Supplementary Information for:

Material Design and Photo-regulated Hydrolytic Degradation Behavior of Tissue Engineering Scaffolds Fabricated via 3D Fiber Deposition

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Synthesis of diacrylate terminated poly (L-lactic acid) macromer (PLADA).

PLADA was synthesized through the esterification reaction of a commercial dihydroxyl terminated poly (L-lactic acid) oligomer (PLADH) (5.00 g) with acryloyl chloride (1.81 g) in the presence of triethylamine (2.02 g) in dichloromethane (150 mL) at 0 ℃ for 12 hours. After the mixture was filtered, the filtrate was added to ethanol to yield a canary yellow precipitate. The obtained product was then dissolved in dichloromethane again and precipitated in ethanol for another two times (Yield: 81.3 %).

The carbon-carbon double bond content of PLADA was determined by iodometry method[1] according to previous literatures. The double bond content of PLADA obtained from PLADH1 and PLADH2 was 1.0894 mmol/g and 1.8288 mmol/g, respectively.

Synthesis of 1, 3-di (3-mercapto propionic acid methyl ester)-2-nitrobenzene (DMMNB).

DMMNB was synthesized by the esterification reaction of 1, 3-di (hydroxymethyl)-2-nitrobenzene and mercaptopropionic acid. The 1, 3-di (hydroxymethyl)-2-nitrobenzene was synthesized according to the literature[2], including two main steps: First, 2-nitro-m-xylene (15.0 g) and sodium hydroxide (6.0 g) were added to water (750 mL) and heated to 95℃. Potassium permanganate (60g) was then added slowly for 3 hours before being refluxed for 20 hours. The mixture was then filtered and the filtrate was acidified with 2N HCl to yield a white precipitate. Second, the 1, 3-dicarboxylic acid -2- nitrobenzene

produced from the first step (2.50 g) was dissolved in THF (12.5mL) and cooled with an ice bath. 1M Borane-THF (59.0mL) was then added dropwise and the reaction was stirred for 48 hours. The THF was removed under vacuum and the product was dissolved in ethyl acetate (20mL) and washed with water (3×eq. vol.). Ethyl acetate was removed under vacuum and the product 1, 3-di (hydroxymethyl)-2-nitrobenzene was recrystallized with ethyl acetate and hexanes.

For the synthesis of DMMNB, 1, 3-di (hydroxymethyl)-2-nitrobenzene (0.80g) and mercaptopropionic acid (1.86g) were dissolved in toluene (30mL). 0.05 g of toluene-p-sulfonic acid was added as catalyst. Then the mixture was stirred and kept refluxing overnight at 116 ℃ under nitrogen atmosphere. Thereafter, the toluene was removed under reduced pressure. The crude product was dissolved in 50 mL of CH_2Cl_2, washed with saturated $NaHCO_3$ aq. (3×100 mL) and then distilled water (3×100 mL), and dried with anhydrous $MgSO_4$. After the removal of $MgSO_4$ by filtration and CH_2Cl_2 by evaporation under reduced pressure, the product was further purified by silica gel chromatography (Yield: 56.5%). All of the above synthesis processes were performed in dark condition and the obtained DMMNB was stored in a sealed black container under 20℃ until needed.

