

# Metal-free “Click” Chemistry for the Development of Peptide-based Biomaterials

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Hydrogels can be injected into localized surface tumors for the consistent release of anti-cancer drugs over a specific period of time. This project used metal-free “click” chemistry to develop novel biocompatible and temperature-sensitive peptide-based hydrogels which form at 37°C. These hydrogels are quick and possibly cheap to synthesize as the ultrashort peptides are only 6 amino acids long. Gelation time can be customized to complement various anti-cancer drugs with different characteristics. Ultrashort peptides ILVAGK-NH<sub>2</sub> (IK<sub>6</sub>-NH<sub>2</sub>) and LIVAGK-NH<sub>2</sub> (LK<sub>6</sub>-NH<sub>2</sub>) were synthesized and purified (60% yield). When 3-azidopropionic acid (75% yield) reacted with the ultrashort peptides, azide-functionalized ultrashort peptides N<sub>3</sub>-IK<sub>6</sub>-NH<sub>2</sub> and N<sub>3</sub>-LK<sub>6</sub>-NH<sub>2</sub> were generated. Propiolic acid ester-functionalized polyethylene glycol (PEG) was synthesized (98% yield). A copper-free azide-alkyne “click” reaction occurred between azide-functionalized ultrashort peptides and alkyne-functionalized PEG-propiolate. At 37°C, clear hydrogels PEG-(triazole-*IK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub> and PEG-(triazole-*LK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub> were formed. The compounds were characterized by HPLC-MS, <sup>1</sup>H and <sup>13</sup>C NMR. Minimum gelation concentration was 5 mg/mL for PEG-(triazole-*IK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub> and 10 mg/mL for PEG-(triazole-*LK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub>. Minimum gelation time was 8 minutes for 10 mg/mL of PEG-(triazole-*IK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub> and 70 minutes for 10 mg/mL of PEG-(triazole-*LK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub>. PEG-(triazole-*IK*<sub>6</sub>-NH<sub>2</sub>)<sub>3</sub> hydrogel was easier to generate than parent peptide *IK*<sub>6</sub>-NH<sub>2</sub> hydrogel, which had a minimum gelation concentration of 20 mg/mL and a minimum gelation time of 25 minutes. In summary, novel biocompatible and temperature-sensitive hydrogels were developed quickly and cheaply. They can potentially deliver anti-cancer drugs to treat localized surface tumors more effectively.

## Awards Won:

Fourth Award of \$500