Utilisation of Novel Polymer Surfaces and Topographies to Promote hiPSC-Cardiomyocyte Maturation

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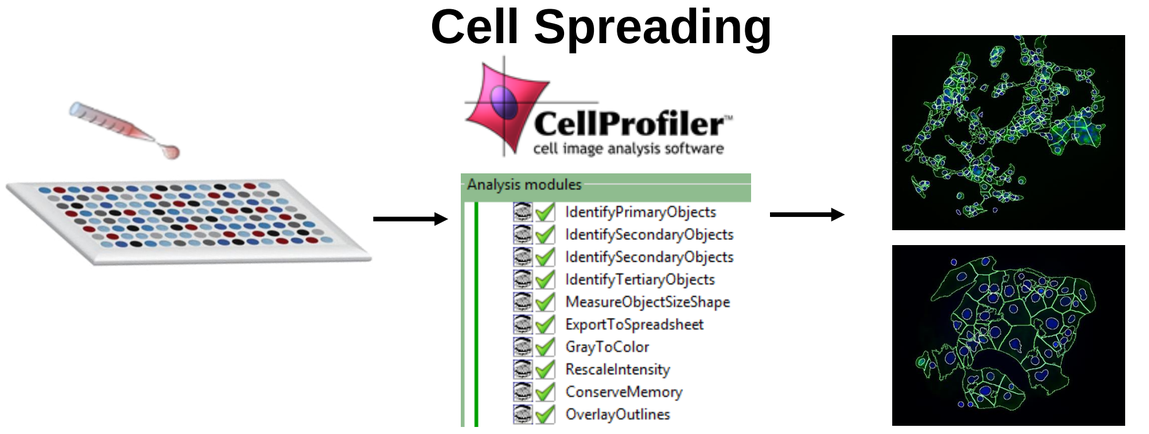
Introduction

