Investigating the Ige-FcεRI Axis in Human Cutaneous Squamous Cell Carcinoma

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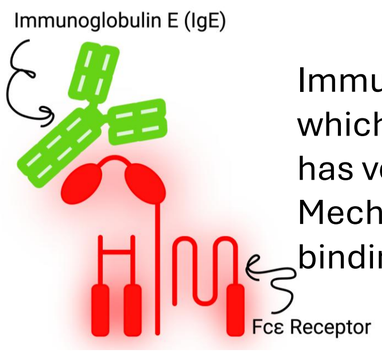
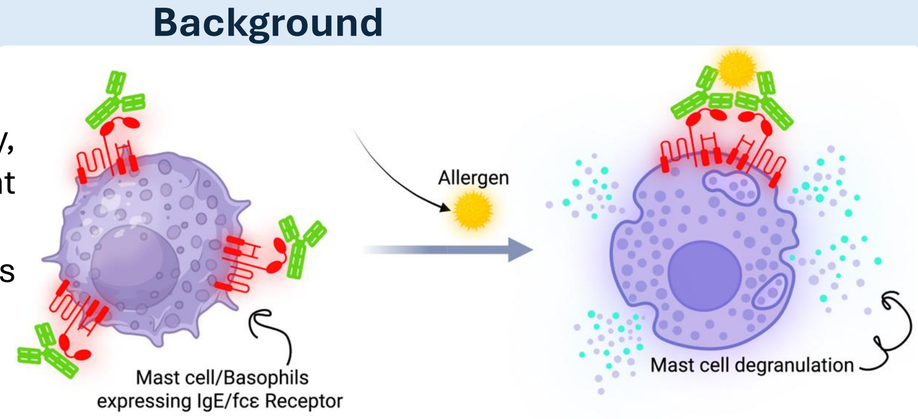
Background

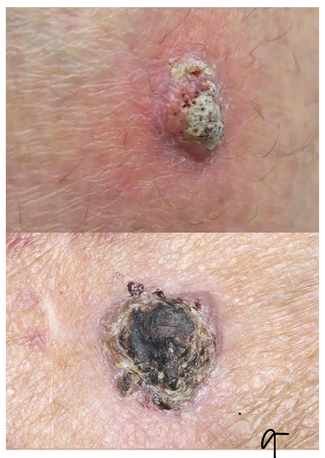


Immunoglobulin E (IgE) is a type of antibody, which is produced by Immune cells and that has very potent immunological function.
Mechanism of action of IgE involves its binding to the high affinity receptor FcεRI.



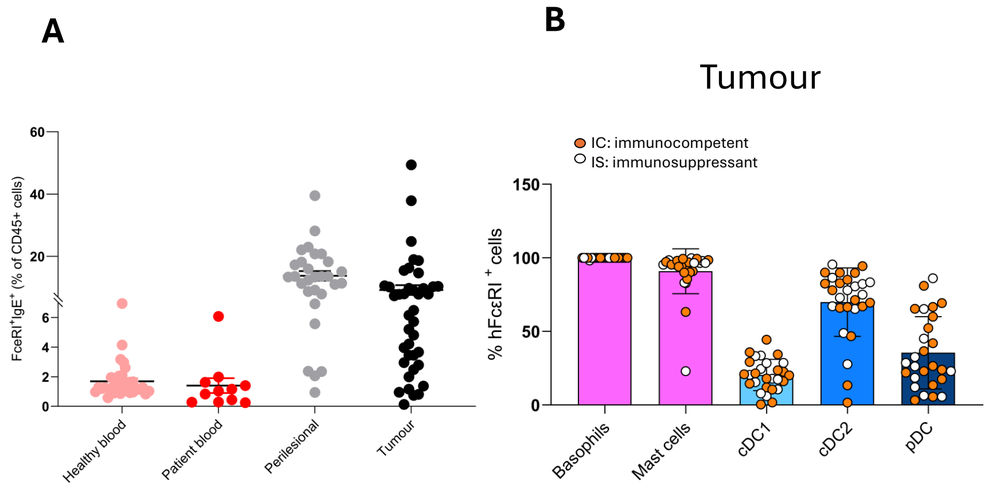
In an allergic reaction, allergen cross-link with IgE bound on the surface of Basophils and Mast cells and cause release of mediators such as histamine which cause hives and wheezing!

