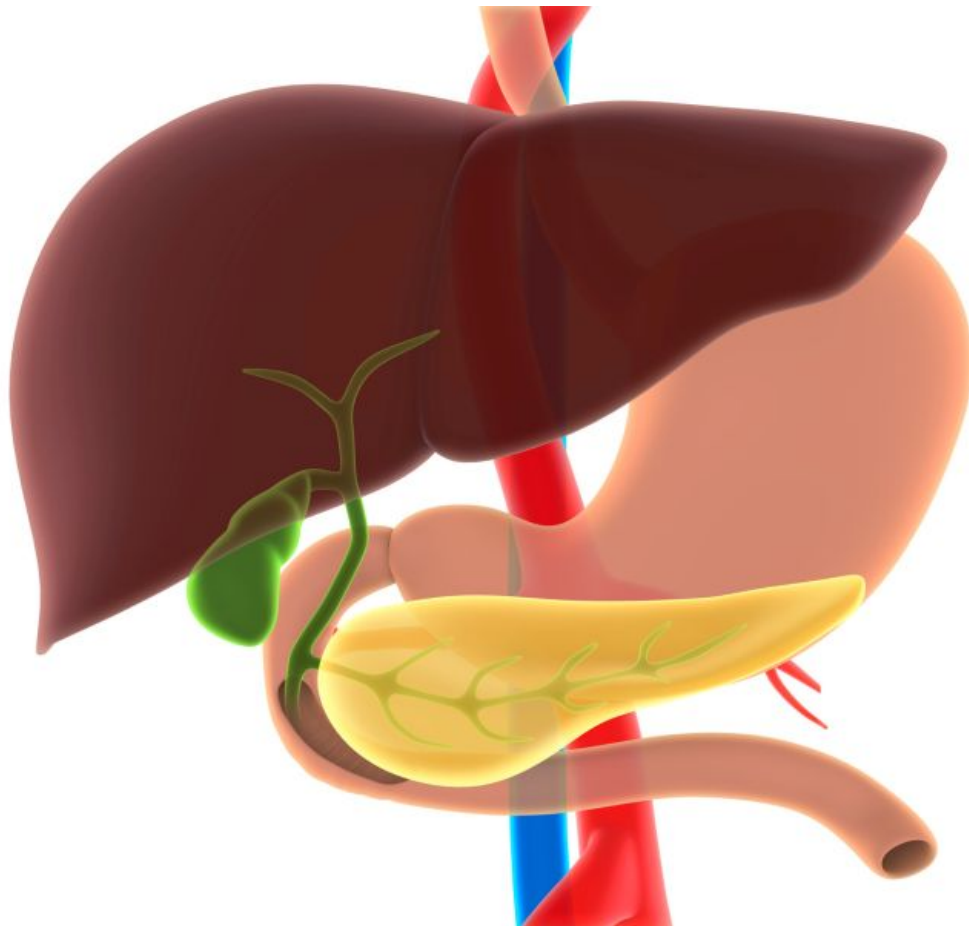


Islet-released mediators impact transplant outcome

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(HealthDay)—Cytokines and chemokines produced by pancreatic islets

in response to inflammatory and metabolic stress include interferon gamma-induced protein 10 (IP-10/CXCL10), which is associated with poor islet transplant outcomes, according to a study published in the September issue of *Diabetes*.

Gumpei Yoshimatsu, M.D., Ph.D., from the Baylor Research Institute in Dallas, and colleagues examined the physiological role of "isletokines" produced by [pancreatic islets](#) in response to inflammatory and [metabolic stress](#).

The researchers found that for patients undergoing [islet transplants](#), islets released multiple inflammatory mediators within hours of infusion. Among the highest-released was IP-10; high levels correlated with poor islet transplant outcomes. The contribution of donor islet-specific expression of IP-10 to islet inflammation and loss of beta-cell function in islet grafts was confirmed in transgenic mouse studies. Treatment of donor islets and recipient mice with anti-IP-10 neutralizing monoclonal antibody blocked the effects of islet-derived IP-10. IP-10 gene induction was mediated by calcineurin-dependent NFAT signaling in [pancreatic beta cells](#) in response to oxidative or inflammatory stress. P38 and JNK MAP kinase (MAPK) activity were required for the sustained correlation of NFAT and p300 histone acetyltransferase with the IP-10 gene, which differentially regulated expression of IP-10 and subsequent release of protein.

"These findings elucidate an NFAT-MAPK signaling paradigm for induction of isletokine expression in beta-cells and reveal IP-10 as a primary therapeutic target to prevent beta-cell-induced inflammatory loss of graft function after islet cell transplantation," the authors write.

The study was funded in part by Roche Diagnostic Corp.

More information: [Abstract](#)

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