Tuesday Afternoon, October 19, 2010

Biomaterial Interfaces
Room: Taos - Session BI1-TuA

Bacteria on Surfaces
Moderator: L.J. Gamble, University of Washington

2:00pm **BI1-TuA1 High Throughput Methodologies for the Discovery of Materials Resistant to Biofilm Formation**, *A.L. Hook, J. Yang, C.-Y. Chang*, University of Nottingham, UK, *D.G. Anderson, R. Langer*, Massachusetts Institute of Technology, *S. Atkinson, P. Williams, M.C. Davies*, ***M.R. Alexander***, University of Nottingham, UK

Biofilm formation leads to a 1000 times increase in antibiotic tolerance compared with planktonic bacteria and is associated with 80% of hospital acquired infections, resulting in $3.0 billion in excess health-care costs each year in the U.S alone. Thus, new materials for biomedical devices that prevent biofilm formation would offer enormous benefits to the health industry and patient welfare. Polymer microarrays are emerging as a key enabling technology for the discovery of new biomaterials.[1] This platform enables a large combinatorial space to be rapidly screened by a biological assay to identify new materials that fulfil a given performance criterion.[2] Furthermore, utilising a high throughput surface characterisation approach the surface chemical and physical properties of each material can be understood and related to the biological performance in order to understand the material-biological interaction.[3] A method for forming polymer microarrays has been developed using contact printing to deposit nanolitre volumes of premixed acrylate monomer and initiator to defined locations on a poly(HEMA) coated glass slide with UV photo-initiation.[4] We have developed a high throughput bacterial attachment assay based on GFP transfected pathogens that is compatible with the polymer microarray format. In our high throughput strategy we initially produced an array containing hundreds of unique materials that was designed to maximise the combinatorial space explored. From this array 'hit' monomer compositions were identified that were used to design a second generation array that explored systematic variations in material compositions in order to focus onto the optimal material composition. This has been utilised to identify new materials that resist the formation of bacteria and show promise for implementation to various biomedical devices such as urinary tract catheters that are susceptible to bacterial colonisation.

[1] A. L. Hook, D. Anderson, R. Langer, P. Williams, M. C. Davies, and M. R. Alexander, *Biomaterials* **2010**, *31*(2), 187.

[2] Y. Mei, S. Gerecht, M. Taylor, A. J. Urquhart, S. R. Bogatyrev, S. W. Cho, M. C. Davies, M. R. Alexander, R. S. Langer, D. G. Anderson, *Adv. Mater.* **2009**, *21*(27), 2781.

[3] A. J. Urquhart, D. G. Anderson, M. Taylor, M. R. Alexander, R. Langer, M. C. Davies, *Adv.Mater.* **2007**, *19*(18), 2486.

[4] D. G. Anderson, S. Levenberg, R. Langer, *Nat.Biotechnol.* **2004**, *22*(7), 863.

2:20pm **BI1-TuA2 Surface Self-Assembled PEG Gel Particles to Control Bacteria-Biomaterial Interactions**, ***Y. Wu***, *Q. Wang, M. Libera*, Stevens Institute of Technology

The fact that desirable tissue cells and undesirable bacteria compete for the surface colonization of an implanted biomaterial is now well recognized. When bacteria win this competition, the resulting infection can lead to device failure with substantial consequences to both the patient and the health-care system. We are developing poly(ethylene glycol) [PEG] -based gel particles with which to modify surfaces and differentially control surface interactions with both tissue cells and bacteria. We are particularly interested in modulating the surface cell adhesiveness at micro/nano length scales with the goal of reducing staphylococcal adhesion while still enabling the adhesion, spreading, and proliferation of desirable tissue cells. In short to preserve healing while reducing the probability of infection. We have synthesized anionically charged PEG-acrylic acid (AA) copolymer hydrogel particles by inverse emulsion polymerization and used a bottom-up electrostatic self-assembly approach to modify otherwise cell-adhesive surfaces with cell-repulsive gel particles. Zeta potential measurements confirm that the gel particles are negatively charged because of the acid groups. SEM imaging and dynamic light scattering show that the particle diameters range from ~10's to ~ 100's of nm. We have electrostatically deposited them on both polylysine-modified silicon wafers and titanium metal coupons. By varying the concentration of gel particles in solution and the deposition time, we can control the area density of particles deposited on the substrate surface to levels of ~ 0.1 – 2 particles/sq micron. Immunofluorescence imaging shows that, relative to unmodified Si and PLL primed Si, PEG-modified Si has substantially lower colonization by *S. epidermidis* after innoculation and 4 hrs of culture. Confocal imaging of PEG-modified surfaces after 4 days of osteoblast culture show good osteoblast spreading and proliferation. SEM images indicate that the osteoblasts grow over the cell-repulsive particles while adhering to the remaining adhesive surface. Such surfaces may be useful in reducing the susceptibility of biomedical devices to biomaterials-associated infection.

2:40pm **BI1-TuA3 Some Strategies and Results for Antibacterial Coatings**, ***H.J. Griesser***, *K. Vasilev, H. Ys, C.P. Ndi, S.S. Griesser, S. Al-Bataineh, S. Semple*, University of South Australia **INVITED**

Bacterial attachment and subsequent biofilm formation might be reduced by application of a thin coating that deters bacterial colonisation. For biomedical devices a coating should also allow good attachment of human tissue to facilitate wound healing, or for catheters and contact lenses be lubricious and not bio-adhesive. Requirements differ for antibacterial coatings for different implants and devices; accordingly we have used different approaches for the fabrication of several antibacterial coatings. For long-lasting effect, we prefer the approach of covalently immobilising antibacterial molecules; we have also investigated the alternative approach of release of silver ions. This presentation will review advantages and disadvantages of various approaches, and discuss open questions.

Our strategies are based on plasma polymer thin film coatings, because this approach can be transferred to coat many polymeric, metallic and ceramic materials. Plasma polymers with chemically reactive surface groups enable covalent immobilisation of antibacterial compounds onto their surface. Alternatively, we load plasma polymer coatings with silver nanoparticles, from which Ag^+ ions can outdiffuse. Organic antibacterial compounds investigated were furanones, novobiocin, and serrulatanes, the latter are novel substituted diterpenes extracted from Australian plants used in traditional medicine. The chemical composition of coatings was assessed by XPS and ToF-SIMS to ensure that the intended coatings were achieved. Samples were tested for bacterial attachment and for biofilm formation, as well as for mouse 3T3 fibroblast cell attachment.

Surface-immobilised furanones, Novobiocin, and serrulatanes reduced bacterial attachment by up to 99.8%. While large biofilm communities formed on control surfaces within 48 hrs, these coatings prevented biofilm formation. Plasma polymer coatings loaded with Ag nanoparticles also were effective; Ag^+ delivery can be adjusted via the properties and thickness of the plasma polymer film and the silver loading. Testing of coatings with m3T3 fibroblast cell cultures showed, however, that in many cases there were adverse effects. Silver in particular affected 3T3 cells. With organic antibiotics, the surface density appears important and an optimum must be found between deleterious cell effects and antibacterial effectiveness.

Important questions remain: do surface-immobilised antibiotics act as in solution, as quorum sensing inhibitors (furanones) or gyrase inhibitors (Novobiocin)? Do in vitro and in vivo tests correlate? How to mitigate adverse effects on mammalian cells? Why is there contradictory literature especially on Ag?

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