

Temperature

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Saverio Cinti, John T. Garretson, Harvey J. Grill, Allen S. Levine & Paul Trayhurn

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Tim Bartness, Ph.D. (1953-2015)

Tim Bartness (Fig. 1) was a friend, mentor, collaborator and leader to many scientists, younger and older, across a variety of disciplines. He died September 24, 2015 at the age of 62 after a one-year battle with multiple myeloma. Tim not only helped educate many of us, but also challenged us to think critically and to laugh heartily about both the bad and the good we experienced in life. Tim was dedicated to science and to those around him. He worked diligently on his research right up the very end until he no longer could.

During his graduate school days in Robert Waldbillig's laboratory (Waldbillig trained with Neal Miller, a true pioneer in the neuroscience of motivated behavior) Tim studied the neural control of food and water intake focusing on serotonergic circuits. Following this he worked with Neil Rowland on energy systems related to insulin, metabolic efficiency and diabetic animal models. He spent further post-doctoral time with George Wade, Bruce Goldman and John Morley and Allen Levine. During that time he began the work on photoperiod and obesity in Siberian hamsters that he would become noted for. He also investigated neuropeptidergic control of food intake, effects of cold exposure on body composition and food intake, and further studies on metabolic efficiency.

In 1988 he was hired as an Assistant Professorship at Georgia State University, reaching full Professor in 1996 and Regents Professor in 2007. Tim's work at Georgia State was funded by a host of competitive grants from the National Institutes of Health and the National Science Foundation. One of his NIH grants was funded for 27 years, including a NIDDK MERIT award for 10 years. More remarkable is that each of Tim's submitted NIH grant proposals was awarded funding on the first submission without revision every time. His university recognized his efforts with the establishment of a Center for Obesity Reversal under his direction.

Tim's research led to a better understanding of the biology of adipose tissue, both white (WAT) and brown (BAT). He published extensively on the sympathetic and sensory nervous system innervation of these tissues and the neural control of WAT lipolysis and BAT thermogenesis. Tim's early studies helped define the mechanisms by which seasonal changes in photoperiod led to a 30% loss of body fat (from 50% to 20%) in Siberian hamsters. He evaluated foraging and hoarding animal behavior as well as melatonin receptor signaling associated with photoperiodism. He found that the duration of nocturnal melatonin secretion encodes day length cues and results in seasonal obesity via the central sites of the sympathetic nervous system (SNS) outflow to WAT.

Tim was a major contributor to the science linking, bidirectionally, the brain and white and brown adipose tissues. He was the first to define pre- and post-ganglionic sympathetic innervation of WAT using viral tract tracing, which was at the time a novel technique. His laboratory demonstrated the central nervous system (CNS) origins of SNA outflow from the brain to WAT. And soon after this, he and his colleagues also reported the CNS origins of the SNS efferent pathways that innervate BAT.

Tim never lost his interest in photoperiodism. Following up on earlier work, he demonstrated that melatonin receptor mRNA co-localized with CNS sympathetic nervous system outflow neurons. He and his colleagues found that alterations in the photoperiod would activate these circuits and result in increased norepinephrine turnover (sympathetic drive) within SNS neurons innervating WAT. Tim collaborated with others to identify key neurotransmitter systems involved in sympathetic outflow to white adipose tissue using PRV tract tracing with in situ hybridization. These key systems include melanocortin 4-receptors, mutations of which account for the most significant single gene defect that results in human obesity.

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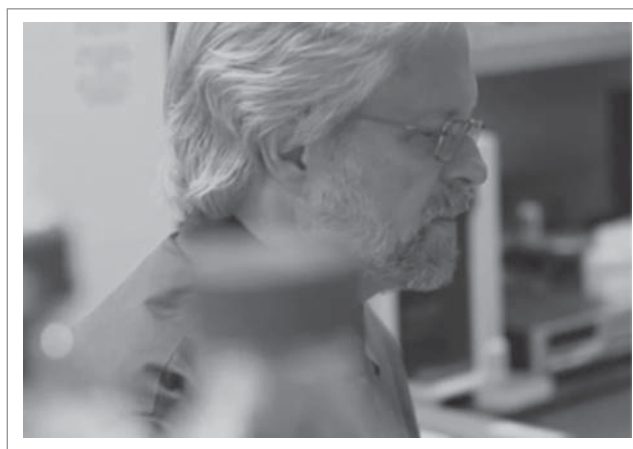


Figure 1. Still image of Timothy J. Bartness (from video by Alex Dreuter, georgia state university college of arts and sciences).

