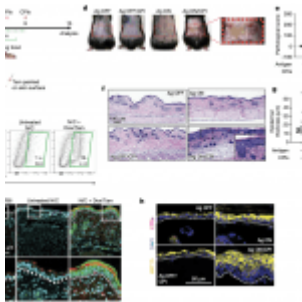


Making cancer immunotherapy safer



[Cancer immunotherapy](#) has revolutionised the treatment landscape for various types of cancer by harnessing the power of the immune system to combat tumours. Specifically, immunotherapies that inhibit checkpoint receptors like [PD-1](#), which curtail the ability of T cells to target cancer cells, have emerged as preferred options for treating solid cancers.

The use of PD-1-blocking agents can lead to unintended consequences, as T cells may attack not only cancer cells but also healthy tissues. This phenomenon results in severe and potentially life-threatening side effects, which can diminish the benefits of immunotherapy.

A recent study has provided valuable insights into the underlying mechanisms through which [PD-1 maintains the integrity of healthy](#) tissues (Figure 1). These findings have the potential to aid scientists in predicting, treating, or even preventing the side effects associated with PD-1-blocking immunotherapies.

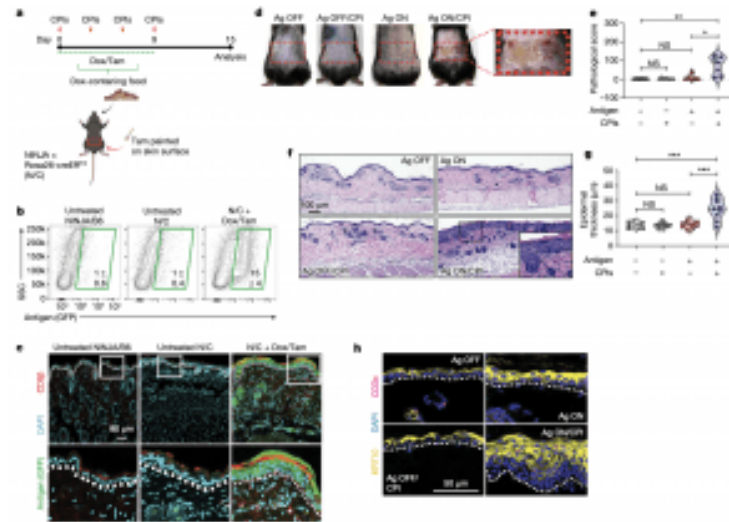


Figure 1: Skin-specific antigen induction and CPIs lead to local cutaneous disease. a, Experimental schedule. b, Frequencies of antigen-expressing (GFP +) skin cells from the indicated conditions (outlined in green; percentages of GFP + cells are shown). Data are mean \pm s.d. $n = 5$ (untreated NINJA, B6 and N/C) or 7 (N/C + Dox/Tam), representative of 4 experimental repeats. c, Confocal microscopy of skin from the indicated conditions. The dotted line indicates the epidermis (top)–dermis (bottom) interface. The outlined region is magnified in the bottom row. $n = 3$, representative of 2 experimental repeats. d, Representative images of the back of experimental mice treated as indicated. The red rectangle indicates the Tam-treated area that expresses the NINJA antigens. $n = 6$ (Ag ON) or 7 (Ag OFF, Ag OFF/CPI and Ag ON/CPI), representative of 3 experimental repeats. e, Pathological scores by experimental

*condition. * $P = 0.0112$, ** $P = 0.0023$; NS, not significant by two-tailed t-test. $n = 6$ (Ag ON) or 7 (Ag OFF, Ag OFF/CPI and Ag ON/CPI), representative of 3 experimental repeats. f, Haematoxylin and eosin (H&E) staining of skin sections from the indicated conditions. Inset shows an expanded view of the outlined area. $n = 6$ (Ag ON) or 7 (Ag OFF, Ag OFF/CPI and Ag ON/CPI), representative of 3 experimental repeats. g, Quantification of epidermal thickness under indicated conditions. *** $P = 0.0006$ (Ag ON/CPI versus Ag OFF), *** $P = 0.0008$ (Ag ON/CPI versus Ag ON); NS, not significant by two-tailed t-test. $n = 3$ ROIs per mouse for 3 mice, representative of 3 experimental repeats. h, Confocal microscopy of skin from the indicated conditions. Dotted line shows the epidermis (top)–dermis (bottom) interface. $n = 5$.*

For the study, researchers employed innovative mouse models designed to elucidate the role of PD-1 in preventing T cells from attacking healthy skin. By blocking PD-1 and mimicking the effects of immunotherapy, the researchers observed the development of skin disorders in the mice, like those observed in cancer patients receiving PD-1 inhibitors.

These research findings lay the foundation for the future development of enhanced immunotherapies that can mitigate or prevent adverse events. By gaining a better understanding of the vital role played by [PD-1 in safeguarding normal tissues](#)

[from T cell](#)-mediated damage, scientists can strive towards devising strategies that maximize the therapeutic benefits of PD-1 blockade while minimizing harmful side effects.

Journal article: Damo, M., et al., 2023. [PD-1 maintains CD8 T cell tolerance towards cutaneous neoantigens.](#) *Nature*.

Summary by Stefan Botha