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HDAC6 Impairs Diabetic Wound Healing by Regulating the Expression of IL-1β and IL-10 in a Mouse Model

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Chronic diabetic wounds involve sustained activation of M1 macrophages with IL-1β expression and suppression of M2 macrophages with reduced IL-10 expression. So in delayed diabetic wounds, high glucose is activating some factors which cause the imbalance between proinflammatory to pro healing phenotypes of macrophages. For the first time we have found that HDAC6 is one of the factors which is up regulated in delayed diabetic mice wounds induced by high glucose. To confirm our hypothesis, the resident peritoneal macrophages were stimulated with high glucose with or without HDAC6 inhibitor, TubastatinA (TSA). Macrophages treated with TSA showed reduced secretion of IL-1β with increased acetylation of α-tubulin with neither effect on inflammasome activation nor maturation of IL-1β and also increased IL-10 expression. To determine the expression of HDAC6 in diabetic wounds C57BL/6 mice were treated with 5 consecutive doses of streptozotocin (45mg/kg). After 5 weeks of consistent hyperglycemia, wounds were induced using 6mm biopsy punches and the expression of HDAC6 was determined at different time intervals post wounding. We found a significant upregulation of HDAC6 on day 3 and day 10 post wound induction. IL-1β expression was up regulated while IL-10 expression was reduced in diabetic wounds on day 10. Topical treatment with TSA gel showed accelerated wound closure in TSA group with reduced IL-1β and increased IL-10 expression. Wound healing parameters was evaluated using ELISA, RT-PCR, western blotting, immunohistochemistry and masons trichome staining.