

# The impact of anaesthesia and anaesthetic techniques on immune function and populations in patients undergoing surgical resection of breast cancer

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**BACKGROUND:** Despite advances in surgical treatments for breast cancer, it remains a major cause of morbidity and mortality. Established literature indicate that a robust immune system is associated with better outcomes, yet increasing evidence suggest that the operative process can be immunosuppressive, especially with use of certain anaesthetic regimens.

**AIMS:** In breast cancer patients undergoing surgery: 1) Assess whether changes in the different immune population subsets of peripheral blood mononuclear cells (PBMCs) occur. 2) Investigate *in vitro* changes in immune function. 3) Investigate if specific **drugs given during anaesthesia** contribute to immunosuppression.

**METHODS:** Blood samples were collected from breast cancer patients (n=20) pre-operatively (baseline), post-anaesthesia, and post-operatively. Isolated PBMCs underwent flow cytometry to identify immune populations and any changes following anaesthesia. Enzyme-linked immune absorbent spot (ELISpot) assays using PBMC antigen-challenges for IFN- $\gamma$  production to assess immune function post-anaesthesia and post-operatively. Finally, *ex vivo* single anaesthetic drug spike-in ELISpots were used to isolate and determine specific drug effects on immune activity.

**RESULTS:** All ELISpot stimulants showed highly significant decreases in immune response post-operatively. Natural killer cell response decreased post-anaesthesia (p<0.0001) and

post-operatively ( $p < 0.0001$ ) from baseline (Figure 4-3). T cell response also decreased in response to viral (EBV, CMV) and breast cancer (MUC1) antigen challenges post-operatively ( $p < 0.0001$ ,  $p = 0.0027$ ,  $p = 0.0002$ ). Functional dose-dependent decreases were also observed in single drug spiking experiments (Figure 4-5 T cells, 4-6 NKs). No major significant changes in PBMC populations were found in flow cytometry.

**CONCLUSION:** Immune activity is suppressed by both anaesthesia and surgery. Specific anaesthetic drugs caused immunosuppression *ex vivo* and support further investigation and potentially guideline changes in anaesthetic regimens for cancer surgeries. Flow cytometry suggest PBMC populations are not affected by anaesthetic drugs or surgery so the observed decreases in IFN- $\gamma$  producing cells are specific to drug and stress-induced functional suppression rather than cell loss.