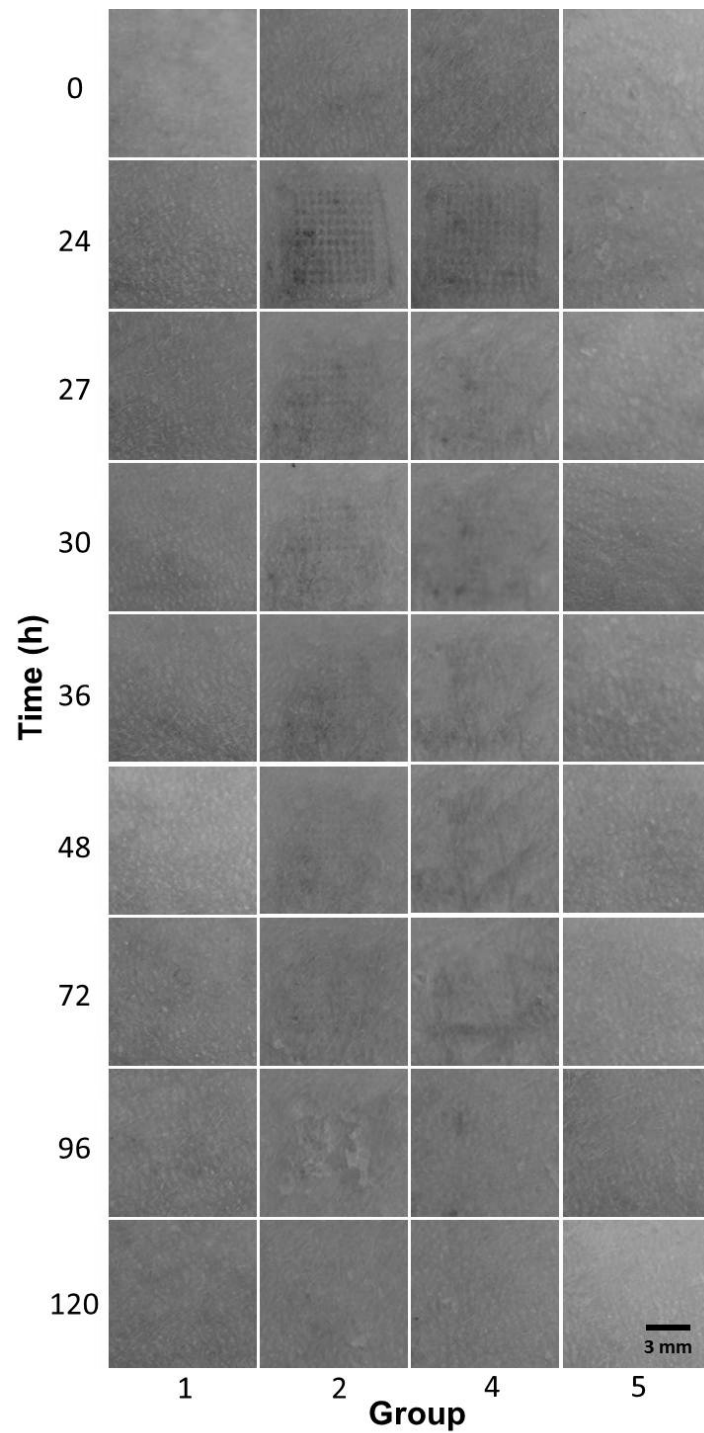


## **Supplementary Information**

Dissolving Microneedle Patch for Transdermal Delivery of Human Growth Hormone

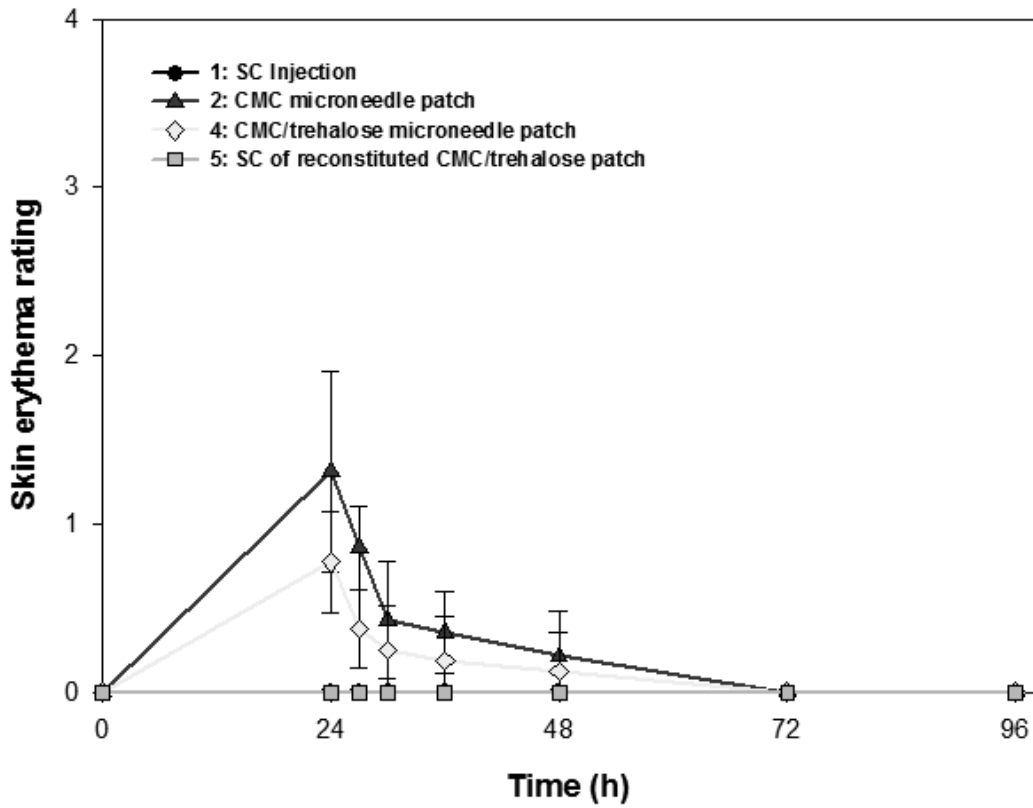
Jeong Woo Lee, Seong-O Choi, Eric I. Felner and Mark R. Prausnitz