Based on these neuroanatomical studies, Tim's laboratory then pursued physiological consequences of WAT sympathetic denervation using local micro-injections of neurotoxins that selectively destroyed sympathetic nerves. Such denervation blocked lipolysis stimulated by cold exposure, exercise, fasting and photoperiod change in hamsters. Based on Tim's results it is now understood that sympathetic drive to WAT initiates lipolysis. Tim and his colleagues also discovered that SNS innervation of WAT regulates adipocyte proliferation, an important part of the biology of obesity. Tim and his lab found that sympathetic denervation, but not sensory denervation, resulted in greatly increased adipocytes proliferation. It is now known that obese rodents and humans have decreased sympathetic activity to WAT, which could result in enhanced fat cell number.

More recently Tim's laboratory was the first to describe the sensory pathway connecting and informing the CNS of afferent events occurring in the fat pad. His laboratory used H129, a virus that progresses in the anterograde direction, which labels the sensory pathway connecting WAT to the brain involving a spinal sensory, but not parasympathetic connection. Together with Gary Schwartz and continued with Johnny Garretson, Tim used electrophysiological recordings from WAT sensory nerves, demonstrating that such sensory nerves monitor certain aspects of lipolysis. Tim and his colleagues proposed that the transmission of such WAT afferent information would be a key integrated element in the brain's efferent control of lipid mobilization.

The above is a very brief summary of some of Tim Bartness's landmark work (see [Table 1](#)). It is already clear that his students and collaborators will continue investigating this important line of research established by Tim.

At this point, we will include some personal comments about Tim by the authors of this obituary.

Words on mentorship: John T. Garretson

"The best way to motivate scientists is to engage them, encourage them, and stay out of their way," a quote by Jim Austin (2012) in his *Perspective: On Motivation* that permanently resided on Tim's email signature. This was his way, and one could in fact test this by changing the locks on the lab door and measuring the many months it would take him to find out. Where was he then? In his office, and always with the door open, easily found at the source of eclectic jazz riffs echoing through the hallways. Each week Tim met with every undergraduate, master's, and Ph.D. student, postdoc, senior scientist, and technician in lab member one-on-one sessions ([Fig. 2](#)). When we met, we talked about our data, our wins, our losses, our futures and our lives. His door was literally and figuratively always open for us and for anyone else who dared. He was our fearless leader, our mentor, our friend, and is and will forever be missed.

His mentorship style was unique and admirable. Instead of forcing or shaming students to produce the data 'we predicted,' he instead encouraged us to find meaning and enthusiastically discover the truth of a seemingly strange result on our own but help from him always at the sideline. "The data never lie," he would say, meanwhile

Table 1. Landmark publications of Timothy J. Bartness.

