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# Novel hierarchical tantalum oxide-PDMS hybrid coating for medical implants: One pot synthesis, characterization and modulation of fibroblast proliferation

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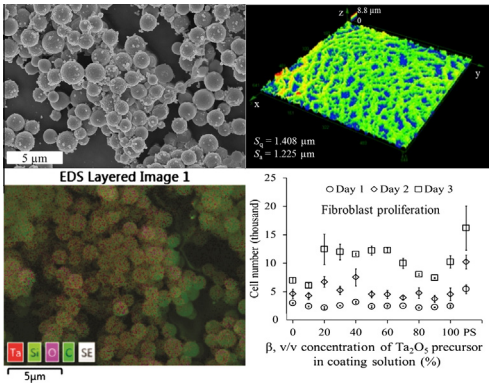
## GRAPHICAL ABSTRACT

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## ABSTRACT

Surface properties such as morphology, roughness and charge density have a strong influence on the interaction of biomaterials and cells. Hierarchical materials with a combination of micron/submicron and nanoscale features for coating of medical implants could therefore have significant potential to modulate cellular responses and eventually improve the performance of the implants. In this study, we report a simple, one pot wet chemistry preparation of a hybrid coating system with hierarchical surface structures consisting of polydimethylsiloxane (PDMS) and tantalum oxide. Medical grade, amine functional PDMS was mixed with tantalum ethoxide which subsequently formed $Ta_2O_5$ *in situ* through hydrolysis and condensation during coating process. The coatings were characterized by SEM, EDS, XPS, confocal scanning microscopy, contact angle measurement and *in vitro* cell culture. Varying PDMS and tantalum ethoxide ratios resulted in coatings of different surface textures ranging from smooth to submicro- and nano-structured. Strikingly, hierarchical surfaces containing both microscale (1–1.5 μm) and nanoscale (86–163 nm) particles were found on coatings synthesized with 20% and 40% (v/v) tantalum ethoxide. The coatings were similar in term of hydrophobicity but showed different surface roughness and chemical composition. Importantly, higher cell proliferation was observed on hybrid

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surface with hierarchical structures compared to pure PDMS or pure tantalum oxide. The coating process is simple, versatile, carried out under ambient condition and requires no special equipment.


## 1. Introduction

Surface architecture is an important factor that can directly affect the interactions of cells and biomaterials. For example, modifying implant surfaces properties such as roughness and morphology to achieve desirable cellular response has been a strategy to improve osseointegration in bone implants. Several studies have shown that increases in the surface micron and sub-micron roughness led to improved osteoblast differentiation and eventually fasten the fracture healing rates [1,2]. Recent studies on implant surface modification highlight the importance of mimicking the hierarchical structures of native tissue such as bones [3] and blood vessels [4]. Surfaces containing micron/sub-micron and nanoscale features have been manufactured on metal, alloy, metal oxide, and polymer surfaces [3,5–13]. For example, Gittens et al. introduced nanoscale features on micro/submicro scale Ti surfaces that were either sand-blasted or unmodified [9]. They found increased osteoblast cell differentiation, osteocalcin production, and significantly higher local factor osteoprotegerin production, suggesting promoted bone formation *in vitro*. Similar results were obtained by Jeon et al. on hierarchical structured poly(ε-caprolactone) surfaces, which were showed to retain higher osteoblast-like-cell MG-63 viability and enhance calcium deposition compared to smooth surfaces [14]. These studies suggested that adding nanoscale features on microscale roughness surfaces should be considered for implant performance optimization. In addition, some studies demonstrated that nanoscale roughness in the absence of micro scale surface roughness decreased osteoblast proliferation highlight the importance of multi-scale roughness [15–17].