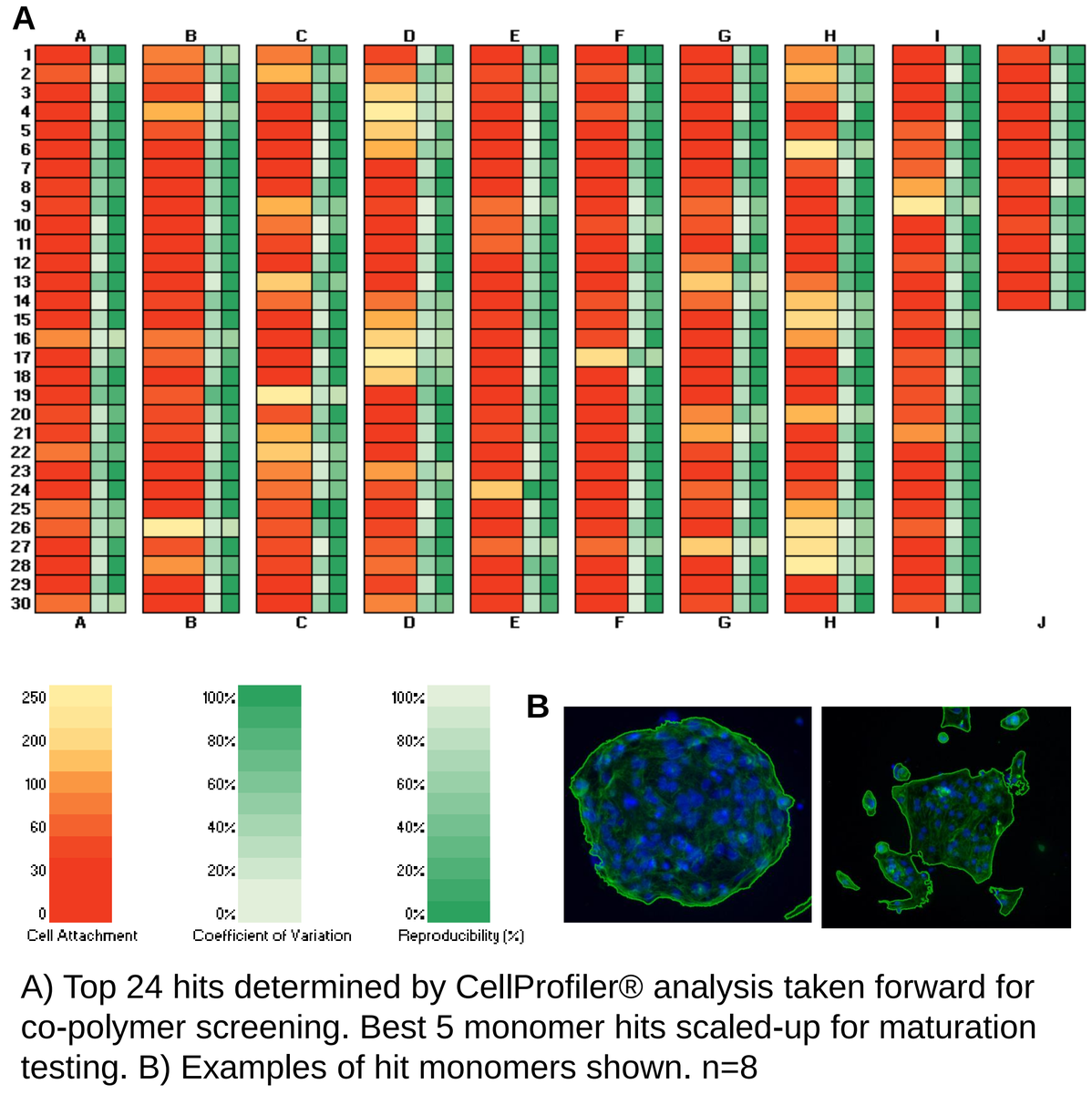
- Drug development in today's market can take 10-15 years and exceed $1 billion in costs
- Cardiotoxicity accounts for the majority of failures during drug development, and market recalls after product launch
- In recent years hiPSC derived cardiomyocytes are being developed for drug testing, however they currently resemble a foetal phenotype.
- To generate more mature cardiomyocytes new approaches will be taken including; the use of novel 2D polymer substrates, which can then be combined with beneficial topographies in an '2.5D' format and eventually brought together in a particle-based 3D culture system.
- Materials and culture systems created during this project will also exclude; the use of serum and additional surface coating (e.g. Vitronectin/Matrigel)

2D Polymer Screen for hiPSC-CM Attachment & Cell Spreading



284 Monomers Screened for hiPSC-CM Attachment & Cell Spreading Results

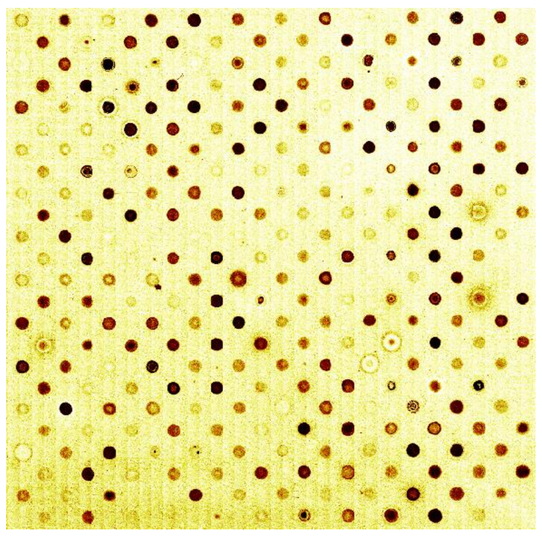
- hiPSC-CMs differentiated in monolayer culture
- Single cell collagenase-based dissociation
- Cultured for 1-week before analysis
- A-actinin staining to reveal sarcomeric structure



