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Therapeutic strategies to restore intratumoral immune activity in human cancer

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Stellingen behorend bij het proefschrift:

“Therapeutic strategies to restore intratumoral immune activity in human cancer”

1. Exhausted tumor-infiltrating T cells are not inert but can be functionally reinvigorated by therapeutic intervention such as checkpoint blockade or cytokine signals. – *this thesis*.
2. PD-1 blockade responses are initiated by rapid, non-transcriptional functional responses of intratumoral dysfunctional T cells and made durable by subsequent expansion and recruitment of lymph-node resident progenitors. – *Kurtulus et al., Immunity, 2019; Siddiqui et al., Immunity, 2019; Yost et al., Nat Med, 2019; this thesis*.
3. In the context of chronic antigen exposure, the immune system safeguards tissues by decoupling transcriptional activation from effector execution, establishing two separable modules that independently regulate T cell function. – *Philip & Schietinger, Nat. Rev. Immunol, 2022; this thesis*.
4. Interleukin-2 remains a promising therapy, particularly for patients not-responding to checkpoint blockade, if delivered to the right subset. - *this thesis*.
5. Intratumoral CD4 T cells should receive equal attention as CD8 T cells in immunotherapy research, as they can be critical — and in some tumors even dominant — determinants of the intratumoral response to checkpoint blockade. – *Alspach et al., Nature, 2019; this thesis*.
6. RNA tells the story of intention; proteins tell the story of action (*Tan et al., Immunity, 2017*). A complete understanding of anti-tumor immune responses requires looking beyond transcriptional changes. – *this thesis*.
7. Although murine models show model-specific variation in tumor-immune infiltrates, they collectively recapitulate only a subset of human tumor-immune microenvironment (*Courau et al., BioRxiv, 2025*), underscoring that the study of human tumors is essential for clinical translation.
8. The biggest challenge in immunotherapy today is not discovering new drugs, but finding the right patients for existing ones.
9. Science advances not only through experiments, but through the excitement we pass on to those who follow.
10. Time spent in or on the sea is a legitimate intervention for scientific burnout.
11. Working with patient material is not a right but a privilege.