Docket #: S22-164

Use of Piezo Inhibitors for the Prevention of Skin Scarring

Skin wounds invariably heal by developing fibrotic scar tissue, which can result in devastating disfigurement, growth restriction and permanent functional loss. Despite a plethora of clinical options and an enormous consumer market for scar treatment; no current therapeutic strategy prevents or reverses this fibrotic process. Inventors at Stanford developed a novel method of use of Piezo1 and Piezo2 inhibitors in the prevention of skin scarring. Piezo channels are mechanosensitive ion channels that mediate stretch sensation. Piezo1 and Piezo2 inhibitors inhibit cellular mechanical signaling, an important contributor to scarring and fibrosis. Using a mouse model of wound healing, we find that a single dose of piezo1 or piezo2 treatment (local injection) reduces scarring and fibrosis, specifically via adipocytes as they are mechanically sensitive. Aside from physically offloading wound tension through specialized wound dressings, no effective therapy for skin scarring exists. No targeted molecular agents have been able to reduce scar burden while not comprising or delaying wound repair. The novel method not only reduces scarring, but also improves scar appearance and allows for regrowth of skin elements such as hair follicles and sweat glands (absent in scars), which are highly significant outcomes for patients suffering from skin scarring.

Applications

- Scar prevention in the skin
- Inhibition of mechanical sensing in adipocytes
- Treatment of organ fibrosis

Advantages

- Currently, there is no effective drug that can overcome skin fibrosis in the skin. The inventors have provided a drug that not only inhibits fibrosis in the skin, but has potential in other organs where fat accumulation contributes to organ fibrosis.

Publications

- Griffin MF, Talbott HE, Guardino NJ, Guo JL, Spielman AF, Chen K, Parker JBL, Mascharak S, Henn D, Liang N, King M, Cotterell AC, Bauer-Rowe KE, Abbas DB, Diaz Deleon NM, Sivaraj D, Fahy EJ, Downer M, Akras D, Berry C, Cook J, Quarto N, Klein OD, Lorenz HP, Gurtner GC, Januszyk M, Wan DC, Longaker MT (2023). Piezo inhibition prevents and rescues scarring by targeting the adipocyte to fibroblast transition. *bioRxiv* **(Preprint)**. 2023 Apr 4:2023.04.03.535302. PMID: 37066136; PMCID: PMC10103999.

Patents

- Published Application: WO2023211728
- Published Application: 20250195474

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