

## PMOXA-based dual-functional antimicrobial surfaces

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**INTRODUCTION:** Millions of implants are surgically implanted every year with high expectations of biomaterial performance from surgeons and patients. However, bacterial infection presents a serious concern for human implant surgery, which can lead to the need for re-operation. Thus, there is high interest in developing new antimicrobial coatings to fight bacterial infections. Recently, we have published a report where we presented poly(2-methyl-2-oxazoline) (PMOXA) as a non-fouling polymer, potential PEG substituent for rendering surfaces resistant to protein adsorption<sup>1</sup> and bacteria adhesion<sup>2</sup>. Our current research aims at developing combined *biopassive-bioactive* (dual-functional) antimicrobial platforms, where antimicrobial compound (*bioactive*) will be immobilized on top of inert (*biopassive*) PMOXA-coated metal oxide surfaces (figure 1).

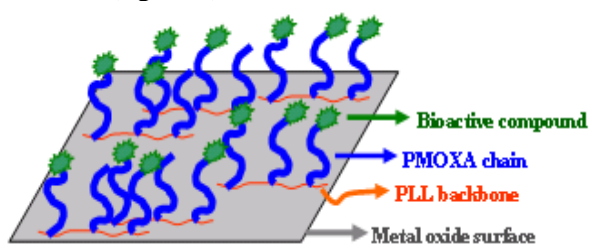


Figure 1. Schematic diagram of PMOXA-based antimicrobial coating

**METHODS:** PMOXA was synthesized through the living cationic polymerization of 2-methyl-2-oxazoline as previously reported<sup>1</sup>. This type of chemistry enables the incorporation of functional groups at defined positions along the polymer chain. Alkyne functionality was introduced to the PMOXA chain at  $\alpha$ -terminus by initiating the living cationic polymerization of 2-methyl-2-oxazoline with a propargylic-initiator. The reaction was terminated with carboxy derivative-terminator; this allows grafting of the polymeric chain from the  $\beta$ -terminus to poly(L-lysine) (PLL) backbone, resulting in graft copolymer, that is alkyne PLL-g-PMOXA. The chemical structure of the resulted polymers was characterized by NMR and MALDI-TOF. “Click” chemistry is utilized for bioconjugation between alkyne PMOXA and azide-functionalized antimicrobial agent (in our case antimicrobial peptides). Surface modification is based on spontaneous assembly from aqueous buffer solutions. Optical Waveguide Lightmode

Spectroscopy (OWLS) was used to *in-situ* monitor polymer adsorption onto metal-oxide coated waveguides and the subsequent exposure to full human serum.

**RESULTS:** We have synthesized alkyne PLL-g(3.2)-PMOXA and NMR has confirmed the expected chemical structure. The grafting ratio of 3.2 was chosen based on our previous results<sup>1</sup> (i.e. grafting ratio that gave high adsorbed polymer mass and low protein adsorption). OWLS measurements showed that the polymeric coatings of alkyne PLL-g(3.2)-PMOXA are protein resistant, where the detected masses were 220 ng/cm<sup>2</sup> for copolymer and < 2 ng/cm<sup>2</sup> for protein. Moreover, the results from first trials on developing protocols for bioconjugation by means of “click” reaction on model compounds look promising, as shown by NMR.

**CONCLUSIONS:** Alkyne PLL-g-PMOXA with grafting ratio of 3.2 was synthesized and the polymer bulk structure was characterized. OWLS confirmed the nonfouling properties of the synthesized alkyne PLL-g-PMOXA polymer.

**OUTLOOK:** Our efforts are now focused on establishing protocol for “click” reaction on model compounds and then applying it for bioconjugation of antimicrobial peptides and alkyne PLL-g-PMOXA. Then perform detailed surface characterization on the resulted surfaces before investigating their biopassive and bioactive properties.

### REFERENCES:

- <sup>1</sup> R. Konradi, B. Pidhatika, et al (2008) *Langmuir* **24**(3):613-616.
- <sup>2</sup> Pidhatika, B.; Möller, J.; Vogel, V.; Konradi, R. *CHIMIA International Journal for Chemistry* 2008, in press.

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