Primary Research Article Title	Authors	Journal	Year
Photoperiodic Control of Body Weight and Energy Metabolism in Syrian Hamsters (<i>Mesocricetus auratus</i>): Role of Pineal Gland, Melatonin, Gonads, and Diet	Timothy J Bartness, George N Wade	Endocrinology	1984
Distributed forebrain sites mediate melatonin-induced short-day responses in Siberian hamsters	Claudia Leitner, Timothy J Bartness	Endocrinology	2010
Central nervous system origins of the sympathetic nervous system outflow to white adipose tissue	Maryam Bamshad, Victor T Aoki, M Gregory Adkison, Wade S Warren, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	1998
CNS origins of the sympathetic nervous system outflow to brown adipose tissue	Maryam Bamshad, C Kay Song, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	1999
Direct innervation of white fat and adrenal medullary catecholamines mediate photoperiodic changes in body fat	Gregory E Demas, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2001
Sympathetic innervation of white adipose tissue and its regulation of fat cell number	Robert R Bowers, William TL Festuccia, C Kay Song, Haifei Shi, Renato H Migliorini, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2004
Melanocortin-4 receptor mRNA is expressed in sympathetic nervous system outflow neurons to white adipose tissue	C Kay Song, Raven M Jackson, Ruth BS Harris, Denis Richard, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2005
White adipose tissue lacks significant vagal innervation and immunohistochemical evidence of parasympathetic innervation	Antonio Giordano, C Kay Song, Robert R Bowers, J Christopher Ehlen, Andrea Frontini, Saverio Cinti, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2006
Differential sympathetic drive to adipose tissues after food deprivation, cold exposure or glucoprivation	Nilton A Brito, Marcia N Brito, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2008
Anterograde transneuronal viral tract tracing reveals central sensory circuits from white adipose tissue	C Kay Song, Gary J Schwartz, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2009
Central sympathetic innervations to visceral and subcutaneous white adipose tissue	Ngoc Ly T Nguyen, Jessica Randall, Bruce W Banfield, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2014
Short and long sympathetic-sensory feedback loops in white fat	Vitaly Ryu, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2014
Brown Adipose Tissue Has Sympathetic-Sensory Feedback Circuits	Vitaly Ryu, John T Garretson, Yang Liu, Cheryl H Vaughan, Timothy J Bartness	The Journal of Neuroscience	2015
Effects of food deprivation and restriction, and metabolic blockers on food hoarding in Siberian hamsters	Timothy J Bartness, Marion R Clein	AJP – Regulatory, Integrative and Comparative Physiology	1994
Partial lipectomy, but not PVN lesions, increases food hoarding by Siberian hamsters	Andrea D Wood, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	1997
Agouti-related protein increases food hoarding more than food intake in Siberian hamsters	Diane E Day, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2004
Peripheral ghrelin injections stimulate food intake, foraging, and food hoarding in Siberian hamsters	Erin Keen-Rhinehart, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2005
Peroxisome Proliferator-Activated Receptor γ Controls Ingestive Behavior, Agouti-Related Protein, and Neuropeptide Y mRNA in the Arcuate Hypothalamus	John T Garretson, Brett JW Teubner, Kevin L Grove, Almira Vazdarjanova, Vitaly Ryu, Timothy J Bartness	The Journal of Neuroscience	2015
Central ghrelin increases food foraging/hoarding that is blocked by GHSR antagonism and attenuates hypothalamic paraventricular nucleus neuronal activation	M Alex Thomas, Vitaly Ryu, Timothy J Bartness	AJP – Regulatory, Integrative and Comparative Physiology	2015
Review Article Title	Authors	Journal	Year
Photoperiodic control of seasonal body weight cycles in hamsters	Timothy J Bartness, George N Wade	Neuroscience & Biobehavioral Reviews	1986
The timed infusion paradigm for melatonin delivery: what has it taught us about the melatonin signal, its reception, and the photoperiodic control of seasonal responses?	Timothy J Bartness, J Bradley Powers, Michael H Hastings, Eric L Bittman	Journal of Pineal Research	1993
Neural and hormonal control of food hoarding	Timothy J Bartness, Erin Keen-Rhinehart, Megan J Dailey, Brett JW Teubner	AJP – Regulatory, Integrative and Comparative Physiology	2011
Neural innervation of white adipose tissue and the control of lipolysis	Timothy J Bartness, Yang Liu, Yogendra B Shrestha, Vitaly Ryu	Frontiers in Neuroendocrinology	2014



Figure 2. Tim Bartness Lab (2014). People from left to right (back): Dr. Laura Szymanski, Alex Thomas, Dr. Timothy J. Bartness, Dr. Fabiana Evangelists, Nick Johnson, Dr. Vitaly Ryu, Johnny Garretson; left to right (front): Ngoc Ly Nguyen, Sierra Williams, Eleen Zarebidaki, Jennifer Mendes.

giving us critical skills to create the perfect experiments needed to disprove our hypothesis always as in the style of John Platt's (1964) *Strong Inference*. He cared, and was very good at it. His passion for good data and even for small wins was infectious, spreading to us all in a way that now seems impossible to have come from only one man. Always available by email when not in person, it was common to have more than 20 back and forth emails about life and science later than midnight on Sunday. Tim showed us the meaning of motivation, of perseverance, of creativity, of discipline, all leading by example. He fought for what he believed in and most often it was fighting for his students: for our success.

