Adipose tissue macrophage specific deletion of SH2 domain-containing protein tyrosine phosphatase 1 (SHP-1) improves glucose homeostasis in obese insulin resistant model

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Introduction: SHP-1 is a non-receptor protein tyrosine phosphatase expressed predominantly in the hematopoietic cell. Improved glucose utilization & insulin sensitivity in viable motheaten mice expressing low levels of functionally deficit SHP-1 protein introduced the metabolic regulatory function of SHP-1. Keeping in mind, the role of SHP-1 in macrophage functions, we speculated that SHP-1 might play an important role in polarization of adipose tissue macrophages (ATMs), the hallmark of obesity-induced insulin resistance.
Materials and methods: Glucan particle (GPs) loaded with SHP-1 siRNA was used for targeted silencing of SHP-1 in ATMs. For this, male C57BL/6J mice were divided into four groups (n=15 each): the lean group received a standard rodent diet, the HFD-IR group received a high fat diet (HFD), NT siRNA was injected with GPs containing nontargeting control siRNA in addition to HFD, and the SHP-1 siRNA group was injected with GPs containing SHP-1 siRNA in addition to HFD. The dietary regimen lasted for 16 weeks and GPs containing siRNA were intra-peritoneally injected every alternate day for a period of 2 weeks. At the end of the study, animals were sacrificed and epididymal adipose tissue was collected for further studies.
Results: Our study reported that during diet induced obesity the expression of SHP-1 significantly increases in ATMs. The inflammatory milieu triggers macrophage activation and high levels of SHP-1 expression by activated macrophages (M1 cells). ATM-specific deletion of SHP-1 improves glucose homeostasis by modulating M1 and M2 macrophage population and subset of macrophage phenotype markers in adipose tissue leading to metabolic improvement in the obese insulin-resistant model.
Conclusion: Glucan particle based targeted silencing of SHP-1 recognized an unrevealed function of adipose tissue-specific SHP-1 in modulating adipose tissue physiology and macrophage phenotype and the molecular mechanism behind the improved metabolic character in SHP-1 deficient mice.

Keywords : SHP-1, Adipose tissue macrophages, Obesity induced insulin resistance, Targeted delivery
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