
How Viral Infections Enhance or Prevent Type 1 Diabetes-From Mouse to Man

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More recent evidence shows that viral infections can enhance as well as prevent type 1 diabetes in experimental animal models [Filippi and von Herrath, 2010]. Published findings clearly indicate that the replication levels of the virus [Tracy et al., 2010] as well as the timing of infection [Richer and Horwitz, 2009] in relation to the autoimmune process both play an instrumental role. For example, enteroviruses replicating to higher levels, accelerate type 1 diabetes, whereas lower replication rates result in the prevention of diabetes. In human pancreata, elevated levels of MHC class 1 were detected in many islets which could be an indicator of a persistent infection. When present, the increased MHC affected all islet cells. MHC upregulation was present in a lobular and patchy fashion, and in many but not all cases associated with CD8 infiltration. In vivo tetramer staining showed that many of these CD8s cells were specific for beta cell antigens. It is proposed that it is possible that a persistent viral infection could unmask human islets for recognition by autoreactive CD8 T cells [von Herrath, 2009]. Indeed in animal models upregulation of MHC class 1 on beta cells is a pre-requisite for their destruction.

On the other hand, prevention of diabetes in NOD mice by Coxsackie viruses was associated with "invigorated" Tregs that was present in higher numbers and produced more TGF-beta [Filippi et al., 2009]. This phenomenon was TLR-2 dependent and effects of TLR-2 on TLR as well as on dendritic cells was a contributory factor. Therefore antiviral vaccines targeting for example enteroviruses might be able to influence the prevalence of human diabetes. **J. Med. Virol. 83:1672, 2011.**

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