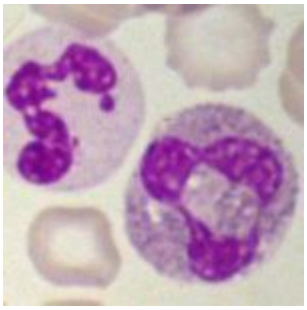
Can neutrophils adopt antigen-presenting cell functions, and if so how?



Neutrophils are well known for their pro-inflammatory properties and neutrophil associated extracellular traps. However, studies have demonstrated that neutrophils also express molecules associated with antigen-presenting cells (APCs) such as MHC-Class II, CD11c and T cell stimulatory marker. These neutrophils termed *neutrophil-derived APCs (nAPCs)* have transcriptional profiles similar to monocyte-derived dendritic cells (DCs). Though they possess APC like properties and can promote T cells responses, not much is known about how neutrophils become nAPCs and whether nAPCs can effectively present to T cells. In this summary, we highlight recent research that investigated whether conversion to nAPCs requires the engagement of their Fcγ receptor (FcγRs) and explore the therapeutic potential of nAPCs.

Using a murine model, authors (Mysore et al., 2021) demonstrated that uptake (endocytosis) of antibody-antigen complexes via binding to the FcγRs converts neutrophils to nAPCs. These nAPCs are fully immunogenic with immunomodulatory properties and can directly activate T cells. Analysis of nAPC frequencies during Systemic Lupus Erythematosus (SLE) suggested that nAPC are associated with SLE severity demonstrated by higher frequencies of nAPC in SLE compared with healthy individuals.

Additionally, researchers demonstrated that antigen-specific nAPCs that activate T cells with anti-tumorigenic properties can be generated by administering anti-FcγRIII conjugated to a defined antigen, and clonal neutrophils harbouring neoantigens from patients with myeloid neoplasms can be converted to immunogenic nAPCs that activate T cells in an antigen-agnostic manner. Both of these approaches may be deployed as T cell-based immunotherapeutic strategies for the treatment of cancer.

Journal Article: Mysore et al., 2021. FcγR engagement reprograms neutrophils into antigen cross-presenting cells that elicit acquired anti-tumor immunity. Nature Communications.

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