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Macrophage ghrelin receptor - A novel regulator for lipid metabolism and inflammation

Chronic low-grade inflammation is a hallmark of obesity, which is associated with metabolic dysfunction and insulin resistance. Gut hormone ghrelin promotes food intake, adiposity and insulin resistance; and ghrelin is functions through ghrelin receptor, Growth Hormone Secretagogue Receptor (GHS-R). To determine the direct effect of GHS-R in macrophages, we generated myeloid-specific GHS-R knockout mice and studied them under chronic and acute inflammatory conditions of diet-induced obesity (DIO) and endotoxin lipopolysaccharides (LPS) treatment. Suppression of GHS-R in myeloid cells attenuated DIO-associated obesity, DIO-induced insulin resistance, and LPS-induced inflammation. The myeloid-specific GHS-R knockout mice showed significant reductions of pro-inflammatory cytokines in the circulation, and pro-inflammatory gene expression in liver, fat and skeletal muscle. To investigate the underpinning mechanism, we isolated bone-marrow-derived-macrophages (BMDM). GHS-R deficient BMDM showed a polarization profile toward anti-inflammatory M2. These data suggest that GHS-R deficiency promotes macrophage anti-inflammatory shift by modulating insulin signaling and mitochondrial energetics. Collectively, our findings indicate that suppression of GHS-R in myeloid-cells promotes anti-inflammatory polarization, decreases inflammatory responses of both diet-induced chronic inflammation and LPS-induced acute inflammation, prompting a healthier lean and insulin sensitive state. Thus, macrophage GHS-R has profound effects on lipid metabolism and inflammation, is a critical molecular link that mediates the cross-talks between immunity, lipid metabolism, inflammation and insulin sensitivity.

Speaker Biography

Yuxiang Sun is an associate professor at Nutrition and Food Science at Texas A&M University, USA. She obtained her PhD from University of Manitoba, Canada. She is a leader in ghrelin research; ghrelin is an important nutrient sensor and metabolic regulator. She has over 65 peer-reviewed publications, many of which are in premier journals such as Cell Metabolism, PNAS, JCI, Diabetes and Aging Cell. Her publications have been cited over 4413 times, and her publication H-index is 29. She is serving as an editorial board member of a number of nutrition and metabolic journals.

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