IgE/FcεRI axis in cutaneous Squamous Cell Carcinoma (cSCC)



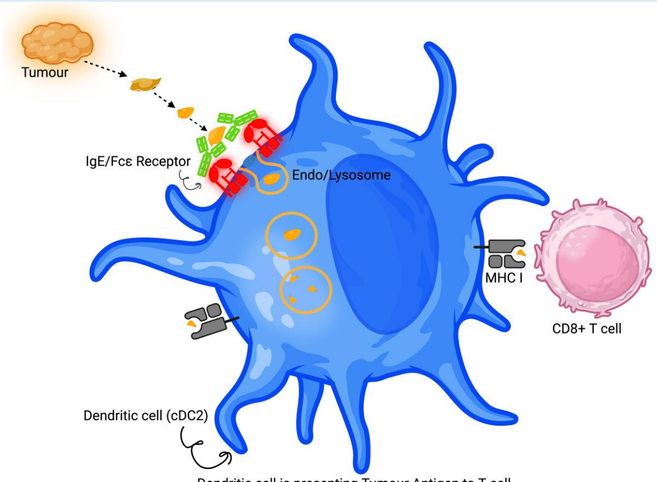
Examples of cutaneous squamous cell carcinoma (cSCC)

Since the early 1990s, non-melanoma skin cancer incidence rates have increased by more than two-and-a-half times (169%) in the UK. This trend is projected to impose a substantial financial burden on the National Health Service (NHS), highlighting the urgent need to understand and prevent this disease through insights into the underlying immunological mechanisms which may guide the development of novel and effective interventions.

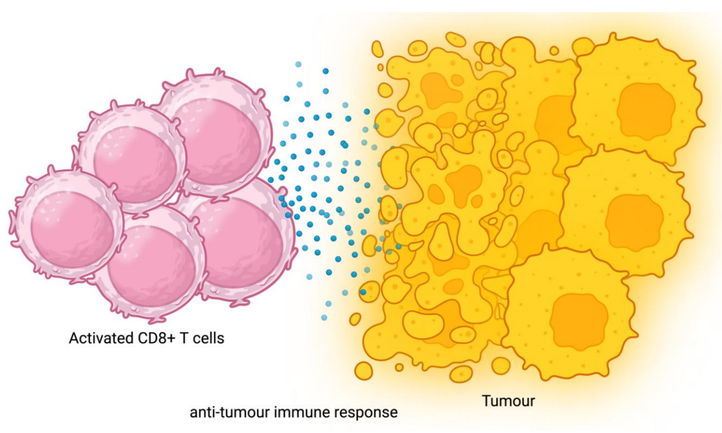


A. Immune cells in the cSCC differ from the blood as they highly express the FcεRI and carry IgE **B.** Among the immune cells, a large proportion of the Dendritic cells (cDC1, cDC2 and pDC) express FcεRI. This is in addition to the traditional expression on basophils and mast cells.

