2023「中技社科技獎學金」

2023 CTCI Foundation Science and Technology Scholarship

境外生生活助學金

Bursary Award for Overseas Students

國立清華大學 National Tsing Hua University

MOST 110-2639-E-007-001-APS

Converging Innovations in Healthcare: Smart Electroactive Dressing for Wound Healing and Monitoring, along with Harnessing β-Glucans-Functionalized Nanocarriers Targeted for Oral Delivery Treament

Nguyen Hoang To Nhien, 3th year Ph.D. Student **Advisor: Hsing-Wen Sung**

Department of Chemical Engineering, National Tsing Hua University, Hsinchu, Taiwan

ABSTRACT

Traditional wound dressings struggle to actively support and monitor wound healing. An electroactive dressing with a polydopamine crosslinked carboxymethyl chitosan conductive hydrogel layer and an interdigitated array (IDA) electrode has been developed. This dressing transmits bioelectrical signals, increasing cellular activity and tissue regeneration in mice with complete skin defects. The IDA electrode detects electrical changes for real-time, noninvasive healing monitoring. Wireless data collection integrated with WIFI aids early infection detection and remote medical intervention.

Desmoplastic tumor microenvironment (TME) worsens pancreatic ductal adenocarcinoma (PDAC) prognosis. Targeted PDAC therapy uses β-glucans-functionalized zinc-doxorubicin nanoparticles (βGlus-ZnD NPs). Oral βGlus-ZnD NPs target microfold cells, cross the intestinal barrier, and are phagocytosed by macrophages to form βGlus@Mϕ. βGlus-ZnD@Mϕ-carrying endogenous macrophages accumulate in tumor tissue through the intestinal lymphatic system. These macrophages produce matrix metalloproteinases, break the desmoplastic barrier, and become M1-like. This modulates the TME, recruiting effector T cells and inducing tumor cell apoptosis. Combined with immune checkpoint blockade, βGlus-ZnD@Mϕ suppresses primary tumor growth and metastasis in PDAC, offering a promising treatment.