This present collection of entries and what has been written elsewhere in Tim's memorial may appear to demonstrate his life's work as a great scientific collection and a logical cohesion of creatively uncovered facts and ideas; however, his life's work was actually us: his lab family. On whom he constantly washed over advice driven by his experience with research, writing, and life at an overwhelming pace. Every moment with him was a learning experience and his advice has been "burned" into us all by means of repetition. Working with Tim, never



Figure 3. Dr. Harvey Grill (left) and Dr. Tim Bartness (right) in New Orleans.

'for' Tim, his academic offspring have inherited 3 primary traits. One) Start early, work hard; 2) Take time to think before you act, it is usually better than acting wrongly then being forced to think; and finally, 3) if you're not having fun, then you're doing it wrong. These were his keys to success, his sources of meaning, and now his legacy for many to follow: I know I will.

Words from colleagues and friends

Saverio Cinti

Dear Tim, I will never forget our friendship.

I will never forget when you came to my 1999 Congress at Portonovo, Italy. The Meeting was a satellite of the Milan European Congress of Obesity, but you came directly from Atlanta to attend the meeting and to propose a collaboration with my group in the field of innervation of white adipose tissue. I was honored by this event that was also the starting point of our long lasting collaboration and friendship.

I will never forget our meeting at the 134th Nobel Symposium "The Adipocyte a Multifunctional Cell" in Gothenburg, Sweden. About thirty scientists from all over the world, but mainly from US were present. We were all quite concentrated on our own research data in order to give the best of our self. In that quite professional atmosphere your kindness, playful spirit and friendship was very important to me and for many other Colleagues present at that event.

I will never forget that you really wanted a couple of watercolor paintings of mine even requesting to buy them. I was honored by your request and, of course, I sent you them as a gift.

I will never forget your invite to your lab to lecture to your students in 2011. I was in a sabbatical period at Harvard and it was a very hard working period and a lonely time for me. When I met you at the airport I really felt "at home" being "only" about 5 thousand miles from my own family. In "my" room I had the satisfaction to see my paintings. Your cats were 2 kids for you and I remember the kind of love you were able to express to them while giving them food and allowing the most affectionate of them to stay in your bed during the night. I still remember our conversations dealing with our most intimate aspects of our own lives and a mutual understanding at the end of that short stay leading to a reciprocal deep friendship although our direct contacts have been and would always be quite occasional. I remember the restaurants, the museum and the numerous frank conversations with laughter that conferred a special mood at that visit.

I will never forget your passion and determination in defense of our scientific data on innervation of adipose tissues when we were in competition with other groups.

I will never forget your prominent contribution to adipose tissues science, perfectly described by colleagues in this paper. Your leadership and behavior in the lab was not different from your wonderful personality. I observed the gratitude of your collaborators for your kindness that together with your expertise created a very lovely and excellent environment in your lab.

I will never forget your spirit and continuous joking with the story of Godfather (me, because Italian) and Consigliori (you, being blond and American).

I will never forget your composed silence during your last year.

I will never forget you Tim, my very good friend.

Harvey Grill

Tim and I were close friends and colleagues (Fig. 3). We shared a grant for a number of years, wrote papers together, and had wonderful brain storming sessions. Over the years we attended many meetings together and in the context of that travel, given our shared a love of music, we invariably spent time going to concerts and listening to and buying music. We introduced each other's keynote addresses at the Obesity Society meeting, read and critiqued each other's Specific Aims pages, and constantly sent each other music we thought the other would enjoy.