Hypothesis

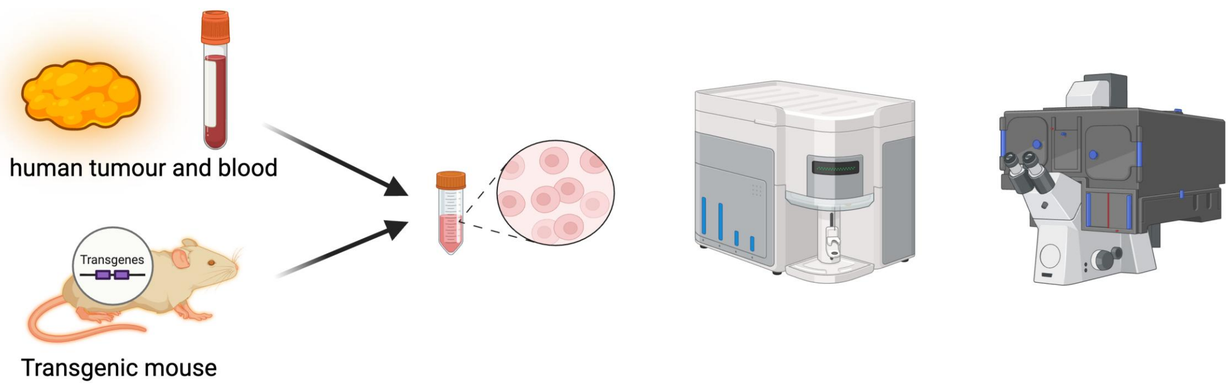


Dendritic cell is presenting Tumour Antigen to T cell



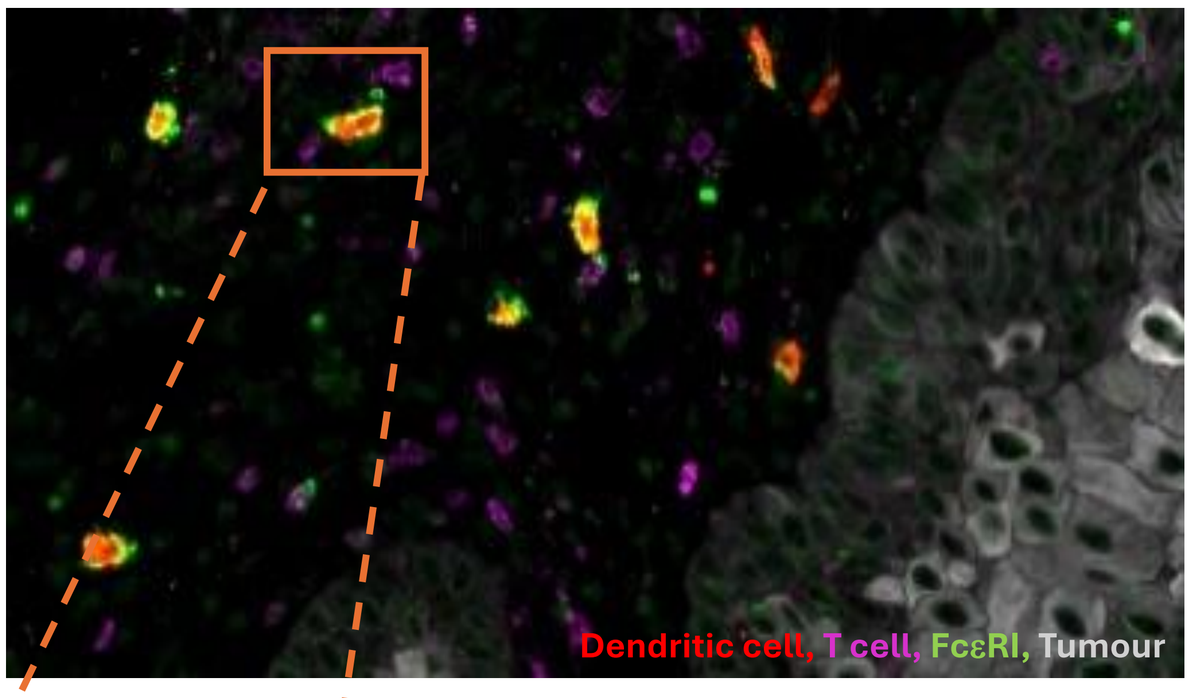
We hypothesise that the IgE/FcεRI axis can enhance anti-tumour responses by a process called 'cross-presentation' whereby tumour antigens are internalised by Dendritic cells and loaded onto MHC class I and presented to CD8 T cell. This process can initiate tumour recognition and tumour elimination by cytotoxic CD8 T cells.