**Figure S1.**



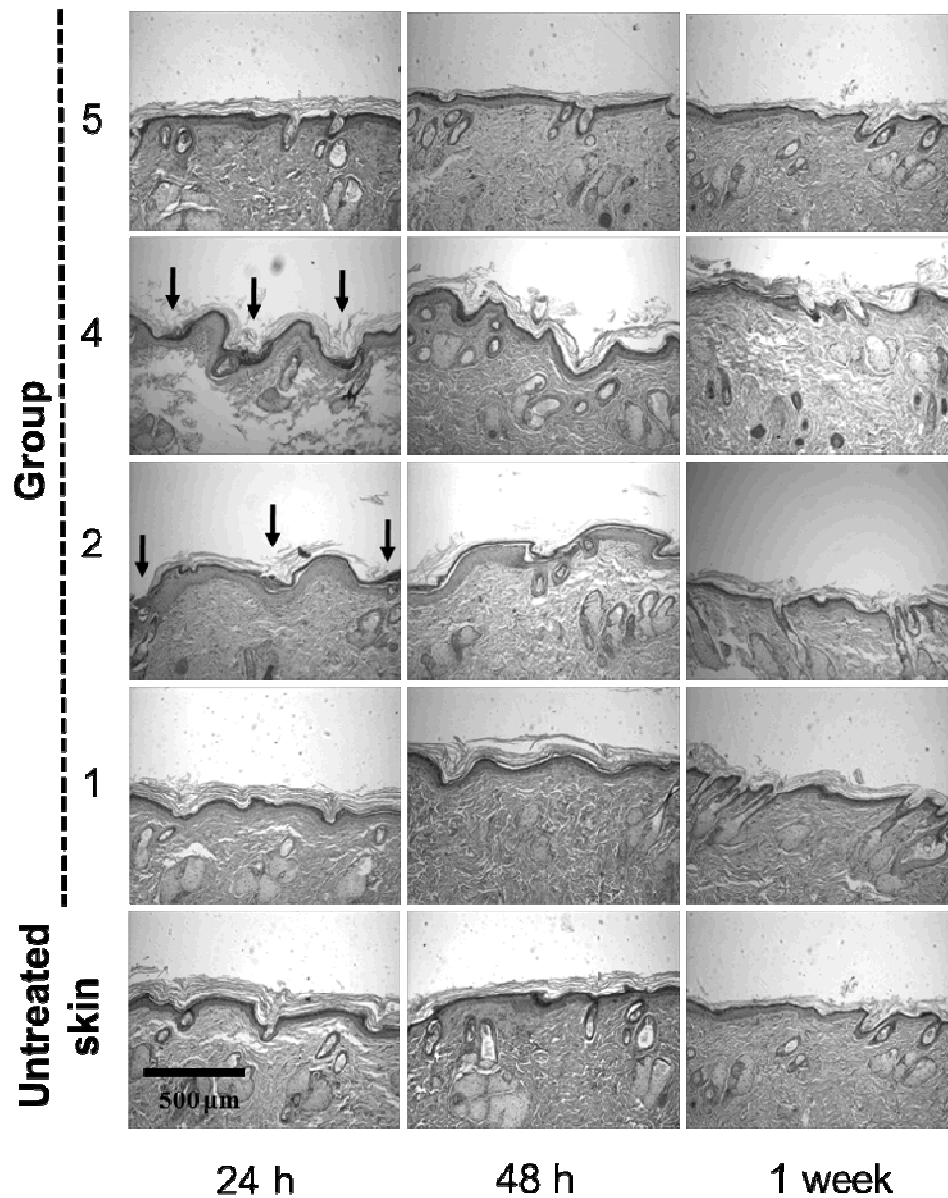
**Figure S1.** Representative images of hairless rat skin in vivo during recovery after hGH administration. Each group is the same group as in Figure S5. The skin was occluded for the first 24 h and unoccluded afterwards.

