Casein microdevices with bioimprinted surface features

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Surface patterning of rigid biodegradable materials with cellular imprints can significantly improve the application of such materials as substrates in tissue engineering and as structural elements in implants[1]. Previous studies have demonstrated the influence of bioimprinted patterns on cell regulation and proliferation when fabricated with non-biodegradable materials such as polystyrene (PS)[2,3]. To combine the advantages of bioimprinting and biodegradable materials, we have since proposed the incorporation of such biomimetic cell-like surface features onto casein-based biomaterials[3].

Casein microdevices with bioimprinted surface features present a biomedical platform technology for enhancing tissue-engineering applications. In this presentation, we will discuss advantages of surface patterning, introduce the bioimprint platform and show its application to a model cell system. We will show the characterization of the biomaterial substrate, the fabrication of devices using an optimized process with significantly improved replication resolution[4] and the use of these devices in a cell-culture context.

Figure 1 shows atomic force microscopy (AFM) images of an individual fixed C2C12 mouse muscle cell and its imprints on PDMS and casein. C2C12 cells were chosen as they provide a model to study differentiation on patterned substrates[5]. To quantify the replication quality we compared cross-sections of the same cell at four stages, as shown in Fig. 2. For use as cell-culture substrates, casein film degradation time is controlled by transglutaminase (TG) crosslinking. Casein solution is mixed with TG with concentration of 10 U per gram of casein, which leads to an increase in the film degradation time from 2 hours to in excess of 14 days when immersed in media. C2C12 cells grown on these substrates exhibit normal morphologies and excellent proliferation, as shown in Fig. 3. Devices with optimized pattern replication and crosslinking can now be used to influence cell alignment and phenotype, thus adding biomimetic functionality to biodegradable substrates and implant surfaces.

1. W. Y. Tong, et al. Biomaterials **33** (31), 7686-7698 (2012).
2. I. Mutreja, et al. Biofabrication **7** (2), 025002 (2015).
3. A. Hashemi, et al. Journal of Vacuum Science & Technology B **33** (6), 06F901 (2015).
4. A. Hashemi, et al. MNE 2016, Vienna
5. L. Murray, V. Nock, J. Evans and M. Alkaisi, Journal of Biomedical Materials Research Part A (2016).

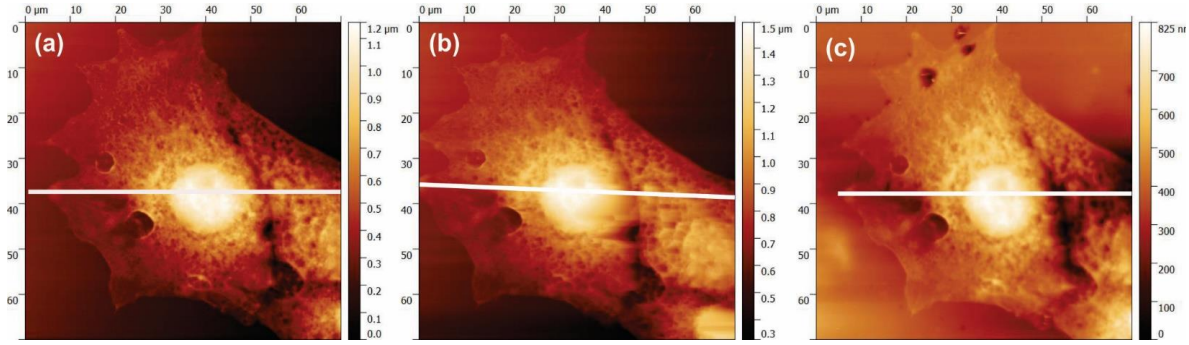

Figure 1 Atomic force microscopy images of a fixed C2C12 cell on glass and its replication onto PDMS and casein: (a) Fixed cell on glass slide, (b) inverted image of negative cell replica bioimprinted into the PDMS master mould, (c) positive imprint onto final casein film after plasma and polyvinylpyrrolidone (PVP) treatment of the PDMS mould.

