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SYMPOSIUM

Importance of Interleukin-1 and Interleukin-1 Receptor Antagonist in Short-Term Glucose Sensor Function *in Vivo*

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Abstract

Background:

The importance of the interleukin (IL)-1 cytokine family in inflammation and immunity is well established as a result of extensive *in vitro* and *in vivo* studies. In fact, much of our understanding of the *in vivo* importance of interleukin-1beta (IL-1B) is the result of research utilizing transgenic mice, such as overexpression or deficiencies of the naturally occurring inhibitor of IL-1 known as interleukin-1 receptor antagonist (IL-1RA). For the present studies, we utilized these transgenic mice to determine the role of IL-1B in glucose sensor function *in vivo*.

Methods:

To investigate the role of IL-1B in glucose sensor function *in vivo*, we compared glucose sensor function in transgenic mice that (1) overexpressed IL-1RA [B6.Cg-Tg(Il1rn)1Dih/J] and (2) are deficient in IL-1RA (B6.129S-*Il1rn*^{tm1Dih}/J), with mice that have normal levels of IL-1RA (C57BL/6).

Results:

Our studies demonstrated that, during the first 7 days post-sensor implantation (PSI), mice deficient in IL-1RA had extensive inflammation and decreased sensor function when compared to normal or IL-1RA-overexpressing mice.

Conclusion:

These data directly support our hypothesis that the IL-1 family of cytokines and antagonists play a critical role in controlling tissue reactions and thereby sensor function *in vivo* during the first 7 days PSI.

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Abbreviation: (CGM) continuous glucose monitoring, (DPI) days post-implantation, (HES) hematoxylin eosin stain, (icIL1RA) intracellular interleukin 1 receptor antagonist, (IL) interleukin, (IL-1B) interleukin-1beta, (IL-1RA) interleukin-1 receptor antagonist, (IL-1RA-KO) interleukin-1 receptor antagonist knockout mice (B6.129S-*Il1rn*^{tm1Dih}/J), (IL-1RA-OE) interleukin-1 receptor antagonist overexpressing mice (B6.Cg-Tg(Il1rn)1Dih/J), (IL-1R) interleukin-1 receptor, (IL-1RN) interleukin-1 receptor antagonist gene designation, (LCF) leukocyte chemotactic factor, (MQ) macrophage, (PMN) polymorphonuclear leukocyte, (PSI) post-sensor implantation, (sIL-1RA) soluble interleukin-1 receptor antagonist, (TNF) tumor necrosis factor, (VEGF) vascular endothelial growth factor

Keywords: angiogenesis, biosensor, diabetes, fibrosis, inflammation, interleukin-1, interleukin-1 receptor antagonist, tissue responses

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