck Research Laboratories
Northwestern University & MSSM
University of Colorado, Denver
University of California, San Diego
Zafgen, Inc
Washington University, St. Louis
Children's Hospital Oakland Research Institute
Yale University

"The continued evolution of the TRI has been positive and the institute is now in position to execute on important research initiatives, expand its intellectual horizons, and solidify a national reputation."

*– David D'Alessio, M.D. Chief, Division of Endocrinology, Metabolism and Nutrition
Duke University Medical Center*



Top: Ron Krauss and Rob Deininger | Bottom: Sam Klein, Andrea Dunaif, Steven R. Smith, Bob Eckel, Dan Kelly, and David Kendall (L) Sam Klein, Andrea Dunaif, Ron Krauss

TRI Faculty

“It takes a team working in concert to successfully conduct larger clinical trials and studies that include biospecimen collection and participant phenotyping. It makes science more fun, and it is next to impossible to blaze that trail by yourself.”

– Paul M. Coen, PhD

Steven R. Smith, MD

**Senior Vice President and
Chief Scientific Officer, AdventHealth**

Joined: August 2009



Steven R. Smith, MD is a translational researcher, specializing in endocrinology and metabolism, who leads AdventHealth’s research vision by serving as the Senior Vice President and Chief Scientific Officer.

Dr. Smith is an established scientist who joined the organization during the conceptual phase of the TRI in 2009. He served as the founding Scientific Director handing that position to Dr. Goodpaster two years ago. During his career, he has contributed over 250 research publications; his science bridges the gap between cell/molecular biology and clinical care also called translational science.

Dr. Smith’s research is focused on obesity, the metabolic origins of disease. He contributed to our understanding how individuals differ in their ability to adapt to diets high in fat, and how obesity leads to type 2 diabetes. Using the translational medicine approach, Dr. Smith discovered that many obese people have an inability to burn fat and discovered a new hormonal control system to increase fat and energy metabolism. Most importantly, the discovery that the inability to burn fat is programmed into muscle cells provides a novel way to identify and test new treatments for obesity and diabetes.

In a project started over a decade ago and recently funded by the NIH, Dr. Smith has been pushing the scientific envelope to understand why and how

people store adipose tissue in different places on their body (i.e. pear-shaped, apple-shaped, etc.). Given that an apple shape increases risk for diabetes, cardiovascular disease and other diseases, his fundamental science on the hormonal and epigenetic control of adipose tissue is revealing new insights into how adipose tissue develops and grows. Ultimately, he hopes to discover new ways to control where fat is stored to treat and prevent metabolic diseases.

In another NIH-funded study, he focused on further understanding how diet changes the gut microbiome. Many diseases have been linked to dysbiosis of the gut microbiome. *“This work is important because we have known for years that obesity and the microbiome are linked yet we don’t really know how and why. Our work, powered by the people and enabled by technologies at the TRI allowed us to solve this mystery.”*

As Dr. Smith celebrates 10 years of the TRI’s growth and success, he does not lose sight of what makes the Institute stand out. *“It’s not just about the building and the technology. It’s really about the bright, dedicated people we’ve recruited from all over the world. We share ideas, methods and challenge each other to drive the science forward. We’re very excited about the team and the progress of the last decade.”*

Key Publication:

Fat Distribution in Women Is Associated with Depot-Specific Transcriptomic Signatures and Chromatin Structure

Featured in: *Journal of the Endocrine Society*

Reference: Divoux A, Sandor K, Bojcsuk D, Yi FC, Hopf ME, Smith JS, Balint BL, Osborne TF, **Smith SR**. Fat Distribution in Women Is Associated with Depot-Specific Transcriptomic Signatures and Chromatin Structure. *Journal of the Endocrine Society*. 2020. doi: 10.1210/jendso/bvaa042.

In this paper, we report that the preferential accumulation of fat in the upper body (apple shape) is associated with changes in DNA structure supporting our global hypothesis that the epigenome is partly responsible for the development of metabolic diseases, such as type 2 diabetes.

Anna Casu, MD

Associate Investigator

von Weller Family Chair in Type 1 Diabetes Research

Joined: September 2018



Anna Casu, MD is a physician endocrinologist and researcher who studies advanced therapies for type 1 diabetes and their metabolic implications. Her research also includes exploring the relationship between the exocrine and the endocrine pancreas, which influences type 1 diabetes.

Hailing from Sardinia, Italy, home to one of the highest incidence rates of type 1 diabetes, Dr. Casu originally wanted to become a neurologist before discovering her passion for diabetes research. It was more than just an intellectual connection with her research field of choice, as she herself was diagnosed with type 1 diabetes herself at age six.

Dr. Casu joined the TRI team with an extensive back-ground in transplant and endocrinology work through organizations, like the University of Pittsburgh and the University of Cagliari. She was intrigued by the TRI's clinical research approach and how it creates an atmosphere of robust collaboration for scientific inquiry.

Since most type 1 diabetes research focuses on basic science, she believes the patient integration aspect is important to her work. Collaboration across TRI's rich knowledge base of investigators

has only encouraged growth and provided “tools” to further her understanding and impact as a scientist and endocrinologist.

One of her most engaging studies at the TRI involves work on pancreases from organ donors aiming at understanding how the many different types of cells in the pancreas act when diabetes develops. The interaction of these cells could explain why some people develop type 1 diabetes later than others. While findings are still being gathered, the results could ultimately impact the prevention of diabetes, and lead to possible cures.

Endowed with the first ever von Weller Family Chair in Type 1 Diabetes Research, created to attract and fund groundbreaking diabetes researchers, Dr. Casu plans to use her studies to gain a better understanding of how the pancreas microenvironment drives pancreatic islet function and resilience to external insults. This can be done through methods her laboratory is developing on ex vivo pancreas perfusion and imaging, along with cell-to-cell interaction in cell co-cultures. The result of these efforts could provide applications for delayed evolution of type 1 diabetes in older adults, after acute pancreatitis or pancreatic cancer.

Paul M. Coen, PhD

Associate Investigator

Joined: September 2013



Paul Coen, PhD is a clinical translational investigator who brought his expertise in mitochondrial energetics within aging and obesity to the Translational Research Institute's portfolio. His work is also integral to collaborations on some of TRI's largest projects, including MoTrPAC and SOMMA.

Originally from Dublin, Ireland, Dr. Coen jumped “across the pond” to earn a PhD in Exercise Physiology at Purdue University in 2008. He then completed a post-doctoral fellowship in Metabolism at the University of Pittsburgh School of Medicine before joining his colleague and mentor, Bret Goodpaster, PhD at the TRI in 2013. He viewed the move to Orlando, working with the unique research team, as “a once in a lifetime career opportunity” to conduct his NIH career development award and to continue his professional development.

Dr. Coen was awarded his first R01 from the NIH as a principal investigator in 2018 and was promoted to Associate Investigator one year later. He points towards the TRI's commitment to team-based science as a key factor in the organization's success. The collaborative-based environment unifies researchers to be creative and, together, conduct more impactful scientific research.

This is exemplified through his contributions to the SOMMA study, in which he works closely with Dr. Bret Goodpaster and Dr. Lauren Sparks. Dr. Coen provides scientific and technical oversight for muscle tissue collection at the clinical sites, including the successful execution of mitochondrial assays in biopsy specimens of nearly 800 participants.

In his independent work, he is currently leading the REST study, investigating the molecular and biochemical underpinnings of human skeletal muscle atrophy and exercise-supported recovery in older adults with type 2 diabetes. Understanding the relationship and factors between diabetes and muscle atrophy could make a profound impact in minimizing a public health problem for older adults.

Dr. Coen believes there is a lot more to discover in this area and hopes to gain more attention and funding to support the ground-breaking research and innovation conducted at the TRI. His goal is to continue contributing to the TRI's success and to advance its scientific mission to extend and improve lives through discoveries and cures for common diseases, like obesity, diabetes and cardiovascular disease.

Key Publication:

Characteristics of adult-compared to childhood-onset type 1 diabetes

Featured in: *Diabetic Medicine*

Reference: **Casu A**, Kanapka LG, Foster NC, Hirsch IB, Laffel LM, Shah VN, DeSalvo DJ, Lyons SK, Vendrame F, Aleppo G, Mastrandrea LD, Pratley RE, Rickels MR, Peters AL. Characteristics of adult- compared to childhood-onset type 1 diabetes. *Diabetic Medicine*. 2020. doi: 10.1111/dme.14314.

Type 1 diabetes diagnosed in adulthood has similar clinical characteristics, diabetes management, acute complications and suboptimal glycemic control as that diagnosed in childhood, but it is often mistreated as type 2 diabetes at onset and has a lower use of insulin pumps.

Key Publication:

Skeletal muscle transcriptome response to a bout of endurance exercise in physically active and sedentary older adults

Featured in: *American Journal of Physiology, Endocrinology and Metabolism*

Reference: Aliza B Rubenstein, J Matthew Hinkley, Venugopalan D Nair, German Nudelman, Robert A Standley, Fanchao Yi, GongXin Yu, Todd A Trappe, Marcos M Bamman, Scott W Trappe, Lauren M Sparks, Bret H Goodpaster, Rick B Vega, Stuart C Sealfon, Elena Zaslavsky, **Coen PM**. Skeletal muscle transcriptome response to a bout of endurance exercise in physically active and sedentary older adults. *American Journal of Physiology-Endocrinology and Metabolism*. 2022. doi: 10.1152/AJPENDO.00378.2021.