Pre-characterization of PLADH1 and PLADH2 in terms of the absolute molecular

weight, polydispersity and thermal property is shown in Figure S1 and S2. MALDI-TOF-MS analysis determined the average numerical molecular weight of PLADH1 and PLADH2, which did a great favor to further calculation of molar ratio during the synthesis process. DSC thermograms of PLADH1 and PLADH2 indicated that PLADH1 was in a crystalline state with a melting point of 29.63 ℃, while PLADH2 had an amorphous structure with a Tg of -7.20 ℃. Both PLADH1 and PLADH2 are not possible to be printed using 3DF method originally.
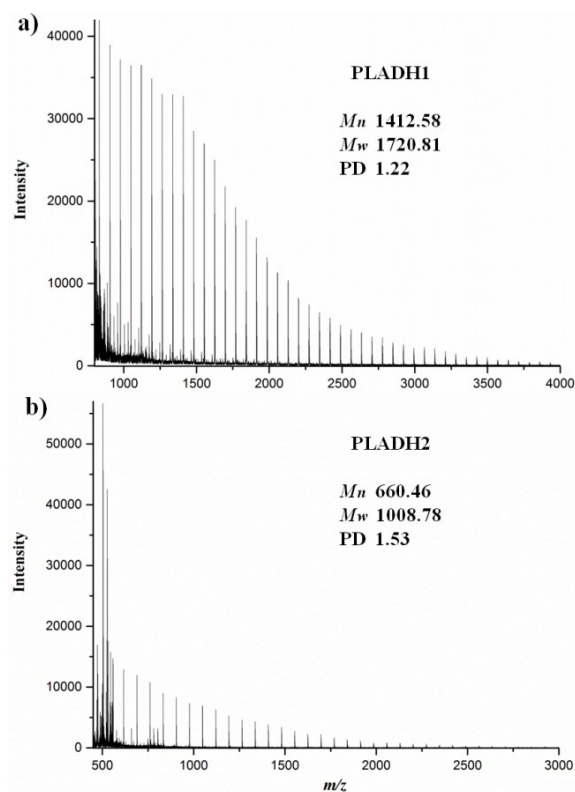
Figure S1. MALDI-TOF-MS analysis of two commercial PLADH oligomers used in this study to determine the absolute molecular weight and polydispersity.
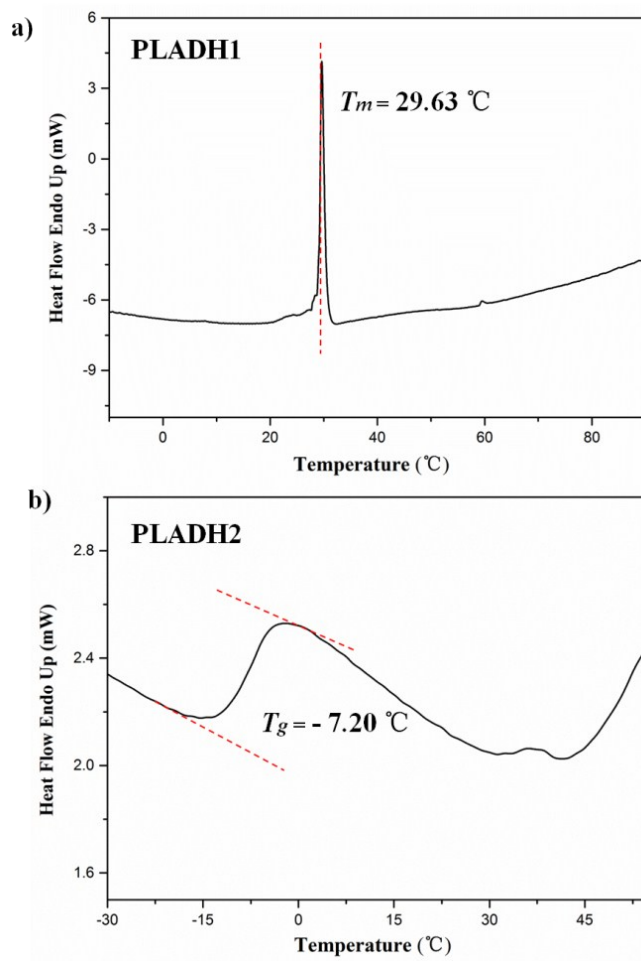
Figure S2. DSC thermograms of PLADH1 (a) and PLADH2 (b), indicating a melting point of

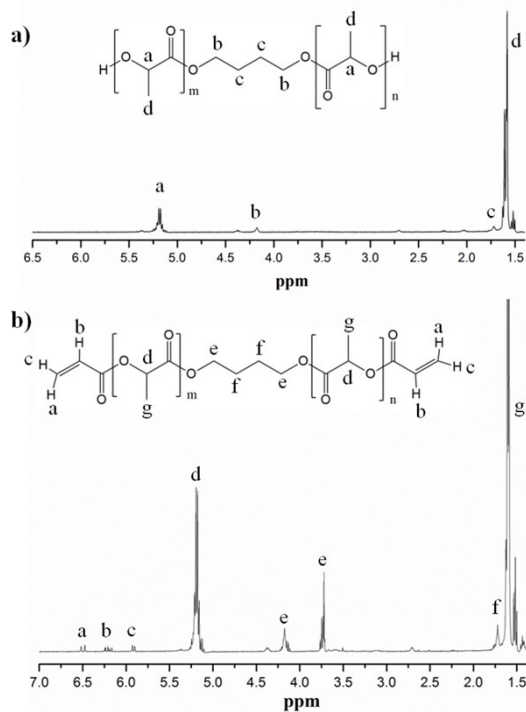PLADH1 at 29.63 ℃ and an amorphous structure of PLADH2 with a Tg of -7.20 ℃.