Our joint interest in the neurobiology of regulatory physiology and in the contribution of a number of regulatory peptides to energy intake, energy expenditure, and thermoregulation sparked many conversations and generated ideas for experiments. We shared the perspective that the neural control of these critical systems was anatomically distributed rather than centered and included but extended well beyond the contributions of hypothalamic neurons. Among my favorite findings from the work we published together are the following two.^{1,2} We determined that hindbrain melanocortin receptor stimulation elevated UCP-1 mRNA expression in BAT that was driven by sympathetic outflow to BAT, abolished by surgical denervation of BAT, and mediated by circuitry intrinsic to the caudal brainstem and spinal cord as these responses were observed in rats with isolated caudal brainstems. Another series of experiments showed that despite surgically eliminating all neural influences of hypothalamic neurons, cold exposure triggered sympathetic energetic and cardiac responses via activation of caudal brainstem and spinal circuitry that were comparable in many, but not in all, respects to those seen in neurologically intact rats. Control rats exposed to 4, 8 or 12 degree temperatures for 6 h periods maintained their core temperature [T(c)] throughout. Similarly, chronic decerebrate (CD) rats maintained T(c) for the 8 and 12 °C exposures, but during 4 °C exposure T(c) declined 2 °C. Tachycardia magnitude was graded with decreases in environmental temperature for control rats, but CDs tachycardia was similarly elevated for all temperatures. Cold increased norepinephrine turnover in BAT, heart, and some white adipose tissue depots in both CDs and controls compared with their respective room temperature controls.

Tim was a dedicated mentor (well described by Johnny Garretson), a tireless advocate for the support of early career investigators, and through his continuous service on NIH Study sections was an exemplary advocate for research support for his areas of science. Tim and I were very close and during his battle with cancer we spoke very often on the telephone. I miss him and wish I could highlight his name on my phone and hear his voice again. I can imagine the sound of his voice and the way he would say “Harv” when he knew I was on the other end.

Allen S. Levine

Tim and I had been colleagues and friends since 1984. I remember the letter Tim wrote to John Morley and me asking to join our laboratory. He was convinced that together with our staff, graduate students and postdoctoral fellows, he would contribute to making this one of the better “feeding labs” in the country. John and I had established a laboratory together at the Minneapolis VA Medical Center in 1979 and were new to the field of food intake regulation. At the time Tim joined our laboratory we had 3 other superb postdoctoral fellows who have had highly successful careers in science, namely Charles Billington, Blake Gosnell and Dean Krahn.

Tim published 10 papers during his time in our laboratory. He contributed a great deal to all of these studies and his broad scholarly interests and persistence moved us into areas of research we had not worked on previously. Asking some of the folks who were in the lab with us in 1982-1986 they remembered that Tim had a wicked sense of humor, was extremely well read in multiple areas of neuroscience and knew the scientific family trees of every young scientist in our field. He also was a master designer of complex experiments. It was a time when our laboratory was like a family. We traveled together to meetings, shared hotel rooms, talked science incessantly and simply had fun.

Tim and I continued to see each other at meetings where we talked about our research, but also shared our love for jazz and blues. I played piano in the Catskill Mountains growing up and wanted to be a jazz musician-Tim studied saxophone as an adult and loved every moment of it. He had a vast CD collection of all types of music and would send colleagues links to some of his favorite tunes. During the last year of Tim’s life we talked often. Despite our speaking about when we should retire, I felt that Tim loved his lab much too much to stop working. Even during his darkest hours he was reading and writing and working with his students. Tim served as an external reviewer of the Minnesota Obesity Center, which I directed, and he wrote a thorough review even when he was ill.

One of the most satisfying moments for me was to nominate Tim as a fellow in the American Association for the Advancement of Science. All of his nomination letters were stellar and he was named a fellow several years

ago. I have always been proud of Tim's accomplishments and loved him dearly. We will all miss Tim and I will miss calling up "little Tim" on the phone and hearing him say bye "Big Al."

