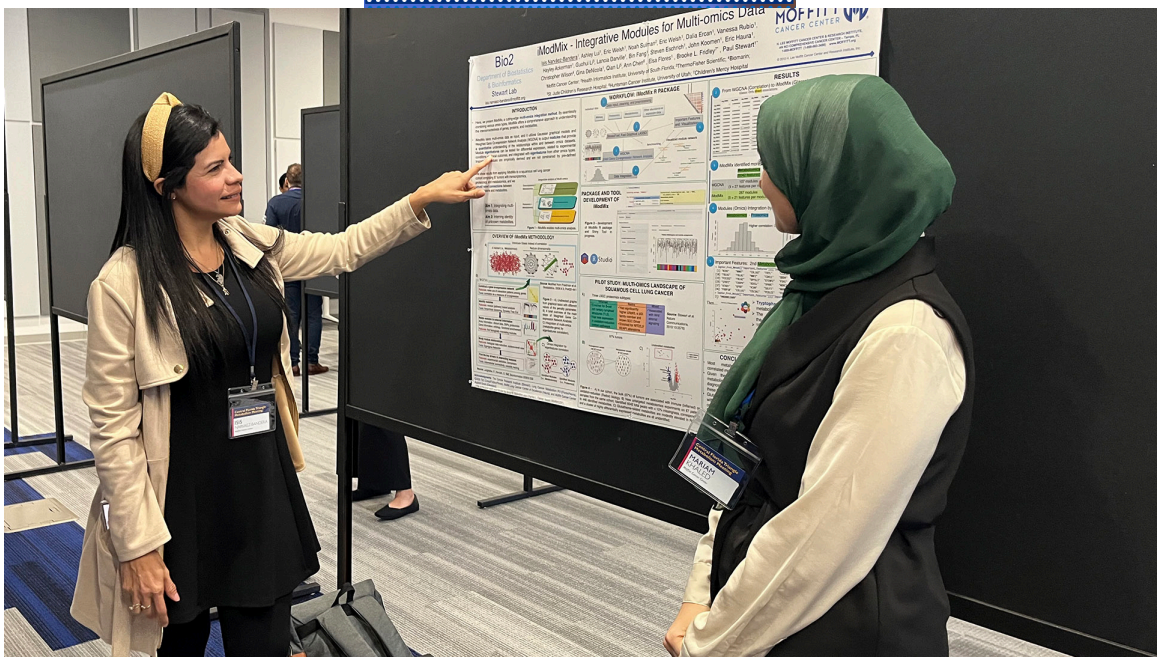

Johns Hopkins All Children's Hosts the 2024 Central Florida Triangle Metabolism Meeting

By **Randolph Fillmore** on 05/09/2024

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Researchers from four Central Florida medical institutions — Johns Hopkins All Children's Hospital, the H. Lee Moffitt Cancer Center and Research Institute, the AdventHealth Translational Research Institute for Diabetes and Metabolism and the University of Florida — co-sponsored the second annual Central Florida Triangle Metabolism Meeting, held March 14-15 on the Johns Hopkins All Children's Hospital campus in St. Petersburg, Florida.

The conference title highlights the collaborative partnership among these four major central Florida Research organizations, focused on metabolism and physiology and emphasizes that the regulatory principles of fundamental metabolism are deeply rooted in all physiologic processes. The symposium provided an opportunity for cross-disciplinary biomedical researchers to present their recent research and to continue to explore unifying theory of metabolism.

Close to 100 attendees pre-registered for the event and an additional 25-50 people logged onto the video conference link to participate in the two-day event. “We could not have handled this event without the skilled assistance of Lorenzo Thomas, who expertly handled all the logistics as our academic coordinator,” says Timothy Osborne, Ph.D., conference co-organizer, associate dean for basic research, director of the Institute for Fundamental Biomedical Research at the Johns Hopkins All Children’s Hospital, and professor of medicine in the Division of Endocrinology, Diabetes and Metabolism of the Johns Hopkins University School of Medicine. “This collaboration among institutions has proven a tremendous success.

“This second annual Central Florida Triangle Metabolism Meeting was sub-themed around metabolic control through the central nervous system and cancer. This year, the conference featured two keynote lectures, each emphasizing this year’s focus on the brain, which also integrated our conference with two special lectureship programs at Johns Hopkins All Children’s.

“On the first day of the meeting, Joel Elmquist, D.V.M., Ph.D., from the University of Texas Southwestern Medical School, delivered the Vice Dean’s Lecture which is a semi-annual event hosted by Dr. George Jallo. On the second day of the meeting, Tamas Horvath, D.V.M., Ph.D., professor and chair of the Department of Comparative Medicine at Yale University, delivered the Pediatric Grand Rounds Lecture, which is a weekly event hosted by the Continuing Medical Education program.”

Keynote Address

Joel Elmquist, D.V.M., Ph.D., director of the Center for Hypothalamic Research and vice chair of research in the department of internal medicine at the University of Texas Southwestern Medical School, offered a keynote address titled “SF-1 Targets in the Hypothalamus: A Molecular Link Between Energy Balance and Exercise.” His lecture described laboratory experiments using animal models and focusing on steroidogenic factor-1 (SF-1) transcription factor and its role in the ventromedial nucleus of the hypothalamus (VMH), a complex brain structure important for neuroendocrine functions, including glucose regulation and also social and sexual behaviors.

The researchers aimed at developing a better understanding of the functions of SF-1 in the VMH by looking at what happens when those genes are “knocked out” in one group of laboratory animals as compared to control groups that maintained those genes.

Their ongoing investigations into SF-1 and VMH, as well as other genes, are ultimately aimed at shedding light on metabolism in humans to be potentially informative with regard to human metabolism and metabolic diseases.