**Figure S2.**



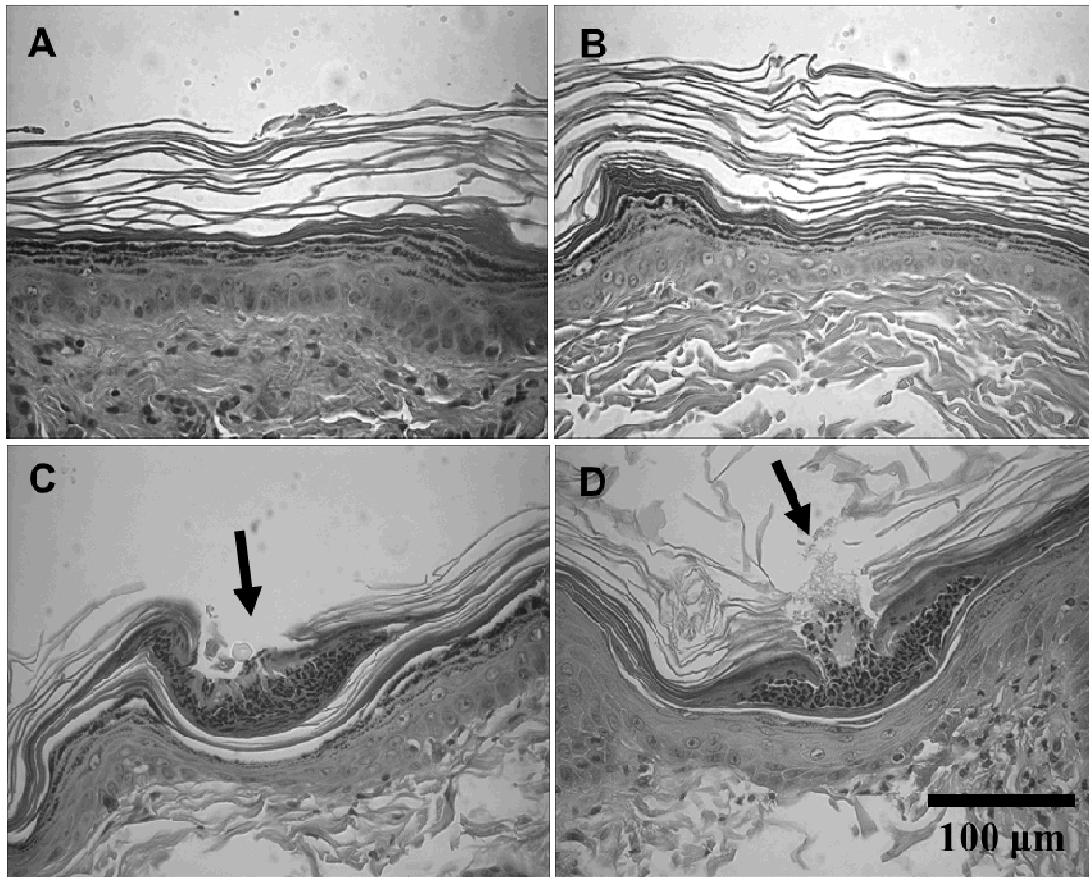
**Figure S2.** Skin erythema rating after treatment with microneedles. Erythema scale: 0 = normal skin, 1 = slight, 2 = mild, 3 = moderate, and 4 = severe erythema. Each group is the same as defined in Figure S5. Skin erythema was not rated during the first 24 hours, because it was occluded and could not be seen. No edema was seen in any groups. Data points represent the average  $\pm$  standard deviation for  $n \geq 4$  for up to 72 hours.

