Polypeptide-Gold Nanorod Solders for Laser Tissue Repair

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Statement of Purpose: Approximately 1.5 million people suffer from colorectal cancer and inflammatory bowel disease in the United States. Following standard surgical anastomosis in intestinal and colorectal surgery leakage can occur, which can result in infection and life-threatening consequences. In this study, we demonstrate crosslinking of elastin-like polypeptides (ELPs) with gold nanorods (GNRs) results in plasmonic nanocomposites, with high efficacies for welding ruptured intestinal tissue following near infrared (NIR) laser irradiation. Thermal damage resulting from the laser welding in areas near the weld site was characterized via IR imaging and histological staining. This study demonstrates the utility of laser tissue welding using plasmonic polypeptide nanocomposites, and indicates the translational potential of these materials in intestinal and colorectal repair..

Methods: GNRs were synthesized via the seed-mediated method. Elastin-like polypeptides, containing twelve cysteine residues (C_{12}ELP) in the repetitive sequence, were generated via recursive directional ligation. C_{12}ELP-GNRs nanocomposites were synthesized by self-assembly of C_{12}ELPs on GNRs via gold-thiol bonds at 4°C resulting in GNR-C_{12}ELP dispersions, followed by phase separation (coacervation and maturation) of these nanoassemblies resulting in the irreversible formation of solid-phase nanocomposites at 37 °C. Fresh porcine small intestines were purchased with a 4 mm full thickness incision was applied at the center of intestine section (4x1 cm, ~0.1 cm thick). The incision edges were brought into contact with one another, and a nanocomposite (1 cm diameter) was applied on top of the serosa layer and across the incision with full contact. NIR Laser irradiation (20 W/cm^2) was applied vertically at a speed of 1 mm/second across the nanocomposite for 5, and 7 minutes. During welding, tissue samples were imaged using an IR camera every 30 seconds to track thermal changes. Following welding tissue samples were fixed and stained for histological evaluation

Results: Self-assembly of thermally responsive C_{12}ELPs via gold-thiol bonds on GNRs resulted in the formation of well-dispersed nanoassemblies at 4°C. Incubation of the nanoassemblies at 37°C overnight led to temperature-triggered, entropy-dominated phase transition of C_{12}ELP, which, in concert with GNR-thiol and intra- and inter-molecular cysteine-cysteine cross-linking, resulted in the formation of maroon-colored plasmonic nanocomposites as precipitates (Figure 1). The absorbance spectra of nanocomposites demonstrated both, transverse (520 nm) and red-shifted longitudinal bands (~800 nm) characteristic of the embedded gold nanorods.

Figure 1. Digital image of GNR (5.4 wt%)-C_{12}ELP nanocomposite

Irradiating ruptured intestines using nanocomposites containing 5.4 wt% GNR with NIR laser resulted in a recovery of ~47% of ultimate tensile strength when compared to intact intestine (Figure 2). In addition, recovery of burst and leakage pressures from 2% to 49%, and 2% to 78%, respectively were observed.

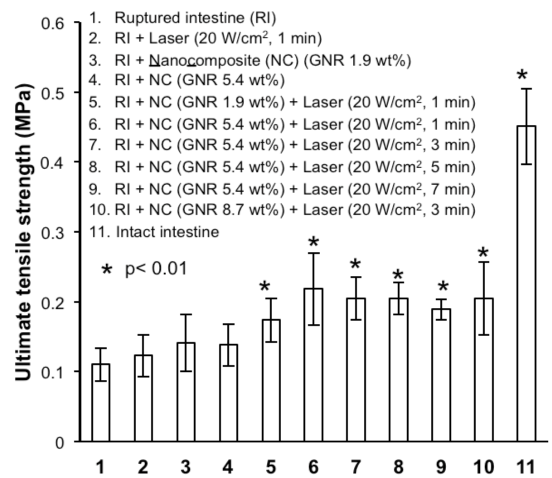

Figure 2. Ultimate tensile strength of intact ruptured, and nanocomposite-laser repaired tissue.

Charring of tissue around site of laser irradiation is visible, indicative of thermal damage. IR images before and immediately after laser tissue welding show an increase in bulk temperature of the tissue samples. Histological evaluation is also indicative of thermal damage away from the wound closure site.

Conclusions: In this study, we investigated biocompatible gold nanorod hybrid elastin-like polypeptide nanocomposites as plasmonic biomaterial 'solders' for NIR laser welding for intestinal tissue repair. Engineered cysteine-containing ELPs (C_{12}ELPs) were selected mainly due to their elasticity, thermal response, stability, and biocompatibility. Gold nanorods were employed with the dual purpose of crosslinking ELPs leading to a stabilized matrix. GNR-C_{12}ELP nanocomposites were able to successfully repair ruptured intestinal tissue upon laser irradiation, with minimal tissue charring and shrinkage. Thermal damage in areas away from wound site were also evaluated using IR imaging and histological staining. These nanocomposites possess tremendous translational potential in the repair of intestinal and colorectal tissues in several diseases, including cancer