This study found that muscle transcript signatures associated with oxidative capacity and immune cells underlie important phenotypic and clinical characteristics of older adults who are endurance trained or sedentary. Despite divergent phenotypes, the temporal transcriptional signatures in response to an acute bout of endurance exercise were largely similar among groups. This data provides new insights into the transcriptional programs of aging muscle and the beneficial effects of endurance exercise to promote healthy aging in older adults.

Karen Corbin, PhD, RD

Investigator

Joined: February 2015



Karen Corbin, PhD, RD is a registered dietitian and scientist who studies human nutrition, metabolism and the gut microbiome. After five years of clinical work in nutrition, she learned about the scientific field on a molecular level, earning a master's and PhD in Molecular Medicine at University of South Florida. After her post-doctoral fellowship and Research Assistant Professorship at the University of North Carolina at Chapel Hill, she discovered an interest in studying the molecular mechanisms driving the initiation and progression of diseases, such as fatty liver, obesity and diabetes.

Reflecting on her first impressions of the TRI during the interview process, Dr. Corbin cites Dr. Steven R. Smith's vision, the institute's advanced capabilities in human metabolism and the "promise of making AdventHealth a living laboratory where we would capitalize on clinical data" as some of the most intriguing factors.

During her time at the TRI, she has been engaged in more than 25 clinical trials, and has risen from the role of Clinical Research Scientist to Investigator. Most notably, she is working as a co-investigator, in conjunction with Dr. Smith, on a study designed to understand the gut microbiome's quantitative impact on energy utilization by the human host, specifically as it relates to colon bacteria known

to influence several aspects of health. This could ultimately expand on previous work that has not accounted for the gut microbiome's unique impact on calorie absorption, ultimately redefining our understanding of nutrition.

In the future, Dr. Corbin looks to successfully complete a study in collaboration with Dr. Torfay Roman from the AdventHealth Fatty Liver Disease Clinic and Transplant Institute and Dr. Benoit Chassaing from Institut National de la Santé et de la Recherche Médicale (INSERM) in Paris, France. The study will examine how the encroachment of the microbiome into the gut lining impacts liver disease. This mechanism, if proven to be important for liver disease, could pave the way for new therapies.

Dr. Corbin's ultimate goal is to contribute to discoveries that will have an impact on clinical care, including scientific communication outside of the lab, which could lead to more efficient discovery and innovation.

"If we are to be good stewards of the amazing intellectual capital that we have here," Dr. Corbin, stated, "we must do everything we can to learn from the data and the samples that we collect, not just in research buildings but in clinical buildings every single day."

James P. DeLany, PhD

Senior Investigator

Joined: February 2018



James DeLany, PhD is a NIH-funded scientist with more than two decades of human obesity and diabetes research. Before arriving at the TRI, Dr. Delany served at Pennington Biomedical Center as an independent researcher and later, the Director of the Stable Isotope Laboratory. After 16 years with the Institute, he became a research associate with University of Pittsburgh – meeting both Dr. Steven R. Smith and Bret Goodpaster along the way. After being invited to join the TRI, Dr. DeLany realized the Orlando-based research center, to which his colleagues had migrated, offered a "vibrant environment" that would allow him to do more with his science.

Dr. DeLany has since brought the challenging "Dynamic PET Imaging" technique to the TRI. This technique provides a well-rounded picture of all phases and aspects of glucose uptake and has benefitted several studies within the TRI. This includes the MatPET study, examining the glucose uptake and the contribution of muscle and adipose tissue in African American women.

Strong preliminary data from this research shows that mitochondrial genetics may play a stronger role in these racial differences than nuclear

genetic ancestry. This joins his extensive past racial disparity research conducted at Pennington Biomedical Center to produce intervention methods, based on findings of lower mitochondrial function in African American women associated with lower insulin sensitivity.

Many aspects of DeLany's research involves extensive collaboration with others inside and outside of the TRI. In another NIH-funded project, partnered with Dr. Steven McGarvey of Brown University, Dr. Delany is employing doubly labeled water, indirect calorimetry, activity monitors and dual energy x-ray absorptiometry to examine energy balance and expenditure in Samoans after the recent identification of the CREBRF missense variant they possess, which is associated with increased obesity.

In the future, he looks to continue expanding his line of research through further progress in his racial disparity studies, considering not only glucose uptake in African American women, but also Hispanic women. He also looks to collaborate in multiple ancillary studies, including one for both the MoTrPAC and SOMMA studies.

Key Publication:

Integrative and quantitative bioenergetics: Design of a study to assess the impact of the gut microbiome on host energy balance

Featured in: Contemporary Clinical Trials Communication

Reference: Corbin KD, Krajmalnik-Brown R, Carnero EA, Bock C, Emerson R, Rittmann BE, Marcus AK, Davis T, Dirks B, Ilhan ZE, Champagne C, Smith SR. Integrative and quantitative bioenergetics: Design of a study to assess the impact of the gut microbiome on host energy balance. Contemporary Clinical Trials Communications. 2020. doi: 10.1016/j.conctc.2020.100646.

This publication describes the design of a study that used two diets as tools to reprogram the gut microbiota to quantify how gut microbial ecology, bioenergetics and metabolites influence host energy balance and ultimately body weight.

Key Publication:

Weight loss and exercise differentially affect insulin sensitivity, body composition, cardiorespiratory fitness and muscle strength in older adults with obesity; a randomized controlled trial

Featured in: American Journal of Physiology Endocrinology and Metabolism

Reference: Brennan AM, Standley, RA, Anthony SJ, Grench KE, Helbling NL, DeLany JP, Cornnell HH, Yi FC, Stefanovic-Racic M, Toledo FGS, Coen PM, Carnero EA, Goodpaster BH. Weight

Loss and Exercise Differentially Affect Insulin Sensitivity, Body Composition, Cardiorespiratory Fitness, and Muscle Strength in Older Adults With Obesity: A Randomized Controlled Trial. Journal of Gerontology Series A-Biological Sciences and Medical Sciences. 2021. doi: 10.1093/gerona/qlab240.

This randomized control trial demonstrated that the addition of exercise to a weight loss intervention elicits important benefits for older obese at-risk adults, many of which are not observed with calorie restriction–induced weight loss alone.

Melissa Erickson, PhD

Investigator

Joined: July 2021



Melissa Erickson, PhD is an up-and-coming researcher developing transdisciplinary studies that bridge the fields of exercise physiology, metabolic pathophysiology and chronobiology. With a PhD in Exercise Physiology from the University of Georgia and post-doctoral training at Cleveland Clinic and Pennington Biomedical Center that focused on obesity and metabolic disease, she is eager to use her knowledge as the Translational Research Institute's youngest Investigator.

While most of her current work resides in building the foundation and funding for her proposed studies, Dr. Erickson is curious about “generating new knowledge” on the relationship between circadian clocks, exercise and the skeletal muscular system. This includes understanding what happens to our bodies during shiftwork, like internal desynchrony – when the circadian clocks in the brain and muscles are out of sync with each other, which may promote illness or negative health consequences.

As she has studied this topic with pioneers, like Dr. Karyn Esser from University of Florida, Dr. Erickson believes this emerging field of work could transform our understanding of how our 24-hour modern lifestyles, characterized by living out-of-sync with our internal biological clocks, impact health. This

could also improve understanding of not only how circadian rhythm disruption is linked to the development of metabolic disease, but also how individuals can time their lifestyle to optimize physiological resilience.

Dr. Erickson cites the TRI's impressive body of work from our senior investigators, especially through the studies of Dr. Bret Goodpaster, in creating the ideal environment to further develop her future studies. She hopes to follow the trajectory of other TRI Investigators before her, like Dr. Lauren Sparks and Dr. Paul Coen, by “working and being supported by the best to achieve benchmarks” on novel research questions.

Alongside championing her future research, she is also involved in on-going AdventHealth studies, like WELL NURSE, led by Jeanette Green, PhD, APRN, which will investigate exercise training in shift-working nurses. This study has the potential to reveal new insight into exercise as a strategy to improve circadian physiology and improve health.

Dr. Erickson credits her scientific development to exceptional teachers and mentors throughout her career. As she cultivates her line of research, she hopes to inspire younger generations. She just received a notice of her first NIH grant award.

Stephen Gardell, PhD

Senior Investigator

Joined: May 2018



Stephen Gardell, PhD is a biomedical researcher trained in biochemistry, molecular biology and pharmacology.

Dr. Gardell received his PhD in Biochemistry from Cornell University and pursued post-doctoral training at the University of California, San Francisco. His career journey took him to the pharmaceutical industry and spanned 21 years at Merck, Bayer and Wyeth. In 2008, Dr. Gardell joined the Sanford Burnham Prebys Medical Research Institute at Lake Nona (SBP) as Associate Professor and Senior Director, Scientific Resources.

It was at SBP that Dr. Gardell was introduced to the TRI and Dr. Smith. Their complementary expertise and common research interests spurred the establishment of a rewarding research collaboration that continues today. When SBP ceased operations at Lake Nona in 2018, Dr. Gardell joined the TRI as a Senior Investigator. The Metabolomics Core that Dr. Gardell established at SBP migrated with him to the TRI.

