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## Differential gene expression of immune related genes in breast cancer tumour and normal adjacent to tumour tissues

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**Background:** The immune response plays a significant role in the post-operative breast tissue environment of breast cancer (BC) patients. The extent of post-operative inflammation and immunosuppression is associated with BC recurrence. Determining the baseline immune profile of normal adjacent to tumour (NAT) tissue may provide an insight into patient outcomes. We aimed to compare the transcriptome of BC tumour and NAT to determine the differential gene expression of immune related genes, pathways and patient outcome.

**Methods:** Matched BC patient tumour and NAT tissues from The Cancer Genome Atlas (TCGA) (n=54) and samples collected in Cork University Hospital (CUH) (n=10) were used. For the CUH cohort ribonucleic acid (RNA) was extracted and sequenced using Illumina Next Generation Sequencing. RNA-Seq read-counts were downloaded from TCGA and provided by BMKGene for the CUH cohort. Differential gene expression was analysed using EdgeR and pathway analysis by Gene Set Enrichment Analysis (GSEA). Genes were significantly different with a false discovery rate (FDR) <0.1 and Log<sub>2</sub>fold change (FC) ≥1.5 and pathways enriched with an FDR <0.25.

**Results:** In both TCGA and CUH patient cohorts, adipogenesis and IL6 JAK STAT3 signalling pathways were

enriched in NAT and IL6, IL10, LEP (leptin), ADIPOQ (adiponectin), CD36 and FABP4 genes of these pathways were significantly higher in NAT compared to tumour tissue (FDR <0.1). Considering high systemic IL6 is negatively associated with patient outcome, TCGA patients were stratified on NAT expression of IL6 and higher NAT IL6 had worse overall survival (P<0.05).

**Conclusions:** Baseline inflammatory and immunosuppressive mediators in NAT are potential predictive biomarkers of patient outcomes.

**Keywords:** Breast cancer (BC); immune expression; tumour microenvironment; tumour; normal adjacent to tumour (NAT)

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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