cell induction was positively correlated with ΔASA values, while cross-reactivity of induced T cells was inversely correlated.

Conclusions Our results indicate that dissimilarity is key for both T-cell induction and discrimination from self. ΔASA may help predict immunogenic non-anchor type neoantigens inducing specific T-cell response from a variety of cancer mutation pools.

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RELEASING THE RESTRAINTS OF \( g^d \) V\( g^d \) T-CELLS IN CANCER IMMUNOTHERAPY

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Background \( g^d \) V\( g^d \) T-cells are a subset of cells with a crucial role in immunosurveillance which can be activated and expanded by multiple means to stimulate effector responses, often exploited in cancer immunotherapy. Little is known about the expression of checkpoint molecules on this cell population and whether the ligation of these molecules can regulate their activity. The aim of this study was to assess the expression of activatory and inhibitory markers on \( g^d \) V\( g^d \) T-cells to assess potential avenues of regulation to target with immunotherapy.

Methods PBMCs were isolated from healthy donors and the expression of activatory and inhibitory receptors was assessed on \( g^d \) V\( g^d \) T-cells by flow cytometry at baseline, following 24 hours activation and 14 days expansion using zoledronic acid (ZA) and Bacillus Calmette-Guerin (BCG), both with IL-2. Activation and expansion of V\( g^d \) cells was assessed by expression of CD69 and by frequency of V\( g^d \) cells, respectively. Production of effector molecules was also assessed following coculture with various tumour cell targets. The effect of immune checkpoint blockade on \( g^d \) V\( g^d \) T-cells was also assessed.

Results \( g^d \) V\( g^d \) T-cells constitutively expressed high levels of NK-associated activatory markers NKGD2 and DNAM1 which remained high following stimulation with ZA and BCG. \( g^d \) V\( g^d \) T-cells expressed variable levels of checkpoint inhibitor molecules at baseline with high levels of BTLA, KLRG1 and NKGD2 and intermediate levels of PD1, TIGIT and VISTA. Expression of checkpoint receptors were modulated following activation and expansion with ZA and BCG with decreased expression of BTLA and upregulation of numerous markers including PD1, TIGIT, TIM3, LAG3 and VISTA. Expression of these markers is further modulated upon coculture with tumour cell lines with changes reflecting activation of these cells with \( g^d \) V\( g^d \) T-cells expressing inhibitory receptors PD1 and NKGD2 producing the highest level of TNF.

Conclusions Our data reveals unique characteristics of V\( g^d \) in terms of their expression of immune checkpoints, which provide a mechanism which may be utilised by tumour cells to subvert \( g^d \) V\( g^d \) T-cell cytotoxicity. Our work suggests different profiles of immune checkpoints dependent on the method of stimulation. This highlights importance of expansion method in the function of \( g^d \) V\( g^d \) T-cells. Furthermore, this work suggests important candidates for blockade by immune checkpoint therapy in order to increase the successful use of \( g^d \) V\( g^d \) T-cells in cancer immunotherapy.

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INTERLEUKIN-10 DRIVES THE DEVELOPMENT OF T REGULATORY TYPE 1 (TR1) CELLS AND IS A TARGET FOR IMMUNOTHERAPY

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Background In recent years, immunotherapy has become a common tool of cancer treatment. In order to define therapeutic targets, it is necessary to understand mechanisms of tumor-induced immunosuppression. In malignant B-cell lymphoma, the effects of the anti-inflammatory cytokine interleukin-10 (IL-10) remain poorly understood.

Methods To investigate the role of IL-10 in a tumor microenvironment, we used \( \lambda \)-MYC-transgenic mice that spontaneously develop B-cell lymphoma. The experiments were performed either in vivo or in vitro and the cell samples were then analyzed by flow cytometry.

Results In MYC tumors, CD4+Foxp3- effector T cells maintained the expression of interferon-\( \gamma \) (IFN-\( \gamma \)), yet became exhausted. Within this population we found a cell fraction of unknown origin coexpressing IFN-\( \gamma \) and IL-10 that increased during disease progression. These cells turned out to be T regulatory type 1 (Tr1) cells, which are known to be immunosuppressive. When exposing homogeneous IFN-\( \gamma \)-producing T helper type 1 (Th1) cells to a MYC tumor milieu in vitro, part of these cells started to express both, IFN-\( \gamma \) and IL-10, and showed an increased level of programmed cell death protein 1 (PD-1). Notably, these changes diminished when an IL-10 neutralizing monoclonal antibody (mAb) was added to the coculture, indicating that IL-10 is necessary for the Tr1 development and is involved in the upregulation of PD-1. In line with these results, we treated \( \lambda \)-MYC mice with anti-IL-10 mAb. This therapy not only led to significantly prolonged survival but also decreased expression of PD-1 on effector T cells and increased proliferation of cytotoxic T cells.

Conclusions In summary, these results showed the importance of IL-10 for the tumor immune escape in lymphoma. IL-10 induced a conversion from Th1 to Tr1 cells and elevated levels of PD-1. Both effects were diminished after IL-10 ablation. Thus, targeting IL-10 might be a promising new approach of immunotherapy.

Ethics Approval All animal studies were approved by Regierung von Oberbayern, approval number 55.2-1-54.

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PHENOTYPIC AND FUNCTIONAL SIGNATURES OF PERIPHERAL AND TUMOR-RESIDENT \( \gamma^\delta \) T CELLS ARE INFORMATIVE FOR OUTCOME OF CHECKPOINT BLOCKADE IN MELANOMA

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Background Immune checkpoint blockade (ICB) set a milestone in cancer immunotherapy, but still only a fraction of patients responds. Thus, there is an urgent need for biomarkers predicting outcome, and also for understanding the responsible mechanisms. \( \gamma^\delta \) T cells constitute a numerically minor subset of 1-10% of the peripheral T cell compartment in healthy people and have a major role in defense against multiple microbial and non-microbial challenges. Unlike the majority of T cells, \( \gamma^\delta \) T cells bind their ligands in an MHC-