Abstract

The Keystone Symposia are held annually to congregate people working in a specific field of research in order to disseminate unpublished findings and allow for networking and establishment of professional contacts and collaborations. With various global locations these conferences attract researchers from all over the world and serve as a catalyst for the advancement of biomedical and life sciences. This year I had the opportunity to present a poster at Keystone Symposia: *Beige and Brown Fat: Basic Biology and Novel Therapeutics*, in Snow Bird, UT, held April 17-22, 2015.

Obesity has reached pandemic proportions worldwide, bringing with it staggering rates of metabolic co-morbidities such as type 2 diabetes and cardiovascular disease. One promising therapeutic option is to increase the amount and activity of brown fat (BAT) in the body. BAT differs from white fat (WAT) in its ability to burn calories instead of solely storing fuel as lipid, due to densely packed mitochondria (the 'power-house" organelle of the cell) with the unique expression of uncoupling protein 1 (UCP1). The presence of UCP1 in the mitochondria allows the cells to dissipate chemical energy as heat through a process termed thermogenesis, which then increases whole body energy expenditure. This specialized role of BAT makes it an appealing target for combating obesity and type 2 diabetes.

We were the first to demonstrate that the growth factor bone morphogenetic protein (BMP)7 is capable of committing stem cells to develop into the brown fat lineage, and it is now well-appreciated that BMPs are important for BAT development and function. Hemojuvelin (HJV) is a BMP co-receptor and has a well-described role in iron homeostasis. Although HJV is expressed in fat tissues (brown and white) and its expression increases in WAT with human obesity, no studies had yet investigated the role of HJV in fat tissue function and BMP signaling in brown fat cells. In this study, we uncovered a novel and important role for HJV in brown fat cells. Mice lacking HJV (KO) displayed a striking pattern of "browning" of WAT, with increased presence of recruitable

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UCP1-positive brown fat cells in WAT, reduced fat pad size, and lower body weight. Browning of WAT is considered an important physiological mechanism by which animals can recruit additional heat producing cells thereby increasing whole body energy expenditure and mitigating obesity and diabetes. In order to determine the cellular and molecular mechanism by which HJV regulates brown fat cell differentiation, we created immortalized undifferentiated brown fat cell lines from HJV KO and control mice. Cells from the KO mice displayed a propensity to differentiate to mature brown fat cells *in vitro*. As early as the undifferentiated stage, HJV KO cells displayed a marked increase in BMP signaling. These undifferentiated brown fat cells also displayed higher mitochondrial activity as measured by oxygen consumption rate in a respirometer. There was also an accompanying increase in glucose uptake and glycolysis in the KO cells, while there was decreased fatty acid oxidation, indicating that the cells may rely on glucose in order to increase mitochondrial activity. Drug delivered inhibition of BMP signaling prevented the accelerated differentiation phenotype in these cells, further supporting that loss of HJV led to increased BMP signaling which mediated the accelerated brown differentiation phenotype. Taken together these data describe a novel role for HJV in brown fat, whereby removal of this co-receptor facilitates brown fat cell differentiation and may be a target for future obesity therapies.

This research investigating energy balance, body weight regulation, obesity, and diabetes is especially relevant for the State of Maine, as we have the oldest population in the nation, and obesity along with diabetes occur disproportionately in an aging populace. Aging research and my GSBSE program are also 'Signature and Emerging Areas' for UMaine research right now. Therefore, attending this meeting was invaluable not only for my professional development, but also for representing the important research we do at Umaine. Any funding provided would be used to offset costs related to traveling to the conference and registering for its attendance.

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Itemized Budget

Item #	Description of Item	Source (Company)	Quantity	Individual Cost	Total Cost (Quantity x Ind. Cost)	Amount Spent	Amount Requested (max GSG award)
1	Registration	Keystone Symposia	1	$550.00	$550.00	$550.00	$300.00
2	Airfare	US Airways Delta American	1	$709.20 $765.00 $734.00	$709.20	$709.20	$550.00
3	Abstract Submission	Keystone Symposia	1	$100.00	$100.00	$0	
4	Lodging	Cabin at Snowbird	6 nights	$100/night	$600.00	$0	
5	Meals	Various	5	$46.00/day	$230.00	$0.00	
TOTAL					**$2,189.20**	**$1,259.20**	**$850.00**

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Budget Explanation

The entire expense of the meeting is outlined in the budget above, and I am requesting that the GSG grant me with $850 to offset the expenses of presenting at this meeting. Greyed out lines of the budget represent expenses covered by my advisor and therefore, are not being included in the total costs incurred by me. I had taken steps within my power to minimize the costs associated with attending this conference as much as possible, i.e. shared lodging and price-discriminatory airfare, but the costs were still substantial. I had applied for funding in the Spring 2015 semester to both the GSG and the School of Biology but did not received funding.

1. Keystone registration is very expensive, and a non-negotiable part of attending the conference. Normal registration rate is $750, however, I registered early enough to qualify for the Early Registration Student Discount Rate of $550. I am requesting the GSG grant me $300 towards offsetting the expense of this registration.
2. Airfare from Bangor, ME to Salt Lake City, UT ranges between $600-$800 well into the spring due in part to the area being an attractive destination for winter sport enthusiasts. Although I attempted to purchase the cheapest tickets possible my departure/return days were constricted by my class schedule. I did purchase the cheapest available option for the days that I could travel, and am requesting a reimbursement grant of $550 from the GSG for this expense.
3. Covered by my advisor, not requesting reimbursement
4. Covered by my advisor, not requesting reimbursement
5. Covered by my advisor, not requesting reimbursement

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