Nanoparticle-Driven Tendon Repair: Role of Vasoactive Intestinal Peptide in Immune Modulation and Stem Cell Enhancement

Yucheng Gao[1, 2], Liu Shi[1, 2], Hao Wang[2], Chuwei Tian[2], Yunfeng Rui[1, 2]
[1] Department of Orthopaedics, Zhongda Hospital, School of Medicine, Southeast University, No. 87 Ding Jia Qiao, Nanjing, Jiangsu, 210009, PR China
[2] School of Medicine, Southeast University, No. 87 Ding Jia Qiao, Nanjing, Jiangsu, 210009, PR China
Email of Presenting Author: gaoyucheng2022@126.com (Yucheng Gao)

Abstract

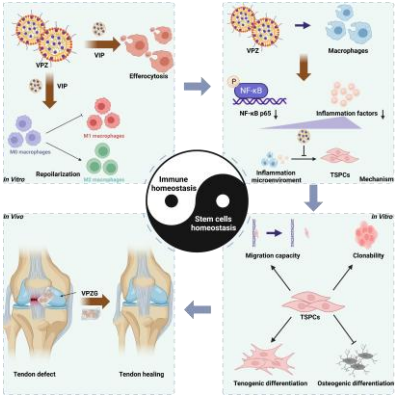
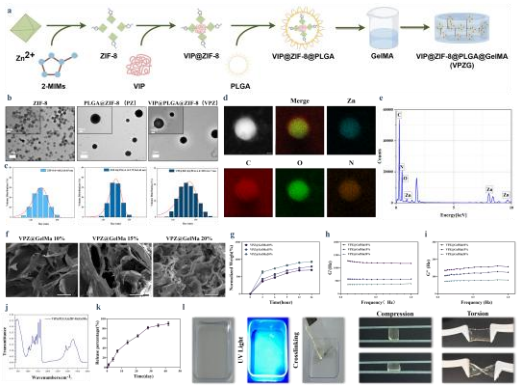
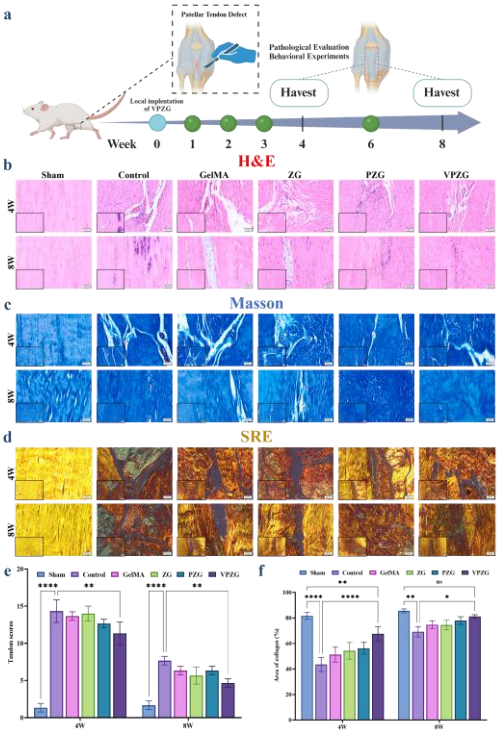
INTRODUCTION: Tendon injuries are common but hard to repair (limited endogenous capacity; current treatments have poor outcomes). Macrophage polarization (M1 proinflammatory/M2 reparative) and tendon stem/progenitor cells (TSPCs) are key for regeneration. Vasoactive intestinal peptide (VIP) aids bone/nerve repair but its tendon role is unclear. Hypothesis: VIP-loaded nanoparticle-hydrogel (VPZG: VIP@PLGA@ZIF-8@GelMa) promotes tendon repair by modulating immune homeostasis and enhancing TSPC function.

METHODS: Synthesized VPZG, characterized via TEM/ELISA (sustained release). Tested macrophage polarization (immunofluorescence/qPCR) and TSPC function (CFU/scratch assay) with LPS-induced inflammation. SD rat patellar tendon defect model (Ethics Approval: 20230301023), implanted VPZG; evaluated tissue via HE/Masson staining.

RESULTS SECTION: VPZG sustained VIP release for 30 days (~50% released in 14 days). VPZG promoted macrophage M2 polarization (Arg-1 ↑, CCR7 ↓), inhibited NF-κB/inflammation (IL-1β ↓, IL-10 ↑), and enhanced TSPC clonogenicity/migration/tenogenic differentiation. VPZG reduced inflammation, improved collagen alignment (collagen area ↑ ~50% at 8w), upregulated tenogenic markers (TNMD ↑), no organ damage.

DISCUSSION: VPZG promotes tendon repair via immune modulation and TSPC enhancement, validating the hypothesis. Limitations: Rat model not replicating human injuries; intercellular communication mechanisms unelucidated.

SIGNIFICANCE/CLINICAL RELEVANCE: (1-2 sentences): VPZG is a translatable strategy to improve tendon repair outcomes (faster recovery, lower re-rupture risk), addressing clinical unmet needs and advancing soft tissue regenerative medicine.

ACKNOWLEDGMENT: Medical key project of Nanjing Health Science and Technology Development Special Fund Project (ZKX24065), Zhongda Hospital Affiliated to Southeast University, Jiangsu Province High-Level Hospital Construction Funds (CZXM-GSP-KY), Winfast Charity Foundation (YL20220525).

IMAGES AND TABLES:
Figure 1. Regulation of immune and stem cell homeostasis to promote healing of patellar tendon injuries by VPZG. VPZ, VIP@PLGA@ZIF-8@GelMa; GelMa-loaded VIP@PLGA@ZIF-8; VPZG, VPZ nanoparticle; VIP, vasoactive intestinal peptide; TSPCs, tendon stem/progenitor cells
Figure 2. Characterization of VPZ and VPZG
Figure 3. VPZG Promotes Patellar Tendon Repair in SD Rats