Figure S3.



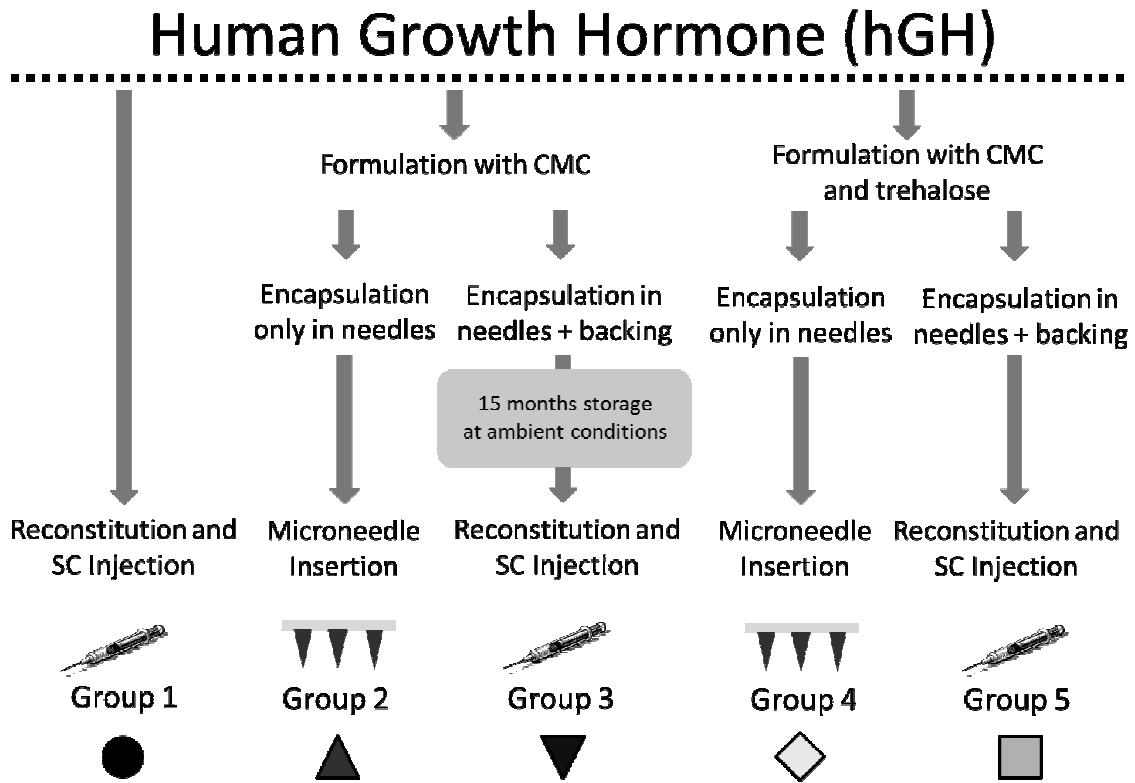
**Figure S3.** Representative histological images of skin biopsied from hairless rats in vivo. Each group is the same as described in Figure S5. At 24 h, Groups 2 and 4 show the sites of microneedle insertion (arrows) and appear to undergo highly localized inflammatory responses (see Figure S4 for magnified views).

**Figure S4.**



**Figure S4.** Representative histological images under high magnification of skin biopsied from hairless rats in vivo. (A) Normal skin (negative control). (B) Subcutaneously injected skin (Group 1). Skin at sites of microneedle insertion 24 h after treatment with a (C) CMC microneedle patch (Group 2) and (D) CMC/trehalose microneedle patch (Group 4). Note the presence of cells at the sites of insertion in (C) and (D) (arrows), which appear to be associated with inflammation.

Figure S5.



**Figure S5.** Summary of hGH formulation and administration. Group 1: subcutaneous injection of hGH, Group 2: CMC microneedle patch encapsulating hGH, Group 3: subcutaneous injection of reconstituted CMC microneedle patch encapsulating hGH after 15 months storage at ambient condition, Group 4: CMC/trehalose microneedle patch encapsulating hGH, and Group 5: subcutaneous injection of reconstituted CMC/trehalose microneedle patch encapsulating hGH.