Dr. Gardell's current research is focused on a molecule called NAD, which is a master regulator of metabolism. He is pursuing a novel drug strategy

to boost NAD synthesis in cells to promote healthy aging and combat a variety of diseases.

Metabolism is not a static process but is highly dynamic. It is an intricate web of chemical reactions in the cell. Some reactions are slow, others are fast. Dr. Gardell uses mass spectrometry and metabolite tracing with stable isotope derivatives of nutrients to unveil how the rates of various metabolic pathways are altered in different diseases, such as cancer, diabetes and sarcopenia.

Dr. Gardell's arrival at the TRI has enabled his long-standing objective to “translate his discoveries from the bench to the bedside.” He looks to continue his metabolism research through future grant support and nurturing fruitful collaborations with his TRI colleagues and beyond.

“The TRI's cutting-edge facilities and resources are second to none and offer promise for supporting a long, thriving research career. I am excited to work and interact with everyone here as we progress towards the common goal of improving lives.”

– Melissa Erickson, PhD
Investigator

Key Publication:

Boosting NAD⁺ with a small molecule NAMPT activator

Featured in: *Nature Communications*

Reference: Gardell SJ, Hopf M, Khan A, Dispagna M, Sessions EH, Falter R, Kapoor N, Brooks J, Culver J, Petucci C, Ma CT, Cohen SE, Tanaka J, Burgos ES, Hirschi JS, Smith SR, Sergienko E, Pinkerton AB. Boosting NAD(+) with a small molecule that activates NAMPT. *Nature Communications*. 2019. doi: 10.1038/s41467-019-11078-z.

We discovered novel chemical agents that activate an enzyme (NAMPT) which produces NAD, a master regulator of metabolism. These agents are promising drug candidates due to their ability to raise NAD in cells, thus reaping health benefits.

Bret Goodpaster, PhD

Scientific Director and Senior Investigator

Joined: September 2013



Bret Goodpaster, PhD is a scientist and triathlete who “walks the talk” of his science. He is keenly focused on discovering the biological origins of human aging, metabolic diseases including type 2 diabetes and obesity, and understanding the health-promoting effects of exercise. This interest was cultivated early on in Dr. Goodpaster’s life, through the competitiveness of youth, living healthy as a young adult and later watching his father undergo heart surgery at 39, after battling obesity and smoking.

With a post doctoral fellowship in Metabolism and a subsequent professorship with the University of Pittsburgh, Dr. Goodpaster became a pioneer in exercise and diabetes research, discovering the “Athlete’s Paradox”. This shifted a paradigm in the field to investigate how and why fat accumulation in muscle causes insulin resistance in some people but not others. He has written over 200 peer-reviewed papers, review articles and book chapters, and served on editorial boards for Diabetes, the American Journal of Physiology, the Journals of Gerontology and others.

Close to 10 years ago, Dr. Goodpaster was unsure about moving his science to Orlando, FL. This changed when he saw an interview with Lars

Houmann wearing a cycling outfit – identifying a common thread of interest and enthusiasm for understanding and living out healthy lifestyles.

Since joining the TRI in 2013, he has spearheaded one of the TRI’s biggest studies, MoTrPAC, as the principal investigator, along with support of several subsequent, related studies. One of these sister studies compares the effects of short-term aerobic vs. resistance training on skeletal muscle mitochondrial function in vivo in older adults. This entire thread of research has impacted the general knowledge of exercise and its effects and will continue to do so for several years to come.

Dr. Goodpaster was promoted to Scientific Director in 2020, taking over for the inaugural Scientific Director, Dr. Steven R. Smith, aiming to expand the TRI into fields of research beyond Metabolism and Diabetes. He looks to continue developing this “world-class clinical-translational research” into much more.

Brian Parkin, MD

Associate Investigator

Joined: September 2021



Brian Parkin, MD is a physician-scientist focused on early detection and prevention of relapsed acute myeloid leukemia and related cancers, particularly in the setting of bone marrow transplantation. Hailing from the Great Lakes region, he received his residency and post-doctoral fellowship in Internal Medicine and Hematology/Oncology respectively at the University of Michigan. With a desire to solve questions he saw in the hospital, he turned to the laboratory to discover more about translational genomics – understanding how DNA mutations and changes affect the outcomes of patients.

“As much as I love and value basic science, it’s that connection with patients that allows us to really ask and answer important questions,” he states. “It provides a priceless resource.”

Upon arriving at the TRI, Dr. Parkin has bolstered the institution’s translational oncology program developing studies that use a combination of ultra-high sensitivity mutation detection methods and cutting-edge single cell immunoproteogenomics. These are used to detect and characterize low-level residual leukemia that often lead to disease relapse. He is especially interested in understanding the mechanisms by which high-risk leukemias, with

TP53 gene mutations, resist chemotherapy and immune surveillance.

While Dr. Parkin is one of TRI’s newest investigators, he shares important plans with the institution.

Dr. Parkin has two primary goals, each focused on building the TRI’s translational oncology program and data pool. He is working in conjunction with the processing lab within the TRI to establish and cultivate a clinically annotated biorepository, collecting specimens from willing patients with acute leukemia or undergoing bone marrow transplants. This will provide a priceless opportunity to study a wide range of patients and understand why some responded to their treatments while others did not. This will aid in zeroing in on clearer medical answers and practices.

Additionally, he looks to further clinical trial development with academic and industry partners with a goal to build sound, correlative scientific aims into clinical trial protocols. This will ultimately provide higher quality, more efficient trials that build on past lessons learned and allow deeper analysis of the results of the trials in the laboratory.

Key Publication:

Metabolic Flexibility in Health and Disease
Featured in: *Cell Metabolism*

Reference: Goodpaster BH, Sparks LM. Metabolic Flexibility in Health and Disease. *Cell Metabolism*. 2017. doi: 10.1016/j.cmet.2017.04.015.

This review of metabolic flexibility highlights the broad concept to explain insulin resistance and mechanisms governing fuel selection between glucose and fatty acids, in particular in obesity and type 2 diabetes.

“We have 10 years of an outstanding foundation around diabetes and endocrine and metabolism programs that provide all the resources we need... but we also have a ground floor opportunity to build an oncology program on that foundation. We do not have to start from scratch, but we have the opportunity to start something new – and that’s very exciting.”

– Brian Parkin, MD
Associate Investigator

Richard Pratley, MD

Senior Investigator

Samuel E. Crockett Chair in Diabetes Research

Joined: April 2011



Richard Pratley, MD is a scientist and active clinician within the field of diabetes research and endocrine studies. He was the first investigator recruited by Dr. Smith over 10 years ago, appointed to oversee the diabetes program within the TRI. Dr. Pratley has since been integral to developing clinical trials and the lab-based approach to pancreas pathobiology at the institute.

With fellowships in geriatric medicine at the University of Michigan and John Hopkins University, Dr. Pratley furthered his career as the Director of the Diabetes and Metabolism Translational Medicine Unit at the University of Vermont. Familiar with Dr. Smith and his work in diabetes and metabolism research, a professional trip to Orlando turned into a recruitment opportunity for the TRI. Dr. Pratley was impressed not only by Dr. Smith's grand aspirations, but the commitment of the AdventHealth leadership behind him.

"There was a consistent story of 'we are committed to doing research. We're committed the fields of diabetes, obesity and metabolism. Not because it's going to make a lot of money, but because this is an important area'... I saw an opportunity to grow (with that commitment)."

Dr. Pratley has gone on to become part of the top 2% of published researchers in the world – with over 150 of his publications being published while with the TRI. He has also bolstered the TRI's type 1 diabetes program, working with the AdventHealth Foundation to raise funds for the von Weller Family Chair in Type 1 Diabetes Research Foundation.

Within type 2 diabetes research, Dr. Pratley continues to cultivate a program focused on understanding the role of circulating miRNAs and extracellular vesicles in inter-organ (pancreas, adipose tissue and muscle) signaling and as biomarkers of disease pathobiology – with help from a Miller Foundation grant.

He also serves as a Co-PI for the WISDM trial, a multicenter trial of CGM in over 200 older individuals with type 1 diabetes. The goal is to determine if the use of continuous glucose monitoring (CGM) can reduce hypoglycemia among older adults with type 1 diabetes, which could result in important public health implications in the future.

Lauren Sparks, PhD

Associate Investigator

Joined: August 2012



Lauren Sparks, PhD is a researcher that specializes on the impact of adipose tissue quality – rather than quantity – on whole body metabolism in the contexts of aging, obesity and exercise. Receiving her PhD and post doctoral fellowship with Pennington Biomedical Research Center at Louisiana State University, Dr. Sparks first met Dr. Smith as a PhD advisor. This mentorship greatly impacted her work and would later bring her to tour and consider the TRI, which she recalled as “a phenomenal visit and ridiculously impressive”. After serving a post-doctoral tenure with Maastricht University in the Netherlands, Sparks joined the TRI as an investigator in 2012.

She vividly remembers early moments of growth, like learning how to write her first grant as an Investigator through collaboration with Dr. Smith. Upon officially receiving the American Diabetes Association Junior Faculty Award, Dr. Sparks ecstatically ran to Dr. Smith's office to celebrate the victory.

