Biocompatibility of Therapeutic Self-Assembled Monolayers for Drug-Eluting Coronary Stents

Gopinath Mani[1], Bysani Chandrasekar[2], Dave M. Johnson[1],
Marc Feldman[2], Devang Patel[2], and C. Mauli Agrawal[1,2].
[1]*The University of Texas at San Antonio*, [2]*The University of Texas Health Science Center at San Antonio*.

Introduction: Commercially available drug-eluting stents (DES) use polymers to coat and release drugs [1]. Evidence suggests that polymer coatings cause adverse reactions to DES [1]. We previously demonstrated the use of self-assembled monolayers (SAMs) to attach and release drugs from metal surfaces [2, 3]. In this study, we investigated the biocompatibility of therapeutic self-assembled monolayers (TSAMs) for potential applications in coronary stent-based drug delivery systems.

Methods: Hydroxyl terminated phosphonic acid and thiol SAMs were coated on titanium (Ti) and Gold (Au) surfaces, respectively. Flufenamic acid, an anti-inflammatory drug, was used as a model and chemically attached to SAMs coated metal surfaces [3]. These TSAMs coated Ti and Au specimens were immersed in tris-buffered saline (TBS) at 37 °C for up to 28 days. The amount of drug eluted in TBS was measured using high performance liquid chromatography. Human aortic endothelial cells (HAECs) were seeded on control, SAMs coated and TSAMs coated Ti and Au surfaces. The viability and proliferation of HAECs were investigated at 1, 3, and 5 days using a MTT colorimetric assay (63 samples). The morphology of endothelial cells was investigated using phase-contrast microscopy at 1, 3, 5, and 7 days (56 samples). The expression of surface adhesion molecule, platelet endothelial cell adhesion molecule (PECAM-1), was investigated using immunofluorescent microscopy. One-way ANOVA and Student Newman Keuls test were used to determine the statistical significance ($p<0.05$).

Results / Discussion: Figure 1 shows the drug release profiles of TSAMs coated Ti and Au surfaces in *in vitro* conditions.

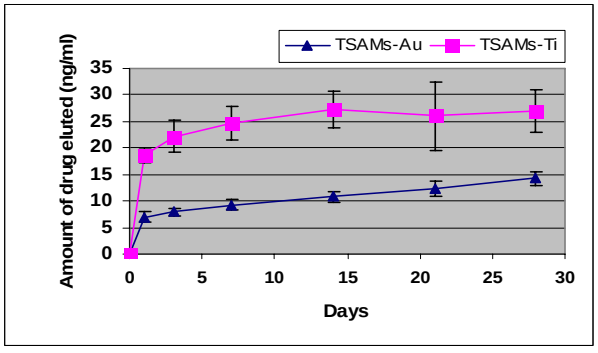

Figure 1. Cumulative drug release profiles of TSAMs coated Ti and Au specimens.

The adhesion of HAECs on SAMs and TSAMs coated metal surfaces is equivalent to that of control metal surfaces and superior to that of plain glass surfaces (Day-1 in Fig 2). The cells continued to proliferate on both SAMs and TSAMs coated metal surfaces (Fig 2). The spreading of HAECs on TSAMs coated metal surfaces with typical polygonal shape indicated that these surfaces are conducive to endothelialization (Fig 3). The expression of PECAM-1 on TSAMs coated metal surfaces indicated that the endothelial cells preserved their phenotype on these surfaces (Fig 4).

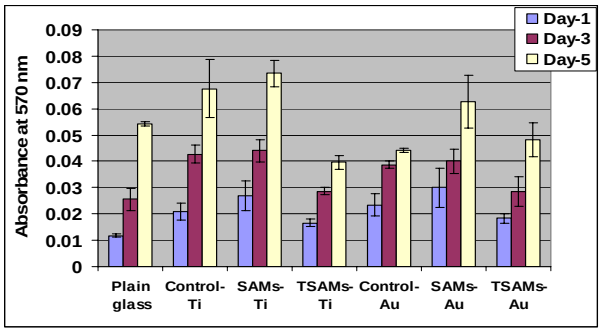

Figure 2. Viability and proliferation of HAECs on control, SAMs coated, and TSAMs coated metal surfaces.

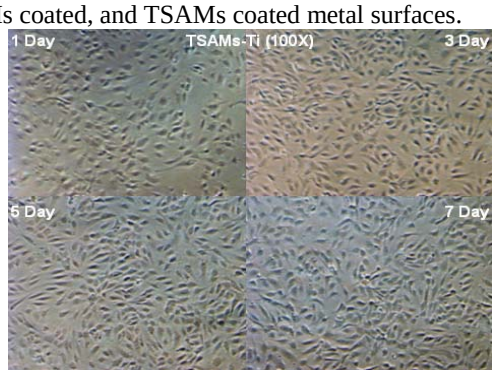

Figure 3. Phase contrast microscopy images of HAECs cultured on TSAMs-Ti surfaces at 1, 3, and 5 days.

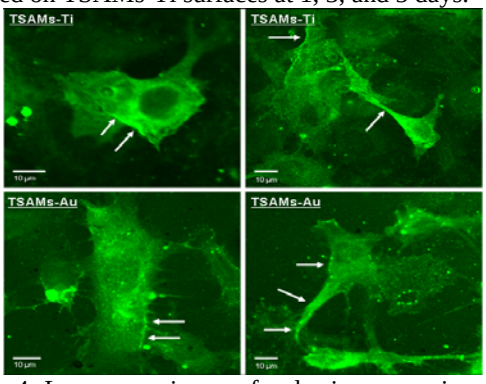

Figure 4. Laser scanning confocal microscopy images of HAECs cultured on TSAMs coated Ti and Au surfaces. Arrows show the expression of PECAM-1.

Conclusions: SAMs and TSAMs do not elicit an adverse response from endothelial cells in *in vitro* conditions. Thus, TSAMs offer a promising technique for coating and releasing drugs from coronary stents or any other metal implant without compromising biocompatibility.

References: (1) Mani G *et al.* Biomaterials 28, 2007, 1689-1710. (2) Mani G et al. Transactions of the 31st SFB 2006, 29, Abstract # 307. (3) Mani G et al. Transactions of the 32nd SFB 2007, 30, Abstract # 4.