Engineering Antioxidant and Oxygen-Releasing Lignin Composites to Accelerate Wound Healing

T.J. Prajapati[1] , A. Kaul[1] , B.W. Padon[1,3] , F. Faruk[1,3] , W.D. Short[1,3] , O. Olutoye[1,3] , L. Yu[1,3] , H. Li[1,3] , O. Jung[2] , S. Jimenez[2] , J. Jung[2] , S. Balaji[1,3]

[1]Baylor College Of Medicine, Pediatric General Surgery, Houston, TX, USA; [2]Louisiana State University, Biological Engineering, Baton Rouge, LA, USA; [3]Texas Children's Hospital, Pediatric General Surgery, Houston, TX, USA

BACKGROUND

Reactive oxidative species are key for initiation of bacterial clearance by neutrophils and macrophages, and migration and proliferation and ECM deposition by fibroblasts, myofibroblast trans-differentiation and blood vessel formation. However, if there is an overabundance of free radicals and ROS, they can be harmful and prevent cellular functions, resulting in excessive inflammation, impaired healing and excessive fibrosis and scarring. This often occurs in impaired wound healing such as Diabetes or infected wounds. Where they tend to stay stuck in this inflammation stage resulting in poor wound healing.

HYPOTHESIS

We *hypothesize* that the oxygen-releasing, antioxidant, ROS-scavenging lignin composites reduce inflammation, promote neovascularization and faster wound healing with improvement is fibrosis and scar formation.

METHODS

- C57BL/6N mice; M/F 8wk
- Create 6 mm stented wounds

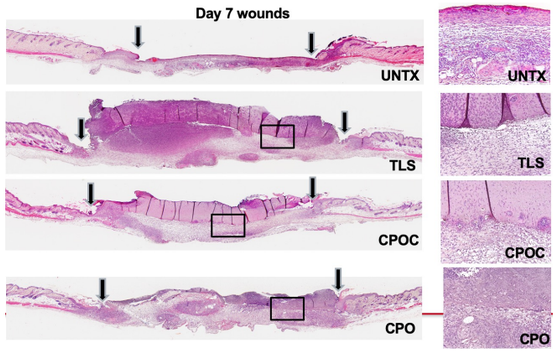
Image wounds every other day
- Camera

Harvest at D7 and D30
- Histology
- IHC

Treatments:

1. GelMA+TLS; **(TLS)**
2. GelMA+TLS+CPO-c (control, non-oxygen producing microparticle; **(CPOc)**
3. GelMA+TLS+CPO (oxygen producing microparticle); **(CPO)**

Control: **(Untreated)**



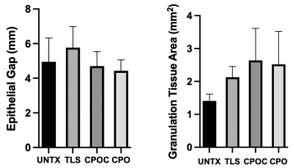


Fig 1: *Day 7 Wound Histology Analysis (HE)* Black arrows indicate epithelial gap. Zoom-ins from the corresponding black box

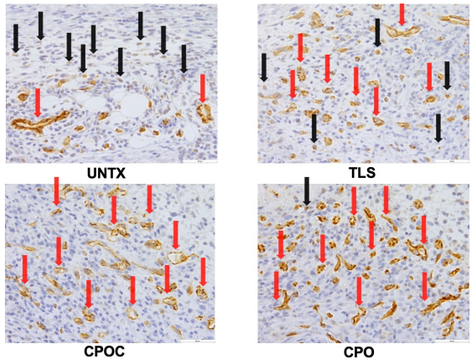
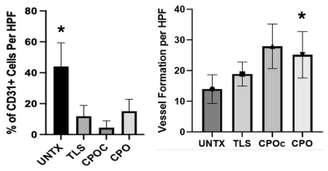


Fig 2: *Day 7 Wound Endothelial and Neovascularization Analysis (CD31+)* Lone CD31+ denoted with black arrows. Lumens denoted with red arrows.



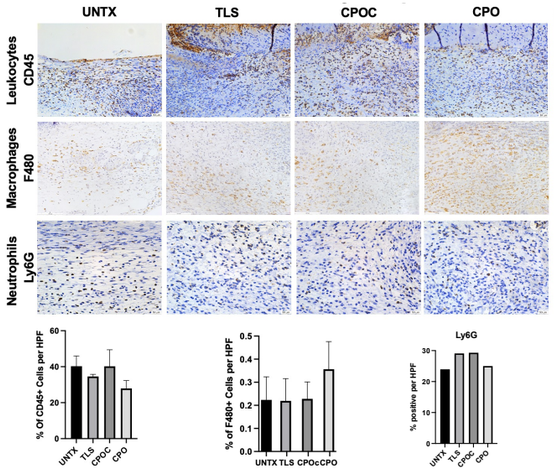


Fig 3: *Day 7 Inflammatory Response Analysis (CD45, F480, Ly6G)*

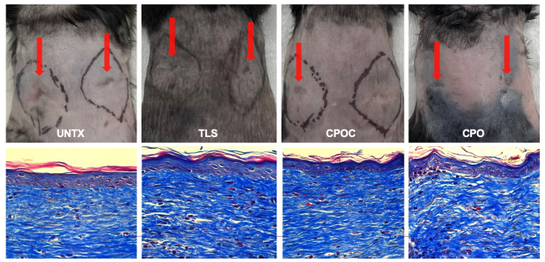


Fig 4: *Day 30 Wound Macroanalysis (Trichrome)* Red arrows indicate location of scar in gross image.

RESULTS

- In vivo data showed that the lignin composite with CPO nanoparticles integrate better on the wound bed and improve the granulation tissue deposition without causing contraction.
- Lignin composite with CPO nanoparticles caused less inflammation, accelerated neovascularization and supported the differentiation of αSMA⁺ fibroblasts and even distribution of these cells across the wound bed at day 7 post wounding.
- Remodeling by day 30 showed much better scar appearance in wound treated with Lignin composite with CPO nanoparticles.

CONCLUSION

Lignin composites with dual antioxidant and oxygen release capacities improve neovascularization and granulation tissue deposition resulting in superior wound repair outcomes. Engineered biomaterials can address unmet needs in clinical wound management for development of novel therapeutics that can promote better wound healing and improve patient outcomes.