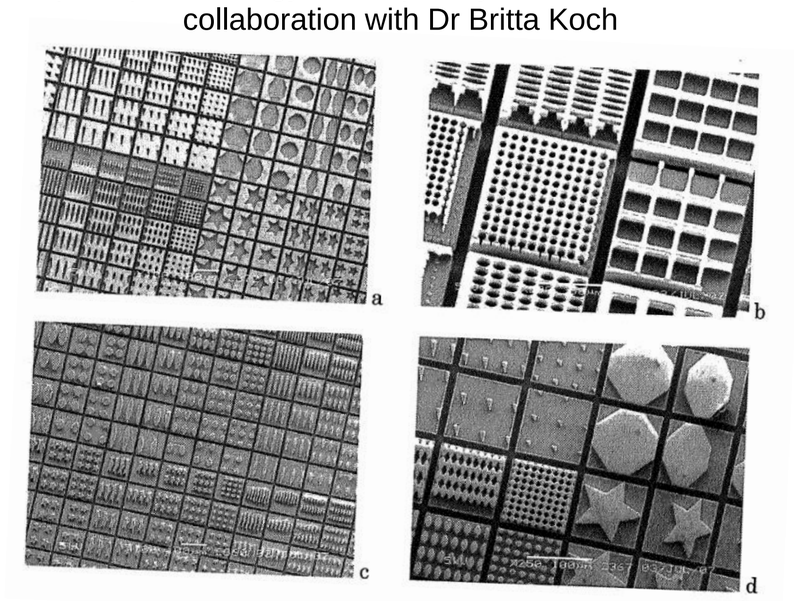
A) Top 24 hits determined by CellProfiler® analysis taken forward for co-polymer screening. Best 5 monomer hits scaled-up for maturation testing. B) Examples of hit monomers shown. n=8

Combining Novel Polymers with New Topographies & 3D Culture to Induce hiPSC-Cardiomyocyte Maturation

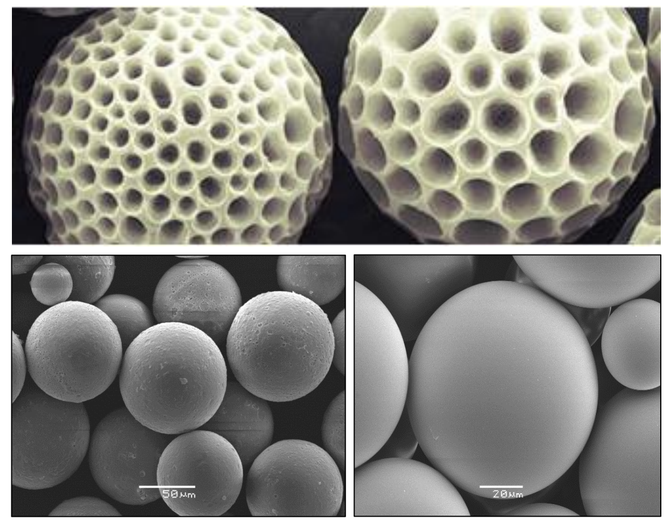
2D Polymer Microarray production with Dr L. Burroughs



Topochip technology developed by Jan De Boer et al. in collaboration with Dr Britta Koch



Microparticle development with control over chemistry, topography, & elasticity by collaboration with Dr Marta Alvarez Paino



Discussion

hiPSC-CMs were seeded at a range of densities on arrays both preconditioned with serum & without serum. A total of 8 biological hits and 24 technical repeats.

Conditioning with serum at lower numbers revealed monomers that support hiPSC-CM spreading. Culturing at higher densities without serum has identified monomers that support the highest density of hiPSC-CMs consistently.

Initial scale-up to 96-well format proved successful for our top hits.

Future Work

Monomer hits selected for scale-up will be tested for any increase in maturation.

Top 24 hits will form co-polymer mixtures to screen for synergistic effects on hiPSC-CM attachment & maturation.

Biomaterials Discovery

This work was supported by the UK Engineering and Physical Sciences Research Council (EPSRC) grant EP/N006615/1 for the University of Nottingham Programme Grant in Next Generation Biomaterials Discovery.