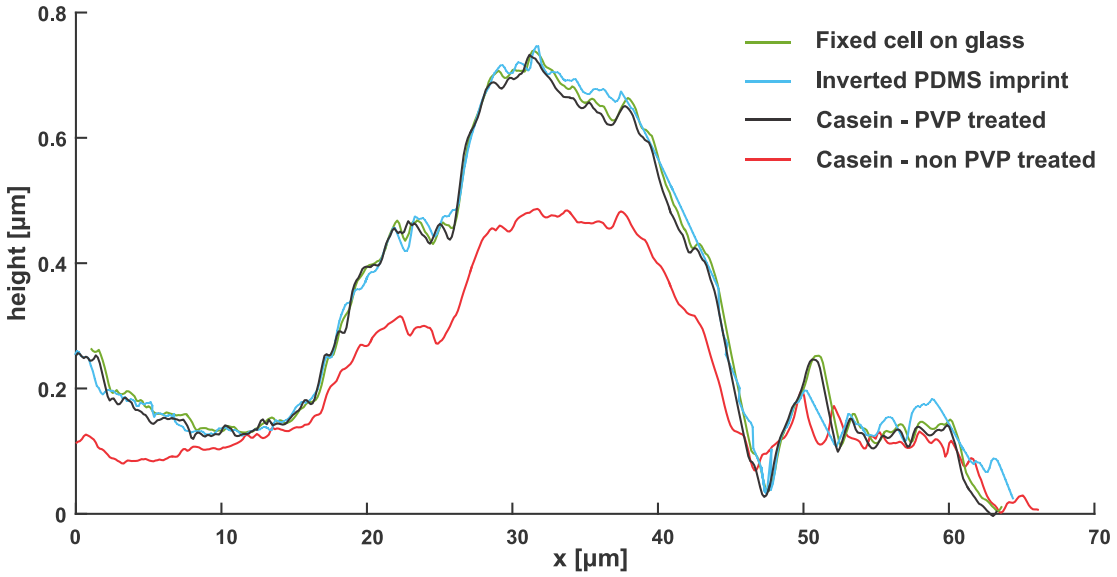

Figure 2 Profiles of the cross-section of the cell shown in figure 1 at different stages of the replication process. The profile of the cross-section on a casein film without PVP treating the PDMS mould is shown here for comparison (AFM image not shown in figure 1). Feature details during the imprint stage can be compared to the original fixed cell.

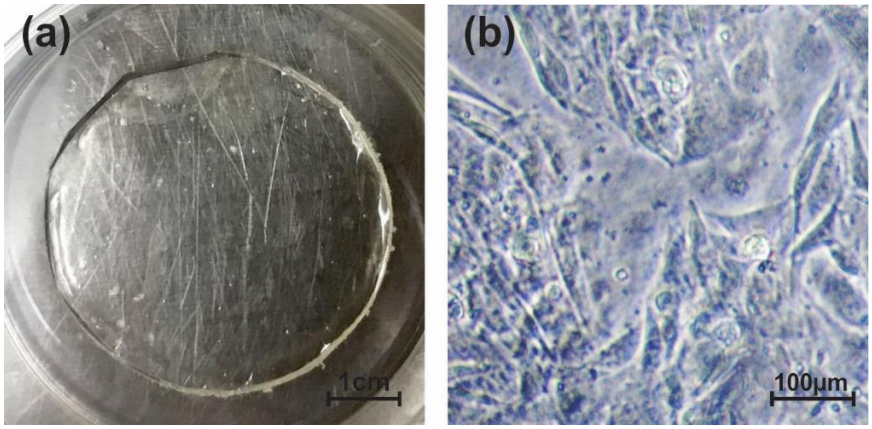

Figure 3 (a) A TG crosslinked casein film, (b) C2C12 cells cultured on the same film after 24h.