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Reference:

Yu, J., Zhang, Y., Yea, Y., DiSanto, R., Sun, W., Ranson, D., Ligler, F.S. Buse, J.B. and Gu, Z. (2015) Microneedle-array patches loaded with hypoxia-sensitive vesicles provide fast glucose-responsive insulin delivery. June 22nd. Proceedings of the National Academy of Sciences of the United States of America. .

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Abstract:

A glucose-responsive “closed-loop” insulin delivery system mimicking the function of pancreatic cells has tremendous potential to improve quality of life and health in diabetics. Here, we report a novel glucose-responsive insulin delivery device using a painless microneedle-array patch (“smart insulin patch”) containing glucose-responsive vesicles (GRVs; with an average diameter of 118 nm), which are loaded with insulin and glucose oxidase (GOx) enzyme. The GRVs are self-assembled from hypoxia-sensitive hyaluronic acid

(HS-HA) conjugated with 2-nitroimidazole (NI), a hydrophobic component that can be converted to hydrophilic 2-aminoimidazoles through bioreduction under hypoxic conditions. The local hypoxic microenvironment caused by the enzymatic oxidation of glucose in the hyperglycemic state promotes the reduction of HS-HA, which rapidly triggers the dissociation of vesicles and subsequent release of insulin. The smart insulin patch effectively regulated the blood glucose in a mouse model of chemically induced type 1 diabetes. The described work is the first demonstration, to our knowledge, of a synthetic glucose-responsive device using a hypoxia trigger for regulation of insulin release. The faster responsiveness of this approach holds promise in avoiding hyperglycemia and hypoglycemia if translated for human therapy.

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