Evaluating the impact of biomaterials on modulating tumour-associated macrophages

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Abstract— **In recent years, biomaterials have been widely used for developing tumour models to help us gain a better understanding of tumour microenvironment (TME). Macrophages, as immune cells, play a significant role in the TME and exhibit plasticity based on their environment. This work aimed to assess the fundamental impact of biomaterials on the functionality of macrophages.**

Keywords— **Biomaterial-macrophage interaction, biomaterials, tumour models, tumour associated macrophages**

I. Introduction

Tumour microenvironment (TME) is a complex and heterogeneous area which plays a critical role in tumour's fate. Among many components present in TME, tumour associated macrophages (TAMs) are among the main cellular components and have a significant impact on tumor metastasis and progression. The importance of macrophages lies in their inherent plasticity, a trait which depends on their microenvironment. Based on their phenotype, these cells can show either anti-tumour or pro-tumour functions. Recently, tumour *in-vitro* models have been widely used to replicate complex TME and enable tracking of cellular activities in the cancer milieu to help having a better understanding of tumour biology. Biomaterials have been extensively used as ECM-like components in the TME, in order to develop these *in-vitro* tumour models. However, certain biomaterials might trigger immune responses, thereby impacting the behaviour of macrophages and consequently impacting the research outputs when employing such models. This work aims to evaluate the impact of commonly used biomaterials on macrophage activities enhancing our understanding of the interaction between macrophages and biomaterials used in *in vitro* models' development [1], [2].

II. Materials and Methods

For cytotoxicity evaluation, alginate solutions (Aspect Biosystem) were prepared by mixing with phosphate-buffered saline (PBS). Collagen solutions were prepared by blending collagen type 1 (rat tail, Ibidi) with Dulbecco's Modified Eagle Medium (DMEM), NaOH, water, and $NaHCO_3$. NaOH and $NaHCO_3$ were added to adjust the pH of collagen.

Following the preparation, each was added to the well plates and incubated at 37 °C for 60 minutes. Collagen preparation should be performed quickly, as there is a risk of partial gelation occurring in the collagen mixture within 5 minutes. After 60 minutes, macrophages (RAW 264.7, ATCC) were seeded on top of the biomaterials and incubated for 24 hours (37 °C, 5% CO_2). Cytotoxicity of the biomaterials was evaluated with 1-(4,5-Dimethylthiazol-2-yl)-3,5-diphenylformazan (MTT) assay 24 hours post cell seeding.

III. Results

As indicated in Fig. 1, MTT assay shows that the cell viability was more than 95% across all samples with alginate and collagen, indicating that these biomaterials do not induce cytotoxicity within the evaluated concentration range. Therefore, alginate and collagen hold promise in cancer research while providing a favorable environment to the cells.

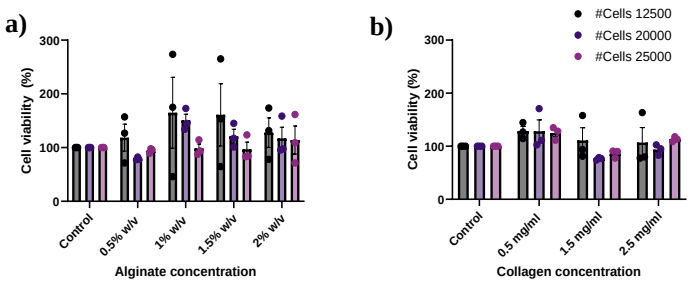

Fig. 1 Cytotoxicity evaluation of (a) alginate, and (b) collagen.

IV. Conclusion

Assessing the impact of biomaterials on macrophages that will be used in tumour models, allows us to select the appropriate biomaterial combinations without triggering unwanted immune responses.

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Conflict of Interest

The authors declare no conflicts of interest related to this research.

References

1. M. Sylvestre, C. A. et al., *Advanced Materials*, vol. 32, no. 13. Wiley-VCH Verlag, Apr. 01, 2020. doi: 10.1002/adma.201902007.
2. C. Wang, et al,, *Biofabrication*, vol. 6, no. 2. Institute of Physics Publishing, 2014. doi: 10.1088/1758-5082/6/2/022001.