Development of Biocompatible Functionalized Polyglycidol-based Scaffolds to Influence Cellular Behavior

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Introduction: Synthetic polymers have contributed significantly to the development of advanced scaffolds for load bearing tissue engineering applications. Despite this, there is still a need to create scaffolds that can simultaneously present multiple biophysical and biochemical properties to better mimic native cellular environments. Polyglycidol has been shown to be a biocompatible polyether polyol, that forms different, sometimes complex, polymeric architectures. Furthermore, it has multiple hydroxyl groups that are capable of numerous chemical modifications. However, little is known about the biocompatibility of modified polyglycidols and their resulting 3-D network. The overarching hypothesis for this project is that changes in the mechanical, structural, and compositional cues within a polyglycidol-based network can be tailored to influence cell responses. Therefore, as a crucial first step, we investigated the biocompatibility of functionalized polyglycidols, and the swelling, degradation, and mechanical properties of polyglycidol based hydrogels. Ongoing studies aim to show that a defined subset of biophysical and biochemical cues can be incorporated simultaneously within the polyglycidol hydrogel. Such an advanced scaffold would allow us to study the synergistic effects of various chemical and physical cues on cellular behavior.

Materials and Methods: Branched polyglycidol and their functionalized derivatives were synthesized using modified literature procedures. The cytotoxicity of the functionalized derivatives against mouse NIH 3T3 and mesenchymal stem cells were evaluated using a MTT as well as a LIVE/DEAD cytotoxicity assay. Polyglycidol-based hydrogels were formed through oxime cross-linking between a keto-functionalized and an aminooxy-functionalized polyglycidol. To tune the crosslinking density of the hydrogels, polyglycidols with different degrees of functionalization were cross-linked. To characterize the hydrogel mechanical properties, rheological and unconfined compression testing were performed. The biocompatibility of the crosslinking process was evaluated with a LIVE/DEAD cytotoxicity kit. These analyses provided data on the biocompatibility, degradation, and mechanical properties of these unique polymeric networks.

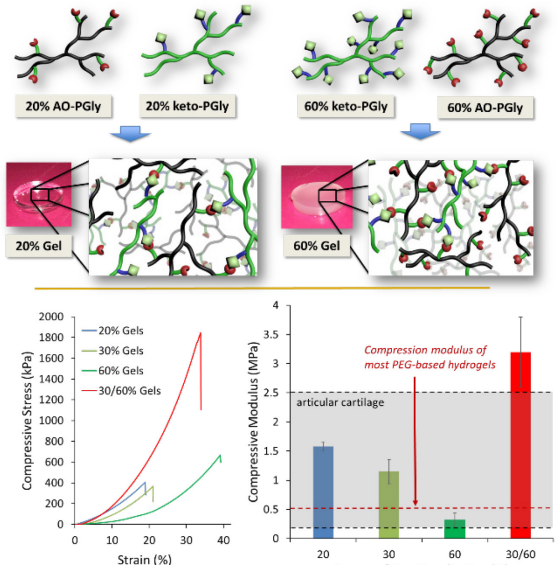

Figure 1. Polyglycidol-based hydrogels formed from their functionalized precursor polymers. These polymeric networks demonstrate mechanical properties like articular cartilage and other load bearing tissues.

Results and Discussion: Biocompatibility of the branched amino-oxy and keto functionalized polyglycidols was confirmed using the MTT Assay. By tuning the ratio of amino-oxy and keto functional groups within the hydrogel network, tunable swelling, degradation, and mechanical properties were obtained. The biocompatibility of the crosslinking process was confirmed via the LIVE/DEAD cytotoxicity analysis. The nature of the crosslinking process allowed for the incorporation of an aldehyde-functionalized RDG peptide which allowed for cell attachment to the hydrogel network. This demonstrates the ability to tune both the biochemical and biophysical properties simultaneously within these hydrogels.

Conclusion: We synthesized aminooxy and keto-functionalized poly(glycidol) derivatives and demonstrated that they are hydrophilic and biocompatible. The results support the hypothesis that the chemical and mechanical properties of polyglycidol-based networks are simultaneously tunable due to the increased number of functional groups. The ongoing studies will elucidate how the combination of keto-functionalized growth factors and various mechanical properties influences chondrogenesis within polyglycidol-based networks.