SMART ELECTROACTIVE DRESSING FOR WOUND HEALING AND MONITORING

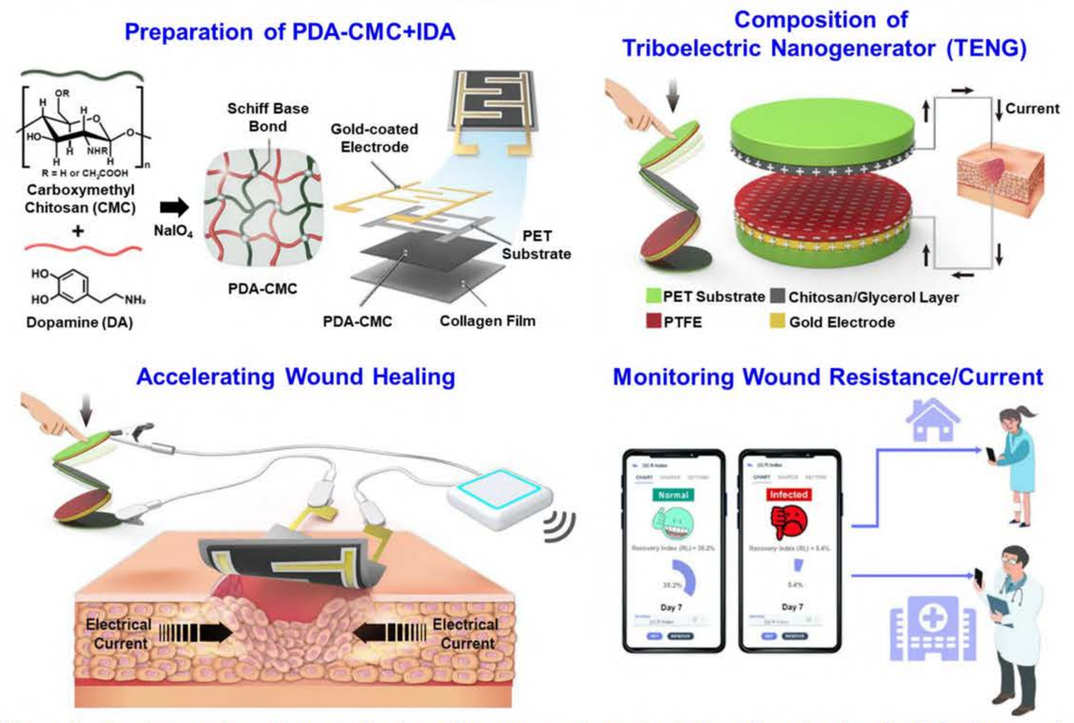


Figure 1. Structure and working mechanism of as-proposed smart electroactive dressing that simultaneously promotes wound healing and noninvasively monitors healing progress. The wound monitoring system is integrated with a self-powered system that can be worn by patients; issue to them early warnings of potential infection; and wirelessly send wound progression data to remote medical staff for dynamic intervention. PET, polyethylene terephthalate; PTFE, polytetrafluoroethylene.

WOUND HEALING AND MONITORING SYSTEM

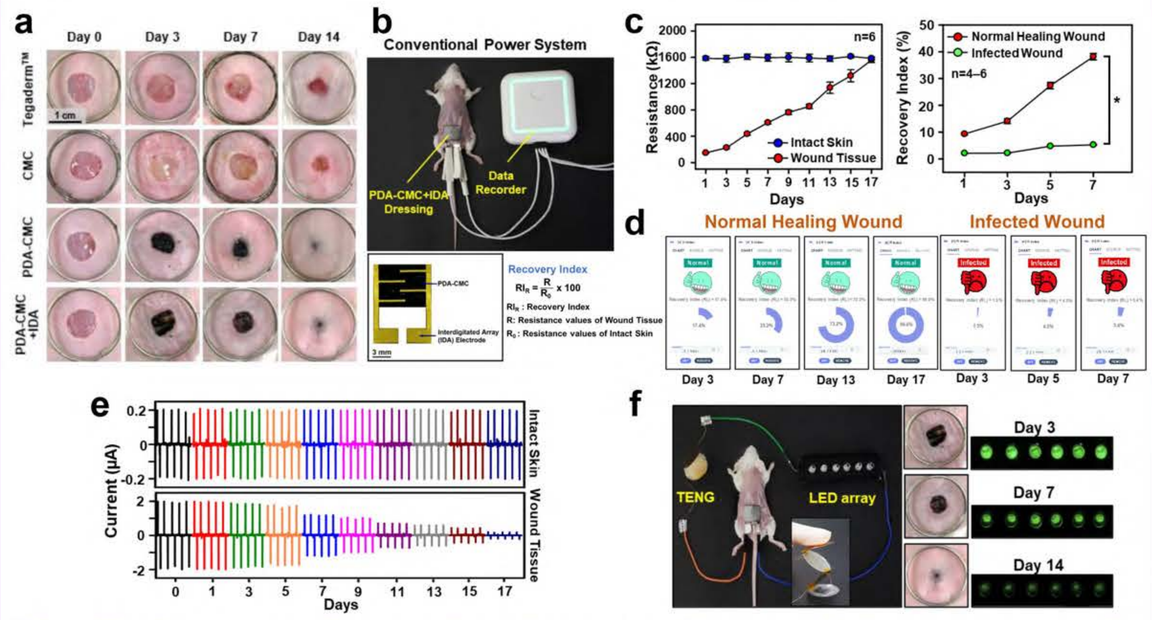
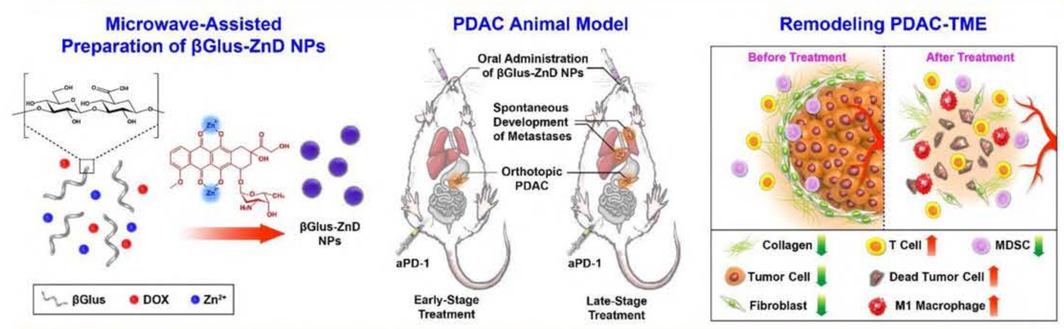


