POSTER PRESENTATION

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Glucose metabolism is linked to the inflammatory status of macrophages

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From Metabolism, diet and disease
Washington, DC, USA. 29-31 May 2012

Background

Macrophages infiltrate adipose tissue at the onset of weight gain and directly contribute to adipose inflammation, insulin resistance, and obesity [1]. The type of fuel substrate utilized by macrophages is central to the formation of obesity, a global epidemic [2]. Our goal is to understand the role of macrophage glucose metabolism in the promotion of inflammation and insulin resistance during high fat diet-induced obesity. We hypothesize that macrophages with *blunted or elevated* glucose metabolism will display *limited or exaggerated* immune responses, and modulate susceptibility to insulin resistance and obesity, respectively.

Materials and methods

GLUT1 is the glucose transporter expressed by macrophages [3]. We manipulated macrophage glucose metabolism using GLUT1 over-expression and deletion techniques *in vitro*, *ex vivo*, and *in vivo*. *In vitro* studies involved over-expression of GLUT1 in RAW264.7 cells. A high fat diet-induced obesity model involving a novel macrophage-specific *Glut1* knockout mouse (*Glut1MΦ^{-/-}*) was used to assess total body weight, glucose tolerance, tissue histological alterations, and gene expression changes resulting from *Glut1* deletion. Bone marrow-derived macrophages (BMDMs), isolated from *Glut1MΦ^{-/-}* mice fed a control diet, were used for measures of polarization, and glucose uptake and metabolism.

Results

GLUT1 over-expression resulted in elevated glucose uptake and metabolism, as well as a hyper-inflammatory state characterized by elevated secretion of MCP-1 and PAI-1, all of which could be blunted with a pharmacologic

inhibitor of glycolysis. Preliminary data suggests that *Glut1MΦ^{-/-}* mice fed a high fat diet were resistant to obesity, remained normoglycemic and demonstrated blunted inflammation in liver and adipose. *Glut1MΦ^{-/-}* BMDMs were viable, but metabolized less glucose at baseline and after LPS stimulation.

Conclusions

The capacity to use glucose as a fuel is correlated to the inflammatory status of macrophages which likely plays an integral role in the promotion of obesity-related insulin resistance. Possible mechanisms linking glucose metabolism to inflammation are being investigated. Understanding macrophage glucose metabolism and inflammation will identify metabolic and/or signaling pathways that will serve as novel therapeutic targets in the treatment of diabetes and obesity.

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Published: 1 June 2012

References

1. Weisberg SR, McCann D, Desai M, Rosenbaum M, Leibel RL, Ferrante AW Jr: **Obesity is associated with macrophage accumulation in adipose tissue.** *J Clin Invest* 2003, **112**:1796-1808.
2. Odegaard JI, Chawla A: **Mechanisms of macrophage activation in obesity-induced insulin resistance.** *Nat Clin Pract Endocrinol Metab* 2008, **4**:619-626.
3. Vats D, Mukundan L, Odegaard JI, Zhang L, Smith KL, Morel CR, Wagner RA, Greaves DR, Murray PJ, Chawla A: **Oxidative metabolism and PGC-1beta attenuate macrophage-mediated inflammation.** *Cell Metab* 2006, **4**:13-24.

doi:10.1186/1753-6561-6-S3-P62

Cite this article as: Johnson et al.: Glucose metabolism is linked to the inflammatory status of macrophages. *BMC Proceedings* 2012 6(Suppl 3):P62.

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