An Engineered Nanosugar Enables Rapid and Sustained Glucose-Responsive Insulin Delivery in Diabetic Mice.

Rong Xu[1], Sukhvir Kaur Bhangu[1,2], Frank Caruso[2], Christoph E. Hagemeyer[1] and Francesca Cavalieri[3]**

1. Australian Centre for Blood Diseases, Central Clinical School, Monash University, Melbourne, Victoria, 3004, Australia
2. Department of Chemical Engineering, The University of Melbourne Parkville, Victoria 3000, Australia
3. School of Science, RMIT University, Melbourne, Victoria 3000, Australia
francesca.cavalieri@rmit.edu.au

Glucose-responsive insulin delivery platforms that are sensitive to dynamic glucose concentration fluctuations and provide both rapid and prolonged insulin release have great potential to control hyperglycemia and avoid hypoglycemia diabetes. Here, we engineered biodegradable and charge-switchable phytoglycogen nanoparticles capable of glucose-stimulated insulin release. The nanoparticles are "nanosugars" bearing glucose sensitive phenylboronic acid groups and amine moieties that allow effective complexation with insulin (95% loading capacity) to form nanocomplexes. A single subcutaneous injection of nanocomplexes showed a rapid and efficient response to a glucose challenge in two distinct diabetic mouse models, resulting in optimal blood glucose levels (below 200 mg dL^{-1}) for up to 13 h. The morphology of the nanocomplexes was found to be key to controlling rapid and extended glucose-regulated insulin delivery *in vivo*. Our studies revealed that the injected nanocomplexes enabled efficient insulin release in the mouse, with optimal bioavailability, pharmacokinetics, and safety profiles. These results highlight a promising strategy for the development of a glucose-responsive insulin delivery system based on a natural and biodegradable nanosugar[1].

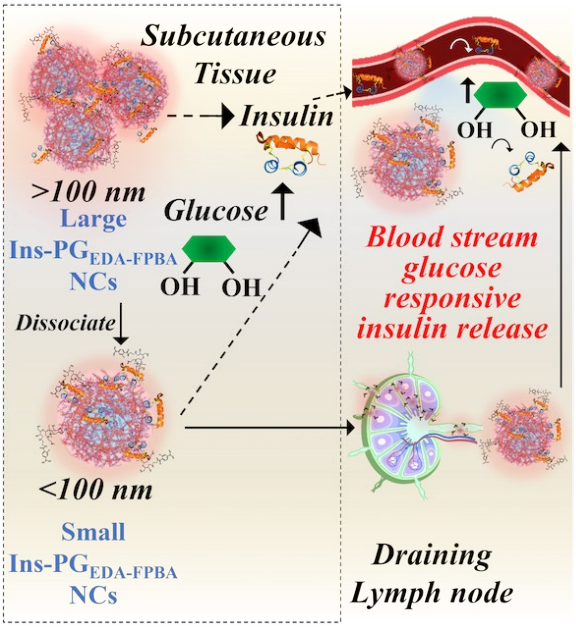

Figure 1: **The architecture and morphology of the nanocomplexes are tailored to control the bioavailability, and pharmacokinetics of insulin through the direct blood capillaries absorption and the lymphatic trafficking.**

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