## Multifunctional Sprayable Hydrogel for Real-time Monitoring and Treatment of Diabetic Wounds

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INTRODUCTION: Diabetic wounds are one of the most frequent problems experienced by people with diabetes mellitus (DM). Chronic diabetic wounds continue to pose a significant problem due to their persistent inflammation and slow healing process. Additionally, accurately assessing the status of the wound solely by macroscopic observation presents a challenge in determining an effective treatment strategy. Therefore, an effective and non-invasive monitoring system that promotes diabetic wound healing is needed to address this "black box".

METHODS: In this study, we designed a multifunctional sprayable hydrogel containing mRNA optical nanosensors (i.e., NanoFlare (NF)) and antibacterial agents (LL37) based on laponite and poly (acrylic acid) (PAA) hydrogel. In addition, the fluorescent signals from NFs were detected and acquired using portable imaging devices in vivo. This study was approved by IACUC.

RESULTS SECTION: The optimal physical properties of laponite+PAA hydrogel were determined for a sprayable hydrogel, as well as the biological properties, which included mechanical properties, cytotoxicity, cell proliferation, and antibacterial effect. Three optical mRNA nanosensors, including COL1A1-NF, PECAM1-NF, and GAPDH-NF, were designed, fabricated, and their efficacy as biomarkers for diabetic wound healing was demonstrated. The application of NFs and LL37-incorporated sprayable hydrogel significantly enhanced wound healing by over 20% in vivo, for both normal and diabetic wounds. In addition, the inflammatory and proliferative stages can be identified by using the fluorescence signal-based Wound Healing Index through PECAM1-NF and COL1A1-NF.

DISCUSSION: The multifunctional sprayable hydrogel designed in this study provides an easy-to-use biomarker-based monitoring system that allows diabetic wounds to be identified, managed, and healed effectively.

SIGNIFICANCE/CLINICAL RELEVANCE: Our study highlights the enormous potential of the multifunctional sprayable hydrogel for promoting wound healing and monitoring the condition of wounds, suggesting significant therapeutic applications in the future.

## REFERENCES:

1. Hwang, J.; Seo, Y.; Jeong, D.; Ning, X.; Wiraja, C.; Yang, L.; Tan, C. T.; Lee, J.; Kim, Y.; Kim, J. W., Monitoring wound healing with topically applied optical NanoFlare mRNA nanosensors. Advanced Science 2022, 9 (18), 2104835.

2. Gao, D.; Zhang, Y.; Bowers, D. T.; Liu, W.; Ma, M., Functional hydrogels for diabetic wound management. APL bioengineering 2021, 5 (3), 031503.

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## IMAGES AND TABLES:

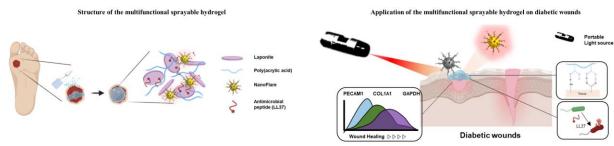


Figure 1. Schematic diagram of the multifunctional sprayable hydrogel.

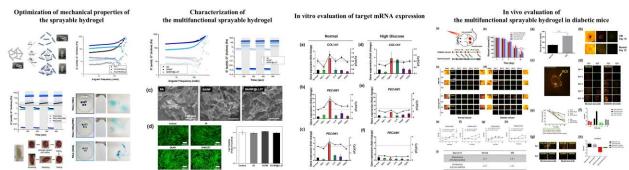


Figure 2. In vitro characterization and in vivo evaluation of the multifunctional sprayable hydrogel.