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Everyone works better together: rational improvements to radio- and immunotherapy combinations

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Stellingen behorend bij het proefschrift getiteld:

Everyone works better together: Rational improvements to radio- and immunotherapy combinations.

1. Failure of anti-cancer combination therapies in the clinic stems from insufficient prior mechanistic understanding of treatment synergies and suboptimal profiling of the patient's tumor immune archetype before treatment. – *this thesis*.
2. Considering the crucial role of lymph nodes in immune education, anti-cancer (immuno) therapies should prioritize the preservation of lymph nodes. Treatment efforts should be directed towards the strategic reprogramming of immune responses within this key anatomical site. – *Reticker-Flynn et al., Trends Cell Biol. 2023; Du Bois, Sci. Immunol. 2021; this thesis*.
3. Rather than being immunologically similar, the co-stimulatory ligands CD80 and CD86 play distinct roles in dictating CD28 co-stimulation across various immune cell types. – *Halliday et al., Front. Immunol. 2020; this thesis*.
4. Dendritic cells are the shepherds to anti-cancer T cell immunity (*Pittet et al., Immunity, 2023*). Consequently, rational improvements to anti-tumor T cell-mediated strategies requires a better understanding of how tumors impact the metabolic and molecular pathways determining the stimulatory status of dendritic cells – *Pittet et al., Immunity, 2023; Pelgrom et al., Cell Res. 2019*.
5. A comprehensive understanding of Tregs, including their developmental trajectory, tissue distribution and subset heterogeneity during both immune homeostasis and tumor development, is essential to improve anti-tumor immunotherapy – *Li et al., Cell, 2018; Miragaia et al., Immunity, 2019; De Simone et al., Immunity, 2016; this thesis*.
6. Radiotherapy can facilitate new T cell priming, even in poorly immunogenic tumors, we just need to identify and remove all underlying bottlenecks that may limit its effectiveness – *this thesis*.
7. In the context of poorly immunogenic tumors, achieving clinical success with anti-cancer immune therapies requires comprehensive targeting of each stage in the cancer immunity cycle. This goal is unlikely to be accomplished with immune checkpoint blockade alone. – *this thesis*.
8. Small in size, immense in impact – Autotaxin, beyond its role in promoting tumor development and invasion, also contributes to the suppression of anti-tumor immunity. – *Konen et al., JCI 2023; Chae et al., Cancer Discov. 2022; this thesis*.
9. “Alone we can do so little; together we can do so much” (*Helen Keller*) – Science is a team effort; the acknowledgements section should therefore not be restricted to a maximum of 800 words.