She has gone on to help the TRI grow by receiving the funding to purchase an instrument of single cell work, called iCell8, which permits the interrogation of the transcriptomes of individual

cells from any tissue in the body. This has enabled investigators to look at the impacts of aging, obesity, hyperinsulinemia and exercise training on individual populations of cells from adipose tissue and the skeletal muscle – positioning the TRI at the forefront of molecular research today.

Through one of her R01 grant projects, a longitudinal, ancillary study to SOMMA, she is assessing the impact of aging on the development of mobility disability in over 800 older adults, through deep phenotyping of the skeletal muscle. She looks to uncover a clearer understanding of how adipose tissue quality affects muscle quality and physical function – a topic which is generally unknown at this time.

Beyond her scientific endeavors, Dr. Sparks looks to train and mentor budding scientists to find their own independent career trajectories, as she was mentored by those before her. The skills she has cultivated throughout her career have called her to lead the TRI and its scientists into the future.

Key Publication:

Effect of Continuous Glucose Monitoring on Hypoglycemia in Older Adults with Type 1 Diabetes: A Randomized Clinical Trial

Featured in: JAMA

Reference: Pratley RE, Kanapka LG, Rickels MR, Ahmann A, Aleppo G, Beck R, Bhargava A, Bode BW, Carlson A, Chaytor NS, Fox DS, Goland R, Hirsch IB, Kruger D, Kudva YC, Levy C, McGill JB, Peters A, Philipson L, Phillis-Tsimikas A, Pop-Busui R, Shah VN, Thompson M, Vendrame F, Verdejo A, Weinstock RS, Young L, Miller KM. Effect of Continuous Glucose Monitoring on Hypoglycemia in Older Adults With Type 1 Diabetes: A Randomized Clinical Trial. JAMA. 2020. doi: 10.1001/jama.2020.6928.

This randomized clinical trial demonstrated that continuous glucose monitoring was effective at reducing hypoglycemia, as well as improving overall glucose control, compared with standard blood glucose monitoring in older adults with type 1 diabetes.

Key Publication:

Exercise Response Variations in Skeletal Muscle PCr Recovery Rate and Insulin Sensitivity Relate to Muscle Epigenomic Profiles in Individuals with Type 2 Diabetes

Featured in: Diabetes Care

Reference: Stephens NA, Brouwers B, Eroshkin AM, Yi F, Cornnell HH, Meyer C, Goodpaster BH, Pratley RE, Smith SR, Sparks LM. Exercise Response Variations in Skeletal Muscle PCr Recovery Rate and Insulin Sensitivity Relate to Muscle Epigenomic Profiles in Individuals With Type 2 Diabetes. Diabetes Care. 2018. doi: 10.2337/dc18-0296.

Some individuals with type 2 diabetes do not reap metabolic benefits from exercise training, yet the underlying mechanisms of training response variation are largely unexplored. We classified individuals with type 2 diabetes (n = 17) as nonresponders (n = 6) or responders (n = 11) based on changes in phosphocreatine (PCr) recovery rate after 10 weeks of aerobic training. We aimed to determine whether the training response variation in PCr recovery rate was marked by distinct epigenomic profiles in muscle prior to training.

Tina Thethi, MD, MPH

Associate Investigator
Joined: July 2019



Tina Thethi, MD, MPH is a practicing endocrinologist and researcher who focuses her studies on the complications associated with obesity and type 2 diabetes, with a specific interest in kidney disease. Recently, she has been focusing on why certain subgroups of patients with and without type 2 diabetes are more susceptible to developing kidney disease.

Dr. Thethi completed her Master of Public Health after finishing her fellowship in Endocrinology and Metabolism at Tulane University. She enjoyed over a decade of medical teaching. She also led the endocrine section at the Southeast Louisiana Veterans Healthcare System as the section chief. Looking to further cultivate her research in kidney disease, she joined the TRI, where she appreciated not only the collaborative science, but the culture of the institution as well.

While her work is to extend the understanding of root causes and early detection of kidney disease, she also believes in the need to study the effects and causes beyond the physical body, relating to the values of whole-person care. Dr. Thethi believes in the TRI's spirit of authenticity and connection, which aligns with her own values. The memories she values most from the institute are that of the

comradery that have contributed to her growth professionally and personally.

"This isn't about a building or project," said Thethi. "It's' about a collective journey." She continues to champion the connective environment that comprises the TRI, which branches from her whole-person approach to research and discovery. "Without connection, you do not have cohesiveness. One must be able to bring people together. You bring people together with energy. "

Dr. Thethi continues her work to understand the heterogeneity seen in kidney disease. In parallel, while in clinic, she also strives to understand the psychological aspects of a patient's life and how their emotional wellbeing and spirituality affects their health. Her goal is to integrate the teaching of spirituality into the practice of medicine. She hopes to study the impact of practicing mindfulness and meditation on disease outcomes. "We are so caught up in the what, instead of the who," she says "(but) who are you? You are the soul."

Past & Current Post-Doctoral Fellows

- Bram Brouwers, PhD
- Elvis Carnero, PhD
- Giovanna Distefano, PhD
- Adeline Divoux, PhD
- Gabiella Garufi, PhD
- Mathew Hinkley, PhD
- Daria Igudesman, PhD
- Zuzana Kovacova, PhD
- Meenu Madan, PhD
- Stephanie Marshall, PhD

- John Noone, PhD
- Yury Nunez-Lopez, PhD
- Maria Pino, PhD
- Sofhia Ramos, PhD
- Robert Standley, PhD
- Natalie Stephens, PhD
- Katie Whytock, PhD
- Tracey Woodlief, PhD
- Reichelle Yeo, PhD
- Xiaolie Zhang, PhD

Past Faculty

- Christian Meyer, MD**
Global Director of Scientific Affairs, Diabetes & Metabolism, Merck
- George Kyriazis, MD**
Associate Professor, Biological Chemistry
Ohio State University

- Magdalena Pasarica, MD**
Professor of Medicine
University of Central Florida

"Being at TRI has brought opportunities to work with other investigators. This has helped me in growing my own research ideas. Undergoing these processes during a pandemic has given a whole new meaning to the understanding of collective energy which has propelled my thinking as a researcher. The moments of joy and laughter over small, but meaningful victories achieved as a team, and the display of camaraderie in the past more than two years are my favorite memories."

– Tina Thethi, MD, MPH
Associate Investigator

"My time at the TRI helped me grow as an independent scientist. At TRI, I became more experienced in identifying gaps in scientific knowledge, formulating critical scientific questions and identify opportunities on how to answer those questions. I also started to be exposed to collaborations with industry partners."

- Bram Brouwers, PhD

"I feel fortunate to have joined TRI during its early days. The atmosphere was full of energy, excitement and optimism. There were many things to figure out, as expected from a newly established research center, but there was a clear vision. This was very motivating for everyone who worked together to make TRI nationally recognized."

- George Kyriazis, MD



Spotlight Studies



"The measure of greatness in a scientific idea is the extent to which it stimulates thought and opens up new lines of research."

- Paul Dirac
Renowned scientist, developer of the quantum field theory and other quantum mechanic theories

D2d

Richard Pratley, MD - Senior Investigator

Diabetes is the seventh-leading cause of death in the United States, responsible for over 80,000 deaths in 2015, according to the Centers for Disease Control and Prevention. While observational studies indicated a connection between higher vitamin D levels and reduction of type 2 diabetes risk, whether supplementation with vitamin D would prevent diabetes in people who were not selected to be deficient was unknown.

The **Vitamin D in Type 2 Diabetes (D2d)** study was an NIH funded, multi-center trial (including the AdventHealth Translational Research Institute), which tested whether taking vitamin D could lower the risk of diabetes in people with a high risk. Over 2,400 adults with pre-diabetes were enrolled and randomized to either 4,000 units of vitamin D per day or a placebo and received blood tests twice per year for an average of two-and-a-half years to monitor for the development of diabetes. Vitamin D supplementation did not significantly reduce the likelihood of developing type 2 diabetes in people with pre-diabetes, who already had normal vitamin D levels. However, among those with pre-diabetes, who had very low vitamin D levels when they joined the study, a reduced risk of developing the diabetes after vitamin D supplementation was observed. Overall, vitamin D supplementation at the doses used in the study was safe and well-tolerated.

DREAM

Anna Casu, MD - Associate Investigator

The body's insulin-producing cells are dispersed throughout the pancreas, a large gland that produces digestive enzymes. This gland can become inflamed during episodes of acute pancreatitis, impairing the function of all pancreatic cells, including those producing insulin. Diabetes mellitus, in and after acute pancreatitis, was historically thought to be a transient phenomenon due to acute

inflammation. However, it is increasingly recognized as one of its late and permanent complications, occurring in as many as 20% of the people who experience acute pancreatitis. This form of diabetes often requires insulin for treatment, resembling type 1 diabetes, but the actual incidence rate of diabetes mellitus following acute pancreatitis and the underlying mechanisms causing it are not known.

