May 8th, 12:30 PM - 1:30 PM

Type 2 Diabetes-Induced Hematopoietic Stem Cell Oxidant Stress Attenuates the Differentiation, Skews M1/M2 Specification of Monocytes/Macrophages and Delays Wound Healing in db/db Mice

Jinglian Yan  
*University of Massachusetts Medical School*

Guodong Tie  
*University of Massachusetts Medical School*

Shouying Wang  
*University of Massachusetts Medical School*

*See next page for additional authors*

---

Follow this and additional works at: [https://escholarship.umassmed.edu/cts_retreat](https://escholarship.umassmed.edu/cts_retreat)

Part of the [Endocrine System Diseases Commons](https://escholarship.umassmed.edu/endocrine), [Endocrinology, Diabetes, and Metabolism Commons](https://escholarship.umassmed.edu/endocrinology), [Physiology Commons](https://escholarship.umassmed.edu/physiology), [Surgery Commons](https://escholarship.umassmed.edu/surgery), and the [Translational Medical Research Commons](https://escholarship.umassmed.edu/cts_research)

---

Yan, Jinglian; Tie, Guodong; Wang, Shouying; and Messina, Louis M., "Type 2 Diabetes-Induced Hematopoietic Stem Cell Oxidant Stress Attenuates the Differentiation, Skews M1/M2 Specification of Monocytes/Macrophages and Delays Wound Healing in db/db Mice" (2013). *UMass Center for Clinical and Translational Science Research Retreat*. 2.  
[https://escholarship.umassmed.edu/cts_research/2013/posters/2](https://escholarship.umassmed.edu/cts_research/2013/posters/2)

---

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Presenter Information
Jinglian Yan, Guodong Tie, Shouying Wang, and Louis M. Messina

Creative Commons License
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License.
Type 2 diabetes-Induced Hematopoietic Stem Cell Oxidant Stress Attenuates the Differentiation, Skews M1/M2 Specification of Monocytes/Macrophages and Delays Wound Healing in db/db Mice

Jinglian Yan, Guodong Tie, Shouying Wang, Louis M. Messina

Department of Surgery, University of Massachusetts Medical School, Worcester, MA 01655

Corresponding author: Louis M. Messina, MD
Email: Louis.Messina@umassmemorial.org

Abstract:

Rationale: After recruitment to wounds, monocytes differentiate into macrophages which play a central role in all stages of wound healing. Wound healing is significantly delayed in type 2 diabetics. Although accumulating evidence suggests that delayed wound healing in type 2 diabetics is related to macrophages specification into M1/M2 phenotypes, the mechanism remains unknown.

Objective: This study tested the hypothesis that type 2 diabetes induces hematopoietic stem cells (HSCs) oxidant stress that reduces their differentiation towards monocytes and skews the specification of M1/M2 phenotype, thereby causing delayed wound healing.

Methods and Results: HSCs were sorted from bone marrow of WT and db/db type 2 diabetic mice. DCF staining showed significant oxidant accumulation in HSCs from db/db mice which was reversed by the antioxidant, N-acetylcysteine (NAC). Bone marrow monocyte concentration (FACS analysis of cell surface markers f4/80, cd14 and cd115) was significantly lower in db/db mice than in WT mice. NAC also reversed the reduced differentiation towards monocytes.

Wound closure rate was significantly delayed in db/db mice. Macrophages were isolated from wounds and their concentration and M1/M2 phenotype were quantified by flow cytometry. During the inflammatory phase of wound healing, macrophage concentration was decreased and the proportion of M1 macrophages was lower in db/db mice than in WT mice. During new tissue formation phase, macrophage concentration was decreased and the proportion of M2 macrophage was lower, but M1 macrophage was higher in db/db mice than in WT mice. During tissue remodeling phase, macrophage concentration was increased and M1 macrophage remained higher in db/db mice, but no difference was observed in the proportion of M2 macrophages. The reduced differentiation of HSCs towards monocytes and the delayed wound closure phenotype of db/db mice could be transferred to WT mice by transplanting db/db HSCs into lethally irradiated WT mice.

Conclusion: Type 2 diabetes-induced HSC oxidant stress impairs HSC differentiation towards monocytes, skews the M1/M2 specification of macrophages and thereby accounts for the delayed wound healing. Type 2 diabetes-induced HSC oxidant stress may be a heretofore unrecognized critical regulator of dysinflammation in type 2 diabetics.