MEDICAL THERAPIES AND PHARMACOLOGY

TRANSDERMAL DELIVERY OF NANO AND MACRO MOLECULES VIA TEMPORAL PRESSURE WITH INSULIN AS PROOF OF CONCEPT

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Introduction: Current transdermal drug delivery strategies require high doses of chemical enhancers, fragile biomolecules, or sophisticated equipment to overcome the skin barrier, and they are only effective for hydrophobic small molecule drugs (<500Da).

Objective: Here, we report a novel pain-less topical delivery using temporal pressure technology.

Materials and Methods: This delivery procedure was optimized in vivo in both mice and rabbits with 0.28MPa pressure for 1 minute and 5minutes utilizing polystyrene nanoparticles and dextran molecules of different sizes. Last but not least, we delivered topical insulin across the skin in diabetic mice model via temporal pressure.

Results: Post temporal pressure, >2-fold improvement of fluorescent polystyrene nanoparticles (up to 500nm) and fluorescent tag dextran molecules (up to 20kDa) were observed to penetrate the epidermis and 430 µm deep into the dermis. This technology generates superficially invisible micropores of ~3 µm2 in size in the epidermis. Elevated expression of gap junction protein connexin-43 and a reduced expression of tight junction protein in the epidermis facilitated the delivery of these nanoparticles and macromolecules. The temporal pressure technology effectively regulated the blood glucose in type 1 diabetes mice. We achieved 80% reduction in blood glucose which lasted >7 hours without compromising the skin barrier.

Conclusions: The described work is the first demonstration, to our knowledge, of insulin, nanoparticles of 500nm and macromolecules of 20kDa to enter the skin using a non-invasive temporal pressure technology. This can be translated from bench to bedside for

both clinical and academic scientists who aim to deliver big molecules and nanoparticles non-invasively across the skin.