Figure 2. Results of wound healing and monitoring that was powered by a conventional power source and a self-powered system, TENG. (a) Photographs of wounds taken at different times. (b) Photograph of experimental setup and as-prepared smart electroactive dressing (PDA-CMC+IDA). (c) Resistance values of intact skin and wound tissue, and wound recovery index obtained from a normally healing wound and an infected wound. (d) Images captured from smartphone, showing cyclic diagram of wound recovery index. (e) Output currents collected from intact skin and wound tissue. (f) Photograph of wound monitoring system with a commercial LED array, showing illumination of a normally healing wound, obtained at different times.

ORALLY ADMINISTERED NPs as "PRECISION-GUIDED STEALTH MISSILES" for TARGETED PANCREATIC CANCER THERAPY



βGlus-Functionalized NPs as "Precision-Guided Stealth Missiles"

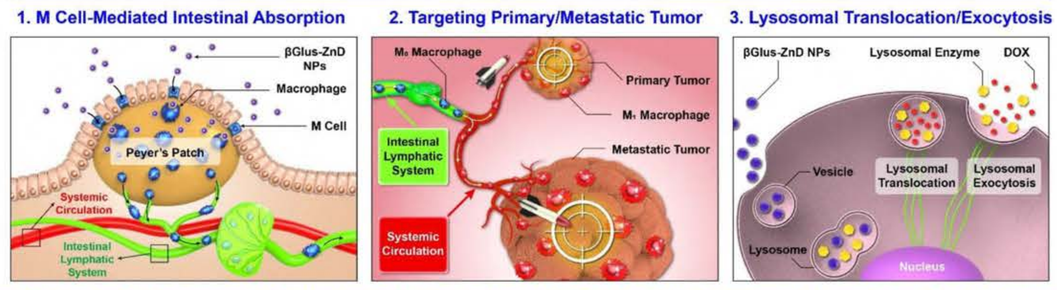


Figure 3 displays the composition/structure of the as-proposed βGlus-ZnD NPs; their oral delivery route and therapeutic mechanism in an orthotopic mouse model of desmoplastic pancreatic tumor are also shown. Following oral administration, the βGlus that are exposed on the surfaces of the particles target the Dectin-1 receptors on M cells. Upon their M-cell transcytosis, the βGlus-ZnD NPs are phagocytosed by the endogenous immune cells that reside in the intestinal lymphatic system (ILS), such as macrophages (Mϕ, which also express abundant Dectin-1 on their cellular membranes). The Mϕ that hitchhike βGlus-ZnD NPs (βGlus-ZnD@Mϕ) responds to tumor-related chemokine/cytokine cues, transiting through lymphatic vessels, entering systemic circulation, and eventually homing in on the tumor site. The hitchhiking Mϕ are endogenous, and so are excluded from immune reactions; thus, this Mϕ-mediated drug delivery platform may act as a "precision-guided stealth missile" for targeted PDAC therapy.

