POST NEOADJUVANT CHEMOTHERAPY TISSUES ENRICHED IN A DISTINCT CD27^+ CD21^- CXCR5^- ATYPICAL DOUBLE NEGATIVE (DN2) B CELLS, WITH POTENTIAL ROLE IN PURINERGIC SIGNALLING IN EARLY BREAST CANCERS

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Background B cells exhibit diverse phenotypes and function and the complex interplay between different B cell subsets in the context of chemotherapy treated breast cancers remains unclear. Here, we investigate the dynamic changes in the B cell immune landscape before and after neoadjuvant chemotherapy (NACT) treatment across different breast cancer subtypes.

Methods Treatment naïve, mid-treatment and post-NACT breast tumour, matched lymph node, blood and serum samples were profiled for B cell subsets and cytokines by flow cytometry, cytometry by time-of-flight (CyTOF) and Luminex technologies. Ex vivo autologous tumour organoid and immune cells cocultures to functionally assess the B-cell interactions across breast cancer subtypes were performed. Multiplex spatial analysis method was used to explore the dynamics of double negative B cell cellular crosstalk within the tumour and axillary lymph nodes. The results are being associated with treatment outcomes. Expression and activity of purinergic ectoenzymes within B cell subsets were also assessed by flow cytometry and high-performance liquid chromatography. Current work focusses on how these changes (especially with DN2 cells) relate to treatment response are ongoing. Among circulating B, T and NK cells, B cells showed the highest CD73 and CD39 surface expression at baseline, but their expression significantly dropped following NACT especially within the DN2 B cell subset. These ecto-5'-nucleotidases are known to play a critical role in B and T cell interactions. Spatial analyses between these cell types are ongoing.

Conclusions We report for the first time an enrichment of DN cells in breast cancer tumour tissue, specifically the expansion of DN2 cells in post NACT residual tissue. Functional analyses of tumour-infiltrated B-cells suggest that mechanistically, B-cell subgroups may contribute to immune surveillance and point to an important role of purinergic signalling in early breast cancers. Our study highlights the requirement for further investigation into the role of DN B cells in the context of chemo/immunotherapy resistance in breast cancers. Clinical trials are ongoing to further investigate the role of DN B cells in the context of chemo/immunotherapy resistance in breast cancers.

Ethics Approval Samples were collected from breast cancer patients undergoing treatment at Guy’s and St Thomas’ Hospital, London, after written informed consent as part of a non-interventional clinical study (BTBC study: REC No: 13/LO/1248, IRAS ID 131133). This study has local research ethics committee approval and was conducted adhering to the principles of the Declaration of Helsinki.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0936