OMICS Group Conferences
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World Congress on
Endocrinology

August 26-28, 2013 DoubleTree by Hilton, Raleigh, NC, USA

Leptin deficiency turns mast cells from pro-inflammatory cells into anti-inflammatory cells

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Mast cells (MCs) are pro-inflammatory cells participating importantly in diet-induced obesity and diabetes. These cells release pro-inflammatory interleukin-6 (IL6) and interferon-γ (IFN-γ) to induce vascular cell proteases expression and promote adipose tissue neovascularization. Reduced body weight gain and improved diabetes in MC-deficient $Kit^{W\text{-}sh\text{-}W\text{-}sh}$ mice can be reversed by adoptive transfer of in vitro prepared MCs from wild-type (WT) mice but not those from IL6- or IFN-γ-deficient mice. We have recently demonstrated that MCs from leptin-deficient ob/ob mice also failed to reverse reduced obesity and diabetes in $Kit^{W\text{-}sh\text{-}W\text{-}sh}$ mice. White adipose tissue (WAT) from $Kit^{W\text{-}sh\text{-}W\text{-}sh}$ mice receiving MCs from *ob/ob* mice had significantly smaller adipocyte size, fewer inflammatory cell infiltrates, lower pro-inflammatory M1 macrophages, and higher anti-inflammatory M2 macrophages than did WAT from $Kit^{W\text{-}sh\text{-}W\text{-}sh}$ mice receiving WT MCs. In cultured mouse bone marrow-derived macrophages (BMDMs), co-culture of MCs from ob/ob mice protected BMDMs from lipopolysaccharide (LPS)-induced M1 macrophage differentiation and enhanced $CD4^+$ T-cell-induced M2 macrophage differentiation. In contrast, leptin deficiency did not affect $CD4^+$ T-cell and $CD8^+$ T-cell activities in regulating LPS- or $CD4^+$ T-cell-induced M1 and M2 macrophage differentiations. MCs from *ob/ob* mice produced more anti-inflammatory cytokines IL4 and IL13 and less pro-inflammatory cytokine IL6 than did MCs from WT mice. These observations suggest an anti-inflammatory activity of MCs in the absence of leptin. When *ob/ob* mice became obese and diabetic, MC-deficient $Kit^{W\text{-}sh\text{-}W\text{-}sh}$ *ob/ob* mice gained even more body weight and developed more severe glucose tolerance. Therefore, functional expression of leptin from MCs determines MC inflammatory activities and experimental obesity and diabetes.

Biography

Guo-Ping Shi received his doctoral training in Physiology from Harvard University in 1995. He is currently a Biochemist of Cardiovascular Medicine, Brigham and Women's Hospital and an Associate Professor of Medicine, Harvard Medical School. His research team has longstanding interest in the roles of lysosomal cysteine proteases cathepsins and inflammatory cells, mainly mast cells in the pathogenesis of atherosclerosis, abdominal aortic aneurysms, obesity, and diabetes. He has published more than 130 peer-reviewed articles in these fields, and serving as an editorial board member of 8 journals.

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