To address these knowledge gaps, the NIH has assembled a consortium of ten clinical centers across the United States. This consortium, called the Type 1 Diabetes and Acute Pancreatitis consortium (T1DAPC), is made up of experts in diabetes, immunology, pancreatitis and imaging. This team will leverage their collective, multi-disciplinary scientific expertise to perform metabolic studies in patients following a bout of acute pancreatitis. The **Diabetes RElated to Acute pancreatitis and its Mechanisms (DREAM)** study will build a cohort of 1,000 people who have had at least one episode of acute pancreatitis to answer the above-mentioned questions on diabetes in acute pancreatitis. It is hoped that these studies will lead to an improved understanding of the phenomenon and might eventually lead to new ways to prevent and treat the disease. The AdventHealth Translational Research Institute partners with the University of Florida as one of these centers in the T1DAPC.

MAC

Steven R. Smith, MD - Chief Scientific Officer
Karen Corbin, PhD, RD - Investigator

Bacteria in the gut (the gut microbiome) impact how efficiently we extract energy (calories) from food, the effectiveness of some medications and multiple other aspects of human health. No prior studies have quantified the impact of the gut microbiome on energy balance in humans. Integrating Quantitative Energetics Determines the **Microbiome's Contribution to Energy Balance (MAC)** addresses this important knowledge gap. TRI researchers, in collaboration with Arizona

State University, completed a study whose primary objective was to determine differences in energy balance after consuming a Western Diet (control) versus a Microbiome Enhancer Diet intervention intended to optimize the gut microbiome for positive impacts on host energy balance. Our entire understanding of the calorie content of foods does not currently account for how the gut microbiome impacts energy absorption and utilization by the human host. Therefore, the results of this work will help redefine our understanding of the impact of diet on weight regulation and overall health.

MATPET

James P. DeLany, PhD – Senior Investigator

The prevalence of type 2 diabetes is nearly two-fold higher in African American women compared to Caucasian women, but reasons for this racial difference are not understood. Lower insulin sensitivity, a major risk factor for development of diabetes, is reported in African American Women. In our previous work, we demonstrated lower insulin sensitivity in lean, young African American women that was due exclusively to lower peripheral glucose uptake, with normal liver insulin sensitivity.

The application of PET/MRI imaging allows us to explore the specific metabolic steps that are altered and the contribution of adipose tissue and skeletal muscle underlying the lower peripheral glucose uptake in African American women. We have completed imaging studies in six African American and 10 Caucasian women, and we recently received additional funding to explore these mechanisms in Hispanic women, who also have a higher prevalence of type 2 diabetes. Our findings will provide insights into therapeutics that target mechanisms underlying lower peripheral glucose uptake specific to African American and Hispanic women, which may be implemented to decrease obesity-related insulin resistance and diabetes.

RESIST

Lauren Sparks, PhD - Associate Investigator

By 2050 the number of people with diagnosed diabetes in the United States will reach 29 million. Type 2 diabetes (T2D) is typified by aberrations in insulin sensitivity and skeletal muscle metabolism. Considering group averages, exercise training restores skeletal muscle metabolism and insulin sensitivity in individuals with T2D to levels observed in healthy individuals. However, as much as 20% of individuals with T2D do not respond favorably to exercise training in terms of glycemic control and skeletal muscle metabolism. Conclusions about the beneficial effects of exercise are too often drawn based on average responses, and how exercise may benefit people with T2D is unclear. Moreover, little is known about those individuals who do not respond favorably to exercise. The RESIST study was a 3-year clinical study in individuals with T2D funded by the American Diabetes Association to address some of these gaps. We found that this “exercise non-response” in vivo in insulin sensitivity and muscle metabolism can be distinguished in these individuals by muscle molecular profiles prior to starting the exercise intervention. The long-term goal is to provide targets for ways to prevent and reverse these barriers to exercise success and shift the diabetes treatment paradigm, targeting exercise interventions to those most likely to benefit and identifying novel, even non-exercise, approaches to treat those who do not.

MODIFY

Karen Corbin, PhD, RD - Investigator

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disorder in western societies and is on a trajectory for becoming the top indication for liver transplantation. The gut microbiome is a central modulator of multiple host and environmental influencers of liver physiology that could represent a unifying mechanism in NAFLD and related comorbidities.

A Case-Control, Observational, Proof of Mechanism Study to Define Microbiome-Mediated Gut Dysfunction Across the Spectrum of Non-Alcoholic Fatty Liver Disease (MODIFY) is the first human study to evaluate microbiome mechanisms directly in the gut lining by measuring the encroachment of microbes into the normally sterile inner mucus layer. Our study will address critical shortcomings in our current mechanistic understanding of how the microbiome modulates liver physiology.

MoTrPAC

Bret Goodpaster, PhD - Scientific Director and Senior Investigator

Despite decades of research establishing the benefits of exercise to our overall health, we still don’t know precisely what happens deep within the body at a molecular level during and after we exercise. These questions led the Translational Research Institute (TRI) to partner with the National Institutes of Health’s (NIH) **Molecular Transducers of Physical Activity Consortium (MoTrPAC)** six-year research study. Our hypothesis is that there are discoverable molecular transducers that communicate and coordinate the impact of exercise on specific cells, tissues and organs within the body. Identifying and characterizing these specific molecular transducers will help us to better understand how exercise improves health and prevents disease.

The TRI is one of 10 clinical sites across the country that will collect an extensive amount of data using blood and tissue samples from the participants before and after each exercise session, as well as data on fitness, strength and body composition. This extensive research will allow us to better understand the specific factors that influence someone’s response to exercise. Ultimately, we want to be able to take a precision medicine approach — to prescribe and customize the type and amount of exercise to each individual, in order to achieve the best possible health outcome.

NADflux

Stephen Gardell, PhD - Senior Investigator

Nicotinamide adenine dinucleotide (NAD) is a vitally important chemical substance that plays many roles in all cells. Elevated levels of NAD are associated with healthy aging whereas low levels of NAD are linked to a wide variety of diseases. NAD is constantly synthesized and broken down in cells. Determining the rates of NAD synthesis and consumption is crucial to better understand why NAD levels vary in cells. **In Measurement of NAD+ Synthesis in Human Skeletal Muscle**, this is accomplished by metabolite tracing experiments with human volunteers that receive intravenous deuterated nicotinamide (i.e., “heavy” nicotinamide or D4-NAM). D4-NAM is a precursor for NAD in cells that gives rise to “heavy” NAD. Mass spectrometry allows us to discriminate the newly formed NAD (“heavy” NAD) from unlabeled NAD that already existed in the cell. The extent to which “heavy” NAD is enriched in the total NAD pool reveals the NAD biosynthetic flux. Consumption of “heavy” NAD by another set of cell enzymes yields a different “heavy” nicotinamide species (D3-NAM) that can be discriminated from the D4-NAM administered to human volunteers. Hence, the appearance of D3-NAM reveals the NAD consumptive flux.

Why is this important? It is the changes in the rates of NAD synthesis and consumption that are the likely contributors to disease. We will evaluate the impact of acute exercise, aging and other experimental variables on the rates of NAD synthesis and consumption in human subjects. Knowing if NAD synthesis or consumption is abnormal in a particular disease or with aging will focus our attention on the best way to normalize the NAD level in cells and, in turn, improve human health.

10 Year Team Members

"The important thing in science is not so much to obtain new facts, as to discover new ways of thinking about them."

- William Lawrence Bragg, Nobel Prize in Physics recipient (1915) and discoverer of Bragg's law of X-Ray diffraction



PIONEER 4

Richard Pratley, MD - Senior Investigator

The glucagon-like peptide-1 (GLP-1) receptor agonists are highly effective treatments for type 2 diabetes and are associated with significant weight loss. Most are given by subcutaneous injection, which limits utilization for many patients and providers. **A Study Investigating the Efficacy and Safety of Oral Semaglutide versus Liraglutide and versus Placebo in Subjects with Type 2 Diabetes Mellitus (PIONEER 4)**, was a phase 3 clinical trial that compared the effects of the first oral GLP-1 (semaglutide) and an established, once daily, injected GLP-1 (liraglutide). Oral semaglutide was similar to subcutaneous liraglutide in decreasing HbA1c, a measure of blood sugar control, and superior in decreasing body weight. This study is significant, because it demonstrated, for the first time, that oral administration of a GLP-1 receptor agonists produced benefits equivalent to or superior to injection. This could potentially shift the treatment paradigm and lead to earlier initiation of GLP-1 receptor agonist therapy among patients with type 2 diabetes.

REST

Paul M. Coen, PhD - Associate Investigator

Skeletal muscle atrophy occurs during hospitalization or immobilization due to illness and injury and leads to a loss of muscle strength and physical function. The presence of type 2 diabetes (T2D) may exacerbate this health issue, which represents an enormous public health problem. In **The Role of type 2 diabetes on skeletal muscle atrophy and recovery following bed rest in older adults (REST)**, the objective of this NIA supported R01 is to decipher the mechanisms by which mitochondrial energetics and muscle lipids underlie early muscle catabolic responses to immobilization. Through innovative time course studies and measurements in serial human muscle biopsies conducted at the TRI, and through collaborations with experts in lipidomics (Dr. Michael Kiebish, BERG) and proteomics (Dr. Ben Miller, Oklahoma

Medical Research Foundation), we will place the etiology of muscle atrophy firmly in the context of mitochondrial biology and will contribute to a better precision medicine approach to prevent and treat disuse atrophy of muscle.

