THE IMPLANTATION SITE IMPACTS THE TUMOUR GROWTH KINETICS AND TUMOUR IMMUNE INFILTRATE IN EO771 AND 4T1 SYNGENEIC BREAST CANCER MODELS

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Background The preclinical evaluation of novel therapeutic agents, such as immune checkpoint inhibitors, and the identification of potential biomarkers require appropriate animal models. Syngeneic mouse models are commonly utilised as they provide immunocompetent hosts and enable rapid and cost-effective experimental readouts. In these models, tumour cells can be injected subcutaneously in the flank or orthotopically in the native organ of tumour origin. The selection of the optimal model for assessing a future therapeutic agent necessitates the characterisation of tumour growth and immune cell infiltrates. In this study, we examine how the tumour implantation site influences both tumour growth kinetics and the tumour immune infiltrate composition in two syngeneic breast carcinoma models.

Methods Female, 6 weeks old BALB/c or C57BL/6 mice were inoculated with 4T1 or EO771 breast carcinoma cells respectively. Cells were implanted subcutaneously (SC) on the left flank, or orthotopically into two mammary fat pad sites (MFP2 and MFP9). Tumours were harvested at day 14 (4T1) or 21 (EO771) post inoculation and characterised using multicolour flow cytometry for both lymphoid and myeloid populations. The growth kinetics of tumours were also followed until the animals reached ethical tumour limits.

Results In both syngeneic models, MFP9 implanted tumours demonstrated the best overall growth. For the 4T1 model, total cell viability reduced significantly in the SC implanted tumours, but in the EO771 model viability was consistent between all sites. MFP9 grown tumours in both models showed a significant increase in B cell infiltration which was significantly correlated with an increase in tumour infiltrated T cells with either a central memory or a naïve like phenotype. MFP2 displayed a similar elevated B cell infiltration but more sporadically and only in the 4T1 model, while SC grown tumours showed no increased B cell infiltrate in either of the 2 models.

Conclusions In the above study we demonstrated that tumour location impacts both the tumour growth kinetics and the composition of the tumour immune infiltrate in both the 4T1 and EO771 syngeneic models. The MFP9 implantation site exhibited the best overall tumour growth kinetics in both models with a more variable tumour immune infiltrate rich in B and T lymphocytes.

Ethics Approval All animal work was carried out under UK Home Office legislation, ASPA 1986, Agenda resource management (Alderley Park) AWERB

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