

## Roles of Toll-like Receptors on Islets in allogeneic Islet Transplantation

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### Roles of Toll-like Receptors on Islets in Allogeneic Islet Transplantation

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**Purpose:** Toll-like receptors (TLRs) on antigen presenting cells (APCs) play important roles in bridging innate and adaptive immunity. Recently, their roles have also been demonstrated in epithelial cells as well as T cells beyond APCs. We investigated the roles of toll-like receptors on pancreatic islet cells in allogeneic islet transplantation together with roles of toll-like receptors on the recipient side.

**Methods and Materials:** After islet cells were stimulated by polyinosinic:polycytidylic acid (poly I:C) and lipopolysaccharide (LPS), expression of chemokines, cytokines, and procoagulants in islet cells were measured using reverse transcriptase polymerase chain reaction (RT-PCR). To assess roles of toll-like receptors on the recipient side in allogeneic islet transplantation, islets from wild type Balb/C mice were transplanted to streptozotocin-induced diabetic MyD88 knockout, trif knockout, or wild type C57BL6/J mice. Next, we transplanted islets from wild type, MyD88 knockout, trif knockout, or TLR4 knockout C57BL6/J mice to streptozotocin-induced diabetic Balb/C mice in order to assess roles of TLRs on the donor side. Blood glucose levels were monitored to assess islet graft survival.

**Results:** Murine islet cells expressed TLR3 and TLR4 at resting status. Various chemokines (RANTES, IP-10, MCP-1), cytokines (type I interferon), induced nitric oxide synthase (iNOS) and procoagulant (tissue factor) were upregulated in islets in response to TLR ligands. These inductions by TLR activation were abrogated in experiments using TLR4 knockout mice. When islets from MyD88 KO, trif KO, or TLR4 KO C57BL6/J donor mice were transplanted to diabetic Balb/C mice, their islet allograft survivals were not better than the wild type group. There was also no significant difference in islet allograft survival between MyD88 KO, trif KO, and wild type recipients. However, some cases with MyD88 KO recipient showed very long term allograft survival.

**Conclusion:** Toll-like receptors on islet cells can mediate immune activation in vitro. However, roles of toll-like receptors in allogeneic islet transplantation across major mismatch barriers were limited both in the recipient side and in the donor side.

**Key Words:** 토르양 수용체, 췌도, 이식

Toll-like receptor, Islet, Transplantation