However, preparation methods for achieving hierarchical structures are still lacking and substrate specific. On metallic substrate such as Ti, Ti alloys and Al, two steps methods are commonly used to initially create a microscale surface then subsequently grow nanoscale features on top [18]. A variety of techniques were used for creating micro-roughed surfaces, including sand-blasting, grit blasting, or acid etching using a mixture of HF and $H_2SO_4$ [9,12,19]. Nanoscale features were produced by controlled oxidation, sputtering, or $H_2O_2/H_2SO_4$ treatments [9,12,19]. On a polymer surface, Kim et al. reported a fascinating technique to produce hierarchical surfaces by using real lotus and taro leaves, which possess natural hierarchical structure. The leaves were imprinted on a PDMS substrate to create a negative imprint, which then was used to produce a positive surface with hierarchical structures on polyethylene oxide and poly(ε-caprolactone) [14,20]. Zhang et al. reported a simple method to produce micron-nano structured surface in Nylon by swelling surface in formic acid followed by immersing in coagulant bath to induce precipitation [21]. Other methods such as electrospraying and capillary force lithography [22–24] were also reported but most require multiple steps and/or special equipment.

Herein, we present a versatile coating system to provide substrates with both micron/submicron and nanoscale surfaces, which can be applied on both metal and polymeric surfaces. The coatings were made in a simple one-step modified sol-gel process involving the hydrolysis and co-condensation of PDMS polymer and tantalum (Ta) ethoxide to produce tantalum oxide ($Ta_2O_5$) – PDMS hybrid material. We use commercially available medical grade PDMS which has functional groups to bind to reactive surfaces such as metals or activated polymers. $Ta_2O_5$ was chosen because it is a biocompatible, corrosion resistant metal which has been used for orthopaedic implant coatings to provide excellent bone in growth and attachment [25,26]. The surface features of the coatings were fine-tuned by carefully adjusting the concentration of each component. The coatings were characterized and *in vitro* fibroblast response was explored as an example of their ability in regulating cellular activities.

## 2. Materials and methods

### 2.1. Materials

Ta ethoxide, ethanol, and hexane were from Sigma Aldrich (St. Louis, MO, USA). Medical grade PDMS (Dow Corning MDX4-4159) was from Ingredients Plus (Rydalmere, NSW, Australia). Its chemical structure is presented in Fig. 1. Greiner Bio-One tissue culture 96-well microplates were from Interpath Services (Heidelberg West, VIC, Australia). 3T3 fibroblast cells were from ATCC (Manassas VA, USA). Cell culture media and supplement (MEM, foetal bovine serum, and penicillin streptomycin) and fluorescent dye 4′,6-diamidino-2-phenylindole (DAPI) were from Life Technologies (Melbourne, VIC, Australia).

### 2.2. Precursor preparation and coating formulation

The hybrid coatings were formulated using a modified sol-gel synthesis method similar to previously described processes [27–29]. Briefly, Ta ethoxide and PDMS solutions (10% v/v) were prepared in ethanol and hexane/isopropanol mixture (70/30 v/v) respectively. The precursors were combined in a glass vial to make a working solution of different volume percentage of Ta ethoxide β. The mixtures were allowed to age at room temperature for 15 min before 20 μL of the mixtures were dispensed into each well of 96-well polystyrene (PS) tissue culture plates. Tissue culture treated polystyrene (PS) was used as the model substrate for our coating because the treated surface has hydrophilicity similar to common implant surfaces where tissue ingrowth is desired [30–33]. This is also for the ease in subsequent *in vitro* biological characterization of the coatings. The plates were left for 15 min in air at room temperature and then inverted to remove liquid excess from the wells. The plates were dried overnight at room temperature in a fume hood before collected for further analysis. Wells without any coating were used as controls.

### 2.3. Coating surface characterization

#### 2.3.1. Surface roughness and morphology

The surface roughness and morphology of the coatings were evaluated using a laser confocal microscope (LCM, LEXT, Olympus,

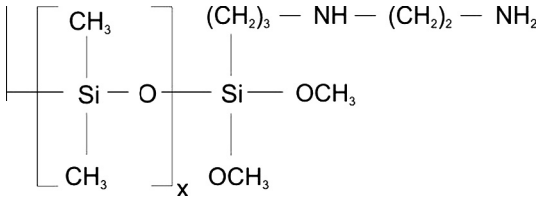


**Fig. 1.** Structure of an amine methoxy-groups modified PDMS as used in this study.