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# Obesity and breast cancer: Investigating the impact of adipose tissue macrophage phenotype on HER2+ breast cancer patient outcomes

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**Background & Aim:** In their lifetime, 1:8 women will be diagnosed with breast cancer. However, 27% of breast cancers in the UK population are preventable, with 9% linked to obesity. Macrophages can be polarized towards the anti- (M2), leading to the production of immunosuppressive factors IL-10 and ARG1 or via iNOS stimulation, pro-(M1) inflammatory subtype. Moreover, inflammatory foci termed Crown-Like Structures (CLS) i.e. dead adipocytes circumscribed by macrophages have recently been identified in breast tissue histology. It has been proposed that obesity induces breast Adipose Tissue Macrophages (ATMs) to form CLS. The study aims to investigate the phenotype of ATMs forming CLS using immunohistochemistry techniques.

**Method:** Formalin-fixed paraffin-embedded breast tissue samples were collected correlating to a database of 235 HER2+ breast cancer patients treated in Southampton. Immunohistochemistry was conducted on the Leica BondMax Autostainer using antibodies against: CD68, CD163, iNOS and ARG1. Immunoreactivity was assessed using light-microscopy. Monocyte-derived macrophages skewed in the laboratory towards the M1 or M2 phenotype served as controls.

**Result:** 37% of cases were positive for CLS, which were primarily (83.8%) observed in clusters at the tumor-adipocyte interface. The majority of ATMs associated with CLS expressed the pro-inflammatory M1 phenotype (iNOS+/CD68+ and ARG1-/CD163+ or CD68+). No statistically significant association was observed between obesity (BMI≥30) and the formation of CLS. Instead CLS were positively associated with other (↑CD16/↓CD32B) intra-tumoral markers (pro inflammatory) suggesting that their formation likely resulted from the inflammatory influences of the tumor microenvironment. Moreover, CD163 proved a macrophage-specific but not M2-specific marker; as both cohort ATMs and controls displayed CD163+/CD68+ dual-positivity irrespective of macrophage phenotype.

**Conclusion:** In this HER2+ breast cancer cohort, ATMs comprising CLS express the pro-inflammatory M1 phenotype. However, CL occurrence was not statistically associated with obesity (BMI≥30). Understanding the mechanism of CLS formation may offer targets for interventions to reduce risk or improve prognosis of breast cancer.

## Biography

Alicia Y Lefas is currently working as a Senior House Officer at Chelsea and Westminster Hospital in London, UK. She has completed her graduation from Southampton University Medical School with Bachelors in Medical Sciences. Her interests are in cancer research studies.

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