SOUL

Tina Thethi, MD, MPH - Associate Investigator

Backed by the North American National Leader Panel, the **Semaglutide cardiovascular outcomes trial in patients with type 2 diabetes (SOUL)** study utilizes the TRI as one of its research sites. SOUL is a randomized, double-blind, multi-center, international trial of more than 9,000 subjects sponsored by Novo Nordisk to evaluate whether oral semaglutide, in comparison to placebo added to standard of care lowers the risk of cardiovascular events in patients with type 2 diabetes, who are at high risk for cardiovascular disease. Given that oral semaglutide, Rybelsus, is the first oral glucagon like receptor-1 receptor agonist (GLP1-RA), SOUL is a pivotal trial in its field.

WELL NURSE

Melissa Erickson, PhD - Investigator

Shiftwork requires one to be awake and active at times that are out of sync with our internal circadian clocks, and this may challenge our physiology in ways that promote weight gain and type 2 diabetes risk. However, our fundamental understanding of how shiftwork impacts our metabolic health is only in its infancy, as most research-to-date is derived from animal models or epidemiology. A new study at AdventHealth aims to find answers to these questions by studying how our body's metabolism is impacted during nightshift work. Investigators will also test if regular exercise improves our biological resilience to shiftwork by impacting our internal circadian clocks.



Tavis Cross

Manager, Clinical Research Unit
Joined: August 2012

Tavis Cross is a SOCRA-Certified Research Professional and U.S. Army veteran with over 20 years of health care experience. His manager, and later mentor, urged him to continue pursuing higher education and worked with him to find the right role within the institution at the time – a Clinical Research Assistant on the night shift. The friendships and working relationships that have grown over the years have made his career journey even sweeter, with the traditions and team-building events that are at the forefront of the TRI culture.



Heather Cornell, PhD

Senior Research Scientist, Imaging
Joined: September 2011

Heather Cornell, PhD is a proven imaging scientist who has “grown up” as a researcher alongside the Translational Research Institute. Since joining the TRI, she has developed and optimized the MRI, DEXA and Fibroscan acquisition and quality procedures through her leadership of the Imaging CORE. Dr. Cornell points to TRI personnel as not only a key factor in her growth, but also a strength that sets the Institute apart. The team-based atmosphere has fostered the perfect learning environment amid challenges, promoting creativity and teamwork.



Parvin Guevara

Research Assistant II
Joined: April 2011

Parvin Guevara is a Research Laboratory Assistant with over 20 years of experience in the field. Parvin has enjoyed watching the TRI's growth and the subsequent new studies they have taken on – which have expanded their fields of expertise by leaps and bounds. This has not only grown her skillset within the Lab, but also the comradery she shares with other team members within the Research Lab.

10 Year Team Members



Cherie Shook

Research Associate, Imaging
Joined: January 2012

Cherie Shook is an imaging technician certified in radiology, CT, and MRI scanning, with over 30 years of experience in the field. She joined the team after developing a strong working relationship with Heather Cornnell, PhD, assisting with the magnetic imaging equipment. The synergy between Shook and Cornnell has defined the Imaging CORE’s abilities over the years. Each is able to see data from a different perspective, which creates a well-rounded collaboration – something Shook notes as a defining characteristic of the TRI.



Josh Smith

Research Laboratory Senior Manager
Joined: June 2011

Intrigued by the “bench to bedside” premise of the TRI, Josh Smith came to the Institute and has risen to the a leadership role for a skilled, 18-member team, “moving at the speed of science.” Alongside being a key contributor to the design and oversight of the 2nd floor Research Lab and 3rd floor Research Oncology and Precision Medicine Labs, Smith was integral to the development of the TRI biorepository. Throughout his time at the TRI, Smith has seen and experienced the Institute’s culture of professional growth and collaboration.



Fanchao Yi, PhD

Senior Data Scientist, Biostatistics
Joined: September 2011

Fanchao Yi, PhD is a biostatistician who has assisted in research at the TRI by providing statistical support for translational research studies over the past 10 years. Through his role, he has served investigators “like a sidekick” throughout all stages of the scientific research process, including experiment design, randomization process, data collection and cleaning, modeling and publication. He believes the strong teamwork and collaboration aspect sets the Institute apart from the rest.

10 Year Team Members



Adeline Divoux, PhD

Independent Scientist, Imaging
Joined: January 2012

Adeline Divoux, PhD is a French researcher specializing in work with bariatric surgery specimens and human adipose tissue to aid understanding of obesity complications. She was referred to Dr. Smith and the TRI by a friend and was subsequently impressed by the budding team’s culture and by Dr. Smith’s warmth, reputation, and vision. Today, seeing TRI as a “leading institute for clinical research”, Divoux looks to continue mentoring young investigators and post-docs within the institute.



Rebecca Zuvich Essner, PhD

Senior Research Scientist, Genomics
Joined: September 2011

Rebecca Zuvich Essner, PhD is a senior researcher studying genomics, population health and implementation science through AdventHealth Genomics and Personalized Health. Starting at the TRI as a post-doctorial scientist, she most fondly remembers how quickly she gained “a sense of belonging” as a new hire due to the warmth and openness of her fellow team members.



Michelle Estee

Regulatory Specialist I
Joined: May 2012

Michelle Estee is one of the several professionals who believe they have truly “grown up” at the TRI through countless memories, experiences and challenges. Originally drawn to AdventHealth’s values, Estee joined the TRI and gleaned a first-hand look at real-time clinical research complemented by an academic-based environment. From day one, she could sense the team’s energy, warmth and “family-like” atmosphere. which was supported by countless fun memories and team-building events.

Faculty Academic Collaborations In The US

The map displays 25 yellow location pins across the United States, representing faculty academic collaborations. The pins are distributed as follows: 3 in the West (California, Washington, Oregon), 1 in the Mountain West region (New Mexico), 1 in the Great Plains (Nebraska), 1 in the Midwest (Illinois), 2 in the Great Lakes (Michigan, Indiana), 1 in the Northeast (New York), 4 in the Mid-Atlantic (Pennsylvania, Maryland, Delaware, Virginia), 1 in the Southeast (Alabama), 1 in the South (Texas), 1 in the Gulf Coast (Louisiana), 1 in the Southeast (Georgia), 1 in the South (Florida), and 3 in the Northeast (New Jersey, Connecticut, New York).

Academic Collaborations

- Arizona State University – **Tempe, AZ**
- Ball State University – **Muncie, IN**
- Brown University – **Providence, RI**
- California Pacific Medical Center – **San Francisco, CA**
- Childrens Hospital of Philadelphia – **Philidephia, PA**
- Columbia University – **New York City, NY**
- Duke University – **Durham, NC**
- Henry Ford Health System – **Detriot, MI**
- Moffitt Cancer Centers – **Tampa, FL**
- Mount Sinai Hospital – **New York City, NY**
- Oregon Health & Science University – **Portland, OR**
- Pacific Northwest National Laboratory –**Richland, WA**
- Pennington Biomedical Research Center – **Baton Rouge, LA**
- Pennsylvania State University – **University Park, PA**
- St. Luke's Roosevelt Institute for Health Sciences – **Chesterfield, MO**
- Sanford-Burnham Medical Research Institute, Inc. – **La Jolla, CA**
- The Ohio State University Medical Center – **Columbus, OH**
- Tufts University – **Sommerville, MA**
- University of Alabama, Birmingham – **Birmingham, AL**
- University of Chicago – **Chicago, IL**
- University of Colorado – **Denver, CO**
- University of Florida – **Gainesville, FL**
- University of Iowa – **Iowa City, IA**
- University of Michigan – **Ann Arbor, MI**
- University of North Carolina – **Chapel Hill, NC**
- University of Pittsburgh – **Pittsburgh, PA**
- University of South Alabama – **Mobile, AL**
- University of South Florida – **Tampa, FL**
- University of Texas / MD Anderson – **Austin, TX**
- University of Texas Health Science Center, San Antonio – **San Antonio, TX**
- Wake Forest University – **Winston Salem, NC**
- Yale University – **New Haven, CT**

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Arizona State University – **Tempe, AZ**
Ball State University – **Muncie, IN**
Brown University – **Providence, RI**
California Pacific Medical Center – **San Francisco, CA**
Childrens Hospital of Philadelphia – **Philidephia, PA**
Columbia University – **New York City, NY**
Duke University – **Durham, NC**
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University of South Florida – **Tampa, FL**
University of Texas / MD Anderson – **Austin, TX**
University of Texas Health Science Center, San Antonio –
San Antonio, TX
Wake Forest University – **Winston Salem, NC**
Yale University – **New Haven, CT**

Influential Leadership



Randy Haffner, PhD
Senior Executive Vice President and CEO, Central Florida Division

As one of the key leaders within the AdventHealth system, Randy Haffner believes in the importance of learning as an organization through research. This insight should be demonstrated through the lives of the people that are able to access care that otherwise would not be available to them. He is proud of the past decade of discovery and looks forward to the future, where he hopes to see the TRI and AHRI bolster their partnerships and take their research to new heights.

“The TRI was this idea of how do we narrow the distance between the researcher and the bedside...in the 32 years that I've been here, the approach that we take relative to specific disease status is remarkably different. It's because of the advancements in technology and the advancements in understanding.”



