



University of Nottingham

Combinatorial Material-Topography Screening: The ChemoTopo Chip

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Aim

Next Generation Biomaterials Discovery



 Adding dimensionality to traditionally flat biomaterial screening approaches

Concept

Exploit biomaterial chemistry and topography to achieve desired cell response

Polymer microarray technology¹

27 chemistries 35 topographies

TopoChip platform²

Discovery of bespoke polymers for applications in medicinal devices and regenerative medicine

Rationale

- Limits of traditional cell culture on polystyrene
 - Biochemically-induced, non-mature cell phenotypes
 - Planar, non-native cell environment
- Deficiency in number of clinically-relevant biomaterials
- Lack of understanding: biomaterial design parameters



Sample fabrication: Thiol/ene chemistry, Surface-initiated polymerisation

Fabrication route:

Photomask

Photolithography, DRIE



Silicon master Drop-casting, UV curing

Silicon Master:

ChemoTopo Chip master, collaboration: Maastricht University

Moulding of base polymer:

Deposition of chemistries:

- Surface-initiated polymerization of chemistries to pendant thiol groups of pre-formed chip³
- Monomer functionality determines c(photoinitiator)

Verification of polymer grafting: ToF-SIMS

Silanised glass

Diacrylate-co-trithiol

Chemistry of interest

Separate topography transfer and immobilisation of chemistries to account for a range of polymer properties.

Film composition affects:

 Surface free thiol groups FT-IR (ATR):

Feature integrity

Cell experiments:

Human mesenchymal stem cell morphology after 3d

• 2D control, varying chemistry

• One topography, varying chemistry

• Three chemistries, 35 topographies

Conclusions

References

- Successful fabrication of ChemoTopo Chip by surface-initiated polymerisation of chemistries to microtopographies
 - Integrity of microfeatures
 Verification of surface modification for (meth)acrylates/ (meth)acrylamides
- First cell assay to confirm suitability of samples (compatibility with cell culture, immunocytochemistry, microscopy)
 - Modulation of primary hMSC morphology and potentially proliferation by both chemistry and topography

Outlook

- Upscale protoype fabrication to full-scale sample production, verify protocol robustness
- Full sample characterisation (FT-IR, ToF-SIMS, WCA, XPS, AFM)
- High-throughput screening to identify hit polymer + microtopography combinations for improved stem cell maturation or reduced biofilm formation
- Correlation of surface properties with cell response: computational modelling to derive structure-property relationships

¹ D. G. Anderson *et al. Nat. Biotechnol.* 22, 863-866 (2004).
 Y. Mei *et al. Nat. Mater.* 9, 768-778 (2010).
 A. Patel *et al. Curr. Opin. Solid State Mater. Sci.* 20, 202-211 (2016).
 ² H. V. Unadkat *et al. PNAS* 108, 16565-16570 (2011).
 F. F. B. Hulshof *et al. Biomaterials* 137, 49-60 (2017).
 ³ V. S. Khire *et al. Adv Mater.* 20, 3308-3313 (2008).

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