Figure S3. ^{1}H NMR spectra of reactant PLADH (a) and resulted PLADA (b). The comparison

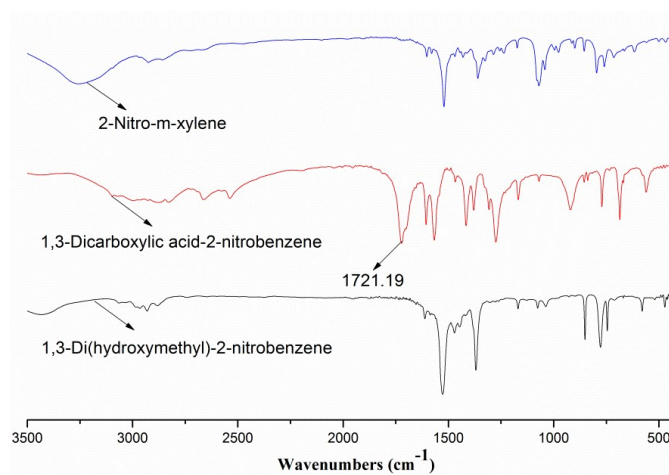confirms the introduction of acrylate double bonds into PLADA molecules.

Figure S4. IR spectra of 2-nitro-m-xylene, 1, 3-dicarboxylic acid-2-nitrobenzene and 1, 3-di

(hydroxymethyl)-2-nitrobenzene. A typical peak at 1721 cm^{-1} corresponded to –C=O stretching occurs

in the spectrum of 1, 3-dicarboxylic acid-2-nitrobenzene and disappears after the following reduction

reaction, which confirms the successful synthesis of 1, 3-di (hydroxymethyl)-2-nitrobenzene.
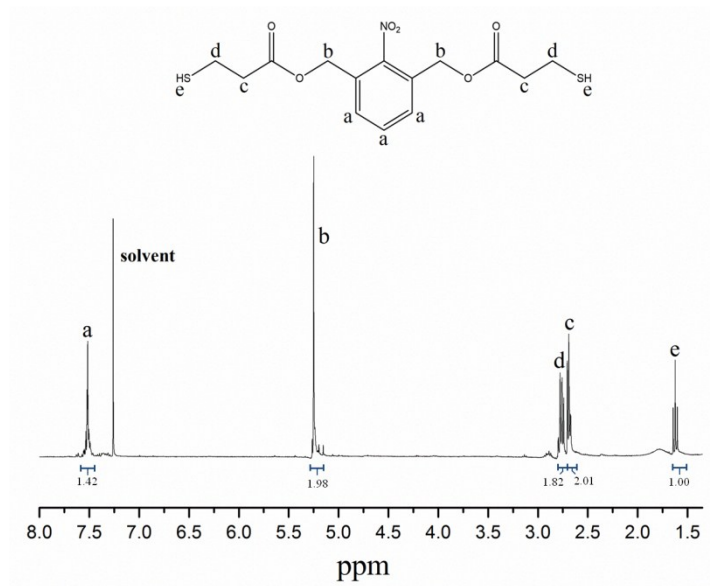
Figure S5. ^{1}H NMR spectrum of DMMNB. All of the hydrogen signals and peak integrals are well

assigned with the proposed H.

GPC traces in Figure S6 compares the influence of the reaction time (Figure S6a) and

stoichiometric ratio of DMMNB to PLADA (Figure S6b) on the molecular weight and

polydispersity of resultant PLANB. It could be found that the reaction time was not a

significant factor to the reaction of PLANB generation owing to the molecular weight

changed a little as time increased from 6h to 14h, 22h and 30h, although a tiny narrowness

of polydispersity after 22h reaction could be seen, which was attributed to the high activity

of thiol-acrylate reaction. Figure S6b showed the stoichiometric ratio of DMMNB to

PLADA could affect the final molecular weight and polydispersity of PLANB. The main reason lied in the wide-distribution of the molecular weight of original commercial reactant PLADH may add difficulty to the precise calculation of molarity of PLADA. According to the pre-observation of molecular weight and distribution of PLANB, an optimal mole ratio of 1:1.05 (DMMNB/PLADA) under the reaction time of 22 h was used for further synthesis.
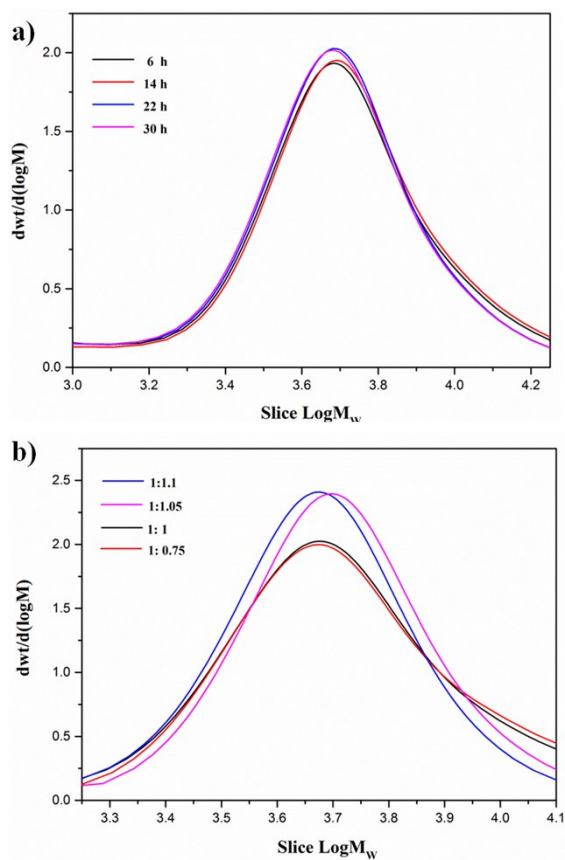

