An ex vivo porcine skin model was then used to evaluate the potential for the peptide gels to disrupt S. aureus biofilms in burns, and this was then translated into an in vivo porcine burn model to evaluate the safety of the peptides gels and reduction of bacterial burden compared to silver sulfadiazine. The impact of H2S on blood perfusion and wound healing were evaluated using laser Doppler scanning of the burns and histopathological imaging.

Results: Both the S-FE and C-FE peptide hydrogels exhibited reduction in S. aureus in planktonic or biofilm form, indicating an antimicrobial effect of the peptide itself. H2S-releasing S-FE gel which had a better antimicrobial effect in general, suggesting the inhibitory effects of H2S gas. The S-FE and C-FE dipeptide gels suppressed the bacterial ability to grow biofilm. Moreover, the S-FE had a significant antimicrobial effect on an established biofilm compared to C-Fe and a bacterial only group which could indicate the gas ability to infiltrate the biofilm to impact the bacteria directly. The impact of the gels in infected ex vivo porcine skin shows a significant decrease in bacterial burden determined by reductions in both CFUs and photon count emitted from the bioluminescent bacteria. An antimicrobial effect was noticed with the S-FE group compared to the other groups as the infection was cleared before day 14 compared to its control which persisted to day 21. There was no clear acceleration of wound healing with any of the treatments. There were no negative impacts of the dipeptide hydrogels on the health of the animals.

Conclusion: The S-FE and C-FE inhibited bacterial growth, thereby limiting biofilm formation or disrupting established biofilms, and S-FE showed better effects than C-Fe. These antimicrobial H2S-releasing dipeptide hydrogels provide a promising new approach to treat wound infections.

Adoptive Transfer Of Tolerogenic Dendritic Cells Promotes Angiogenesis And Wound Healing

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Purpose: Dendritic cells (DCs) are a heterogeneous cell population which critically regulates the adaptive immune response. Depending on their activation status, DCs can also promote peripheral immune tolerance, thus limiting the activation of the immune system and tissue damage. Cell based therapy approaches using DCs have been approved by the FDA and clinical trials using DC immunotherapy are being performed against a variety of cancer types. However, the role of DC therapy for wound healing has not yet been investigated.

Methods: Hematopoietic stem cells (HSCs) were isolated from the bone marrow of green fluorescent protein (GFP) expressing mice and differentiated into DCs over a 7 day in vitro culture period. Tolerogenic DCs (TDCs) were induced by stimulation of cultures with 1,25-dihydroxyvitamin D3 (1α,25(OH)2D3), lipopolysaccharide or dexamethasone and the angiogenic potential of the cells was evaluated by endothelial cell (EC) tube formation assays in transwell as well as direct co-cultures. The protein levels of 52 cytokines were measured in the conditioned media of DC cultures using Luminex multiplex assays. The ability of TDCs to accelerate wound healing was evaluated by treating splinted excisional wounds in C57BL6/J mice weekly with pullulan-collagen hydrogels seeded with 1α,25(OH)2D3-stimulated TDCs, unstimulated DCs or blank hydrogels.

Results: EC tube formation assays showed a significantly higher EC branch number and length when co-cultured with TDCs treated with 1α,25(OH)2D3 over a 7 day culture period. Tolerogenic DCs were induced by stimulation of cultures with 1,25-dihydroxyvitamin D3 (1α,25(OH)2D3), lipopolysaccharide or dexamethasone and the angiogenic potential of the cells was evaluated by endothelial cell (EC) tube formation assays in transwell as well as direct co-cultures. The protein levels of 52 cytokines were measured in the conditioned media of DC cultures using Luminex multiplex assays. The ability of TDCs to accelerate wound healing was evaluated by treating splinted excisional wounds in C57BL6/J mice weekly with pullulan-collagen hydrogels seeded with 1α,25(OH)2D3-stimulated TDCs, unstimulated DCs or blank hydrogels.

Conclusion: Our data indicate that the induction of tolerogenicity in DCs by 1α,25(OH)2D3 enhances their secretion of VEGF, thus promoting EC tube formation and accelerating wound healing. Given their ready availability from human blood through established leukapheresis protocols and easy multiplication in...
vitro, TDCs are promising candidates for novel autologous cell-based therapy approaches for wound healing.

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Galvanotactic Smart Bandage For Wireless Wound Healing

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Background: Approximately thirty million people in the United States suffer from diabetes. The prevalence of diabetic foot ulcers (DFUs) in this population is 13%. There is a pressing need to develop effective therapies to treat chronic wounds robustly. Current standard of care wound dressings are passive and cannot actively respond to variations in the wound environment. Smart bandages are well positioned to address these challenges with their ability to integrate (bio)sensors for real-time monitoring and active wound care treatment. Current smart bandage technologies have demonstrated significant promise in their ability to sense physiological conditions. This includes detecting pH of the wound, temperature, oxygen, moisture, mechanical and electrical changes. To our knowledge there have not been significant advancements in incorporating sensing technologies to deliver active wound care. We believe this can be achieved using a multidisciplinary approach combining electrical and chemical engineering with the fundamentals of cellular and biomolecular processes in wound healing directed towards high resolution, in situ tissue regeneration.

Methods: A flexible printed wireless stimulator was designed and fabricated to deliver directional energy across a wound gradient. Subsequently a low impedance PEDOT:PSS electrode was designed to optimize the skin and stimulator interface, producing a robust gel with tunable adhesion properties. The smart bandage was evaluated in an excisional diabetic and C57BL6/J murine wound healing model. A parabiosis model was used to evaluate circulating cell migration into the wound bed. Single cell analyses were performed to evaluate changes in cell populations as a direct result of induced electrical stimulation. In vitro validation was performed to elucidate in vivo results.

Results: Wireless electrical stimulation resulted in significantly accelerated wound closure, when compared to controls, in both a diabetic and C57BL6/J murine excisional wound healing model. Complete epidermal recovery was observed, with a thicker collagen network and increased dermal thickness. Greater neovascularization and appendage formation were observed in the treatment groups. Single cell analyses revealed higher proliferation and remodeling regulatory markers expressed across treated groups. In vitro co-culture validation experiments demonstrated accelerated proliferation, mitotic rate and tube formation when compared to controls.

Conclusion: Our data demonstrates the functionality of a robust wireless interface for wound healing. This novel treatment modality will integrate AI processing components for the development of a closed-loop functional stimulator. By combining the domain expertise of nanofabrication, mechanotransduction, fibrosis and molecular/cellular analyses, we are developing a novel chronically stable and robust smart bandage that will pave the way for the next generation of palliative wound care.

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The Osseointegrated Neural Interface For Prosthetic Control: A Chronic, Percutaneous, Rabbit Model

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