**FUNCTIONAL INACTIVATION OF MAST CELL ENHANCES SUBCUTANEOUS ADIPOSE TISSUE BROWNING THROUGH SEROTONIN IN MICE**

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**Objectives:** This study is in order to examine whether MCs in the SAT affect systemic energy expenditure and adipose tissue thermogenesis under protean environmental and stimulatory conditions and relative mechanism.

**Background:** Adipose tissue browning and systemic energy expenditure provide a defense mechanism against obesity and associated metabolic diseases. In western diet-fed mice, inactivation of mast cells (MCs) ameliorates obesity and insulin resistance along with improved metabolic rate. Yet, a direct role of MCs in adipose tissue thermogenesis and browning remains unclear.

**Methods:** Norepinephrine (NE)-stimulated metabolic rates were detected in 12 weeks old MC-deficient *Kitw-sh/w-sh* mice, MC-stabilized wide-type (WT) mice and MC reconstituted*Kitw-sh/w-sh*mice. Moreover, thermogenic program and associated molecular regulators, PDGFRα+ bipotential adipocyte precursors were assessed in adipose tissues. Finally, tryptophan hydroxylase 1 inhibitor, LX1031 was used to identify the critical participation of serotonin in mast cell-regulated browning and thermogenesis.

**Results:**Here we report that, in the context of mice on a chew diet, norepinephrine (NE)-stimulated metabolic rate is increased in MC-deficient *Kitw-sh/w-sh* mice and MC-stabilized wide-type (WT) mice. Such functional inactivation of MCs enhances thermogenesis and browning in subcutaneous adipose tissues (SAT), but not in brown (BAT) and epididymal adipose tissues (EAT). MC reconstitution to SAT blocks the aforesaid changes in *Kitw-sh/w-sh* mice. Mechanistic studies demonstrate that functional inactivation of MCs not only elevates the numbers of PDGFRα+ bipotential adipocyte precursors but also accelerates beige adipocyte differentiation in SAT. Using tryptophan hydroxylase 1 inhibitor, we show that MC-derived serotonin inhibits SAT beige adipocyte biogenesis and systemic energy expenditure.

**Conclusion:**Together, functional inactivation of MCs or inhibition of MC serotonin synthesis in SAT promotes adipocyte browning and systemic energy metabolism in mice.