Figure S6. GPC traces showing the influence of reaction time (a) and stoichiometric ratio of reactants (b) on the molecular weight and polydispersity of PLANB.
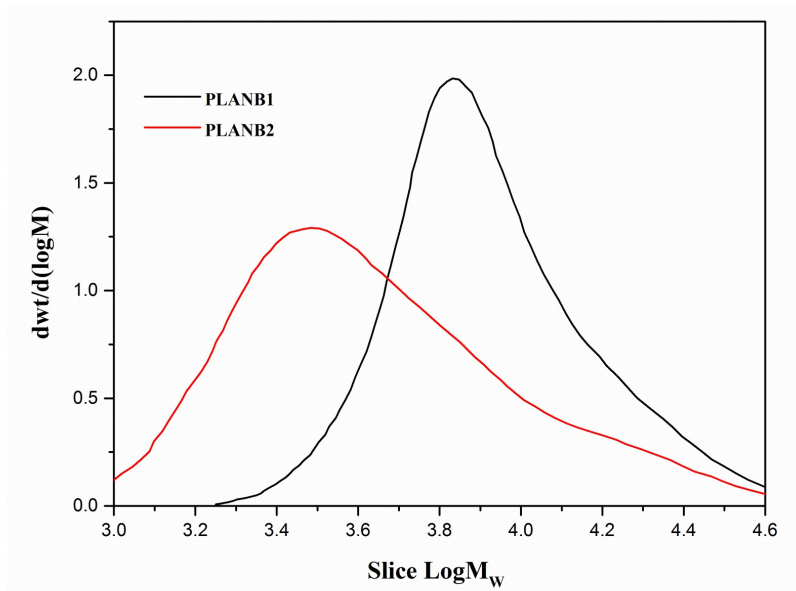
Figure S7. GPC curves of PLANB1 and PLANB2 with different molecular weights.
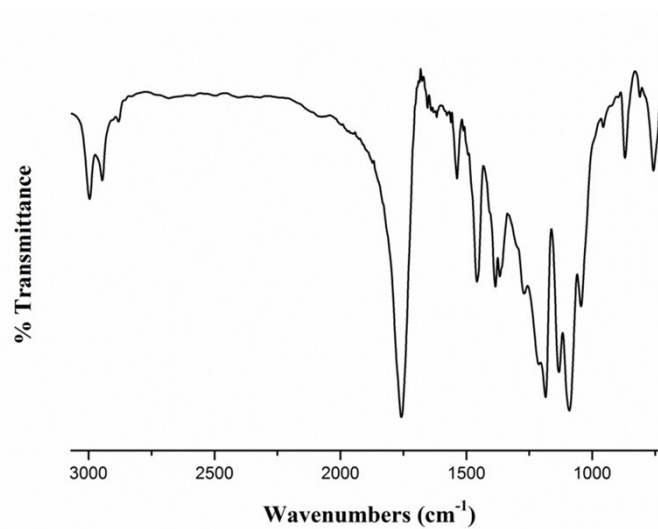

