The proinflammatory effects of macrophage-derived NADPH oxidase function in autoimmune diabetes

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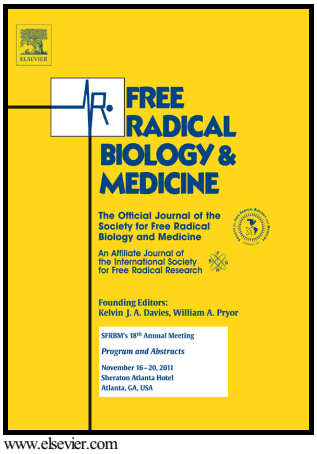

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PII: S0891-5849(18)30802-5
DOI: https://doi.org/10.1016/j.freeradbiomed.2018.04.581
Reference: FRB13749

To appear in: *Free Radical Biology and Medicine*

Received date: 4 January 2018
Revised date: 22 April 2018
Accepted date: 27 April 2018

Cite this article as: Joseph M. Feduska and Hubert M. Tse, The proinflammatory effects of macrophage-derived NADPH oxidase function in autoimmune diabetes, *Free Radical Biology and Medicine,* https://doi.org/10.1016/j.freeradbiomed.2018.04.581

The proinflammatory effects of macrophage-derived NADPH oxidase function in autoimmune diabetes

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Abstract

Type 1 diabetes (T1D) is an autoimmune disease culminating in the destruction of insulin-producing pancreatic β-cells. While ultimately a T cell-mediated disease, macrophages play an indispensable role in disease initiation and progression. Infiltrating macrophages generate an inflammatory environment by releasing NADPH oxidase-derived superoxide and proinflammatory cytokines. The synthesis of reactive oxygen species (ROS) is acknowledged as putative factors contributing to autoimmunity and β-cell damage in T1D. In addition to direct lysis, free radicals collectively participate in β-cell destruction by providing a redox-dependent third signal necessary for islet-reactive CD4 and CD8 T cell maturation and by inducing oxidative post-translational modifications of β-cell epitopes to further exacerbate autoimmune responses. This review will provide an overview of macrophage function and a synergistic cross-talk with redox biology that contributes to autoimmune dysregulation in T1D.