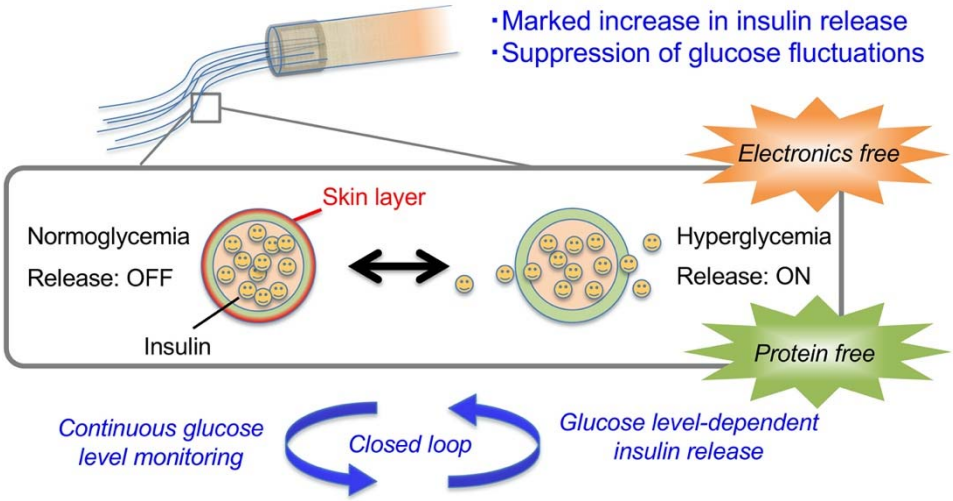
News Release

Title

Hollow fiber-combined glucose-responsive gel technology as an *in vivo* electronics-free insulin delivery system

Key Points

- **Closed-loop artificial pancreas was developed on the "electronics-free" and "protein-free" basis**
- **Combination of synthetic boronate gel with hemodialysis hollow fibers markedly increased insulin release *in vivo***
- **Our device ameliorated glucose fluctuations, in addition to average glucose levels, without inducing hypoglycemia in diabetic rats**



Summary

There is a growing body of evidence that not only sustained elevation of blood glucose levels but also the glucose fluctuation represents key determinants for diabetic complications and mortality. Current closed-loop insulin therapy option is limited to the use of electronic-based system, although it poses a number of technical issues with high cost. Here we demonstrate an electronics-free, synthetic boronate gel-based insulin-diffusion-control device technology that can cope with glucose fluctuations and potentially address the electronics-derived issues.

In this report, we combined the gel with hemodialysis hollow fibers to increase insulin release for clinical translation and scaled suitable for rats, serving as a subcutaneously implantable, insulin-diffusion-active site in a manner dependent on the subcutaneous glucose. Continuous glucose monitoring test revealed that our device not only normalizes average glucose level of rats but also markedly ameliorates the fluctuations over timescale of a day without inducing hypoglycemia, to our knowledge, for the first time using an electronics-free system *in vivo*, and that leads to the prevention of diabetic complications. With inherent stability, diffusion-dependent scalability, week-long sustainability as well as remarkably acute glucose-responsiveness, this boronate gel-based technology may offer a low-cost alternative to the current electronics-based approaches.

Research Background

There is a growing body of evidence that not only sustained elevation of blood glucose levels but also the glucose fluctuation represents key determinants for diabetic complications and mortality. Current closed-loop insulin therapy option is limited to the use of electronic-based system, although it poses a number of technical issues; high cost, burdensome sensor calibration, risk of electronic failures, and so on. Among many efforts of developing "electronics-free" or chemically-driven alternatives, formulations based on glucose oxidase and sugar-binding lectins such as Concanavalin A are the two major approaches. However, their inherently unstable (due to the protein denaturation) and toxic nature yields in a generally short duration of function. As a result, it remains to be elucidated whether these systems appropriately ameliorate the daily fluctuation of blood glucose levels *in vivo*.

Research Results

In sharp contrast to the above, our study focuses on an "electronics-free" and "protein-free", synthetic boronate gel-based insulin-diffusion-control device technology that can cope with glucose fluctuations and potentially address the electronics-derived issues. In this report, we combined the gel with hemodialysis hollow fibers to increase insulin release for clinical translation and scaled suitable for rats, serving as a subcutaneously implantable, insulin-diffusion-active site in a manner dependent on the subcutaneous glucose. We assessed the therapeutic effect of the device on glucose metabolism in streptozotocin-induced type 1 diabetic rats (conditions with absolute insulin deficiency). Continuous glucose monitoring test also revealed that our device not only normalized average glucose level of rats but also markedly ameliorated the fluctuations over timescale of a day without inducing hypoglycemia.

Research Summary and Future Perspective

With inherent stability, diffusion-dependent scalability, week-long sustainability as well as remarkably acute glucose-responsiveness, this boronate gel-based technology may offer a remarkably economic alternative to the current electronics-based closed loop systems to treat diabetes and glucose spikes.

Publication

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