Cytokine-mediated regulation of immunity during persistent viral infection

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Stellingen behorend bij het proefschrift

Cytokine-mediated regulation of immunity during persistent viral infection

1. Emerging evidence revealed that IL-27 positively regulates the expansion of stem-like TCF1+ CD8 subset. Hence, IL-27 signaling could be exploited in combination with immune checkpoint therapy to augment self-renewing T cells in chronic infections and cancer. (this thesis)

2. B cells are essential source of IL-27 during persistent LCMV infection. The role of B cells in producing IL-27 should be explored in other disease to improve our understanding of IL-27 biology and determine potential therapeutic targets. (this thesis)

3. Location matters: deletion of B-cell-specific IL27 cannot be compensated by myeloid-derived IL-27 which comprise the majority of IL-27p28^{+} splenocytes during Clone 13 infection. This indicates the requirement for IL-27 specifically in areas where B cell-T cell interactions occur. (this thesis)

4. The combination of Jak inhibitor and immune checkpoint blockade surprisingly rescued T cell exhaustion and likely has clinical implications during cancer treatment. (this thesis)

5. Given that B cells and tertiary lymphoid structures (TLS) are associated with better response to immunotherapy in cancer patients, better understanding of the mechanism by which TLS and B cells enhance antitumor response is required to develop novel therapeutic strategies that can further improve cancer therapy. (Cabrita *et al.,* Nature. 2020 Jan;577(7791):561-565.)

6. Despite the identification of many cytokines that regulate the functions of CD8 T cells, cytokine-directed therapies will remain scientifically challenging until we understand the specific mechanism of actions that each cytokines have on CD8 T cells. (Hashimoto *et al.,* Cold Spring Harb Perspect Biol. 2019 Jan 2;11(1):a028464.)

7. Identifying transcription factors and molecular pathways that protect stem-like TCF1+ CD8 T cells from being terminally exhausted is crucial for improving the effectiveness of anti-PD-1 immunotherapy. (Im *et al.,* Nature. 2016;537(7620):417-421. doi:10.1038/nature19330)

8. Given that tumor infiltrating IgA were shown to mediate both cytolytic killing by T cells and antibody-dependent phagocytosis in human ovarian cancer, the roles of tumor-infiltrating B cells should be explored in other cancer types. (Biswas,. *et al.*, Nature 591, 464–470 (2021))

9. Meaningful research collaborations can inspire scientists and yield big rewards.

10. One quality that many great scientists have in common is perseverance.

11. Education is a powerful tool that can be used to improve our society.

12. Science is like a marathon. To reach the finish line, you will need to keep going.

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20 September 2022