Figure S8. FTIR spectrum of PLANB scaffold after printing which shows unchanged chemical structure compared with PLANB before printing in Figure 1a: 2995 and 2926 cm^{-1} (-C-H stretching from $-CH_3$ and $-CH_2$), 1750 cm^{-1} (-C=O stretching), 1650 cm^{-1} (C=C stretching), 1530 cm^{-1}(-NO$_2$ stretching), and 810 cm^{-1} (=C-H bending).
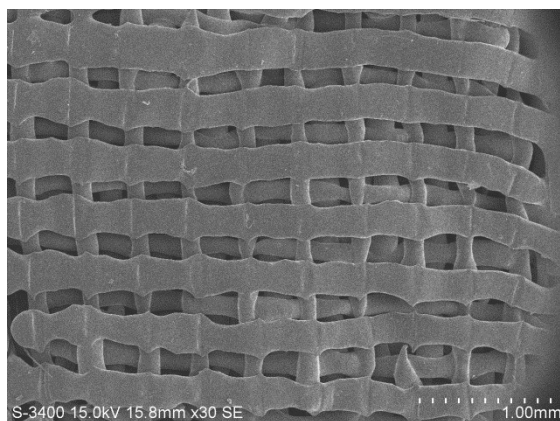
Figure S9. SEM image of preliminary mix-printing of PLANB1 and PLLA (Mw 10000) with the

weight ratio of 5:1. The mix-printing requires a small difference between the flowability of the mixed

polymers at the printing temperature. Otherwise, the extrusion of melted polymers will be ununiform

and lead to the failure of mixture printing. Although the strands here are not as smooth as the PLANB

scaffold, it shows the possibility of scaffolds printing by mixing PLANB with other mixable

polyesters. The morphology of the mix-printed scaffold could be improved by carefully selection of
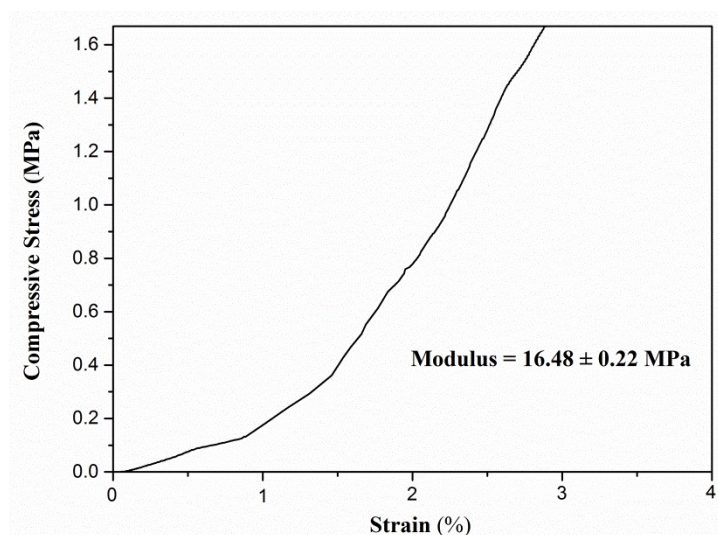
printing parameters.

Figure S10. The compressive stress-strain curve of PLANB1 scaffold, indicating a much higher

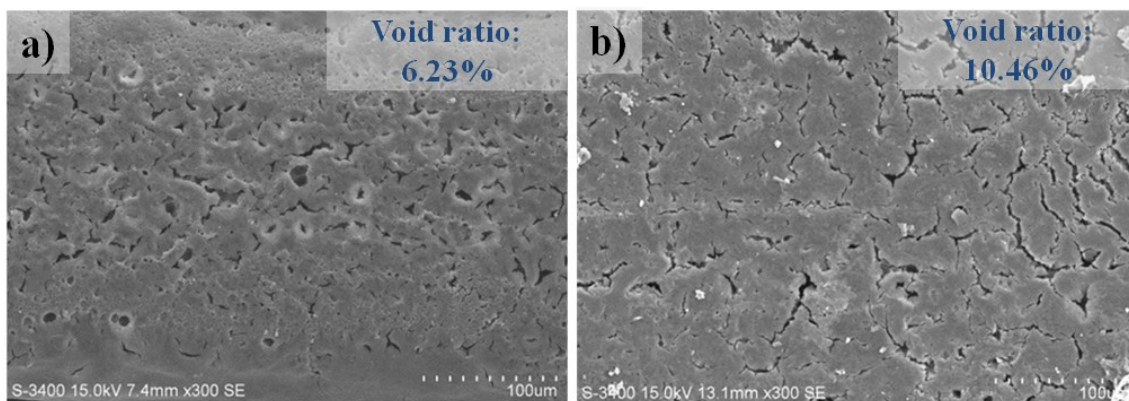modulus compared with other 3D-printed PLA scaffolds.

Figure S11. SEM images of strand surface of PLANB1 scaffold after 10-day (a) and 20-day (b) degradation in the context of hydrolysis combined with a daily photo-irradiation (320-500 nm, 30 mW/cm^2 for 15 min).

References

1. O.-W. Lau and S.-F. Luk, *Analyst,* 1987, **112**, 1269-1272.
2 . D. Han, X. Tong and Y. Zhao, *Macromolecules,* 2011, **44**, 437-439.