A novel 3D polymeric tool for accurate screening of the performance of immunodiagnostic polymeric microneedles

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INTRODUCTION: Melanoma is the most lethal skin cancer, having a rapid increase of occurrence over the past 30 years[1].To date, the most effective treatment for melanoma is the early diagnosis, which is followed by surgical resection. Therefore, in order to improve these disappointing statistical figures, it is essential to develop efficient diagnostic tools for rapid detection of the disease's specific markers. Minimally invasive microneedles (MNs) are promising candidates, as they enable rapid and pain-free protein biomarker detection *in situ*. However, validating the developed microneedle (MN) systems remains a bottleneck. To date, the most commonly used systems for *in vitro* microneedle validation are either homogeneous solutions that contain the target antigen to be detected by the MNs or excised animal skin. Animal skin strikes many similarities with the human skin, however the animal skin properties, such as stiffness, elasticity, porosity, which vary between different patients cannot be easily tuned/ tailored [2]. Furthermore, antigen solutions can be informative for a preliminary evaluation of the MN arrays, but they are not representative models of *in vivo* skin structure and biomarker concentration. Biomaterial based 3D structures can simulate important skin tissue features, such as stiffness, elasticity, porosity, structure, extracellular matrix presence that can vary between different patients, different skin types and with ageing. Moreover, they can provide a realistic structural environment for the penetration and action of MN. Therefore, these biomaterial based 3D structures have great potential as screening tools for MN evaluation. *The aim of this work was to validate the S100 expression, a marker that is upregulated in melanoma, on a microporous polymer based 3D melanoma model. S100 expression in the model was confirmed using a novel immunodiagnostic microneedle device.*

METHODS: 3D polymer (PU) based microporous scaffolds (5x5x2.5mm^3) were developed using the Thermally Induced Phase Separation (TIPS) method, as described previously[3]. The porosity was 80% and the pore size 100-120 μm. Thereafter, the metastatic melanoma cell line A-375 was injected and cultured in those scaffolds for 5 weeks. Evaluation of cell distribution within the PU matrix was conducted with Scanning Electron Microscopy (SEM). Viable (live) cells were visualised *in situ* with confocal laser scanning microscopy (CLSM) of several sections of each scaffold. Furthermore, the detection of the S100 marker was carried out with PLA microneedles both on the 3D scaffold and for the cell culture supernatants. The PLA microneedle device was produced, surface modified and coated with the S100 antibody as previously described, followed by the detection of the antigen via immunoassay analysis on the microneedle surface[4].

RESULTS: The MN device was able to detect the S100 secretion from the melanoma cells in the scaffold after 35 days of a viable culture, producing a clear and visible detection signal similar to the one detected for the positive control samples. However, S100 gradients were not detected in the cell culture supernatants, suggesting that this versatile scaffolding tool can be an advantageous low cost animal free tool to be use as a surrogate for the *in vitro* evaluations of the MNs.

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