ANTITUMOR EFFICACY AND COMBINATION with IMMUNO CHECKPOINT BLOCKADE

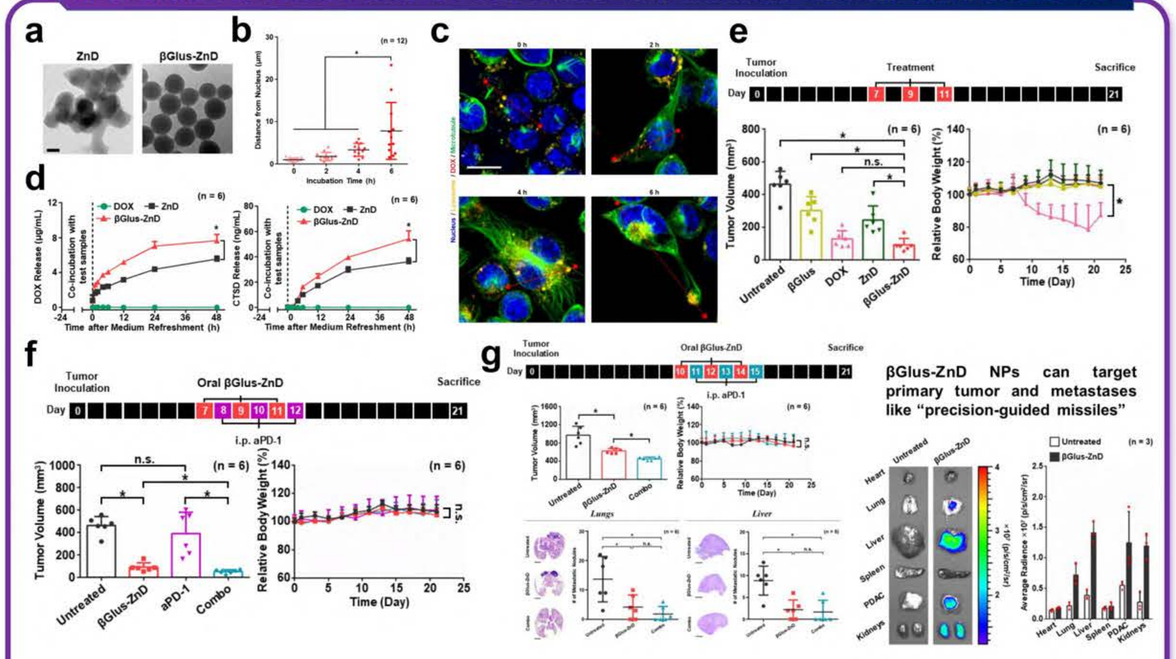


Figure 4. Results of characterization and therapeutic efficacy of βGlus-ZnD NPs. (a) TEM images of ZnD/βGlus-ZnD NPs. Scale bar = 100 nm. (b,c) CLSM images of lysosomal trafficking within RAW264.7 cells that had been pretreated with βGlus-ZnD NPs for predetermined intervals. (d) Profiles of lysosomal exocytosis of DOX and CTSD. (e) Antitumor efficacy and TME modulation in early-stage PDAC model. (f) Antitumor efficacy and TME modulation following ICB therapies. (g) Antitumor efficacy and TME modulation in a late-stage PDAC model.

PUBLICATIONS

1. Nhien Nguyen†, Zhong-Hong Lin†, Snigdha Roy Barman†, Chiranjeevi Korupalli, Ni-Xuan Song, Yen Chang, Fwu-Long Mi, Hsing-Wen Sung*, Yu-Jung Lin*. "An Integrated Smart Electroactive Dressing and Self-powered System that Promotes Wound Healing and Noninvasively Monitors Healing Progress". *Nano Energy* 2022, 99, 107393.
2. Kuan-Hung Chen†, Nhien Nguyen†, Tun-Yu Huang†, Yu-Jung Lin, Yu-Tzu Yu, Hsiang-Lin Song, Jui-To Wang, Khanh Nguyen, Hsin-Lung Chen, Li-An Chu, Hui-Hua Kenny Chiang, Hsing-Wen Sung. "Macrophage-Hitchhiked Orally Administered β-Glucans-Functionalized Nanoparticles as "Precision-Guided Stealth Missiles" for Targeted Pancreatic Cancer Therapy". *Advanced Materials* 2023, 2304735 (†Equal Contribution)
3. Chiranjeevi Korupalli†, Hui Li†, Nhien Nguyen, Fwu-Long Mi, Yen Chang, Yu-Jung Lin*, Hsing-Wen Sung*. "Conductive Materials for Healing Wounds: Their Incorporation in Electroactive Wound Dressings, Characterization, and Perspectives". *Advanced Healthcare Materials* 2020, 2001384.

財團法人 中技社 CTCI FOUNDATION