Paul Trayhurn

I first came to know of Tim in 1985 through Dr George Wade who at the time was spending a sabbatical with me at the Dunn Nutrition Laboratory in Cambridge, UK. George talked eloquently of Tim who had been a post-doctoral fellow with him at the University of Massachusetts. A short while later Tim and I made contact, and a collaboration ensued while I was at the University of Alberta, Canada, in which we investigated the effects of high fat diets on hibernation and adipose tissue function in the Turkish hamster (*Mesocricetus brandti*). At the time, Tim was particularly interested in dietary lipid and hibernation, and Turkish hamsters offered a valuable model. The project was very much driven by Tim and our role in Edmonton was to examine what were (and are) the major biochemical indices of thermogenic capacity in brown adipose tissue – mitochondrial content, cytochrome *c* oxidase activity and the amount of uncoupling protein-1. The results were published in the *Journal of Comparative Physiology B* in 1991, and although not dramatic they demonstrated for me the very real pleasure of collaborating with Tim.

Our next substantial interaction was in 1993, immediately prior to the "Life in the Cold" Symposium in Colorado. We were both planning to attend that meeting and Tim invited me to visit him and his group in Atlanta prior to going to Colorado. At the time I was based in Aberdeen, Scotland, and flew to Atlanta from Glasgow via Washington. His children were with him at the airport and I remember vividly that he had conjured up the image of someone coming from an exotic land who might be wearing strange clothes (kilt and sporran) and speaking with an impenetrable accent. Instead, they saw (with much disappointment) a tired Englishman who through jet-lag was incapable of reproducing a Scottish accent - and indeed was almost incoherent in his own standard English. I stayed at Tim's house during my visit and recall with great affection his warm and generous hospitality.

Tim and I maintained occasional contact thereafter, and I was deeply impressed by his developing studies on the central origins of the innervation to the adipose tissues, both brown and white, and on the role of the SNS in regulating adipocyte proliferation and function. His use of pseudorabies virus (PRV) as a retrograde tracer from adipose tissue to brain areas was pioneering and extremely influential. The series of pivotal investigations by him and his group cemented his reputation internationally, and I was able to encourage his invitation to speak at meetings that I was involved in organizing, including the Symposium on "New Developments in Adipose Tissue Biology," in Portonovo, Italy, arranged and hosted by Saverio Cinti, and the Summer 2004 Meeting of the UK Nutrition Society on the "Biology of Obesity," held in Dublin, Ireland. Tim's presentations at these and other meetings were invariably committed, scholarly, and intense - and everyone knew that they were listening to someone special.

Our final collaboration was when a PhD student and I at the University of Liverpool, UK, were studying nerve growth factor in white adipose tissue, both in relation to the growth and maintenance of the innervation of the tissue and the putative role of NGF in the inflammatory response within fat. To help explore this, Tim sent white adipose tissue depots from the dwarf hamsters (*Phodopus campbelli*) that he was working with at the time where one side of the depot had an intact innervation while the other had been surgically denervated. We were concerned to examine the expression of NGF and other adipokine genes, but came up against the difficulty that because of sequence differences our probes would not hybridize with mRNA from *Phodopus campbelli*. As a consequence, we had to sequence certain mRNAs and many will be surprised to know that among Tim's many scientific contributions are partial sequences (deposited in gene databases) of nerve growth factor and leptin from dwarf hamsters.

The last time Tim and I met was in Liverpool a decade or so ago when he and Ruth (Harris) were visiting her relatives in the North of England. After talking science in the lab with Tim's customary engagement, we visited Liverpool Metropolitan Cathedral (known locally as "Paddy's wigwam," because of the Irish connection and the design of the building), on the edge of the University campus. So my final memory of Tim is saying farewell in unusually bright sunlight outside this unique and iconic building – how very fitting.

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Saverio Cinti

University of Ancona, School of Medicine, Ancona, Italy

John T. Garretson


*Georgia State University Neuroscience Institute
Center for Obesity Reversal, Atlanta, GA, USA*

Harvey J. Grill

University of Pennsylvania, Department of Psychology, Philadelphia, PA, USA

Allen S. Levine

*University of Minnesota, Morrill Hall (Room 110)
100 Church Street, Minneapolis, MN 55455, USA*

 aslevine@umn.edu

Paul Trayhurn

*University of Liverpool, Obesity Biology Research Unit, Liverpool, UK
& University of Buckingham
Buckingham Institute for Translational Medicine, Buckingham, UK*