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TSG-6 produced by hMSCs delays the onset of autoimmune diabetes by suppressing Th1 development and enhancing tolerogenicity

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Affiliations + expand

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Abstract

Genetic and immunological screening for type 1 diabetes has led to the possibility of preventing disease in susceptible individuals. Here, we show that human mesenchymal stem/stromal cells (hMSCs) and tumor necrosis factor-α-stimulated gene 6 (TSG-6), a protein produced by hMSCs in response to signals from injured tissues, delayed the onset of spontaneous autoimmune diabetes in NOD mice by inhibiting insulitis and augmenting regulatory T cells (Tregs) within the pancreas. Importantly, hMSCs with a knockdown of tsg-6 were ineffective at delaying insulitis and the onset of diabetes in mice. TSG-6 inhibited the activation of both T cells and antigen-presenting cells (APCs) in a CD44-dependent manner. Moreover, multiple treatments of TSG-6 rendered APCs more tolerogenic, capable of enhancing Treg generation and delaying diabetes in an adoptive transfer model. Therefore, these results could provide the basis for a novel therapy for the prevention of type 1 diabetes.

Figures

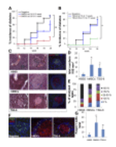

FIG. 1. Systemic administration of hMSCs or...

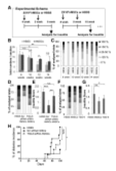

FIG. 2. Administered hMSCs reduced insulitis by...

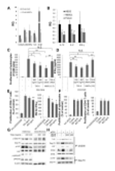

FIG. 3. hMSCs or TSG-6–suppressed Th1 cytokine...

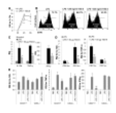

FIG. 4. TSG-6 suppressed APC activation in...

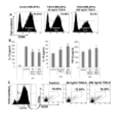

FIG. 5. TSG-6–generated tolerogenic APCs. Expression of...

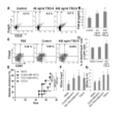

FIG. 6. TSG-6-BM APCs delayed diabetes in...

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