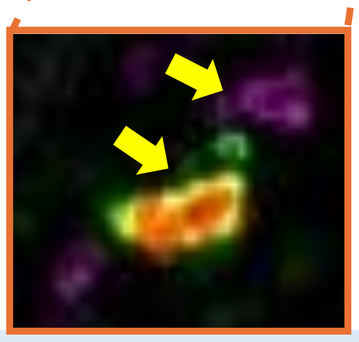
Methods



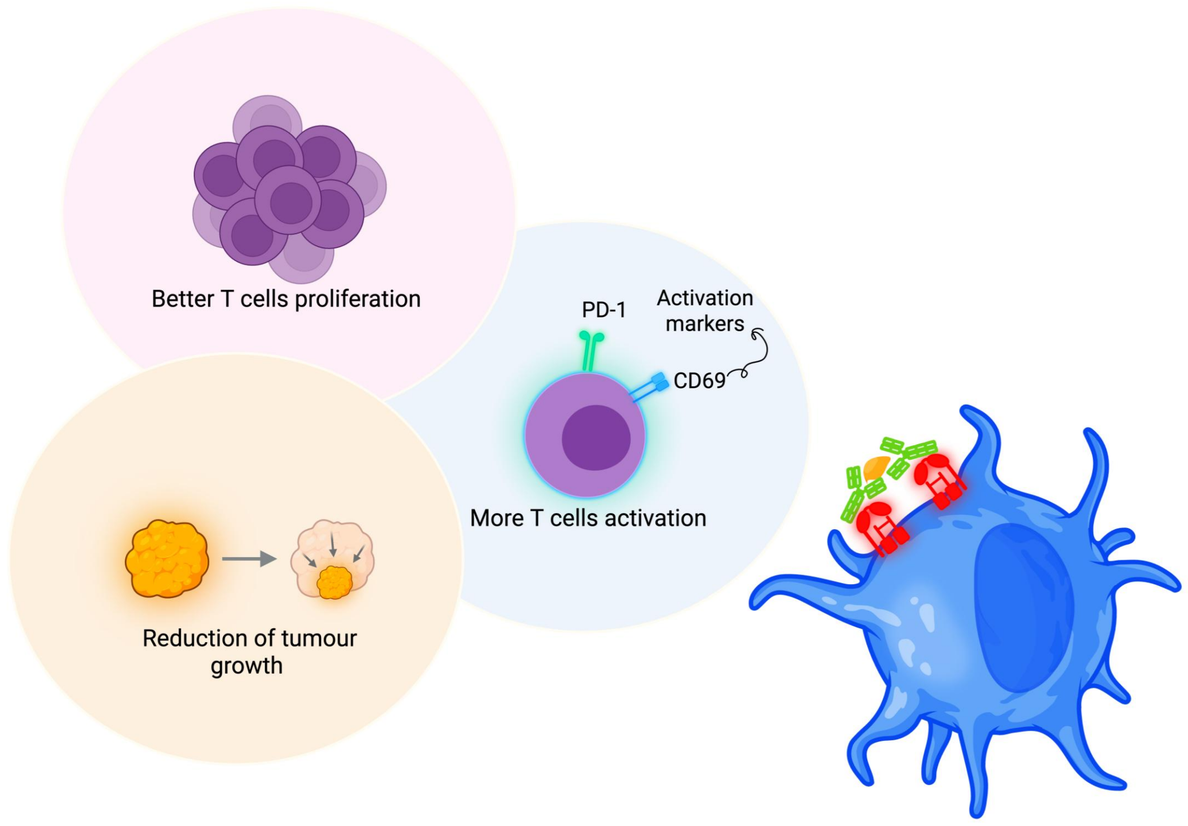
Cell suspension from both human tumour and blood and transgenic mouse tissues were analysed using flow cytometry or imaged via confocal microscopy.

Results





Example showing Dendritic cells (Red) expressing FcεRI (Green) on the surface are co-localising with CD8 T cells (Purple) in a human cSCC tumour sample.



CD8+ T cells expand better and get more activated in the presence of IgE, which is bound to its high affinity receptor on the surface of dendritic cells (cDC2. This leads to better tumour control and a reduction in the frequency and size of the cancer.

The IgE–FcεRI axis contributes to suppression of tumour growth through enhanced DC cross-presentation and CD8+ T-cell–mediated immunity in cSCC. Further understanding of these mechanisms may inform new immunotherapeutic approaches for cSCC and potentially other solid tumours.