Lars Houmann
Retired, AdventHealth Corporate Chief Operating Officer

Lars Houmann was a lead force in ensuring the TRI was created and led by a visionary who would transform the endeavor. He firmly believed it was the organization's “duty” to get involved in research – elevating AdventHealth into the level of an academic medical center that focuses on high quality service and safety. The TRI was designed to advance our academic standing, improve patient care and drive economic development in central Florida. Houmann was also set on hiring Dr. Smith as the TRI's lead, flying to Texas to discuss it personally with him and seal the deal.

“The TRI represents a commitment to something greater than ourselves. We're doing it not because we'll make more money, but because we'll improve patient care and clinical outcomes. It's our duty to advance care.... I am proud of Steve Smith, and the legacy of the TRI, and how much that has influenced people to be disciplined, to think, to organize and articulate. I'm so proud of what it has become.”
(Chief Executive Officer, Florida Hospital, Central Florida Division)



David Moorhead, MD
Executive Vice President and Chief Clinical Officer

David Moorhead, MD played a key role as AdventHealth's Chief Clinical Officer during the development of the TRI, which at first served as a joint venture with the incoming Sanford Burnham Medical campus in Medical City. The TRI stood as the catalyst to streamlining fundamental oversight of research at AdventHealth. Moorhead ultimately points to the TRI's leader, Dr. Smith as the “driver” who clarified the vision of what the TRI could become.

“We never had the aspiration to be a basic science institution. We felt we had huge opportunities to do clinical research. With Steven's help, it morphed from potentially ad hoc clinical research that had the interest of particular clinicians to a commitment that the research needed to have substantive transformational implications.” (Chief Clinical Officer)



Rob Deininger
CEO, AdventHealth Orlando

Rob Deininger remembers how detailed and involved AdventHealth's senior leadership was in moving the TRI from a concept to reality. As the Vice President of Research Operations for AdventHealth Orlando, engagement reflected how important research was to be “front and center” within the organization. Even today, he is still just as invested in the TRI's success and its future.

“The level of care that is delivered as a result of research being a part of clinical care is clearly a differentiator. We are getting better in everything from registries to retrospective studies. Our patients get better care today than 10 years ago, in part because of the research infrastructure that's been built and the commitment to quality that drives the TRI.” (Vice President, Research Operations)



Donna Lamb
President and Chief Executive Officer, National Resident Matching Program

Donna Lamb remembers how the inception of the TRI “felt trailblazing”. After a couple of attempts to initiate cancer research, the organization leaned into the idea of a metabolism focus. This eventually evolved into discussing translational research. They sought to answer the question: “What can we do differently using new strategies in research that will make a difference in the world and offer a lasting impact? The TRI was the result.”

“It was pretty exciting at the time. There was nothing like it in Orlando. It was a true collaboration that would allow us to create competency within the AdventHealth system that not only did it not have, but it never even dreamed of having. It was an effort to be forward thinking and look at chronic diseases of the community and figure out how we can do things differently.” (Founding Director of the Translational Research Institute)



Terry Owen
Consultant, AdventHealth Leadership Institute

Terry Owen recalls AdventHealth leadership narrowing the field down to Dr. Smith as the first-pick leader to bring about the vision of the TRI. Passionate about bringing research to the then Florida Hospital, he believed this endeavor had the potential to elevate the enterprise to new heights, all while paying respect to the Adventist legacy in health care.

Owen believes the legacy of the TRI will continue to improve patient care, lead to better treatment algorithms and strengthen pathways in both business and health care.

“If we were going to get to the next level of care for AdventHealth Orlando, we knew we needed to get into the research component to attract the best clinicians, thought leaders and team members... to look at the horizon to new learning...” (Senior Executive Officer)



Brian Paradis
CEO, C-suite Growth Advisors

Brian Paradis recalls how important research was to AdventHealth's growth strategy to generate “local-level” impact and enhance AdventHealth's credibility as an aspiring health care system. The TRI was the beginning of a continuous journey to become a learning health care system. Paradis sees that the Institute has not only influenced health care through its scientific work, but also redefined the culture of the organization “to think different and ask different questions.”

“There was something about the notion of translational research...it wasn't just research for curiosity's sake but had intentionality about affecting people and health care... It was the missing piece of a larger vision – a space that was different, new and less encumbered to accomplish things.” (Chief Operating Officer, Florida Hospital, Central Florida Division)

AdventHealth Research Institute Leadership



Rob Herzog
Vice President of Research Operations

Rob Herzog has overseen all branches of the institute’s research departments and core support services since 2014. During that time, he has seen first-hand how impactful the TRI has been in advancing AdventHealth as an organization, and enhancing their service of care. TRI’s roots have since produced groundbreaking research infrastructure and resources in other areas of health research, like neuroscience and oncology.

Looking forward to AdventHealth’s vision for 2030, research is key to becoming an influential brand founded on quality, safety, and unparalleled compassion delivered to patients.

“The “T” in TRI could just as easily be transformational. Not only has the TRI brought about powerful new scientific knowledge, it has served to teach our organization and our community what is possible when leading scientific minds have access to great technology and great clinicians delivering world-class care.

It is this combination of exceptional whole-person care and globally recognized research that will cause others to look at AdventHealth as the model for how healthcare is being transformed.”



Valerie Landrio McDevitt, JD
Executive Director, Research Services

Valerie Landrio McDevitt, JD brings almost 20 years of academic research administration experience to her role directing the Research Services department – a centralized team that supports all the administrative aspects of grants, human subject’s research, and technology transfer. Even before joining AdventHealth, she was aware of the TRI and its national reputation.

“The TRI stands out as unique,” said McDevitt. “... it would be difficult to successfully build anything like it in an academic environment. The specialized facility alone provides scientific and clinical research opportunities that few other academic research centers, much less hospital systems, can explore. AdventHealth has just the right combination of leadership, top tier researchers, and facilities to continue its upward trajectory- positively impacting our patients and advancing scientific knowledge in key areas effecting Floridians.”



Christopher Davis, PhD
Executive Director, Research Operations

Chris Davis, PhD has illustrated how the benefit of first-hand scientific experience transforms the leadership and outcomes of research operations. Before rising to a leadership role, he first came to the TRI as a Research Scientist in 2012, drawn to institute by Dr. Smith’s clear vision of translational research using human subjects – compared to rat models he experienced through work in the pharmaceutical industry.

He was impressed by TRI’s “wide-eyed” culture, where team members were eager to cultivate an initiative bigger than themselves, believing “anything was possible” to achieve. Since then, with Davis’ “empirical approach” to operations oversight, the Institute has continued to build the infrastructure needed to collect, analyze and learn about their research performance. This ultimately continues to drive TRI’s success, and subsequently AHRI as a whole – leading to better health research data and outcomes.

“As scientists, we don’t know enough, ..and a building like TRI gives you the environment and opportunity to explore... With the commitment to cutting edge translational research, its track record of success in academics and extramural funding, the TRI continues to demonstrate what is possible.”



Shauni Dusan
Executive Director, Health Outcomes Research

Shauni Dusan is the newest member of the AHRI leadership team, overseeing and developing streamlined access and portfolio diversity for research data analytics and metrics across the entire AdventHealth system. She believes the impact of the TRI has launched the AdventHealth system into something bigger than just a system of hospitals. Through their bench to bedside research, AdventHealth is becoming a learning health care system capable of great things to come.

She is particularly interested in how the TRI will generate outcomes research for real-time performance improvement within hospitals. Their model of translational research will continue to accelerate implementation and enhanced care within AdventHealth in the future.

“It’s important to push the envelope in patient care nationally, so we’re not just treating patients based on current protocol,” Dusan said. “Our communities are why we exist. We’re actively engaging in discovering the most effective treatments, so that we can provide our communities with the best possible care.”

The TRI Cores

"The TRI specifically allows faculty members with diverse specializations to engage multiple CORES, which would otherwise be unavailable to them. With this access, the investigators have the freedom to come up with bigger and less restricted ideas, on how to better understand health, metabolism, disease progression and response to interventions. This synergistic combination allows AdventHealth to advance the science behind personalized medicine and ultimately, provide the absolute best patient experience in the industry."

– Heather Cornell, PhD, Imaging Manager

What is a CORE?

A TRI CORE is an operations team led by a subject matter expert that provides researchers access to the latest technology and proven processes to achieve their scientific aims.

Since 2012

Exercise & Bioenergetics Lab



The Exercise & Bioenergetics Lab (EBL) conducts all exercise-related testing and procedures to examine the effects on study participants. Originally contained within two rooms, the lab has since expanded to most of the TRI's third floor. Equipped with a comprehensive array of cardio and strength-training equipment, the EBL works with other departments to facilitate the data needed for any study – all in a "one-stop-shop" environment.

The EBL has been pivotal in many new studies within the TRI, as well as globally, including the MoTrPAC study, serving as one of a few sites in the United States to focus on building a worldwide database of exercise-specific data. Maximal muscle and cardiorespiratory testing are done to gain information on a participant's physical limits and expand the research findings in exercise science.

Calorimetry

The Calorimetry CORE aids TRI studies by measuring metabolic activity and providing methods to understand the energy-related effects of an intervention. These baseline measures provide a metabolic snapshot in relation to efficiency, flexibility. This helps to predict energy intake, eliminating study variables.