Other Selected Presentations

After the keynote address, the conference continued with 20 speakers from over a dozen research institutions and universities across the United States (see box), each presenting their research on metabolism and physiology, covering a wide range of topics, including cancer; glaucoma; metabolic diseases; sensory systems; pulmonary research; fatty liver disease and diabetes; neural metabolism in aging and neurodegeneration; and obesity.

Selected presentation highlights:

Padhu Pattabiraman, Ph.D. (Indiana University) spoke on a potential advancement in the treatment of glaucoma. In his presentation, titled "Novel Mechanistic Insights into the Role of Sterol Regulatory Element Binding Proteins in the Regulation of Intraocular Pressure," Pattabiraman discussed a novel way to reduce high intraocular pressure (IOP) in the eyes, a cause of glaucoma.

According to Pattabiraman, glaucoma is a leading cause of blindness and the goal for slowing the progression of glaucoma rests in finding new ways to lower IOP by keeping open the internal pathway by which the IOP can be "drained." Current treatments depend on eye drops or surgery to lower IOP.

He discussed the experimental use of a small molecule called "fatostatin" to target this pathway and reducing IOP by blocking activation of sterol regulatory element binding proteins (SREBPs), thereby changing the cellular biomechanics in the eye by affecting the lipids that modulate "cell stiffening." Cell stiffening causes pathway blockage and fatostatin helps in restructuring the mechanical forces that cause cell stiffening and, in doing so, potentially lowers IOP.

Mioara Larion, Ph.D., (NIH), who leads the Cancer Metabolism Research Program at the Neuro-Oncology Branch (NOB) at NIH, studies the metabolic needs of cancer cells and how tumors process nutrients for their growth. A goal is to develop targeted metabolic approaches that can delay tumor growth. In her presentation, titled "Brain Tumor Metabolism: An Underexplored Therapeutic Vulnerability," Larion spoke on tumor metabolism and how a "lipid imbalance" can trigger defects in organelles, subcellular structures that perform a variety of functions in the cell. One aspect of her research is related to how targeting that imbalance may induce "apoptosis," or programmed cell death, a process that can kill cancer cells.

She is interested in the metabolic needs of cancer cells and how they process nutrients, in order to develop targeted approaches that delay tumor growth. She and her colleagues are particularly interested in identifying metabolic vulnerabilities in glioblastomas, a fast-growing type of central nervous system tumor that forms from tissues of the brain and spinal cord.

Xiangbo Ruan, Ph.D., (Johns Hopkins All Children's Institute for Fundamental Biomedical Research) spoke on the "Mechanism of impaired amino acid catabolism (the break-down of complex molecules) in fatty liver diseases and type 2 diabetes." For Ruan, impaired amino acid metabolism in the liver is a hallmark of both non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes (T2D). Despite the critical role of impaired AA catabolism linking NAFLD with T2D, a molecular mechanism explaining this dysregulation is unknown. However, Ruan and his colleagues have found a mechanism of action for a human-specific long non-coding RNA (lncRNA). Gene expression is regulated by lncRNAs at multiple levels and plays a role in suppressing amino acid catabolism. This finding may explain impaired amino acid catabolism, present in both NAFLD and T2D.

Aya G. Elmarsafawi, Ph.D., (The H. Lee Moffitt Cancer Center and Research Institute) offered a presentation titled "The polyamine-hypusine axis regulates CD8+ T-cell fate and functions" which was the topic of her Ph.D. studies in the laboratory of John Cleveland, Ph.D., who is the Director of the Moffitt Cancer Institute. Elmarsafawi discussed the role played by CD8+ immune cells in "adoptive cell therapy" (ACT), a recent advancement in cancer immunotherapy that sources the patient's own CD8+ immune cells which are subsequently "reprogrammed" and expanded in the laboratory, then injected back into the patient to boost immunity.

According to Elmarsafawi, strategies that would enhance the function of CD8+ cells are "an urgent clinical need." She explained how the "polyamine-hypusine axis," shown to regulate T-cell function, is a metabolic "checkpoint" that can be exploited to augment to generation of CD8+ cells to improve the efficacy of T-cell based immunotherapies.

Tamas Horvath (Yale University)

Tamas Horvath, D.V.M., Ph.D., professor and chair of the Department of Comparative Medicine and also the director of the Yale "Program on Integrative Cell Signaling and Neurobiology of Metabolism," offered the second keynote lecture titled "Hunger drives life." Horvath explained recent research carried out in his lab that investigated specific neurons that potentially play a role in anorexia nervosa (AN), an eating disorder characterized by an abnormally low body weight that, among other specifics, often may result in addictive exercise to help cause

and maintain low body weight. AN is a condition that is more likely to be fatal in women than in men.

The Yale researchers found that food-restricted mice all died within 72 hours of their compulsive running, but when elevated fats were added to their diet, deaths were prevented and the researchers have hypothesized that a specific neuron that is activated by food restriction, called the “hypothalamic agouti-related peptide” (AgRP), plays a role in determining when anorexia becomes fatal, as the exercise-addicted animals lacking a high fat diet were unable to properly mobilize fuel during food restricted exercise. The finding suggests that those in medical care for anorexia nervosa, and at-risk of dying, may benefit from a high fat diet.

“We were very happy with our attendance this year,” says co-conference organizer Gina De Nicola, Ph.D., from Moffitt Cancer Center’s Department of Metabolism and Physiology and leader of Moffitt’s Metabolism Program. “We had twice as many posters as last year, and the poster session was popular as many great discussions took place around them. Also, the presentations included interesting new themes and new technologies for studying metabolism and physiology.”