Breaking barriers: unraveling response mechanisms to immunotherapy in breast cancer

Blomberg, O.S.

Stellingen behorende bij het proefschrift getiteld

Breaking barriers:

Unraveling response mechanisms to immunotherapy in breast cancer

1. A shift in perspective on immunotherapy, moving from its traditional focus solely on T cells to more holistic view of tumor immunity as an interconnected system, will be necessary to better understand and improve immunotherapy efficacy for breast cancer patients *(this thesis)*

2. Combining unbiased profiling of cancer patient samples with mechanistic studies in clinically relevant mouse models offers a powerful approach for uncovering new mechanisms of immunotherapy response and resistance *(this thesis)*

3. Eosinophils are not merely biomarkers of response but rather play a causal role in immunotherapy response *(this thesis)*

4. Further characterizing eosinophil heterogeneity to determine whether a specific activation state can be linked to anti-tumor immunity and immunotherapy response will be crucial in developing eosinophil engagement strategies *(this thesis)*

5. Immune checkpoint inhibitors inadvertently activate T_{regs} alongside conventional T cells, thereby counteracting the efficacy of immunotherapy. This factor should be considered when treating cancer patients, especially those with high levels of T_{reg} infiltration in the tumor *(Kamada et al., PNAS, 2019; Kumagai et al. Nat. Immunol., 2020; this thesis)*

6. Absence of therapeutic benefit in the primary tumor following neoadjuvant immunotherapy does not preclude the potential therapeutic benefit against the future development of metastatic disease. This suggests the initiation of long-term, beneficial systemic effects of neoadjuvant immunotherapy-based strategies *(Loibl et al., Ann Oncol, 2022; this thesis)*

7. Clinical implementation of immunotherapies is advancing more rapidly than our mechanistic understanding of which patient subgroups may respond and which combination therapies should be rationally explored *(this thesis)*

8. Engagement of systemic immunity is critical for tumor rejection following immunotherapy *(Spitzer et al., Nat. Med., 2020; this thesis)*

9. Organ specific differences in the immunosuppressive network have consequences for metastatic spread and response to immunotherapy *(Kos et al., Ann. Rev. Can. Biol., 2020; this thesis)*