We use methods such as indirect calorimetry and activity monitors to aid in-trials with other leading research centers focused on this field of data. Since inception, the CORE has grown from hosting small-scale procedures on one metabolic cart to large endeavors across a total of three metabolic carts, two whole room calorimeters and two flex room calorimeters.

Since 2012, the Calorimetry CORE has collected over 50,000 hours of energy expenditure measurements, including exercise, pharmaceutical and diet intervention studies.

Clinic

After recruitment, the journey of translational research begins with the Clinic. Located on the first floor of TRI, the clinic enrolls participants, manages all aspects of the study protocols, aids in protocol development and collects various types of data and documentation. Featuring a private waiting area, eight fully equipped exam rooms, a phlebotomy suite and office space for all clinical staff, it creates the foundation for research protocol to be initiated and turned into precise data collection.

In 2012, the Clinic CORE was comprised of three coordinators and two ARNPs, but has since flourished into a team of nine coordinators and five ARNP/RNs.

One of the most challenging and rewarding accomplishments of this team was their

execution of the COVID-19 vaccine trial, called ENSEMBLE. The team was split between the TRI and two satellite locations, six days a week, to enroll nearly 400 participants in the fall and winter of 2020. They continue to manage all active participants and have since provided boosters to over 200 eligible participants.

“I am most proud of... how the Clinic team takes on the challenges, adapts and collaborates with other CORES, and has the skills set to mentor and support other departments within the research institute.”

–Natasha Waters

Clinical Research Unit



The Clinical Research Unit (CRU) comprises 10,000+ square feet of the TRI’s second floor and facilitates research procedures for participants staying overnight for research studies. Operated 24/7 with ACLS certified RNs and Advanced LPNs on call, the CRU CORE is comprised of two branches – one for inpatient testing and another for metabolic research procedures. This includes six private “hospital rooms”, equipped with beds, bathrooms and showers for participants to use during the study.

Like other TRI CORES, the CRU has expanded over one decade, strengthening its procedural capabilities. This is exemplified through the Super-CE study conducted by Dr. Richard Pratley, which required pre- and post-interventional biopsies on at least 30 participants. The CRU CORE rose to the occasion and completed over 80 muscle biopsies, all while navigating the COVID-19 Pandemic.

“Hundreds of participants have graced the halls of the TRI and given their feedback concerning our facility. According to them, what sets us apart from other clinical research facilities is our excellent staff and the facility itself. (They express that) our ability to provide private rooms to study participants has made them more comfortable with staying for longer studies and encouraged them to participate in multiple studies.”

–Tavis Cross

Imaging



The Imaging CORE is key to technology and phenotyping at the TRI. They provide the identification of imaging biomarkers for personalized medicine and facilitate interventions by precisely measuring

changes in the structure and function of the body. It has grown to feature world-class machinery, including 3T Magnetic Resonance Imaging, Dual-Emission X-ray Absorptiometry and Vibration Controlled Transient Elastography. The Imaging CORE non-invasively investigates various markers of health, metabolism, disease progression and response to treatment. Since its inception, it has also expanded its cutting-edge imaging capabilities, including magnetic resonance image segmentation, magnetic resonance methods for imaging the fat content and stiffness of organs and multi-nuclear magnetic resonance spectroscopic techniques, such as proton and phosphorus spectroscopy.

Over the course of the decade, the TRI has maintained its original two imaging team members for the entire decade - growing their skillset along with the CORE. Their commitment to patient safety and attention-to-detail ensures data is high-quality and reproducible.

“The Imaging CORE is unique among other imaging institutions as one of very few research-dedicated, clinical-grade MRI suites that is staffed with a research technologist and a PhD level scientist. This provides faculty, investigators and industry sponsors with the ability to utilize advanced imaging technologies, without having to hire an external expert, and the added benefit of a more streamlined process for both the staff and participants. Our growth and work as a team, our ability to engage with other teams and our resultant data is something I will always be proud of.”

– Heather Cornell, PhD

Metabolic Kitchen



The Metabolic Kitchen supports multiple CORES and investigators within the TRI by implementing all nutrition requirements or data within a study. This includes preparing meals for overnight participants, nutrition counseling, food frequency questionnaires, 24-hour diet recalls and food diary analysis. Featuring commercial-grade equipment, a walk-in cooler, a walk-in freezer and 230-square feet of shelving, the CORE has a team of six highly-trained team members to calculate, prepare and weigh food items for controlled meals and energy intake.

Operating seven days a week for inpatient and outpatient participants, the team constantly adapts to the needs of each new study. This was exemplified through the peak of the COVID-19 pandemic, where staff were required to work remotely and obtain informed consent to aid in the COVID-19 vaccine clinical trial.

The Metabolic Kitchen also serves as a component to AdventHealth’s Dietetic Internship Program, where 16 dietetic interns complete a two-day nutrition research rotation within the CORE. While on site, these interns learn about the responsibilities of a registered dietitian working within research, providing unique, first-hand experiences for research-related career paths.

Medical Team

Medical Team provides integral oversight to research activities within the TRI by serving as the liaisons between clinical and non-clinical disciplines. With a widely diverse medical background across team members, they are responsible for performing study related physical examinations and procedures, which include muscle and adipose tissue biopsies, interpreting study related diagnostic tests and assessing adverse events. The two physician scientists who lead the team, Dr. Richard Pratley and Dr. Tina Thethi, are actively engaged in innovative clinical trials to understand the nature and progression of disease.

The strength of this CORE’s clinical trial abilities was seen during the pandemic, as they were pivotal in restarting research activity amid nationwide uncertainty. The medical team is also involved in quality and regulatory aspects of research, which helps provide well-rounded feedback to the operations team. This collaboration makes the work environment integrative and allows the medical team to grow their expertise.

Recruitment

“Recruitment is the KEY part of our research.”

-Anna Casu, MD

The Recruiting CORE leads all aspects of participant relations, including the facilitation of study opportunities, scheduling appointments, maintaining key information databases and fueling research through marketing strategy. Working closely with Clinical Research Coordinators, the original team of two has expanded over the last decade to encompass a team of seven – including recruiters, a data analyst and manager. Today, the

CORE not only is present at key marketing events and expos to promote the TRI’s research efforts, but they also create materials for newspapers, social media, radio, television and more.

Strong collaboration and teamwork within the CORE is critical to facilitating each study’s particular needs and target audience. Through a streamlined process, they are able to not only bolster participant engagement, but also maintain positive relationships that lead participants to partnering with the Institute again and again.

Research Lab



The Processing Lab CORE within the TRI performs all clinical and translational study logistics, such as collection, processing, storage and shipping of research samples. They also facilitate in-house molecular and phenotypic analysis, along with all responsibilities relating to a biorepository of over two-million parent samples from 98 different studies. All of this is conducted between multiple sites around the Central Florida area.

Beginning over 10 years ago, the CORE housed a single biosafety cabinet, -80C freezer and liquid nitrogen cryo-storage tank at a temporary site. It has since expanded to 13 biosafety cabinets, eight

liquid nitrogen cryo-storage tanks and 32 -80°C freezers. The CORE’s capabilities are unique in the field, with a world-class combination of cutting-edge equipment and a scalable infrastructure, paired with a cohesive team and culture of service.

One of the Research Lab’s greatest accomplishments to-date is the cultivation of their biorepository. During the first year, they collected 12,981 samples, which they easily bested last year through the collection of 67,301 – or roughly 259 samples per day. While the team’s capabilities are strong, their focus will always be toward a commitment to top-tier service, safety and efficiency in all of their responsibilities.

Since 2013

Pharmacy

The TRI Investigational Drug Service Pharmacy supports human clinical research that involves the testing and administration of study prescriptions. They focus on not only the safety and efficiency of medication use, but also control and accountability of medication through the adherence of good clinical practice, DNV, Florida State Board of Pharmacy and other regulatory bodies.

Since 2013, this CORE has filled over 5,000 investigational product prescriptions over the course of 50 studies. They are also the only AdventHealth facility that provides “non-sterile to sterile” injectable drugs, which has aided in several studies at TRI, along with sterile compounding, which has been a key contributor to several studies. The Pharmacy also accomplished the feat of preparing and dosing over 750 Johnson & Johnson COVID-19 vaccines since 2020.

Since 2018

Metabolomics

The Metabolomics CORE at the TRI migrated from Sanford Burnham in 2018. Since its arrival at the TRI, the Metabolomics CORE has expanded its services from targeted metabolomics (the highly quantitative measurement of a few hundred metabolites) to global metabolomics and stable isotope tracing.

This CORE aids in understanding metabolism and its function to clarify disease mechanisms. This provides investigators with key, precise biomarkers to gauge the metabolic processes that govern health and disease.

Senior Investigator and Metabolomics CORE leader, Dr. Stephen Gardell makes an analogy to traffic on a highway. A snapshot of the highway yields information about the numbers of cars but it fails to tell us if the cars are moving. On the other hand, a movie of the highway reveals whether the traffic is stalled or is moving briskly.

Use of metabolite precursors that are decorated with stable isotopes and subsequent detection using mass spectrometry is used to determine the metabolic fate of metabolites and achieve the equivalent of a movie camera view that reveals the flux of different metabolic pathways. This capability promises to broaden our understanding of how altered metabolism causes disease and how these metabolic irregularities can be mitigated to improve health and well-being.

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301 East Princeton Street | Orlando, Florida 32804
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